Attempts to Green the Synthesis of Liquid Crystals

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ABSTRACT

This study presents several green approaches to the synthesis of liquid crystals. In the research, three types of reactions (esterification, Suzuki cross-coupling and amidation) have been considered. A series of sulfonated Starbons (mesoporous carbonaceous materials derived from polysaccharides) have been tested for esterification as catalysts. As a result, sulfonated Starbon was found to have selectivity for *cis*- and *trans*-isomer of 4-pentyl-cyclohexane carboxylic acid. *Cis*-isomer has priority in the reaction. With water-soluble carbodiimide as coupling agent, cyclopentylmethyl ether (CPME) as solvent, and microwave irradiation, a series of *trans*-4-n-alkyl-cyclohexane carboxylic acid 4-cyanophenol esters were synthesized and their liquid crystalline phase transition temperature was determined. Green metrics were applied to assess this reaction with respect to the traditional synthesis. A series of Starbon-Pd were tried in two different solvent systems (ethanol/water and CPME/water) as heterogeneous catalyst for Suzuki reaction. All the Starbon-Pd had a high activity in ethanol/water solvent system. In CPME/water solvent system, only Starbon-500-Pd had a good performance. Starbon-Pd catalyst could be reused approximately 3 times in the Suzuki reaction. With comparison, CPME has been proved that it was a better replacement for THF in Suzuki reaction. A mesoporous structured silica catalyst was applied to amidation for the purpose of generating liquid crystalline amides.

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DECLARATION OF ORIGINALITY

This is to certify that the work is entirely my own and not of any other person, unless explicitly acknowledged (including citation of published and unpublished sources). The work has not previously been submitted in any form to the University of York or to any other institution for assessment for any other purpose.

AIM OF RESEARCH

It has been nearly two decades since conception of green chemistry with lots of research in many green technologies having been developed to reduce the hazards, save resources and energy. Many industries have started their green evolution amidst concerns of corporate social responsibility. Information display has been dominated by liquid crystal industry in the modern society. Liquid crystal industry provides many devices, valuable in daily life. It has made the liquid crystal industry become a multi-billion-dollar industry. A huge industry like this will face environmental problems sooner or later. Therefore, greening the synthetic route of liquid crystal has a great prospect.

In this research, several green technologies (e.g. green solvent, heterogeneous catalyst) will be applied to synthesis of liquid crystals with the aim of making some improvements. Research will focus on common linkages of liquid crystal. Meanwhile green metrics will be introduced to assess reactions in synthesis of liquid crystal. Since no one has tried to green synthetic routes of liquid crystal before, we hope this research would provide a new angle in synthesis and design of liquid crystal.

CHAPTER 1 INTRODUCTION

1.1 Green Chemistry

Green Chemistry was first formulated at the beginning of the 1990s.[1] It also called "sustainable chemistry". Green Chemistry is a philosophy of chemistry. Definition of Green Chemistry is the design of chemical products and processes that reduce or eliminate the use and generation of hazardous substances.[2]

1.1.1 The Twelve Principles[1]

The Twelve Principles of Green Chemistry were introduced in 1998 by Paul Anastas and John Warner. They are the basic rules in Green Chemistry for the design of new chemical products and processes, applying to all aspects of chemistry, such as organic chemistry, inorganic chemistry, biochemistry, analytical chemistry, physical chemistry and chemical engineering.

The Twelve Principles are:

1. Prevention

It's better to prevent waste than to treat or clean up waste afterwards.

2. Atom Economy

Design synthetic methods to maximize the incorporation of all materials used in the process into the final product.

3. Less Hazardous Chemical Syntheses

Design synthetic methods to use and generate substances that minimize toxicity to human health and the environment.

4. Designing Safer Chemicals

Design chemical products to affect their desired function while minimizing their toxicity.

5. Safer Solvents and Auxiliaries

Minimize the use of auxiliary substances wherever possible make them innocuous when used.

6. Design for Energy Efficiency

Minimize the energy requirements of chemical processes and conduct synthetic methods at ambient temperature and pressure if possible.

7. Use of Renewable Feed stocks

Use renewable raw material or feedstock rather than traditional sources whenever practicable.

8. Reduce Derivatives

Minimize or avoid unnecessary derivatization if possible, what requires additional reagents and generate waste.

9. Catalysis

Catalytic reagents are superior to stoichiometric reagents.

10. Design for Degradation

Design chemical products so they break down into innocuous products that do not persist in the environment.

11. Real-time Analysis for Pollution Prevention

Develop analytical methodologies needed to allow for real-time, in-process monitoring and control prior to the formation of hazardous substances.

12. Inherently Safer Chemistry for Accident Prevention.

Choose substances and the form of a substance used in a chemical process to minimize the potential for chemical accidents, including releases, explosions, and fires.

1.1.2 Green technology

1.1.2.1 Starbon

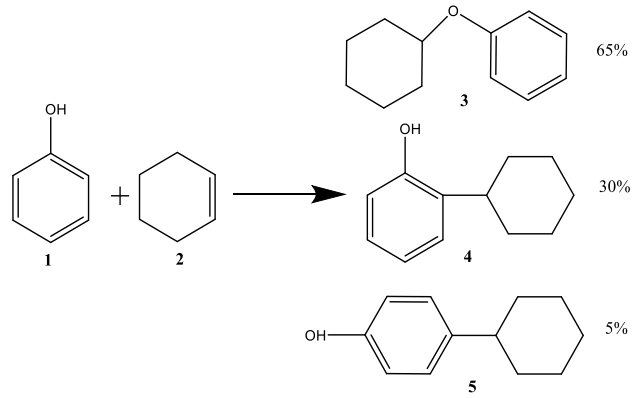
Starbon is a series of mesoporous, carbonaceous materials, originally derived from starch, but now the term extends to other polysaccharides such as pectin and alginic acid.[3] Starbons may be produced in three steps. First step is expansion via gelation and retrogradation to form a porous gel block. Secondly, the porous gel block is dried via careful solvent exchange with ethanol to afford mesoporous starch. On the last step, the resultant mesoporous starch is pyrolysed in different temperatures to give Starbon, for example, Starbon-350 is pyrolysed at 350 ^{o}C.[3]

Depending on the pyrolysis temperature, Starbon can be tuneable between hydrophilic to hydrophobic. Usually, high temperature can create hydrophobic Starbon by pyrolyzing more hydrophilic groups on starch. On the other side low temperature gives hydrophilic Starbon. The indicated properties make Starbon a very good support for loading catalysts.[4]

1.1.2.1.1 Sulfonated Starbon

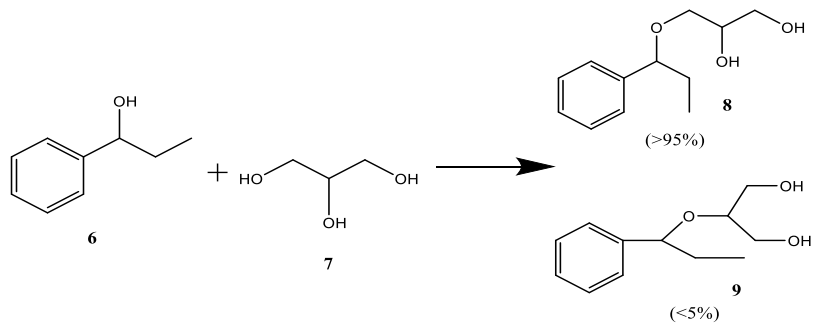
With 95% H_2SO_4, Starbon can be sulfonated at 90 ℃. After washing with methanol and drying at 105 ℃ overnight, sulfonated Starbon can be created. It is one kind of solid acid and seems to be a green replacement for acid catalysts. Sulfonated Starbon can act as a heterogeneous acid catalyst, instead of using homogeneous acid, such as H_2SO_4. Sulfonated Starbon has been reported to successfully catalyze the esterification of oleic acid.[5] It is a potential green solution for avoiding the disadvantages of homogeneous acid catalysts. Sulfonated Starbon can be recycled after reaction[4] and it is non-corrosive.

Acting as a catalyst, catalytic activity of sulfonated Starbon on alkylation and acylation have been studied.[6, 7] When sulfonated Starbon catalyzed the reaction of phenol (**1**) with cyclohexene (**2**), three products (cyclohexyl phenyl ether (**3**), 2-cyclohexylphenol (**4**) and 4-cyclohexylphenol (**5**)) were created (Scheme 1). The reaction completed in 12 hours and cyclohexyl phenyl ether (65%) was the major product while 2-cyclohexylphenol (30%) and 4-cyclohexylphenol (5%) were by-products.[6]



Scheme 1[6] (Alkylation of phenol with cyclohexene)

However, sulfonated Starbon had much better performance in acylation.[7] Sulfonated Starbon had greater conversions (85 %- 99 %) and selectivity (75 %- 99 %) then other solid acid in esterification of different organic acids (succinic, fumaric, itaconic and levulinic) with ethanol. In the reactions of acetic acid with phenyl methanol, (4-Nitrophenyl) methanol and *α*-methyl benzyl alcohol, sulfonated Starbon showed great catalytic activity as well. But the reaction of acetic acid with phenol was very slow with sulfonated Starbon.[7] In addition, Sulfonated Starbon had high selectivity in esterification of glycerol (**6**) with 1-Phenyl-1-propanol (**7**).[8] (Scheme 2)



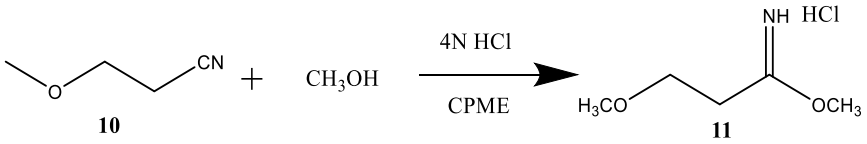
Scheme 2[8] (Etherification of glycerol with 1-phenyl-1-propanol using Starbon-400-SO_3H. Reaction conditions: 2 mmol glycerol, 6 mmol 1-phenyl-1-propanol, Microwave, 300 W, 110 ℃, 3 min, 0.1 g Starbon1-400-SO_3H.)

1.1.2.1.2 Palladium-Starbon

Besides sulfonation, Starbon also is a good support for palladium.[9] Palladium is an expensive metal. The main usage of palladium in organic chemistry is the catalysis of the Suzuki reaction.[10] In traditional Suzuki reactions, palladium or organopalladium are homogeneous catalysts. That means that the catalysts are not typically recyclable. After palladium anchoring on Starbon， palladium will become recyclable. It has been applied on oxidations of glycerol to both glycolic and oxalic acids.[8] In appropriate reaction conditions, palladium-Starbon showed a good catalytic activity and recoverability.

1.1.2.2 Cyclopentyl Methyl Ether (CPME)

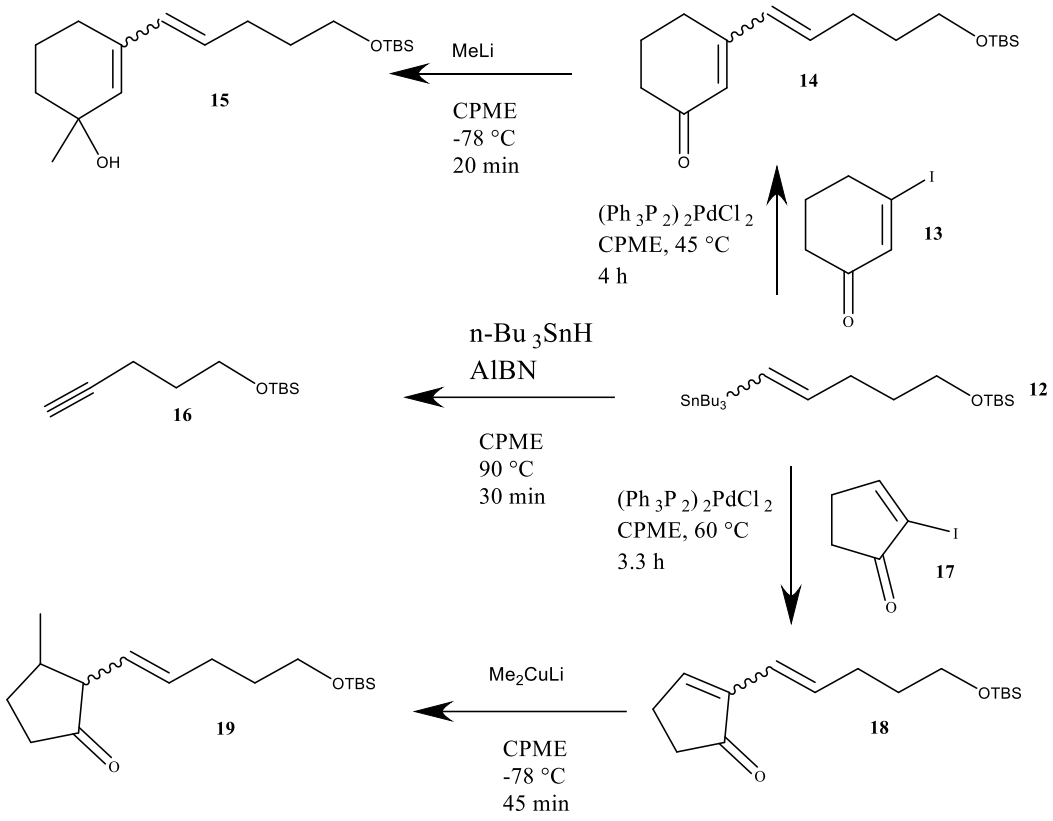
CPME is a novel green solvent which was developed to replace other ether solvents. The human permitted daily exposure (PDE) of CPME is 7.4 mg/day and CPME was manifested that It had negative effects in genetic toxicity and mutagenicity by Antonucci *et al*.[11] CPME is a better option than other common ether solvents, because it is a high hydrophobic solvent, stable under acidic and basic conditions, easy to vaporize and hard to explode.[12] Comparing with tetrahydrofuran which is major solvent in organic synthesis, CPME is much easier to recover. CPME has been applied to many kinds of reaction as an alternative green solvent. CPME was employed as a key solvent to improve the Pinner reaction (Scheme 3) by Watanabe *et al*[13]. According to their result, amount of waste and labour of processing has been reduced.



10 **11**

Scheme 3[13] (Pinner reaction, 0 ℃ 1 h, 0-5 ℃ 48 h)

In addition, there are three types of reactions (a radical addition, a Pd-catalyzed coupling, and an organometallic addition) which were highly efficient with suitable reaction conditions in CPME (Scheme 4)[14]. Because of low vaporization energy and water-immiscibility, CPME was easy to recycle from those reactions and reusable.[14]



Scheme 4[14]

1.1.2.3 Microwave Irradiation Technology

Microwave is a kind of electromagnetic wave. Reaction mixture is heated by microwaves base on ionic conduction mechanism and dipole rotation mechanism. If reaction mixture contains free ions, ions will be migrated by electromagnetic field. When the migration is hindered by other molecules, the electromagnetic energy will transform to thermal energy to increase temperature. This is the ionic conduction mechanism. When polarized molecules were put in microwave radiation space, polarized molecules were affected by the microwaves. With the influence from the electromagnetic field, the dipole molecules would rearrangement along with the direction of electric field. Microwave has alternating electric field which is changing very fast. That will cause the rotation of dipole. When the regular rotation is interfered by other molecules, the electromagnetic energy from microwave will transform to internal energy of molecules. Although nonpolar molecules also can produce some displacement due to electric field polarization, but that almost did not have any contribution. Some of the objects

had free polarized molecules, thus they could be directly heated by microwave; other objects as long as mixed with polarized molecules, could be heated by those polarized molecules in microwave radiation as well.[15] Microwave ovens were designed for use in cooking. In 1986, Gedye[16] and Giguere[17] were the first ones who applied microwave irradiation technology to organic synthesis. This application made some reaction much faster than before. Short reaction time implied higher energy transfer efficiency and less energy waste. Since 1986 microwave-assisted reaction has been widely used on esterification,[18, 19] amidation,[20, 21] Suzuki coupling,[22-25] and other reactions.[26-28] Microwave-assisted technology can shorten the reaction time from hours to minutes.[29] Nowadays, there are two different microwave reactors[30] which have been used for synthesis: one has single vessel and the other has multiple vessels. First kind of microwave reactor is more accurate and efficient by creating standing wave to heat the vessel. But it can only heat one vessel at the same time. The second one is able to heat multiple vessels at the same time by reflecting microwave inside the reactor. It is less accurate and efficient than the first one.[31]

1.1.3 Metrics of Green Chemistry

Metrics is a system or standard measurements: a set of figures or statistics that measure results. It is created for evaluating how green the reaction is.

1.1.3.1 Yield

The most traditional way to assess a chemical reaction is Yield. Yield is calculated by the following equation:

$$\text{Yield} = \frac{moles\ of\ product}{moles\ of\ the\ limiting\ reactant} \times 100\%$$

In this equation, waste, excess, solvent and purification are not considered. It only focuses on product.

1.1.3.2 Atom Economy[32] (AE)

This term, first introduced by Barry Trost in 1995 and was an attempt to promote synthetic organic chemists to seek "greener chemistry". Atom economy is a calculation of how much of the reactants remain in the final product. Final product applies to a single chemical reaction, a series of chemical reaction in a single stage of a multistage synthetic route, or to the entire route to a final product. It is calculated by the following equation:

$$\mathrm{AE} = \frac{Molecular\ weight\ of\ product}{Total\ molecular\ weight\ of\ reagent} \times 100\%$$

In this metric, it can guide you when you design a single or a series reaction to maximize all materials used in the process into the final product.[1] However, in Atom Economy, yield has been assumed to be 100% and excesses of reactants have been ignored. It also does not account for solvents and reagents.[32]

1.1.3.3 Environmental Factor (E-Factor) [33]

E-factor is a calculation of how much of waste would be generated when 1 kg final product was created.[33] It is calculated by the following formula:

$$E - Factor = \frac{Mass\ of\ Total\ Waste}{Mass\ of\ Final\ Product}$$

E-factor is the actual amount of waste produced in the process. It takes the chemical yield into account and includes all reagents solvents losses, all process aids, excluding water however because it would lead to exceptionally high E-factor figures, which eventually makes the comparisons of processes difficult.[34]

1.1.3.4 Process Mass Intensity (PMI)[35]

PMI was first presented by Curzons *et al*. It has been decided to define PMI as the key high-level metric to evaluate and benchmark the greenness of processes and to achieve greater efficiency and novelty in pharmaceutical processes by The

American Chemical Society Green Chemistry Institute Pharmaceutical Roundtable. The equation is presented as follow:

$$\text{process mass intensity(PMI)} = \frac{total\ mass\ in\ a\ \ process\ \ or\ process\ step}{mass\ of\ product}$$

Unlike Yield and AE, PMI does not give a percentage. It is based on mass with boundaries which is set by user. That means all the recyclable materials can be remove from calculating and large amount of solvents as well. This would make the comparison much easier and more obvious.

1.2 Liquid Crystals

To common knowledge, there are three states of matter: gas; liquid and solid. However, at 1888 Austrian botanical physiologist Friedrich Reinitzer discovered a specific phenomenon when he observed the melting behaviour of cholesteryl benzoate.[36] Cholesteryl benzoate melted into a cloudy liquid when it was being heating to 145.5 ℃. This state was persisting at 33 ℃ temperature range until it was heated to 178.5 ℃ and became a clear liquid.[37] Then after purifying and viewing this cholesteryl benzoate through a polarizing light microscope, O. Lehmann realized that the cloudy liquid was a fourth state of matter. Instead of melting from solid to liquid, the cholesteryl benzoate was stabilized at a special state of matter. This state was between the solid and liquid states of matter. Lehmann and Reinitzer decided to name the new state of matter liquid crystals.[37] In this state of matter, molecules not only could flow like liquid but also oriented in a crystal-like way.[38] Liquid crystals have the counterintuitive combination of fluidity and long-range order.[36] This characteristic makes them the best known material in flat panel displays today.[36] Besides the displays application, liquid crystals also can be used on temperature sensors, projection systems, optical computing, fibres with tensile strength greater than steel and some novel pigments.[39]

1.2.1 Historical Perspective[40]

In the latter part of the nineteenth century, some scientists observed several compounds had a bizarre phenomenon that those compounds formed flexible and generated uncommon optical effects under the polarized light. Liquid crystal was first discovered and named by Friedrich Reinitzer in 1888. After this unexpected discovery he did not continue his works on liquid crystal though Otto Lehmann continued study. Daniel Vorländer[41] was the first who successfully synthesized the liquid crystal compounds which had smectic phase. He published his research in 1908. In his research, he found that those compounds which were able to research liquid crystal state were calamitic molecule. He spent his whole life on synthesis of liquid crystal and created hundreds liquid crystals. In 1922 Georges Freidel[42] classified liquid crystal phase into three different type: nematic, smectic and cholesteric phase. This was one of the most important achievement on liquid crystals. However, during the early 20th century, because of lacking of application, research in the area of liquid crystal was treated as a pure scientific curiosity. This situation was retained for 80 years.[43] Research on the synthesis of liquid crystals was resumed after World War II. In 1962, after the synthesis and investigation of a considerable number of new liquid crystal compounds, George Gray and his groups published a book Molecular Structure and the Properties of Liquid Crystals.[44] This book became a guidebook on the synthesis of liquid crystals. In 1965, the first international conference on liquid crystals was held by Glenn H. Brown in Kent, Ohio. Only after 3 years, the first liquid crystal display which was base no dynamic scattering of nematic liquid crystals was demonstrated.[45] This practical application was a revolution on display and gave enterprises a strong motivation to invest in the liquid crystals research. Since then, research on liquid crystals entered a golden age. In 1971, a new electro-optical effect of twisted nematic liquid crystals was discovered which allowed conversion of the rotation of linearly polarized light continuously from $0\,°$ to $90\,°$ by W. Helfrich and M. Schadt.[46] This discovery leaded production of liquid crystal display into industrialization. In 1984, T. Scheffer developed liquid crystal display by using supertwisted birefringence effect (SBE).[47] Currently, liquid crystal display has a much better image quality than before. With the thin-film-transistor liquid-crystal display (TFT-LCD) invented liquid crystals display became the major display on the market until now and this was also the biggest application for liquid crystals.[48]

However, with development of organic light-emitting diode (OLED) display TFT-LCD was no longer the best option on the display market.[49, 50] The whole liquid crystal industry is facing a new challenge.

1.2.2 Classification of Liquid Crystals Compounds

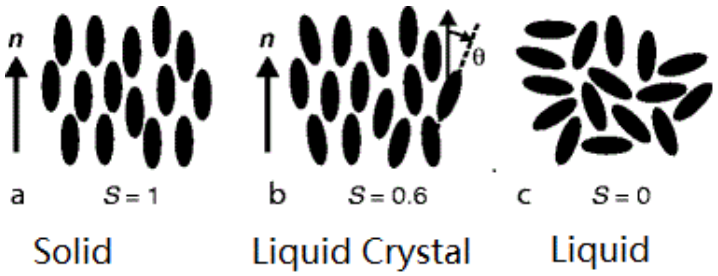
Whether the molecular weight is high or low, the molecule could have the liquid crystals state. Liquid crystalline compounds can be classified into two different categories. The first one is called thermotropic Liquid crystals. In this kind of liquid crystals, the liquid crystal phase is a function of the temperature of material. The other class is lyotropic liquid crystals. In lyotropic liquid crystals the liquid crystal phase is associated with the concentration of materials. This research is focused on the low molecular weight thermotropic liquid crystals.

1.2.3 Types of Liquid Crystalline（mesophase）

G Friedel based on the polarizing microscopy studies, he classified liquid crystalline in to three different types.[42] Those three types are nematic, smectic and cholesteric.[42] Each mesophase has their unique optical texture under a polarizing microscope.

1.2.3.1 The Nematic Phase

The term nematic arises from the Greek word *"**nematos**"* meaning thread-like, because of its thread-like optical texture. Nematic phase is the simplest one in all of mesophases. In this phase, molecules have no positional order but tend to point in the same direction. Because of that, in this phase molecules have good mobility. It can be fluid like liquid. Nematic liquid crystal molecules tend to align along a preferred direction. This direction is called the director （n）. Another important parameter is S which is used to represented the extent of ordering. S is calculated by the formula: $S = 0.5(3\cos^2\theta - 1)$, where θ is the angle between the long axis of each of the individual molecules and the director. S is in the region of 0.4-0.7 (temperature dependent). The Figure 1.2.2.1.1 shows the relationship between n, S and θ.



$$S = 0.5(3\cos^2\theta - 1)$$

Figure 1.1 The relationship between n, S and **θ**

1.2.3.2 The smectic phase

Smectic, this term is derived from the Greek word "***smectos***". ***Smectos*** in Greek means 'soap-like', because smectic was first observed in alkaline soaps. The smectic state is another characteristic mesophase of liquid crystal substances. Molecules in this state show a degree of translational order which is not present in the nematic state. In the smectic state, the molecules maintain the general orientational order of nematic, but also tend to arrange themselves in layers. Motion is only limited to inside these layers, and separate layers are observed to flow past each other. The increased order means that the smectic state is closer to solid state than the nematic.

1.2.3.3 The cholesteric phase

This kind of liquid crystals are usually derivative of cholesterol and this phase was first discovered in derivative of cholesterol, so the mesophase is called cholesteric phase. Technically, it is a special kind of nematic phase. Nowadays it is also called chiral nematic phase because molecules contained a chiral centre. The chiral nematic phase could be considered as a "layered" nematic phase, but those "layers" do not exist. The director in each "layer" are slightly twisted either clockwise or anticlockwise. The distance taken for the director to complete one full revolution (0 °to 360 °) is termed the "pitch length".

1.2.4 Chemical Structures[40]

For those low molecule weight compounds which want to achieve the liquid crystals state, molecules are usually required to have some rigid molecular structures, such as benzene ring and cycloalkane are linked by ester group, to stop internal rotation. Those rigid molecular structures would let molecules stay in order at specific temperatures. But to be a liquid crystal, molecules also need to have fluidity. That would require molecules to have soft group at both ends, like long chain alkane. Liquid crystals are normally rod-, discotic- or bent-core. (Figure 1.2)

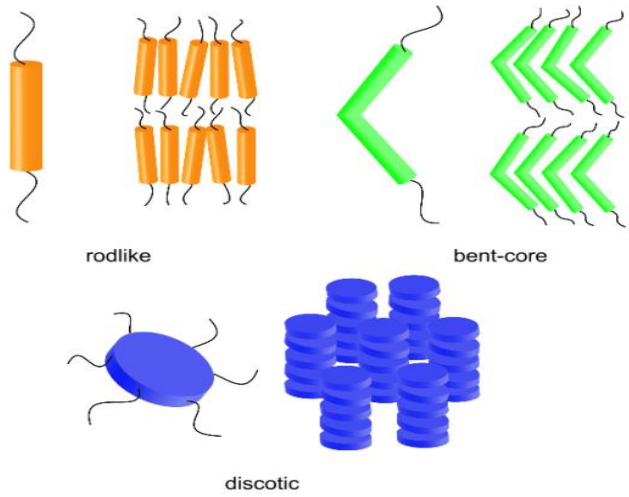


Figure 1.2 Rod-like, discotic or bent-core liquid crystal structures

The general structure of rod-like and bent-core liquid crystals could be drawn like on the Figure 1.3.

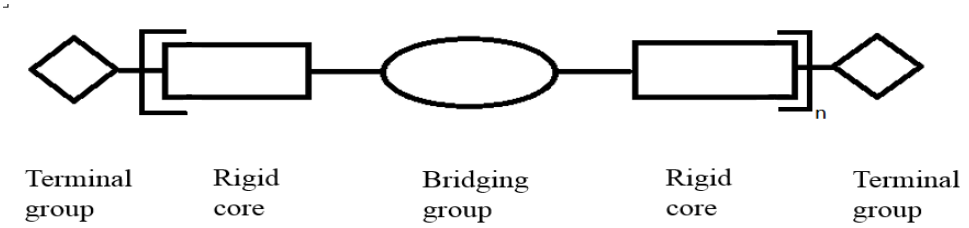
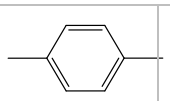
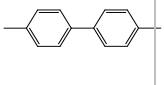
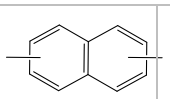
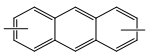
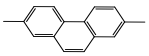
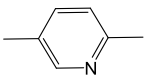
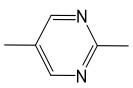
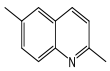
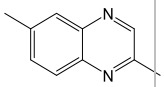
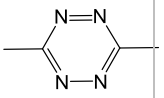
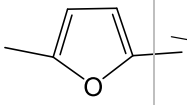
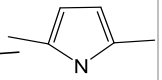
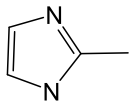
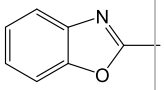
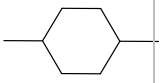
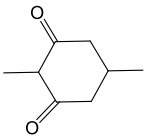
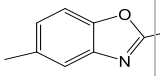


Figure 1.3 The general chemical structure of rod-like and bent-core liquid crystals

For the discotic liquid crystals, the general architecture is the following: one rigid core or multiple connecting rigid cores forming a dish. At the same time several terminal groups are attach to them. But sometimes bridging groups are not necessary. Two directly connected rigid cores with terminal groups could create liquid crystals as well. The following table shows the most usual rigid cores, bridging groups and terminal groups.[51]

Rigid cores					
Standard					
Frequent					
Rare					
					
					
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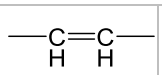
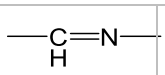
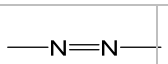
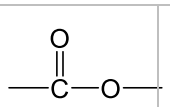
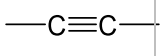
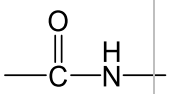
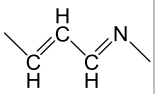
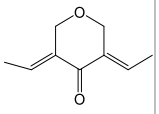
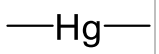
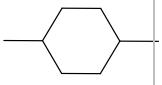
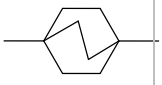
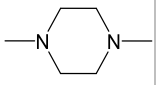
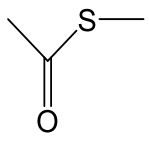
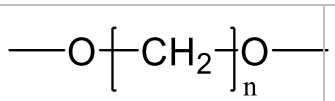
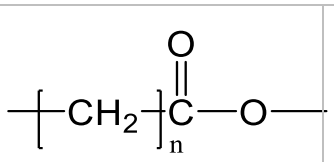
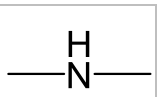
Standard					
Frequent					
Rare					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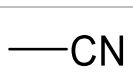
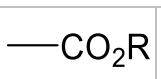
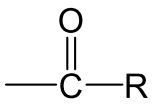
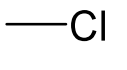
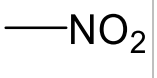
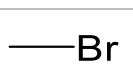
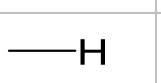
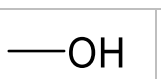
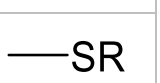
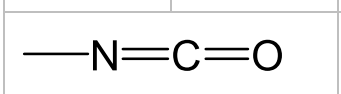
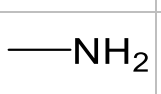
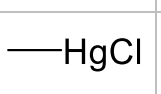
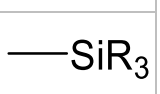
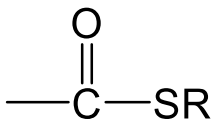
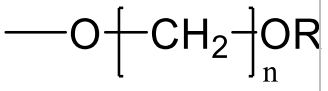
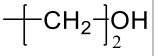
Standard					
Frequent					
Rare					
					
					

Table 1.1 The most usual rigid cores, bridging groups and terminal groups[51]

1.2.5 Synthesis of Liquid Crystal

Most common cores of liquid crystal are the aromatic core units due to the relative ease of synthesis. Usually, electrophilic substitution reaction, such as Friedel-Crafts acylation, bromination and nitration, would be used to functionalize aromatic units. Esterification, amidation and C-C cross-coupling was used to connect different aromatic units.[40]

1.2.5.1 Esterification

The ester bond is present in many liquid crystal molecules, because it is stable and easy to synthesize.[52, 53] Liquid crystals with ester unit usually have low melting point.[40] Esterification not only could be used to provide a bridge to connect rigid cores, but can also have the ability to create terminal groups.[54] Because of that, esterification was a widely used reaction in synthesis of liquid crystal. Esterification in organic chemistry, ester can be created from carboxylic acids used to convert two carboxylic acid molecules into the corresponding anhydride, then using DMAP (4-dimethylaminopyridine) as an acyl-transfer catalyst to react with an alcohol.[55, 56] The mechanism is shown in the Figure 1.4. A Traditional dehydrant for this reaction is N, N'-dicyclohexylcarbodiimide (DCC). DCC is a highly toxic chemical. After reaction DCC would turn into DCU (Dicyclohexylurea), a white solid, making purification difficult. The solvents in this reaction is CH_2Cl_2 which is not eco-friendly and toxic.

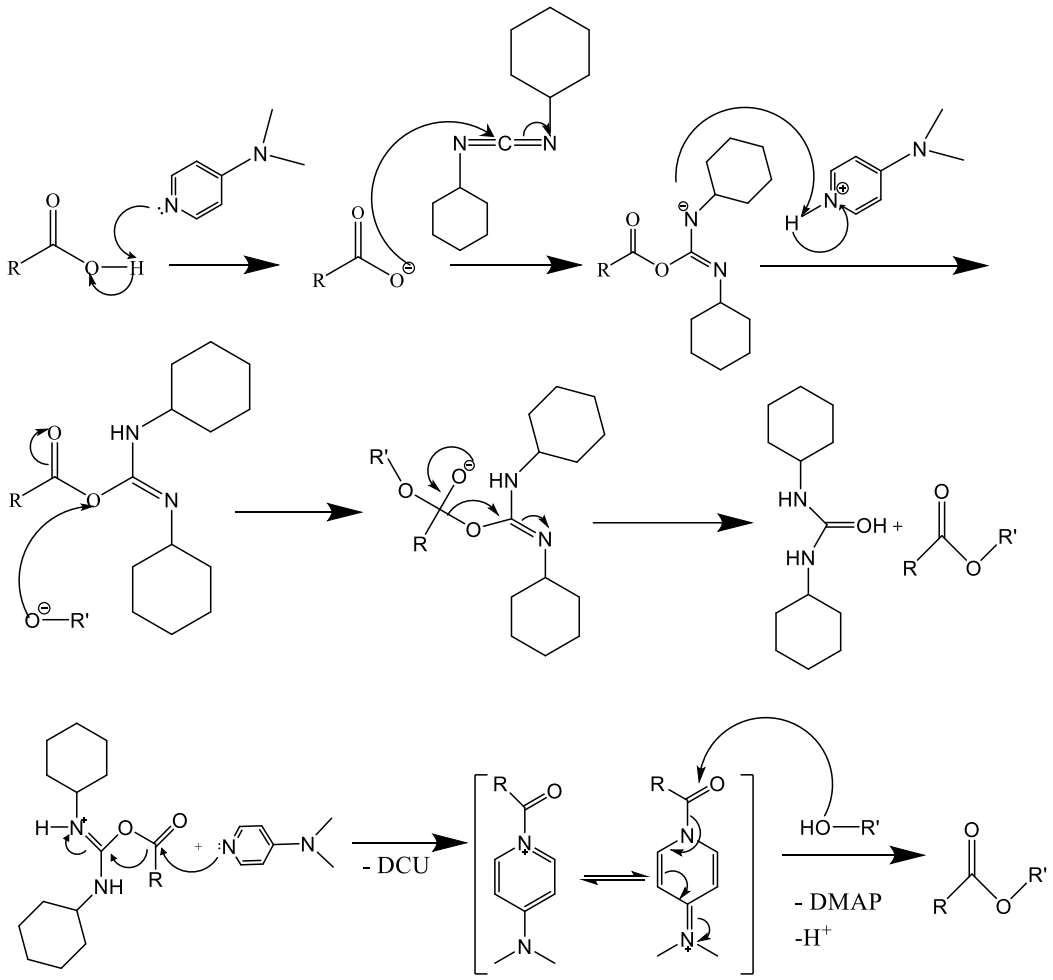


Figure 1.4 The mechanism of Steglich esterification[56]

Development on Steglich esterification was focused on dehydratation. To overcome the disadvantages of DCC, two different types of carbodiimides have been developed. One is N, N'-diisopropylcarbodiimide (DIC) and the other one is 1-Ethyl-3-(3-dimethylaminopropyl) carbodiimides (EDC). DIC is in the liquid state at room temperature. Urea is able to dissolve in organic solvents.[57] So it is applied to synthesize water-soluble products for easy purification. DIC is dermally toxic that needs to be handled carefully.[58] EDC is highly soluble in water and its by-product is soluble in water as well. This property makes purification easy.[59] Extraction is a much easier step than chromatography. The major application of DIC and EDC is in pharmaceuticals or biology to produce amide bonds.[60-64] Few

of them have been applied on synthesis of liquid crystals. DCC has used in the synthesis of ester liquid crystal.[65]

The other way is Fischer–Speier esterification. Fischer–Speier esterification presumes that by using acids as catalysts, carboxylic acids and alcohols combine together and dehydrate with heating.[66] The mechanism of Fischer–Speier esterification which is showed in Figure 1.5 is different from Steglich esterification. For this reaction traditional acids, e.g. sulfuric acid, are the most common catalysts. But traditional acids are corrosive, it makes them become a potential dangerous. Meanwhile, traditional acids are homogeneous catalyst, the typically are not recycled after the reaction.

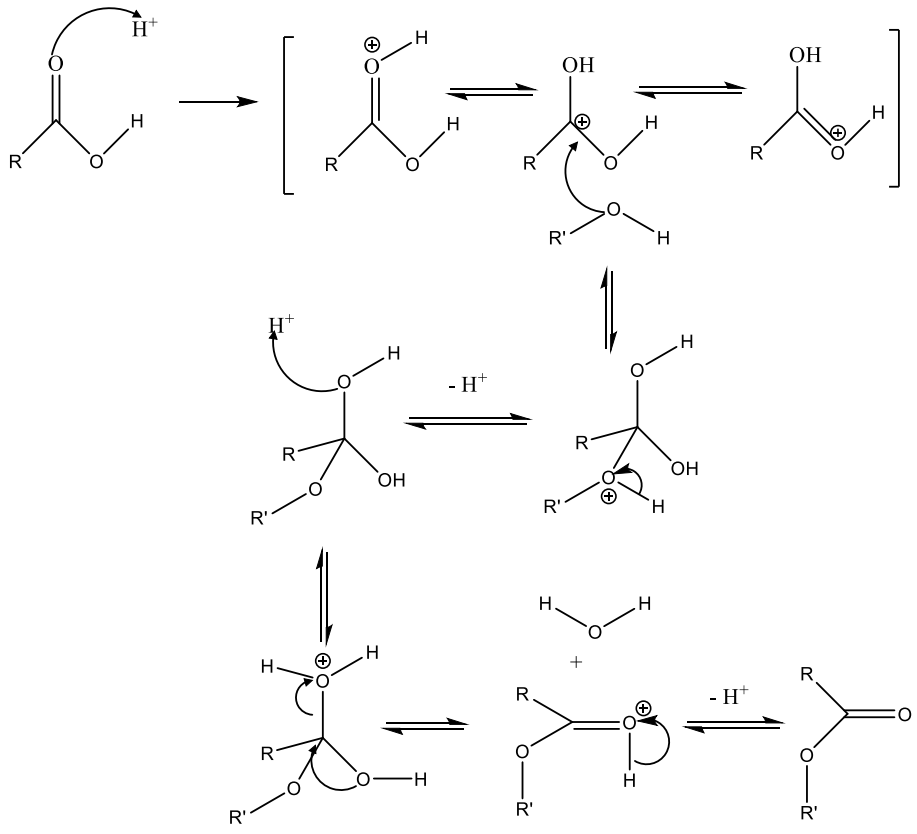


Figure 1.5 The mechanism of Fischer–Speier esterification

Recent research on the improvement of Fischer–Speier esterification is focused on solid acid catalysts. Solid acid is a kind of heterogeneous catalysts. The advantages of solid acid are recyclable, non-corrosive and the waste from reaction is easier to

dispose[67]. Sulfonated Starbon which has been mentioned previously is a kind of solid acids. Several solid acid catalysts were developed during the last decades. Among the different types of solid acids, mesoporous type solid acid catalysts are a good type of solid acid catalysts for esterification, because the characteristics of mesoporous are tuneable. It makes mesoporous have different properties according to reaction condition. Kiyotaka Nakajima *et al*.[68] reported a highly active mesoporous solid acid (Ph-SO_3H HME). It is a mesoporous ethenylene-silic (HME) supported solid acid. Ph-SO_3H HME has highly active sites in ethyl acetate formation. Takagaki, Atsushi, *et al*.[69] invented a sulfonated carbonized D-glucose. It has been tested as solid acid catalyst in esterification of higher fatty acids. Because of density of SO_3H groups, this catalyst had great activity. In addition, there are heteropoly acid loaded MCM-41 catalyst, sulfated zirconia and tin oxide type solid acid catalyst, tungsten trioxide loaded zirconia (WO_3/ZrO_2) type solid acid catalysts.[67] However, the major application for those solid acid catalysts was on esterification and transesterification of biodiesel. No one has tried to practice them on synthesis of terminal group of liquid crystal.

1.2.5.2 Suzuki-Miyaura Cross Coupling Reaction (Suzuki Reaction)[70]

Linking units are not necessary for thermotropic liquid crystals. A direct bond between two cores could provide better rigidity and more stability.[40] There are many way to create a direct bond to connect a core to the others. Among all those C-C coupling reaction, Suzuki reaction has mild reactive condition and good tolerance to functional group (e.g. aldehyde group, ester group, ether group, nitrile group, nitro group and fluorine-based).[71] Those advantages make Suzuki reaction widely used in the synthesis of liquid crystals.

The Suzuki reaction is a coupling reaction which is used for coupling a boronic acid with a haloid by using a palladium(0) complex as a catalyst.[10] The perspective of the palladium catalyst is the best for understanding of the mechanism of the Suzuki reaction (Figure 1.6).

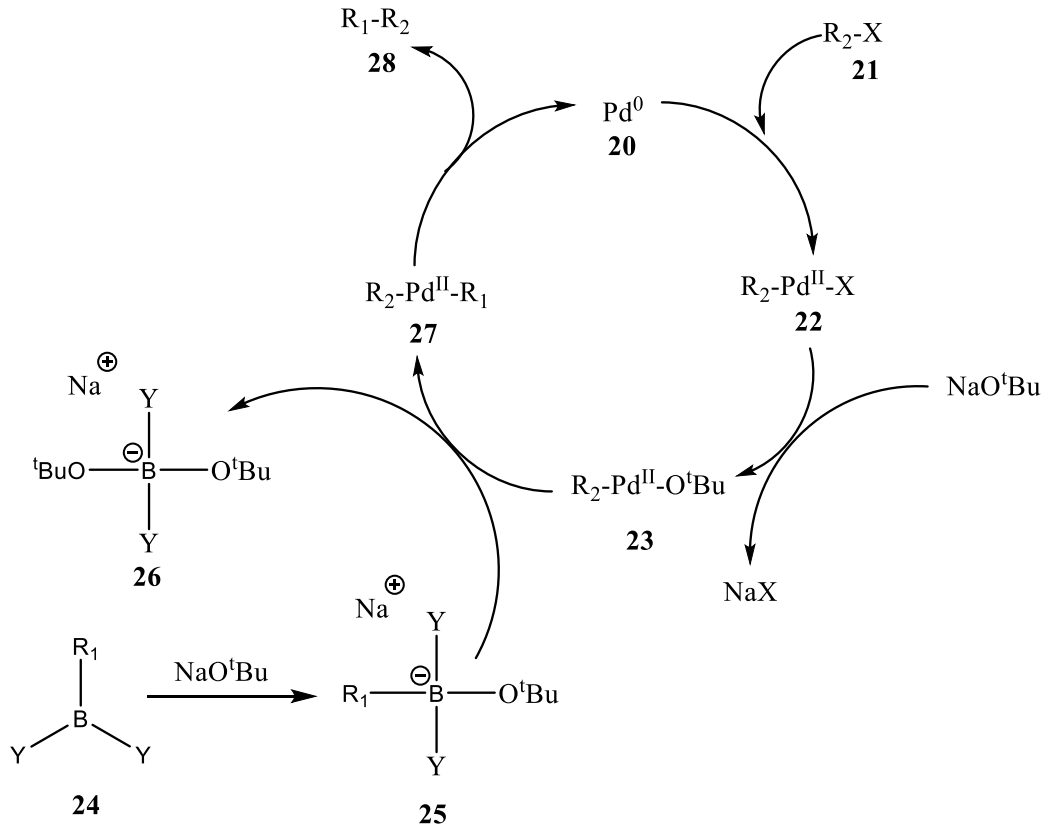
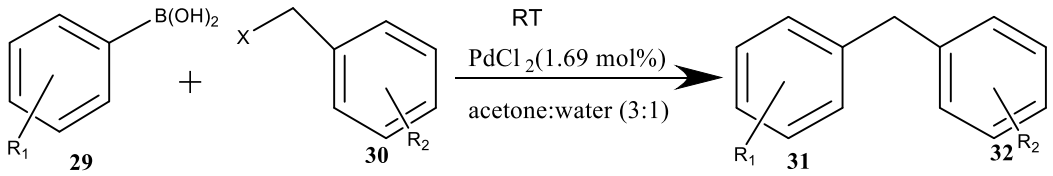


Figure 1.6 The mechanism of the Suzuki reaction

Firstly, palladium underwent oxidative addition to the halide **21** to form the organopalladium species **22**. Secondly, species **22** reacts with alkali give intermediate **23**, which via transmetalation[72] with the boronate complex **25** forms the organopalladium species **27**. Reductive elimination of the desired product **28** restores the original palladium catalyst **20** which completes the catalytic cycle.[73] In the Suzuki coupling catalytic cycle, the alkali has three different roles: Formation of the palladium complex, formation of the borate and the acceleration of the reductive elimination step by reaction introducing alkoxide to the palladium complex.[74] Alkoxide could be replaced by other weak bases depending on the reaction condition. Polar solvents are better than non- polar solvents in this reaction and water will accelerate the reaction.[75] To green this reaction, it has been carried out in supercritical CO_2, solvent-free, water and ionic liquids.[76] However, starting materials of liquid crystals usually cannot dissolve in water. In the following work ethanol and CPME will be used in the reaction as a green solvent. Additionally, the palladium catalyst has been studied as well. There are two kinds

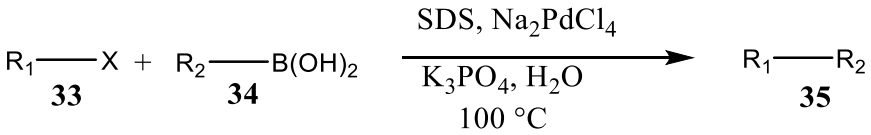
of palladium catalyst to be developed. First one is called ligand-free catalyst. This kind of catalyst is usually Pd^{2+}. [77, 78] B.P. Bandgar[78] used $PdCl_2$ as catalyst for reaction (Scheme 5). Reaction had high yield and good selectivity. First kind of ligand-free catalysts are easy to obtain, but they are unrecyclable, which is their biggest problem.



R 1= H, OMe, OCH 2Ph R 2=H, NO 2, F, Cl, Br, I, X= Cl, Br, I,

Scheme 5[78]

Because palladium is an expensive metal, recycling of palladium is an important step to lower the cost. To achieve this, a second kind of ligand-free catalyst was invented. This kind of palladium catalyst is nanoparticles[79, 80] mesoporous supported[81] palladium. Budarin *et al.*[82] used mesoporous starch as support for palladium to create a palladium catalyst which had high stability, activity and was reusable under various reaction conditions. Saha *et al.*[79] discovered an easy and efficient protocol for the Suzuki coupling reaction (Scheme 6) by using palladium ligand-free nanoparticles. This kind of reaction was able to be carried out in open air and the catalyst is recyclable up to three times without losing activity.



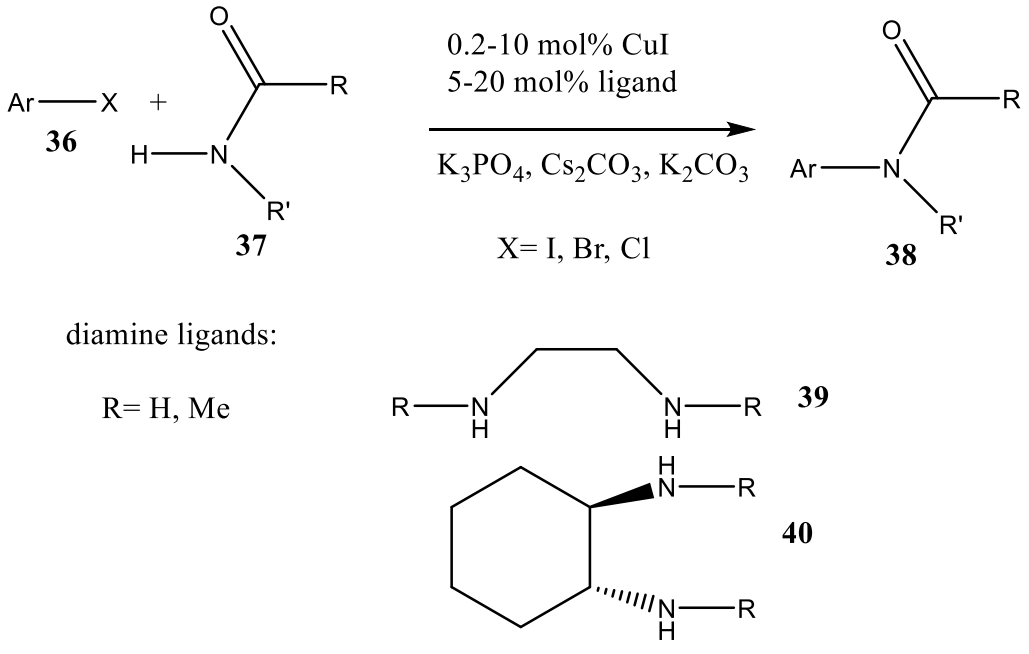
R_1= aryl, heteroaryl R_2= aryl, alkyl X= I, Br

Scheme 6[79]

1.2.5.3 Amidation

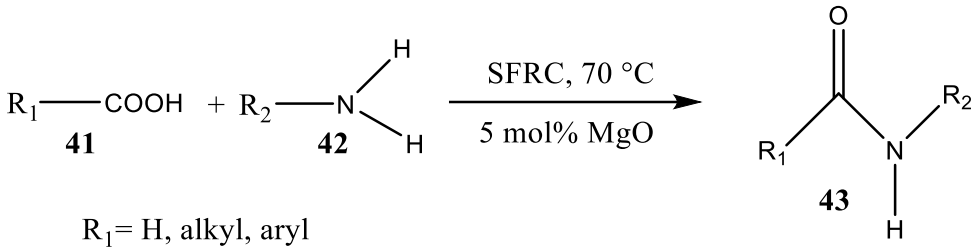
Amide groups were normally not considered, when short chain rod-like liquid crystals were designed. Because intermolecular hydrogen bonds would cause the raising of melting point or destroy molecular order of the mesophase.[83] However, when Y. Matsunaga *et al.*[84, 85] modified the structure of ester-substituted benzene ring, he found that compounds would have more stable mesomorphic phase and larger range of mesomorphic temperatures if ester groups were replaced by amide groups. The major reason was that the amide group could provide intermolecular hydrogen bonds. Those hydrogen bonds induced molecular assembly in one dimension. Since then, the amide group became an important linkage in structure of liquid crystals. It appear on lots of liquid crystal polymers[86, 87] or discotic liquid crystals[88-91].

Klapars *et al.* developed a general and efficient copper catalyst for the amidation of aryl halides.[92] The reaction (Scheme 7) was taken under 0.2−10 mol % of CuI, 5−20 mol % of N,N'-dimethylethylenediamine or trans-N,N'-dimethyl-1,2-cyclohexanediamine and K_3PO4, K_2CO_3, or Cs_2CO_3 as the base with aryl iodides, bromides, and aryl chlorides (in some cases).



Scheme 7[92]

VK Das[93] has created reusable, highly activity and cheap nano-MgO catalyst for amide synthesis under solvent free reaction conditions (SFRC). The reaction (Scheme 8) used carboxylic acid and amines as starting materials under 70 ℃. Catalysts were able to recycle up to 5 times.



R_1= H, alkyl, aryl
R_2= Alkyl, aryl

Scheme 8[93]

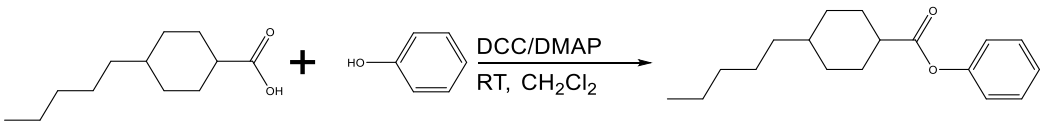
Another green catalyst SBA-15 was invented for catalysing the reaction between carboxylic acid and amino by Comerford *et al.*[94] SBA-15 is the mesoporous structured silica. It is easy and green to obtain by heating silica at 700 ℃.[94] XD Yang *et al.*[95] did the screening of solvent for direct amide synthesis with silica. The result indicated that toluene is the best solvent for the reaction.

CHAPTER 2 EXPERIMENTAL

Sources of every reagents and instruments mentioned in this chapter were as follow: All the starting materials were bought form Sigma-Aldrich, Merck, Fischer and other scientific bands; they were used without any further purification. All the *trans*-4-alkyl-cyclohexanecarboxylic acids were obtained from the Advanced Materials Group of University of York, and used without purification. All the solvent were from Fischer or Sigma-Aldrich and used with no further purification. All NMR works were done by NMR centre of University of York. All GC data came from Agilent 6890N with DB-5HT Column. All IR data came from Vertex 70.

2.1 Esterification

2.1.1 Preparation of *Trans*-4-Pentyl-Cyclohexanecarboxylic Acid Phenyl Ester

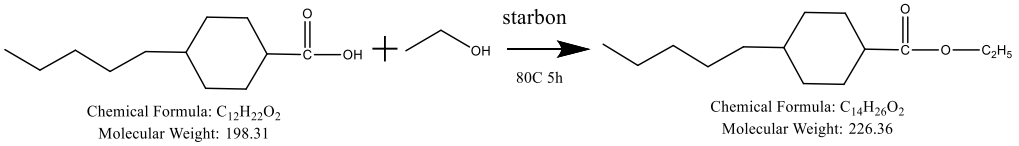


Scheme 9 Synthesis of *trans*-4-Pentyl-cyclohexanecarboxylic acid phenyl ester

A mixture of *trans*-4-pentyl-cyclohexanecarboxylic acid (1.00 g, 5.0 mmol), phenol (0.52 g, 5.5 mmol), DCC (1.03 g, 5.0 mmol), DMAP (0.1 g, 0.09 mmol) and CH_2Cl_2 (20 ml) was stirred at room temperature overnight. The white solid (DCU 1.28 g) from the reaction was filtered and washed by CH_2Cl_2 (10 ml), then was dried in *vacuo* and weighed. The solution was concentrated by rotary evaporation. Then concentrated solution was purified by silica gel column chromatography (mobile phase: 1:1=CH_2Cl_2: petroleum ether 40~60 ℃). The desired fractions were collected and the solvent removed in *vacuo* to get the devised trans-4-pentyl-cyclohexanecarboxylic acid phenyl ester (XZ1), 1.09 g (79.56 % yield), as a pale yellow liquid. Characterization of products (*Trans*-4-Pentyl-cyclohexanecarboxylic acid phenyl ester): IR/cm^{-1}： 2926, 2855 m(C-H_{str}), 1756 s (C=O_{str}), 1493, 1450 m (C-H_{sci}), 1193, 1161, 1122 s(C-O_{str}), 967 w (cyclohexane C-C_{ske}), 736 m (aliph C-C_{ske}); R_f=0.5. ^{1}H-NMR (400 MHz, $CDCl_3$)

δ/ppm: 7.20 (2H, d, J=8 Hz), 7.00 (H, s), 6.83 (2H, d, J=8 Hz), 2.51 (1H, tt, J=12 Hz, 4 Hz), 2.12 (2H, d, J= 16 Hz), 1.85 (2H, d, J=16 Hz), 1.55 (2H, ddd, J=16 Hz, 12 Hz, 4 Hz), 1.39-1.10 (9H, m), 1.06-0.78 (5H, d); ^{13}C-NMR (400 MHz, $CDCl_3$) δ/ppm: 174.0, 154.3, 133.7 (2), 122.8 (2), 118.4, 109.6, 43.7, 37.1, 36.9, 32.2 (2), 29.0 (2), 26.6, 23.0, 14.2;

2.1.2 Preparation of *Trans*-4-Pentyl-Cyclohexanecarboxylic Acid Ethyl Ester



Scheme 10 Synthesis of *trans*-4-pentyl-cyclohexanecarboxylic acid ethyl ester

A series of ethyl esterification reaction was set in different condition (listed on Table 2.1) which followed the method presented below:

A mixture of *trans*-4-pentyl-cyclohexanecarboxylic acid (98%) and ethanol, sulfonated Starbon was stirred at 80 ℃ and refluxed. Using GC traced the reaction at different timing. The crude was filtered to discard catalyst and remove solvent in the rotary evaporator. Dry crude was dissolved in diethyl ether. Diethyl ether was washed with 1 mol/L sodium hydroxide solution twice. Sodium hydroxide solution was kept for recovering 4-pentyl-cyclohexane carboxylic acid. Diethyl ether phase was washed with saturated sodium chloride solution for neutralization. The upper organic phase was separated by using separating funnel. Then the organic phase was dried with anhydrous magnesium sulfate. After drying, anhydrous magnesium sulfate discarded through filtration and diethyl ether was removed by rotary evaporator.

Acid	Mass (g)	Alcohol	volume(ml)	Catalyst	Mass (mg)	Reaction Time(h)	Code	Yield
Trans-4-pentyl-cyclohexanecarboxylic acid (98%)	0.5	Ethanol	10	Sulfonated S300	20	5, 8, 14, 21	XZ 3	N/A
Trans-4-pentyl-cyclohexanecarboxylic acid (98%)	0.5	Ethanol	10	Sulfonated S350	20	5, 8, 14, 21	XZ 4	N/A
Trans-4-pentyl-cyclohexanecarboxylic acid (98%)	0.5	Ethanol	10	Sulfonated S450	20	5, 8, 14, 21	XZ 5	N/A
Trans-4-pentyl-cyclohexanecarboxylic acid (98%)	0.5	Ethanol	10	Sulfonated S550	20	5, 8, 14, 21	XZ 6	N/A
Trans-4-pentyl-cyclohexanecarboxylic acid (98%)	0.5	Ethanol	10	Sulfonated S600	20	5, 8, 14, 21	XZ 7	N/A
Trans-4-pentyl-cyclohexanecarboxylic acid (98%)	0.5	Ethanol	10	Sulfonated S760	20	5, 8, 14, 21	XZ 8	N/A
Trans-4-pentyl-cyclohexanecarboxylic acid (98%)	2	Ethanol	40	Sulfonated S450	80	5	XZ 13	4.8%
Recovered 4-pentyl-cyclohexanecarboxylic acid from XZ13	1	Ethanol	20	Sulfonated S450	40	5	XZ 14	21.8 %
Trans-4-pentyl-cyclohexanecarboxylic acid (98%)	2	Ethanol	40	Sulfonated S350	80	5	XZ 15	11%
Recovered 4-pentyl-cyclohexanecarboxylic acid from XZ14	0.5	Ethanol	10	Sulfonated S450	20	5	XZ 16	42.1 %

Table 2.1 Reaction conditions for preparation of *trans*-4-pentyl-cyclohexanecarboxylic acid ethyl ester

Characterization of products:

XZ13:

^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm: 4.09(2H, q, J=8 Hz), 2.18(1H, tt, J=12 Hz, 4 Hz), 1.93(2H, d, J=16 Hz), 1.78(2H, d, J=16 Hz), 1.40(2H, ddd, J=16 Hz, 12 Hz, 4 Hz), 1.32-1.10 (12H, m,), 0.94-0.80(5H, m,). ^{13}C-NMR (400 MHz, $CDCl_3$) δ/ppm: 176.4, 60.1, 43.7, 37.3, 37.0, 32.4 (2), 32.2, 29.1 (2), 26.6, 22.76, 14.3, 14.2.

XZ14:

^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm: 4.09(2H, q, J=8 Hz), 2.18(1H, tt, J=12 Hz, 4 Hz), 1.93(2H, d, J=16 Hz), 1.78(2H, d, J=16 Hz), 1.40(2H, ddd, J=16 Hz, 12 Hz, 4 Hz), 1.32-1.10 (12H, m,), 0.94-0.80(5H, m,); ^{13}C-NMR (400 MHz, $CDCl_3$) δ/ppm: 176.4, 60.1, 43.7, 37.3, 37.0, 32.4 (2), 32.2, 29.1 (2), 26.6, 22.76, 14.3, 14.2.

XZ15:

^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm: 4.09(2H, q, J=8 Hz), 2.18(1H, tt, J=12 Hz, 4 Hz), 1.93(2H, d, J=16 Hz), 1.78(2H, d, J=16 Hz), 1.40(2H, ddd, J=16 Hz, 12 Hz, 4 Hz), 1.32-1.10 (12H, m,), 0.94-0.80(5H, m,); ^{13}C-NMR (400 MHz, $CDCl_3$) δ/ppm: 176.4, 60.1, 43.7, 37.3, 37.0, 32.4 (2), 32.2, 29.1 (2), 26.6, 22.76, 14.3, 14.2.

XZ16:

^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm: 4.09(2H, q, J=8 Hz), 2.18(1H, tt, J=12 Hz, 4 Hz), 1.93(2H, d, J=16 Hz), 1.78(2H, d, J=16 Hz), 1.40(2H, ddd, J=16 Hz, 12 Hz, 4 Hz), 1.32-1.10 (12H, m,), 0.94-0.80(5H, m,); ^{13}C-NMR (400 MHz, $CDCl_3$) δ/ppm: 176.4, 60.1, 43.7, 37.3, 37.0, 32.4 (2), 32.2, 29.1 (2), 26.6, 22.76, 14.3, 14.2; IR/ cm^{-1}: 2925 s, 2855 m ($C\text{-}H_{str}$), 1733 s ($C{=}O_{str}$), 1450 m ($C\text{-}H_{sci}$), 1377 m ($C\text{-}H_{def}$), 1247 m ($C\text{-}C_{ste}$), 1041 w, 980 w, 733 m ($C\text{-}C_{ske}$).

2.1.2.1 4-Pentyl-Cyclohexanecarboxylic Acid Recovery

Sodium hydroxide eluent from purification was acidized by 36% hydrochloric acid. Diethyl ether was used as extraction agent to extract 4-pentyl-cyclohexanecarboxylic acid from aqueous phase. After extraction, the organic

phase was washed by saturated sodium hydroxide and then the organic phase was dried with anhydrous magnesium sulfate. Finally, magnesium sulfate and diethyl ether were removed to recover the 4-pentyl-cyclohexanecarboxylic acid.

Characterization of products:

Recovery 4-pentyl-cyclohexanecarboxylic acid from XZ13:

IR/cm^{-1}: 2953 w (-OH), 2915, 2850 m (C-H_{str}), 1692 s (C=O_{str}), 1450, 1424, 1336, 1316 m (C-H_{def}), 1257 m (C-C_{ste}), 1039 w, 950 w, 723 m (C-C_{ske}); ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm: 2.23(1H, tt, J=12 Hz, 4 Hz), 1.99(2H, d, J=16 Hz), 1.80(2H, d, J=16 Hz), 1.40(2H, ddd, J=16 Hz, 12 Hz, 4 Hz), 1.33-1.09 (9H, m,), 1.00-0.79(5H, m, H_{ax}, -$\underline{CH}_3$); ^{13}C-NMR (400 MHz, $CDCl_3$) δ/ppm: 183.0, 43.4, 37.2, 37.0, 32.3 (2), 32.2, 28.9 (2), 26.6, 22.7, 14.2.

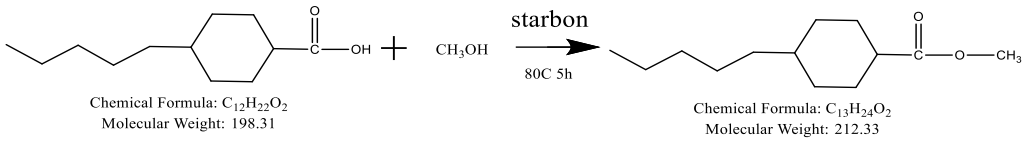
Recovery 4-pentyl-cyclohexanecarboxylic acid from XZ14:

IR/cm^{-1}: 2954 w (-OH),2916, 2850 m (C-H_{str}), 1692 s (C=O_{str}), 1450, 1424, 1336, 1317 m (C-H_{def}), 1258 m (C-C_{ste}), 1040 w, 951 w, 723 m (C-C_{ske}); ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm: 2.23(1H, tt, J=12 Hz, 4 Hz), 1.99(2H, d, J=16 Hz), 1.80(2H, d, J=16 Hz), 1.40(2H, ddd, J=16 Hz, 12 Hz, 4 Hz), 1.33-1.09 (9H, m,), 1.00-0.79(5H, m,); ^{13}C-NMR (400 MHz, $CDCl_3$) δ/ppm: 183.0, 43.4, 37.2, 37.0, 32.3 (2), 32.2, 28.9 (2), 26.6, 22.7, 14.2.

Recovery 4-pentyl-cyclohexanecarboxylic acid from XZ15:

IR/cm^{-1}: 2954 w (-OH), 2920, 2850 m (C-H_{str}), 1693 s (C=O_{str}), 1450, 1426, 1337, 1317 m (C-H_{def}), 1258 m (C-C_{ste}), 1040 w, 951 w, 723 m (C-C_{ske}); ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm: 2.23(1H, tt, J=12 Hz, 4 Hz), 1.99(2H, d, J=16 Hz), 1.80(2H, d, J=16 Hz), 1.40(2H, ddd, J=16 Hz, 12 Hz, 4 Hz), 1.33-1.09 (9H, m,), 1.00-0.79(5H, m,); ^{13}C-NMR (400 MHz, $CDCl_3$) δ/ppm: 183.0, 43.4, 37.2, 37.0, 32.3 (2), 32.2, 28.9 (2), 26.6, 22.7, 14.2.

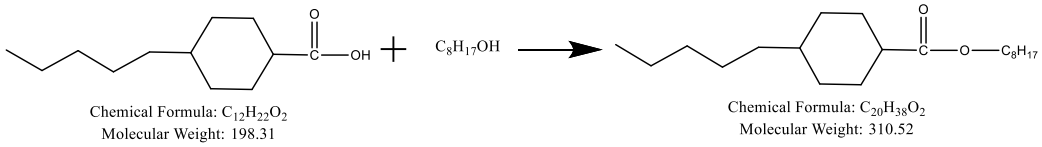
2.1.3 Preparation of *Trans*-4-Pentyl-Cyclohexanecarboxylic Acid Methyl Ester



Scheme 11 Synthesis of *trans*-4-pentyl-cyclohexanecarboxylic acid methyl ester

A mixture of *trans*-4-pentyl-cyclohexanecarboxylic acid (0.5 g 2.5 mmol 98%) and ethanol (10 ml), sulfonated Starbon S450 (20 mg) was stirred at 80 ℃ and refluxed for 5 h. Then the mixture was filtrated to discard sulfonated Starbon and added new sulfonated Starbon S450. Keeping concentration of Starbon at 0.2 mg/ml the system reacted for 5h. Using GC analysed crude before adding new Starbon S450. Changing Starbon catalyst, the procedure was repeated 3 times.

2.1.3 Preparation of *Trans*-4-Pentyl-cyclohexanecarboxylic Acid Octyl Ester



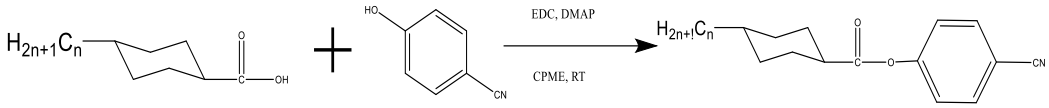
Scheme 12 Synthesis of *trans*-4-pentyl-cyclohexanecarboxylic acid octyl ester

Two different octyl esterification reactions were set in different condition (listed on Table 2.2) which followed the method presented below: A mixture of *trans*-4-pentyl-cyclohexanecarboxylic acid (98%) and 1-Octanol, sulfonated Starbon S450 was stirred and refluxed. The reactions were traced by GC at different timing.

Acid	Mass(g)	Alcohol	Quantity (ml)	Catalyst	quantity(mg)	Reaction Time(h)	Reaction Temperature(°C)	Code
Trans-4-pentyl-cyclohexanecarboxylic acid (98%)	0.5	1-Octanol	10	S450	20	9	80	XZ20
Trans-4-pentyl-cyclohexanecarboxylic acid (98%)	0.5	1-Octanol	10	S450	20	12	80	XZ20

Table 2.2 Reaction conditions for preparation of *trans*-4-pentyl-cyclohexanecarboxylic acid octyl ester

2.1.4 Preparation of *Trans*-4-Alkyl-Cyclohexane Carboxylic Acid 4-Cyanophenol Ester



n=2, 3, 4, 5

Scheme 13 Synthesis of *trans*-4-alkyl-cyclohexane carboxylic acid 4-cyanophenol ester

All the reaction conditions were listed below at Table 3.2. Reactions were operated by following step:

A mixture of *trans*-4-alky-cyclohexanecarboxylic acid (98%), 4-cyanophenol, EDC, and DMAP was stirred at room temperature in CPME (10 ml). The reaction was tracing by GC at different timing. The product could be purified by two ways. The first one: crude was redissloved in 30 ml diethyl ether, then wash by 25 ml HCl (0.1 mol/L) to remove DMAP and EDC and other byproducts. And then 25 ml NaOH (0.1 mol/L) was used to clear unreacted starting materials by washing

crude twice. The upper phase was neutralized with saturated sodium chloride solution (25 ml). The upper organic phase was separated by separating funnel. Then the upper phase was dried with anhydrous magnesium sulfate. After drying, anhydrous magnesium sulfate was filtered to discard and CPME was removed by rotary evaporator to get the final product. The other way was that: The crude was concentrated by rotary evaporation. The concentrated solution was purified by silica gel (20 g) column chromatography (mobile phase: 1:1=CH_2Cl_2 (134 g): petroleum ether 40~60 ℃ (64 g)). The desired fractions were collected and solvent removed in *vacuo* to get the devised final product.

Characterization of products:

Trans-4-ethyl-cyclohexanecarboxylic acid 4-cyanophenol ester (n=2, LC CN C2):

^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm: 7.66 (2H, d, J=8 Hz), 7.20 (2H, d, J=8 Hz), 2.48 (1H, tt, J=12 Hz, 4 Hz), 2.12 (2H, d, J=16 Hz), 1.86 (2H, d, J=16 Hz), 1.54 (2H, ddd, J=16 Hz, 12 Hz, 4 Hz), 1.30-1.11 (3H, m), 1.06-0.81 (5H, d); ^{13}C-NMR (400 MHz, $CDCl_3$) δ/ppm: 174.0, 154.3, 133.6 (2), 122.9 (2), 118.4, 109.6, 43.7, 38.6, 31.2 (2), 29.8, 29.0 (2), 11.5; IR/ cm^{-1}: 2935, 2853 m ($C\text{-}H_{str}$), 2234 m ($C\equiv N_{str}$), 1758 s ($C=O_{str}$), 1600 m ($C=C_{str}$), 1500 m (aromatic systems), 1448 m ($C\text{-}H_{sci}$), 1200 m ($C\text{-}H_{ske}$), 1164 m ($C\text{-}O_{str}$), 1015 w, 954 w, 830 m ($C\text{-}C_{ske}$).

Trans-4-propyl-cyclohexanecarboxylic acid 4-cyanophenol ester (n=3, LC CN C3):

^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm: 7.66 (2H, d, J=8 Hz), 7.20 (2H, d, J=8 Hz), 2.48 (1H, tt, J=12 Hz, 4 Hz), 2.12 (2H, d, J=16 Hz), 1.87 (2H, d, J=16 Hz), 1.54 (2H, ddd, J=16 Hz, 12 Hz, 4 Hz), 1.40-1.10 (5H, m), 1.09-0.80 (5H, d); ^{13}C-NMR (400 MHz, $CDCl_3$) δ/ppm: 174.0, 154.3, 133.7 (2), 122.8 (2), 118.4, 109.5, 43.5, 39.5, 36.6, 32.2 (2), 29.0 (2), 20.0, 14.4; IR/cm^{-1}: 2931, 2859 m ($C\text{-}H_{str}$), 2225 m ($C\equiv N_{str}$), 1749 s ($C=O_{str}$), 1602 m ($C=C_{str}$), 1504 m (aromatic systems), 1446 m ($C\text{-}H_{sci}$), 1207 m ($C\text{-}H_{ske}$), 1161 m ($C\text{-}O_{str}$), 1035 w, 925 w, 835 m ($C\text{-}C_{ske}$).

Trans-4-butyl-cyclohexanecarboxylic acid 4-cyanophenol ester (n=4, LC CN C4):

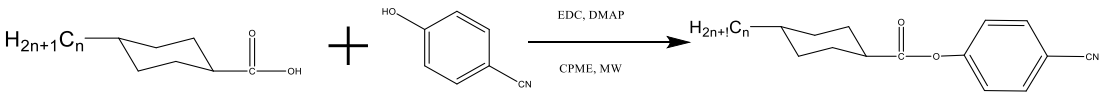
^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm: 7.68 (2H, d, J=8 Hz), 7.20 (2H, d, J=8 Hz), 2.47 (1H, tt, J=12 Hz, 4 Hz), 2.11 (2H, d, J= 16 Hz), 1.87 (2H, d, J=16 Hz), 1.54 (2H, ddd, J=16 Hz, 12 Hz, 4 Hz), 1.35-1.15 (7H, m), 1.04-0.80 (5H, d); ^{13}C-NMR

(400 MHz, $CDCl_3$) δ/ppm: 174.0, 154.3, 133.7 (2), 122.8 (2), 118.4, 109.6, 100, 43.7, 36.9, 32.2 (2), 29.2, 29.0 (2), 23.0, 14.2; IR/cm^{-1}: 2927, 2856 m ($C\text{-}H_{str}$), 2230 m ($C\equiv N_{str}$), 1757 s ($C=O_{str}$), 1602 m ($C=C_{str}$), 1503 m (aromatic systems), 1450 m ($C\text{-}H_{sci}$), 1210 m ($C\text{-}H_{ske}$), 1164 m ($C\text{-}O_{str}$), 1113 w, 972 w, 850 m ($C\text{-}C_{ske}$).

Trans-4-pentyl-cyclohexanecarboxylic acid 4-cyanophenol ester (n=5, LC CN C5):

^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm: 7.66 (2H, d, J=8 Hz), 7.18 (2H, d, J=8 Hz), 2.50 (1H, tt, J=12 Hz, 4 Hz), 2.11 (2H, d, J= 16 Hz), 1.86 (2H, d, J=16 Hz), 1.54 (2H, ddd, J=16 Hz, 12 Hz, 4 Hz), 1.38-1.10 (9H, m), 1.06-0.78 (5H, d); ^{13}C-NMR (400 MHz, $CDCl_3$) δ/ppm: 193.3, 174.0, 154.3, 133.7 (2), 122.8 (2), 118.4, 109.6, 43.7, 37.1, 36.9, 32.2 (2), 29.0 (2), 26.6, 23.0, 14.2; IR/cm^{-1}: 2926, 2856 m ($C\text{-}H_{str}$), 2228 m ($C\equiv N_{str}$), 1759 s ($C=O_{str}$), 1604 m ($C=C_{str}$), 1506 m (aromatic systems), 1452 m ($C\text{-}H_{sci}$), 1212 m ($C\text{-}H_{ske}$), 1166 m ($C\text{-}O_{str}$), 1117 w, 976 w, 859 m ($C\text{-}C_{ske}$).

2.1.5 Preparation of *Trans*-4-Alkyl-Cyclohexane Carboxylic Acid 4-Cyanophenol Ester with Microwave Irradiation



Scheme 14 Synthesis of *trans*-4-alkyl-cyclohexane carboxylic acid 4-cyanophenol ester with MW

All the reaction conditions were listed below at Table 2.3. Reactions were operated through the following steps:

A mixture of *trans*-4-alky-cyclohexanecarboxylic acid (98%), 4-cyanophenol, EDC, and DMAP was dissolved in CPME (5 ml) and heated by microwaves to 100 ℃ in a closed vessel for 3 min. After reaction, crude was redissloved in 30 ml Diethyl Ether, then wash by 25 ml HCl (0.1 mol/L) to remove DMAP and EDC and other byproducts. And then 25 ml NaOH (0.1 mol/L) was used to clear unreacted staring materials by washing the crude twice. The upper phase was

neutralized with saturated sodium chloride solution (25 ml). The upper organic phase was separated by separating funnel. Then the upper phase was dried with anhydrous magnesium sulfate. After drying, anhydrous magnesium sulfate was filtered and discarded. CPME was removed in a rotary evaporator to get the final product.

Acid	quantity (g)	Alcohol	quantity (g)	EDC （g）	DMAP (g)	Reaction Time	Code
Trans-4-ethyl-cyclohexanecarboxylic acid，n=2	0.25	4-cyanophenol	0.15	0.25	0.02	3min	MW LC CN C2
Trans-4-propyl-cyclohexanecarboxylic acid，n=3	0.25	4-cyanophenol	0.15	0.25	0.02	3min	MW LC CN C3
Trans-4-butyl-cyclohexanecarboxylic acid，n=4	0.25	4-cyanophenol	0.15	0.25	0.02	3min	MW LC CN C4
Trans-4-pentyl-cyclohexanecarboxylic acid，n=5	0.25	4-cyanophenol	0.15	0.25	0.02	3min	MW LC CN C5

Table 2.3 Reaction conditions of synthesis of *trans*-4-alkyl-cyclohexane carboxylic acid 4-cyanophenol ester with MW

Another series of reaction was set up for comparison between microwave irradiation and room temperature conditions. Conditions of reactions were listed at Table 2.4.

Acid	quantity(g)	Alcohol	quantity(g)	EDC（g）	DMAP (g)
Trans-4-ethyl-cyclohexanecarboxylic acid，n=2	0.25	4-cyanophenol	0.15	0.25	0.02
Trans-4-propyl-cyclohexanecarboxylic acid，n=3	0.25	4-cyanophenol	0.15	0.25	0.02
Trans-4-butyl-cyclohexanecarboxylic acid，n=4	0.25	4-cyanophenol	0.15	0.25	0.02
Trans-4-pentyl-cyclohexanecarboxylic acid，n=5	0.25	4-cyanophenol	0.15	0.25	0.02

Table 2.4 Reaction conditions for comparison

Each reaction was taken under two different heating modes, which were room temperature, and microwave irradiation. Reactions were monitoring by GC.

Characterization of products:

Trans-4-ethyl-cyclohexane carboxylic acid 4-cyanophenol ester (n=2, MW LC CN C2): ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm: 7.67 (2H, d, J=8 Hz), 7.19 (2H, d, J=8 Hz), 2.48 (1H, tt, J=12 Hz, 4 Hz), 2.12 (2H, d, J=16 Hz), 1.86 (2H, d, 2H, d, J=16 Hz), 1.54 (2H, ddd, J=16 Hz, 12 Hz, 4 Hz), 1.30-1.11 (3H, m), 1.06-0.81 (5H, d); ^{13}C-NMR (400 MHz, $CDCl_3$) δ/ppm: 174.0, 154.3, 133.6 (2), 122.9 (2), 118.4, 109.6, 43.7, 38.6, 31.2 (2), 29.8, 29.0 (2), 11.5.

Trans-4-propyl-cyclohexane carboxylic acid 4-cyanophenol ester (n=3, MW LC CN C3): ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm: 7.66 (2H, d, J=8 Hz), 7.20 (2H, d, J=8 Hz), 2.48 (1H, tt, J=12 Hz, 4 Hz), 2.12 (2H, d, J=16 Hz), 1.87 (2H, d, 2H, d, J=16 Hz), 1.54 (2H, ddd, J=16 Hz, 12 Hz, 4 Hz), 1.40-1.10 (5H, m), 1.09-0.80 (5H, d); ^{13}C-NMR (400 MHz, $CDCl_3$) δ/ppm: 174.0, 154.3, 133.7 (2), 122.8 (2), 118.4, 109.5, 43.5, 39.5, 36.6, 32.2 (2), 29.0 (2), 20.0, 14.4.

Trans-4-butyl-cyclohexane carboxylic acid 4-cyanophenol ester (n=4, MW LC CN C4): ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm: 7.68 (2H, d, J=8 Hz), 7.20 (2H, d, J=8 Hz), 2.47 (1H, tt, J=12 Hz, 4 Hz), 2.11 (2H, d, J=16 Hz), 1.87 (2H, d, 2H, d, J=16 Hz), 1.54 (2H, ddd, J=16 Hz, 12 Hz, 4 Hz), 1.35-1.15 (7H, m), 1.04-0.80 (5H, d); ^{13}C-NMR (400 MHz, $CDCl_3$) δ/ppm: 174.0, 154.3, 133.7 (2), 122.8 (2), 118.4, 109.6, 100, 43.7, 36.9, 32.2 (2), 29.2, 29.0 (2), 23.0, 14.2.

Trans-4-pentyl-cyclohexane carboxylic acid 4-cyanophenol ester (n=5, MW LC CN C5): ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm: 7.66 (2H, d, J=8 Hz), 7.18 (2H, d, J=8 Hz), 2.50 (1H, tt, J=12 Hz, 4 Hz), 2.11 (2H, d, J=16 Hz), 1.86 (2H, d, 2H, d, J=16 Hz), 1.54 (2H, ddd, J=16 Hz, 12 Hz, 4 Hz), 1.38-1.10 (9H, m), 1.06-0.78 (5H, d); ^{13}C-NMR (400 MHz, $CDCl_3$) δ/ppm: 193.3, 174.0, 154.3, 133.7 (2), 122.8 (2), 118.4, 109.6, 43.7, 37.1, 36.9, 32.2 (2), 29.0 (2), 26.6, 23.0, 14.2.

2.2 Suzuki-Miyaura Cross Coupling Reaction

2.2.1 Catalyst Preparation of Starbon-Pd

A range of Starbon (S300, S350, S400, S450, S500 and S600) were contained in a 30 ml sample vial and mixed with 2.5% of weight of Starbon Pd^{2+} (using palladium(II) acetate as source of Pd^{2+}). The mixture was stirred with 10 ml of ethanol overnight. Then the solvent was removed through rotary evaporation. Product was washed with acetone (20 ml) twice and ethanol (20 ml) twice. The final product was dried in oven at 80 ℃ overnight.

2.2.2 Ethanol/water Solvent System for Suzuki Reaction

Two different starting materials: Iodobenzene or 4-Iodoanisole was used to reaction with Phenylboronic acid as model for testing the ethanol/water solvent and catalysts performance by following steps: starting material (2 mmol) dissolved

in different volume ratio of ethanol and water with Phenylboronic acid (2.2 mmol), 0.5 g K_2CO_3 and catalyst (2% weight of starting material) was stirred at 60 ℃. Reaction products were analysed by GC.

2.2.3 CPME/ Water and THF/ Water Solvent System for Suzuki Reaction

Two different starting materials: Iodobenzene or 4-Iodoanisole were used in the reaction with Phenylboronic acid as model for testing the CPME/water solvent and catalysts performance by following steps: starting material (2 mmol) dissolved in different volume ratio of ethanol and water with Phenylboronic acid (2.2 mmol), 0.5 g K_2CO_3 and catalyst (2 % Weight of starting material) were stirred at 60 ℃. Reaction products were analysed by GC. Because CPME is developed for replacing THF. A series of reaction were carried out with THF/water system as well for comparison.

2.2.4 Recycling of Starbon-Pd Catalyst

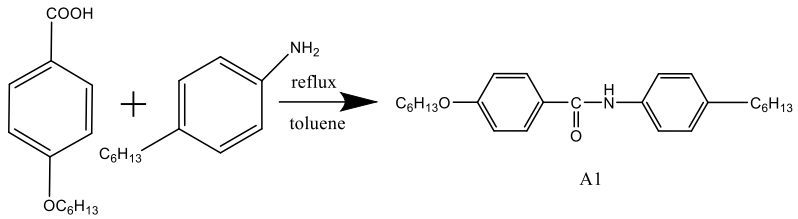
A series of reactions were set up to test the recyclability of Starbon-Pd catalyst. Using Iodobenzene and Phenylboronic acid as starting materials (2 mmol each), the reaction was stirred at 60 ℃ for 3h in 9:1=ethanol: water (V/V) with 0.5 g K_2CO_3 and Starbon-S500-Pd catalyst (5% Weight of starting martial). Reaction products were analysed using GC. After reaction, solution was centrifuged to recover Starbon-Pd catalyst. Recovered Starbon-Pd catalyst was washed by 10 ml acetone 3 times and then dried at 80 ℃. The procedure was repeated 3 times on the same catalyst.

2.3 Amidation

2.3.1 Preparation of activated SiO_2 catalyst

Commercial silica gel was activated at 700 ℃ in muffle furnace for a couple hours. After cooling down at room temperature activated SiO_2 catalyst was obtained and ready for reaction.

2.3.2 Preparation of N-(4-Hexylphenyl)-4-Hexyloxybenzamide



Scheme 15 Synthesis of N-(4-hexylphenyl)-4-hexyloxybenzamide

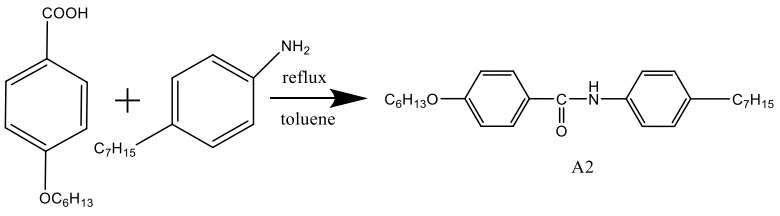
A mixture of 4-hexyloxy benzoic acid (0.5 g, 2.25 mmol), 4-hexylaniline (0.4 g 2.25mmol), and 10%wt activated SiO_2 catalyst was refluxed in toluene (15 ml) for 24 h. After that, SBA-15 was filtered and removed. The crude was cooled down to 4 ℃ for few hours for recrystallization. Crystals were filtered and washed by cold toluene 3 times. The desired fractions were collected and the solvent was removed in *vacuo* to get the devised N-(4-hexylphenyl)-4-hexyloxybenzamide (0.45 g, 52.4 % yield).

Characterization of the product:

IR/cm^{-1}: 3318 m (N-H_{str}), 2930, 2856 m (C-H_{str}), 1637 s (C=O_{str}); ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm: 7.80 (2H, d, J= 8Hz), 7.65 (1H, s), 7.49 (2H, d, J=8Hz), 6.93 (2H, d, J=8Hz), 6.88 (2H, d, J=8Hz), 4.00 (2H, t, J=4Hz), 2.57 (2H, t, J=4Hz), 1.83-1.76 (2H, m), 1.60-1.32 (14H, m), 0.96-0.88 (6H, m);

^{13}C-NMR (400 MHz, $CDCl_3$) δ/ppm: 183.0, 43.4, 37.2, 37.0, 32.3 (2), 32.2, 28.9 (2), 26.6, 22.7, 14.2.

2.3.3 Preparation of N-(4-Heptylphenyl)-4-Hexyloxybenzamide



Scheme 16 Synthesis of N-(4-heptylphenyl)-4-hexyloxybenzamide

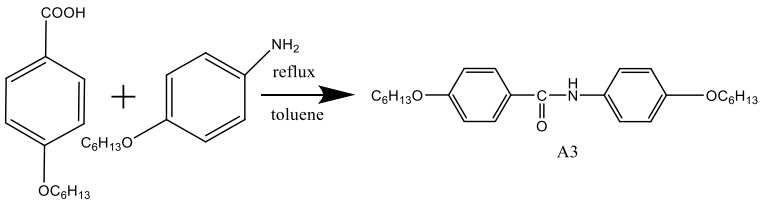
A mixture of 4-hexyloxy benzoic acid (0.5 g, 2.25 mmol), 4-heptylaniline (0.43 g, 2.25 mmol), and 10%wt activated SiO_2 catalyst was refluxed in toluene (15 ml) for 24 h. After that, SBA-15 was filtered and removed. The crude was cooled down to 4 ℃ for few hours for recrystallization. Crystals were filtered and washed by cold toluene 3 times. The desired fractions were collected and the solvent removed in *vacuo* to get the devised N-(4-heptylphenyl)-4-hexyloxybenzamide (0.49 g, 55.1 % yield).

Characterization of the product:

IR/cm^{-1}: 3321 m ($N\text{-}H_{str}$), 2926, 2856 m ($C\text{-}H_{str}$), 1638 s ($C{=}O_{str}$); ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm: 7.81 (2H, d, J= 8Hz), 7.67 (1H, s), 7.51 (2H, d, J=8Hz), 7.16 (2H, d, J= 8Hz), 6.94 (2H, d, J= 8Hz), 4.00 (2H, t, J=4Hz), 2.57 (2H, t, J=4Hz), 1.83-1.78 (2H, m), 1.59-1.24 (16H, m), 0.96-0.88 (6H, m);

^{13}C-NMR (400 MHz, $CDCl_3$) δ/ppm: 183.0, 43.4, 37.2, 37.0, 32.3 (2), 32.2, 28.9 (2), 26.6, 22.7, 14.2.

2.3.4 Preparation of N-(4-Hexyloxyphenyl)-4-Hexyloxybenzamide



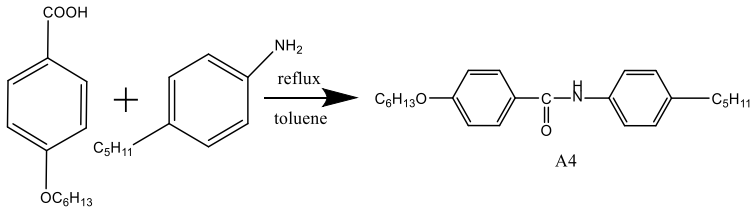
Scheme 17 Synthesis of N-(4-hexyloxyphenyl)-4-hexyloxybenzamide

A mixture of 4-hexyloxy benzoic acid (0.5 g, 2.25 mmol), 4-hexyloxyaniline (0.435 g, 2.25 mmol), and 10%wt activated SiO_2 catalyst was refluxed in toluene for 24 h. After that, SBA-15 was filtered and removed. The crude was cooled down to 4 ℃ for few hours for recrystallization. Crystals were filtered and washed by cold toluene 3 times. The desired fractions were collected and the solvent removed in *vacuo* to get the devised N-(4-hexyloxyphenyl)-4-hexyloxybenzamide (0.62 g, 69.3 % yield).

Characterization of the product:

IR/cm^{-1}: 3318 m ($N\text{-}H_{str}$), 2929, 2856 m ($C\text{-}H_{str}$), 1637 s ($C{=}O_{str}$); ^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm: 7.81 (2H, d, J= 8Hz), 7.68 (1H, s), 7.51 (2H, d, J=8Hz), 7.16 (2H, d, J= 8Hz), 6.94 (2H, d, J= 8Hz), 4.00 (2H, t, J=4Hz), 3.93 (2H, t, J=4Hz), 1.83-1.76 (4H, m), 1.59-1.24 (12H, m), 0.96-0.88 (6H, m); ^{13}C-NMR (400 MHz, $CDCl_3$) δ/ppm: 183.0, 43.4, 37.2, 37.0, 32.3 (2), 32.2, 28.9 (2), 26.6, 22.7, 14.2.

2.3.5 Preparation of N-(4-Pentylphenyl)-4-Hexyloxybenzamide



Scheme 18 Synthesis of N-(4-pentylphenyl)-4-hexyloxybenzamide

A mixture of 4-hexyloxy benzoic acid (0.5 g, 2.25 mmol), 4-pentylaniline (0.37 g, 2.25 mmol), and 10%wt SBA-15 was refluxed in toluene for 24 h. After that, SBA-15 was filtered and removed. The crude was cooled down to 4 ℃ for few hours for recrystallization. Crystals were filtered and washed by cold toluene 3 times. The desired fractions were collected and the solvent removed in *vacuo* to get the devised N-(4-pentylphenyl)-4-hexyloxybenzamide (0.36 g, 43.5 % yield).

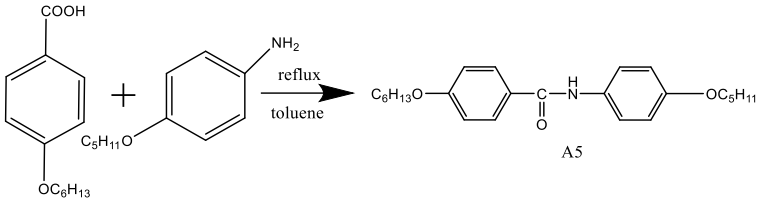
Characterization of the product:

IR/cm^{-1}: 3319 m ($N\text{-}H_{str}$), 2927, 2856 m ($C\text{-}H_{str}$), 1638 s ($C{=}O_{str}$);

^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm: 7.81 (2H, d, J= 8Hz), 7.67 (1H, s), 7.51 (2H, d, J=8Hz), 7.16 (2H, d, J= 8Hz), 6.94 (2H, d, J= 8Hz), 4.00 (2H, t, J=4Hz), 2.57 (2H, t, J=4Hz), 1.83-1.78 (2H, m), 1.59-1.24 (12H, m), 0.96-0.88 (6H, m);

^{13}C-NMR (400 MHz, $CDCl_3$) δ/ppm: 183.0, 43.4, 37.2, 37.0, 32.3 (2), 32.2, 28.9 (2), 26.6, 22.7, 14.2.

2.3.6 Preparation of N-(4-Pentyloxyphenyl)-4-Hexyloxybenzamide



Scheme 19 Synthesis of N-(4-pentyloxyphenyl)-4-hexyloxybenzamide

A mixture of 4-hexyloxy benzoic acid (0.5 g, 2.25 mmol), 4-pentyloxyaniline (0.40 g, 2.25 mmol), and 10%wt SBA-15 was refluxed in toluene for 24 h. After that, SBA-15 were filtered and removed. The crude was cooled down to 4 ℃ for few hours for recrystallization. Crystals were filtered and washed by cold toluene 3 times. The desired fractions were collected and the solvent removed in *vacuo* to get the devised N-(4-pentyloxyphenyl)-4-hexyloxybenzamide (0.54 g, 62.8% yield).

Characterization of the product:

IR/cm^{-1}: 3320 m ($N\text{-}H_{str}$), 2926, 2856 m ($C\text{-}H_{str}$), 1638 s ($C{=}O_{str}$);

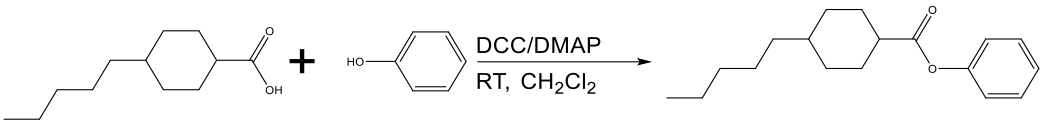
^{1}H-NMR (400 MHz, $CDCl_3$) δ/ppm: 7.80 (2H, d, J= 8Hz), 7.65 (1H, s), 7.49 (2H, d, J=8Hz), 6.93 (2H, d, J=8Hz), 6.88 (2H, d, J=8Hz), 4.00 (2H, t, J=4Hz), 3.94 (2H, t, J=4Hz), 1.83-1.74 (4H, m), 1.52-1.32 (10H, m), 0.96-0.88 (6H, m);

^{13}C-NMR (400 MHz, $CDCl_3$) δ/ppm: 183.0, 43.4, 37.2, 37.0, 32.3 (2), 32.2, 28.9 (2), 26.6, 22.7, 14.2.

CHAPTER 3 RESULTS AND DISCUSSIONS

3.1 DCC/DMAP Esterification

The traditional way to create *trans*-4-Pentyl-cyclohexanecarboxylic acid phenyl ester is through the employment of the DCC/DMAP system. The metrics have been calculated below. Data was collected from experiment 2.1.1



Scheme 9 Synthesis of *trans*-4-Pentyl-cyclohexanecarboxylic acid phenyl ester

3.1.1 Atom Economy

Atom Economy (AE) = [molecular mass of product]/ [Σ molecular mass of reagents]

= 274.41/ (198.3+94.11+206.3)

= 55.02%

Atom Economy shows that only near half atoms in starting material have been used. The other half atoms have been wasted.

3.1.2 E-factor

E-Factor = [mass of waste]/ [mass of product]

= [CH_2Cl_2 (238.8 g) + petroleum ether (97.5 g) + DCU (1.28 g) + DMAP (0.1 g) + silica gel (25 g)] / XZ1 (0.95 g)

= 381.77

According to this two metrics, The DCC/DMAP esterification is not green, even though this reaction has a good yield. Because the final product needs to be purified through a GC column was used to remove the by-product DCU. This step would generate a large amount of waste. And the quantity of DCU was as large as the product. That meant that almost half of atoms in reaction has been wasted. These two results show that the traditional esterification is far from the concepts of green chemistry.

3.1.3 PMI

Process Mass Intensity (PMI) = [total mass used in process or process step]/ [mass of product]

= [CH2Cl2 (238.8 g) + petroleum ether (97.5 g) + acid (1.0g) + phenol (0.52 g) + DCC (1.28 g) + DMAP (0.1 g) + silica gel (25 g)]/ XZ1 (0.95 g)

= 383.15

This data shows that if 1 kg of *trans*-4-Pentyl-cyclohexanecarboxylic acid phenyl ester was created in this way, 383.15 kg material would be used.

3.2 Starbon Esterification

3.2.1 Best Sulfonated Starbon Catalyst

In the series of sulfonated Starbon (S300, S350, S450, S550, S600, S750), sulfonated Starbon S350 has the highest GC peak of product. Because all reaction started at same conditions. Highest peak meant best catalytic efficiency. S350 created the largest peak area than others during the same reaction time, as showing in Figure 3.1 That meant with the same reaction condition sulfonated Starbon S350 had better performance than other sulfonated Starbons.

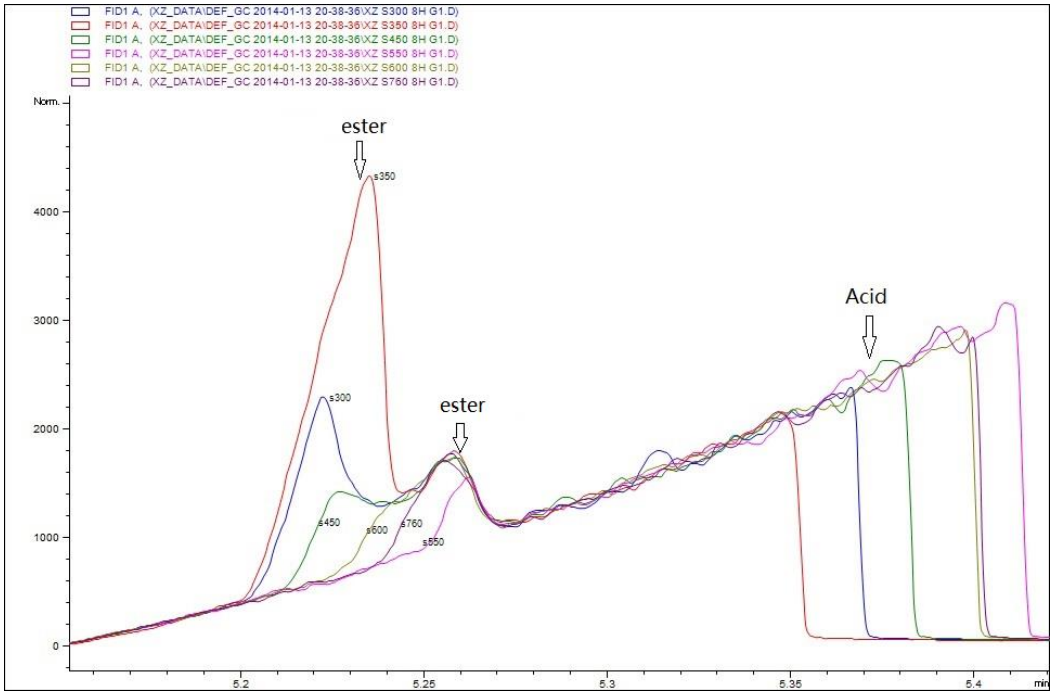


Figure 3.1 GC results of different sulfonated Starbon catalyst at 8h

（Orang: GC result of S350, Blue: GC result of S300, Green: GC result of S450, Yellow: GC result of S500, Purple: GC result of S760, Pink: GC result of S550）

3.2.2 Selectivity on Sulfonated Starbon

Figure 3.2 shows an unexpected peak in the GC results. This phenomenon was found in all kinds of sulfonated Starbon. With tracing reactions at different times for all the sulfonated Starbon catalysts, sulfonated Starbon S450 had most obvious GC results (showed at Figure 3.2). In esterification reaction for 4-pentyl-cyclohexanecarboxylic acid ethyl ester which was catalyzed by sulfonated Starbon, a smaller peak which had longer retention time (5.26 min) was produced first and then the bigger peak which had shorted retention time (5.22 min) was generated. This result suggested two things: one was that in the esterification two reactions were catalysed by sulfonated Starbon. The other thing was that the reaction for smaller peak had higher priority than the reaction for larger peak. In other words, sulfonated Starbon showed selectivity while catalysing this esterification.

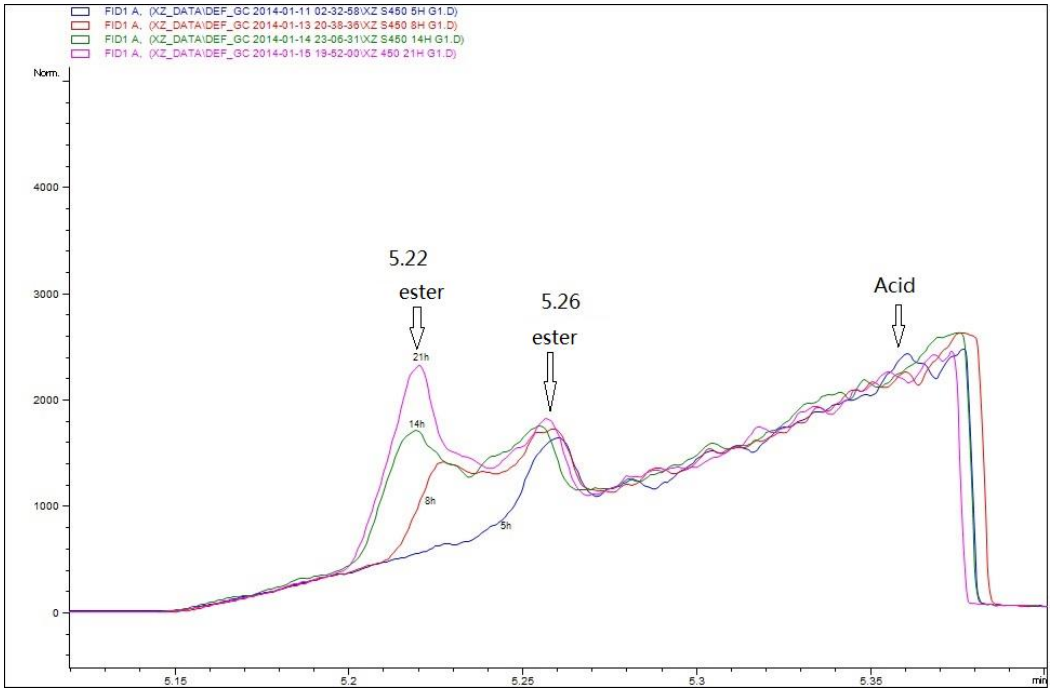
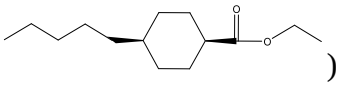


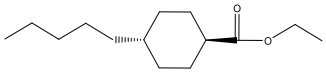
Figure 3.2 GC trace of sulfonated Starbon S450 at different time

(Blue: 5 h, Orange: 8 h, Green: 14 h, Pink: 21 h)

3.2.3 Identification of Products

3.2.3.1 Regular NMR

In order to separate two products, reaction for XZ13 ()

and XZ16 () have been established and the products were purified. Reaction was traced by GC and the product was identified by NMR. GC results were showed in Figure 3.3 and Figure 3.4

In Figure 3.3 the triangular peak is 4-pentyl-cyclohexancarboxylic acid due to the 4-pentyl-cyclohexancarboxylic acid was injected into a nonpolar GC column. After purification, the pure product which smaller peak stood for was obtained. No product which was larger peak stood for has been created in this reaction.

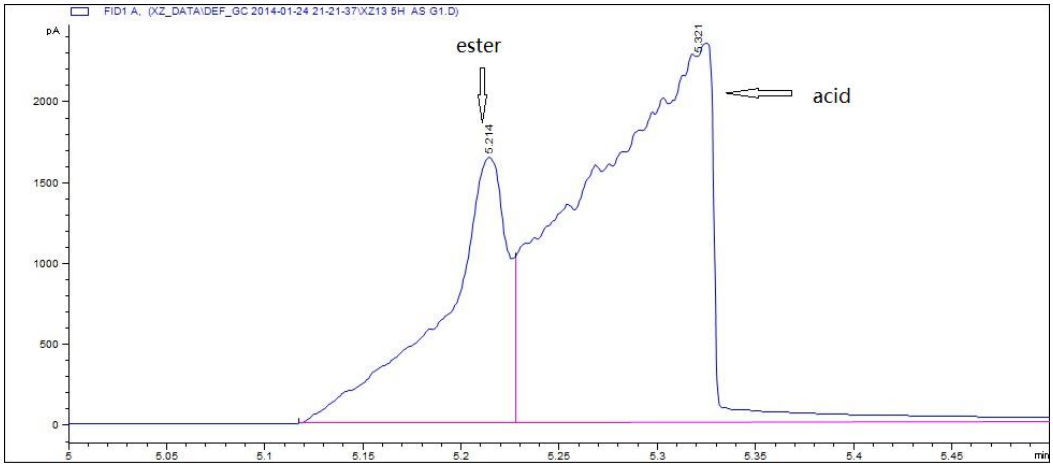


Figure 3.3 GC result of reaction XZ13 at 5h

In this reaction XZ16, starting material was purified and recovered to remove the matter which would produce the smaller peak to obtain the pure product.

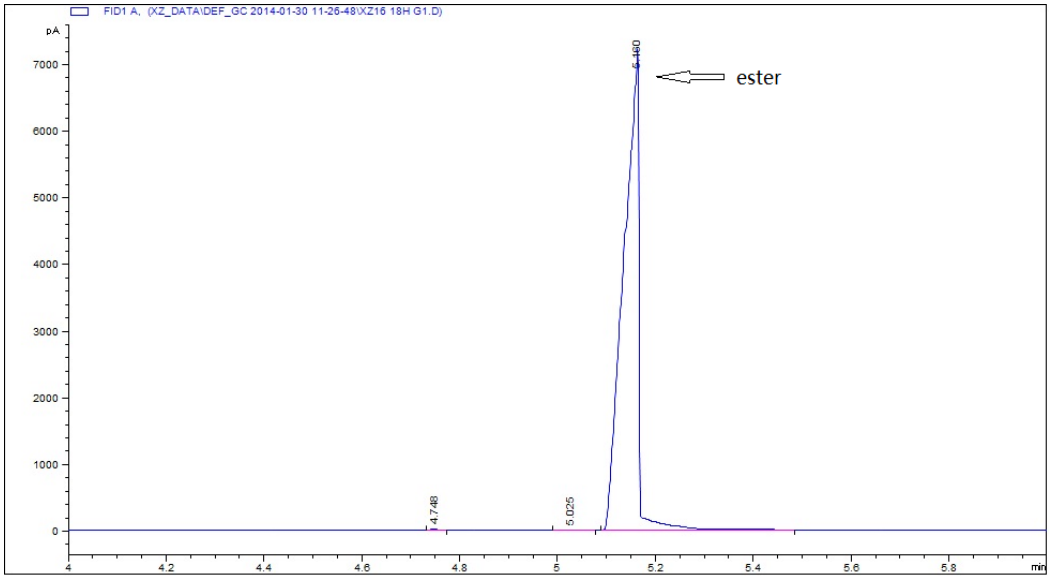


Figure 3.4 GC result of reaction XZ16 at 5h

These two products were analysed by NMR after purification. The results of proton spectrum were showed at Figure 3.5 and Figure 3.6. The results of carbon 13 spectrum were showed at Figure 3.7 and Figure 3.8. The results of HSQC spectrum were Figure 3.9 and Figure 3.10.

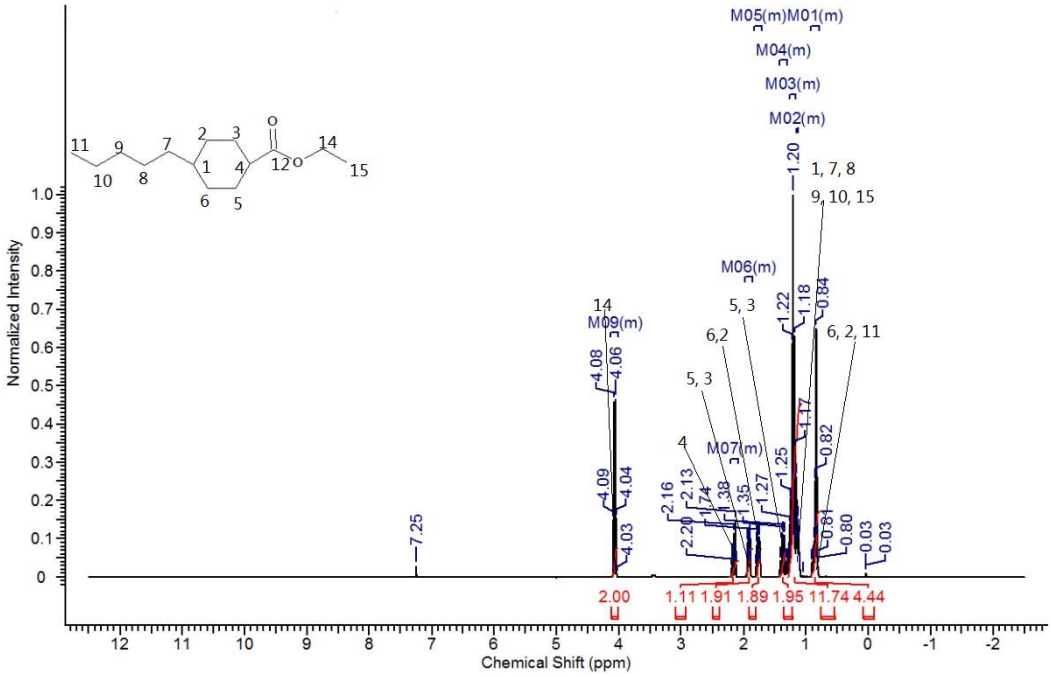


Figure 3.5 NMR proton spectrum of XZ13

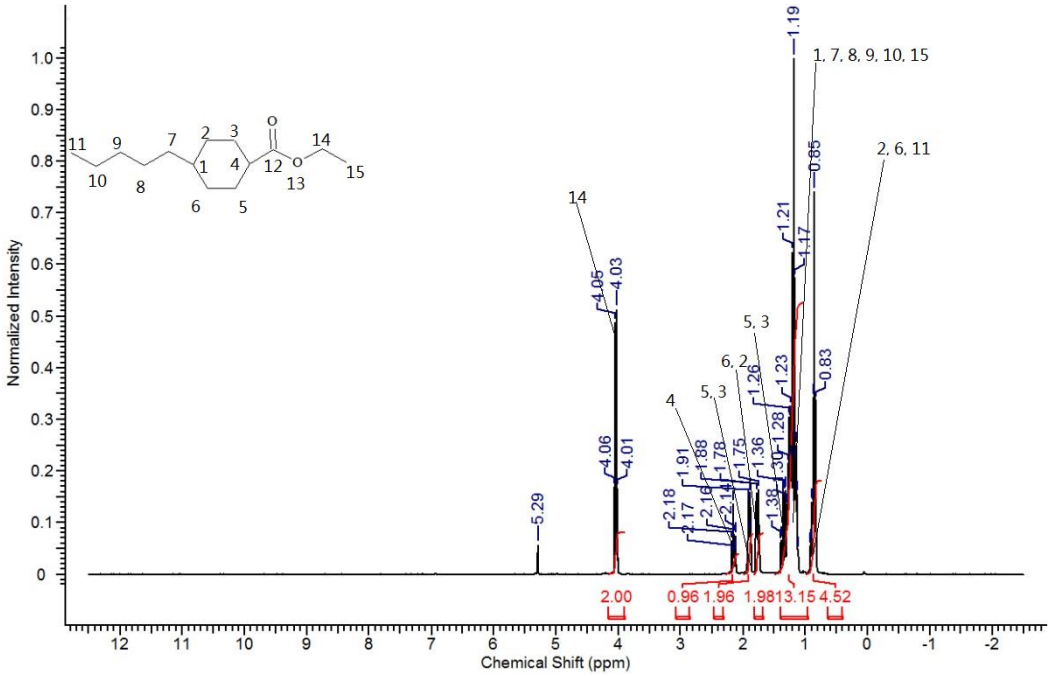


Figure 3.6 NMR proton spectrum of XZ16

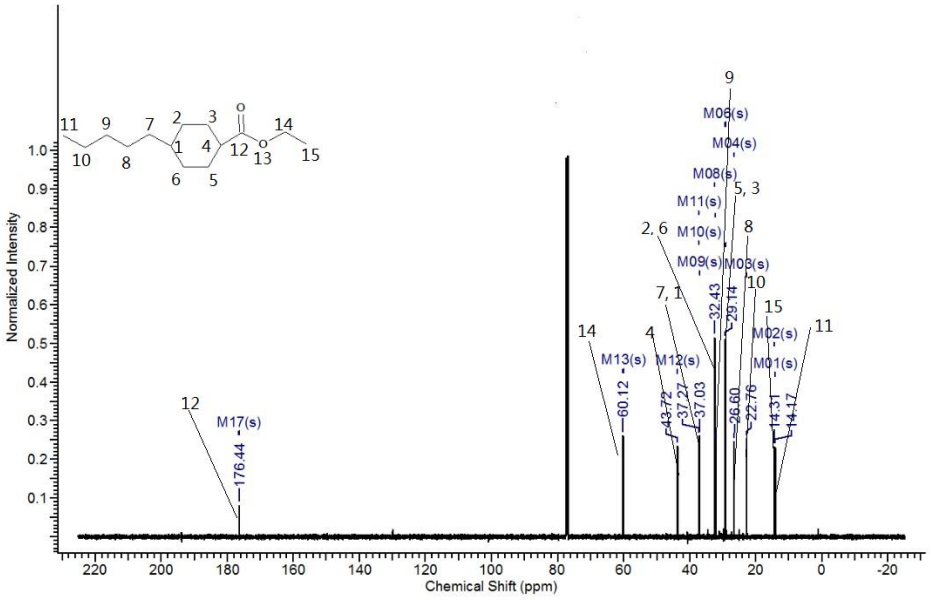


Figure 3.7 NMR carbon spectrum of XZ13

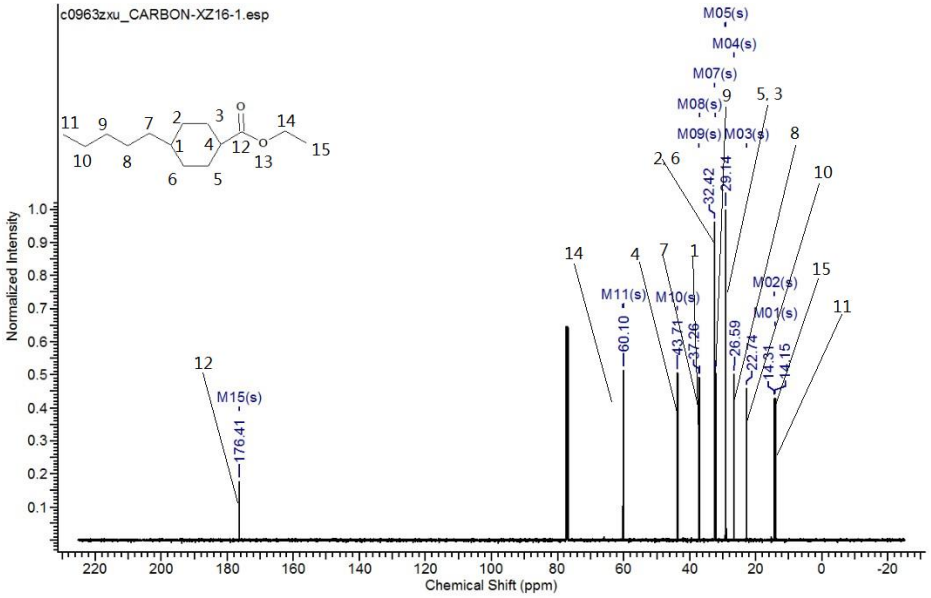


Figure 3.8 NMR carbon spectrum of XZ16

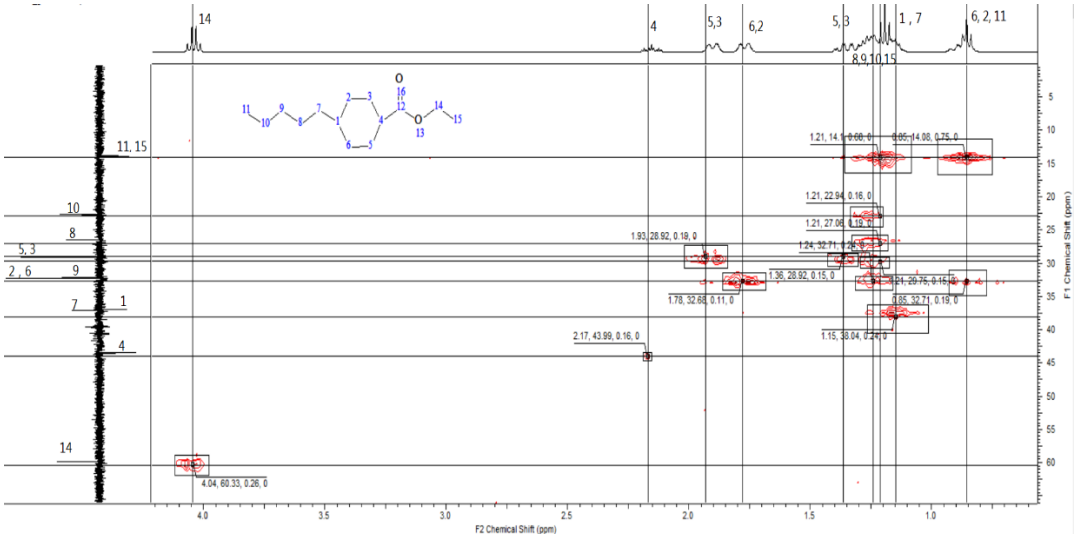


Figure 3.9 NMR HSQC spectrum of XZ13

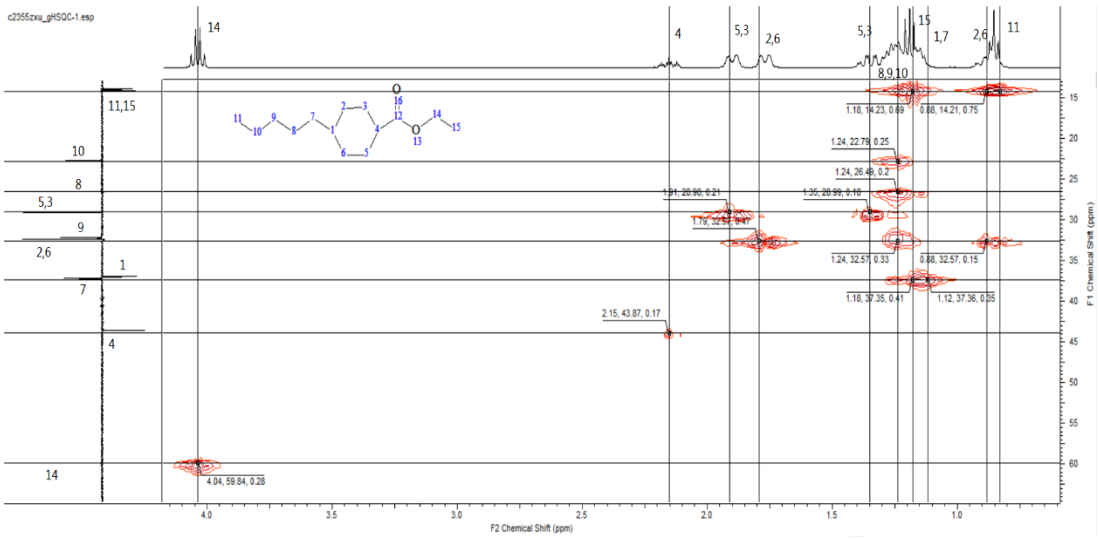
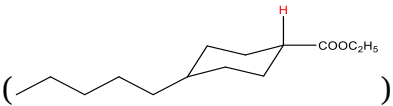


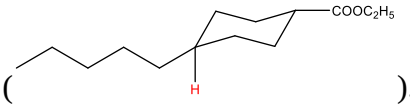
Figure 3.10 NMR HSQC spectrum of XZ16

These six NMR spectrums showed those two products had very similar structure. Protons and carbons were assigned in HSQC spectrums. All the NMR spectrums were the same. And the Mass spectrums proved that they had the same molecule weight. All those evidences implied that both of two peaks could be 4-Pentyl-cyclohexanecarboxylic acid ethyl ester. The reason why they were separated by GC column DB-5HT was that those two products could be two different isomer of 4-Pentyl-cyclohexanecarboxylic acid ethyl ester. One was the *cis*-isomer and the other one was the *trans*-isomer. *Cis*- and *trans*-isomers usually have slight

different on physical property. The carboxylic acid for this reaction was 98% *trans*-isomer commercial reagent. When industry produced 4-Pentyl-cyclohexanecarboxylic acid, hydrogenation was the most common way to created it. In this processing, *cis*-isomer was inevitable. So there could be a few *cis*-isomers in the final commercial reagent. Therefore the larger peak could be *trans*-4-Pentyl-cyclohexanecarboxylic acid ethyl ester and the small peak could be *cis*-4-Pentyl-cyclohexanecarboxylic acid ethyl ester.

3.2.3.2 Nuclear Overhauser Effect (NOE) NMR

NOE NMR was done to identify the conformation of products. NOE spectrum (Figure 3.13) showed: When the proton which linked to same carbon with acyl group (

) was radiated, both products created the same NOE spectrum. That indicated that both products had the same relative position between radiated proton and protons around it. The coupling constants of this proton (J= 12 Hz and 4 Hz) is same in both products. So the proton should be the axial proton. The conformation of this part in both products is fixed. It means that the critical proton was the one that linked to same carbon with alkane (

).

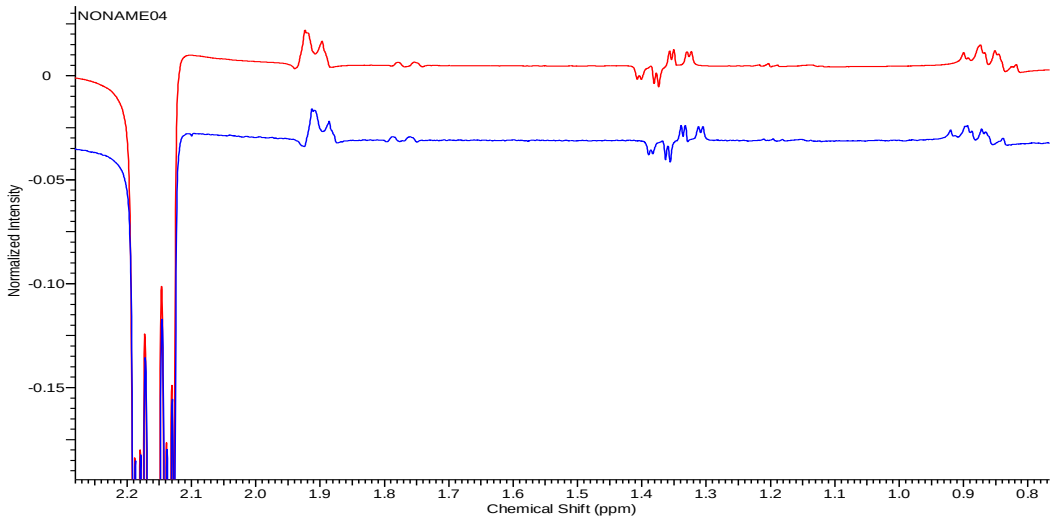


Figure 3.11 NOE spectrum of *trans*- and *cis*-isomer

(Red: *cis*-isomer NOE Spectrum, Blue: *trans*-isomer NOE Spectrum)

3.2.3.3 Low Temperature NMR

At room temperature cyclohexane ring is flipping very fast. Protons are converting between equatorial and axial positions. Room temperature NMR data only shows an average status. This could be the reason why NMR data of those two isomers looked the same.

For further study low temperature NMR analysis has been done. (Figure 3.11 and 3.12) Because low temperature can slow down the flipping of cyclohexane ring the studied two isomers could have different NMR spectrum.

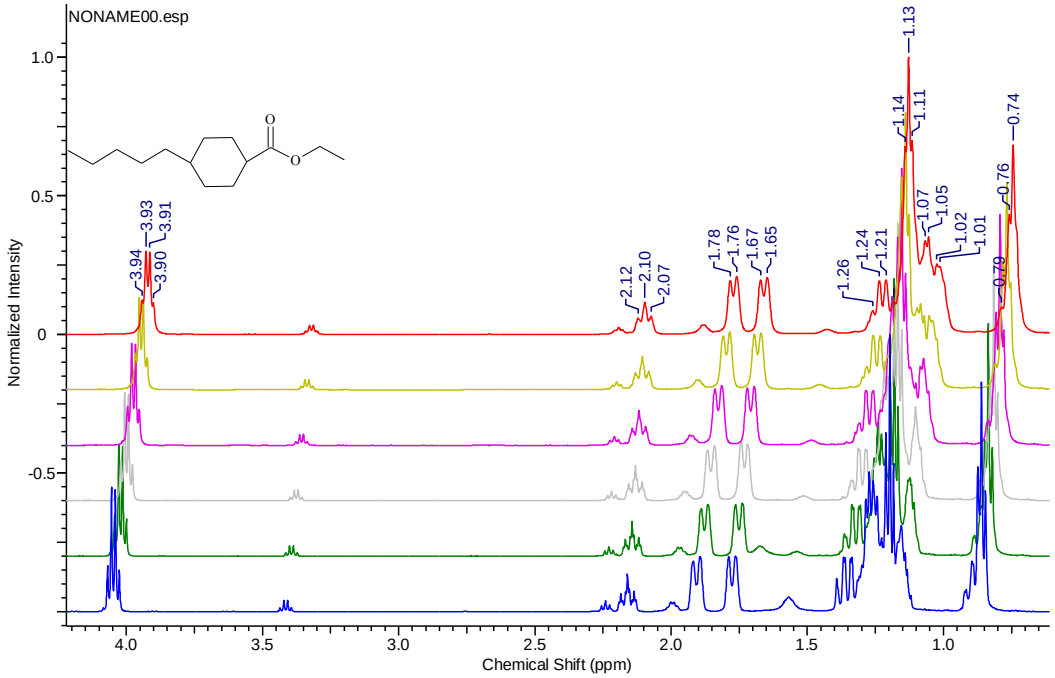


Figure 3.12 Low Temperature proton Spectrum of *cis*-isomer (XZ 13)

(Blue: 25 ℃, Green: 0 ℃, Grey: -20 ℃, Purple: -40 ℃, Yellow: -60 ℃,

Red: -80 ℃)

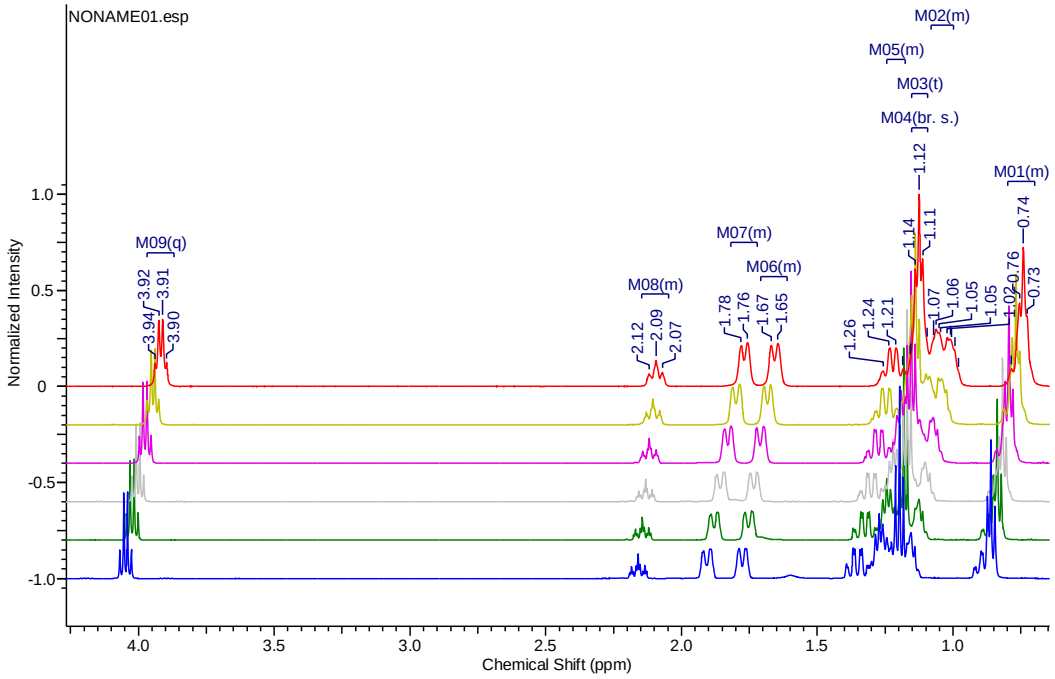


Figure 3.13 Low Temperature proton Spectrum *cis*-isomer (XZ 16)

(Blue: 25 ℃, Green: 0 ℃, Grey: -20 ℃, Purple: -40 ℃, Yellow: -60 ℃,

Red: -80 ℃)

Those figures showed that with dropping temperature, whole spectrum was shifted to the higher field. Peaks between 1.12 ppm and 1.18 ppm shifted to 0.97 ppm and 1.09 ppm. Peaks in this area showed a significant change. The peaks in other areas were look the same. This data confirmed that the part with acyl group were the same in both isomers.

Comparing two -80 ℃ proton spectrum, peaks between 1.07 ppm and 1.05 ppm had an obvious difference. (Figure 3.14) It happened to be the area which the critical proton belonged to. But with interference from alkane chain, it was hard to make the judgment if this difference came from different position of protons. The interference also made coupling constants incalculable. It only could be indirect evidence without coupling constants.

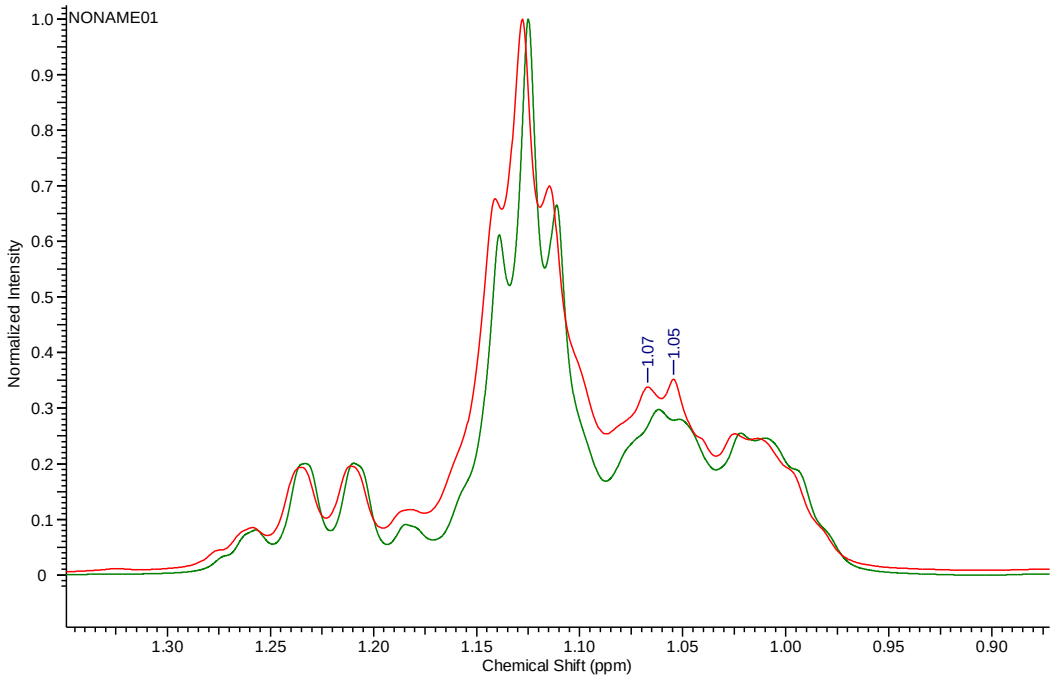


Figure 3.14 Proton Spectrum at -80 ℃

(Red: *cis*-isomer, Green: *trans*-isomer)

However, those evidences showed a strong possibility that sulfonated Starbon had selectivity between *cis*- and *trans*-isomer of 4-pentyl cyclohexane carboxylic acid in the esterification reaction. It also suggested some further work (e.g. using crystallography to make sure those two product are different isomer) to do.

3.2 Reaction Rate of Starbon Esterification

The Figure 3.15- 3.17 manifests peak areas of the reacted mixture for XZ13, XZ14 and XZ16. In those figures, broad triangle peak stood for acid and sharp peak stood for the product.

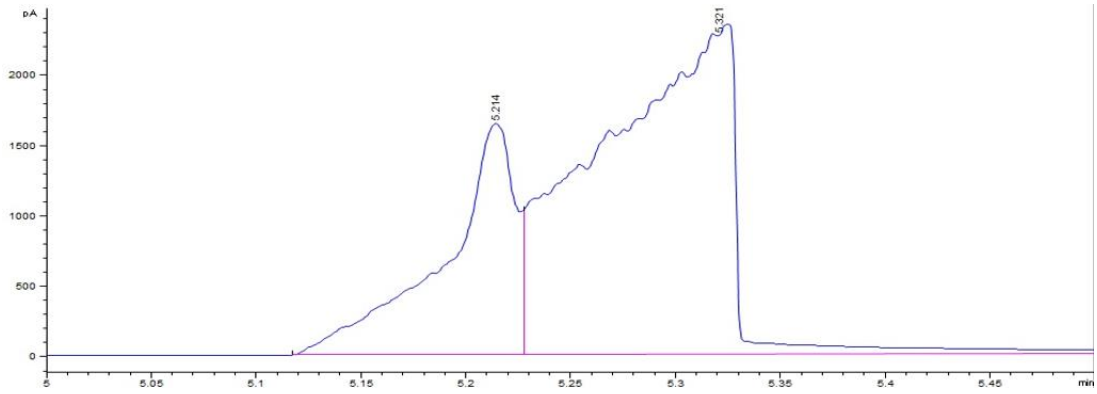


Figure 3.15 Peak Area of crude from XZ13 at 5h

In reaction XZ13, a large triangle peak indicated that there are large amounts of acid which was still in unreacted condition. At this time, only one isomer of product was formed.

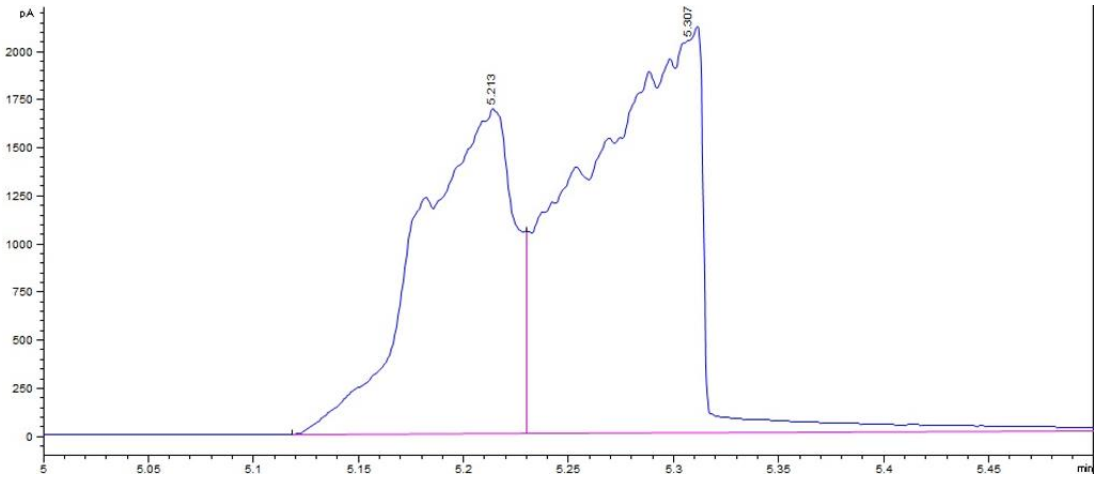


Figure 3.16 Peak Area of crude from XZ14 at 5h

This GC data showed that there still was a lot of acid after reaction in the reaction mixture. But a shoulder peak indicated that some second product had been generated. There were two kinds of products in the reaction mixture.

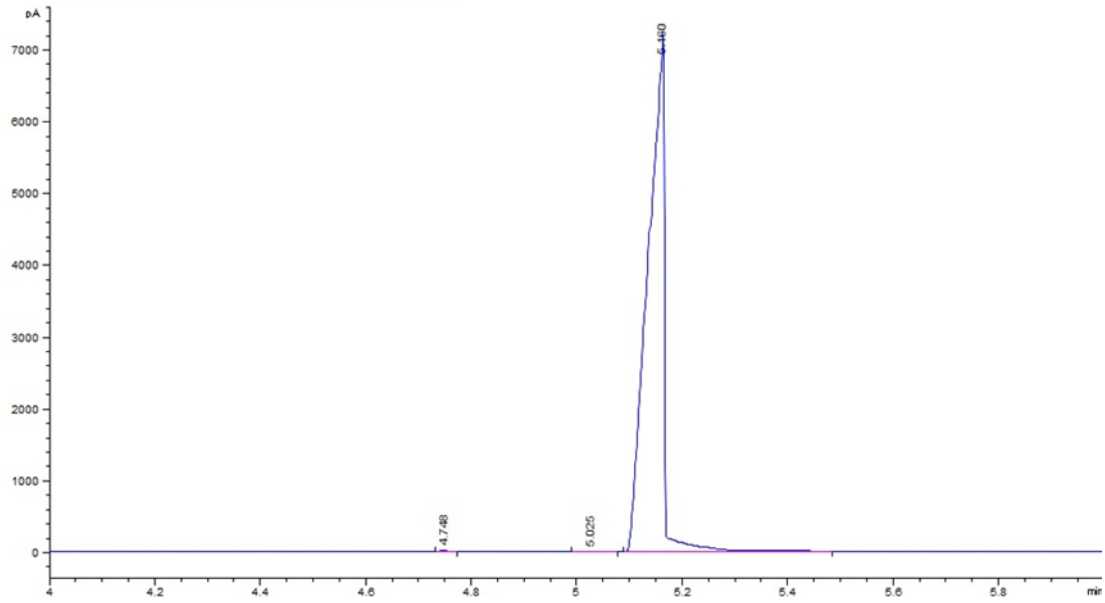


Figure 3.17 Peak area of crude from XZ16 at 5h

The figure 3.17 showed that the esterification reaction proceeded almost completely. No acid has reminded in unreacted condition. This acid was recovered from the reaction XZ14. It was considered as pure *trans*-4-pently-cycloheaxane carboxylic acid. This reaction was much faster than the first two reactions. Due to obtain very pure product for NMR analysis, lots of product was lost in purification step. It cause the yield of product as low as 41%. But it was still much higher than the yield of *cis*-isomer.

The same phenomenon also shows at methanol esterification with 4-pentyl cyclohexane carboxylic acid. The product GC peak area from methyl ester reaction was listed at Table 3.1. Catalyst in the reaction was replace by the brand new one every 5h. With each time replacing the catalyst, reaction would be faster than last time. That should be the reason why increased peak area of product became larger and larger. Because more ester was formed in the same reaction. It proved that the *cis*-4-pentyl cyclohexane carboxylic acid had an ability to slow down the whole reaction by poisoning the catalyst.

Runs	Peak Area of Methyl Ester	Area Increased
1st	3851.1	3851.1
2nd	10126.8	6275.7
3rd	19682.2	9555.4
4th	40286.2	20604

Table 3.1 The product GC peak area from methyl ester reaction

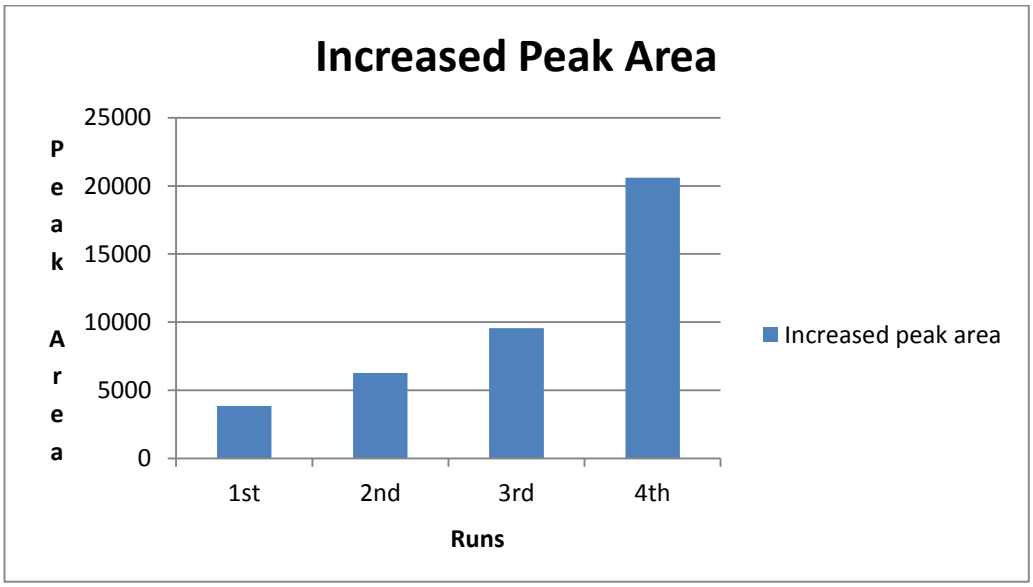


Figure 3.18 Increased peak area of difference time of methyl esterification

Figure 3.18 showed that as the *cis*-isomer was consumed, reaction proceeded faster. Initially, the reaction was slow. Starbon catalysed the *cis*-isomer reaction. After all the *cis*-isomer was gone and the shift to a new catalyst took place, the reaction proceeded faster and faster. This phenomenon showed at both ethanol and methanol esterification of 4-pently-cycloheaxane carboxylic acid. On *trans*-4-t-Butyl cyclohexane carboxylic acids, the *trans* one esterified around 20 times faster than the *cis* ones.[96] The *trans*-isomer acid had a much faster reaction rate in esterification than the *cis*-isomer acid. It seemed to apply to almost all the *cis*- and *trans*-substituted cyclohexane acids. Comparing with *cis*-isomer, *trans*-isomer had

lesser steric effects.[97] It could be a reason to explain that. The different reactivity between two products would be another evidence to prove that two products were two different isomers of 4-pentyl-cyclohexan acid ethyl ester. Those results also showed that the *Cis*-isomer could be a poison for the catalyst. After reaction *cis*-isomer would attach to surface of catalyst or block the holes of catalyst to stop *trans*-isomer connect to catalyst. So the reaction rate would be dragged down.

The Figure 3.19 showed the GC data of crude from the reaction XZ20

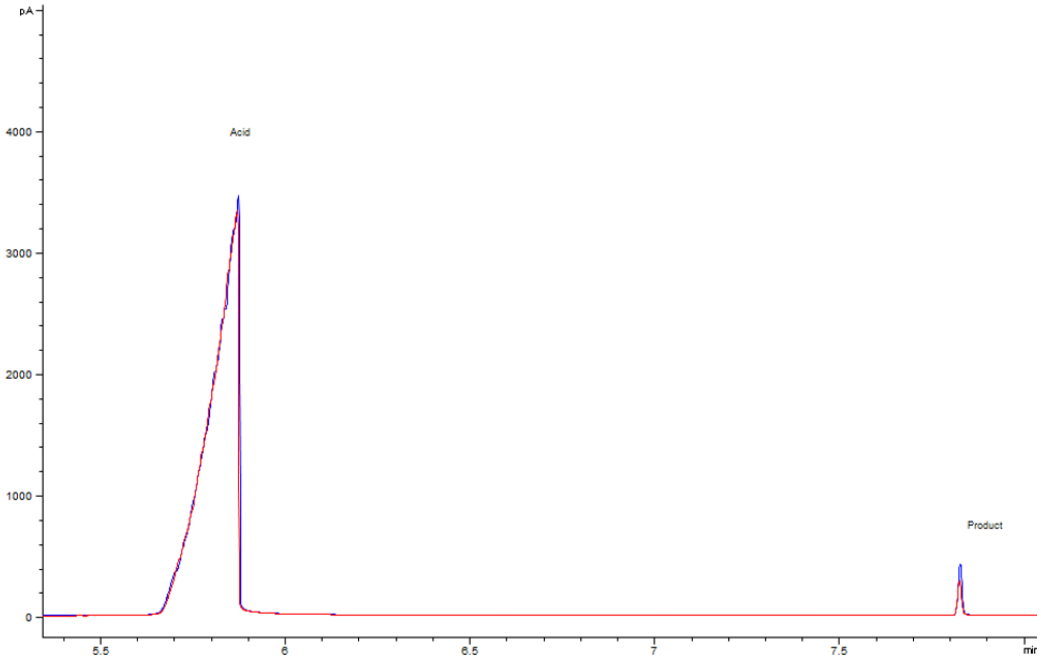


Figure 3.19 GC data for XZ20

(Red: reacted at 9h Blue: reacted at 12h)

The GC data showed that after 9h and 12h reaction, only a few Products have been created. Peak areas for 9h is 217 and 314 for 12h. Lots of acid reminded at unreacted condition.

Comparing with ethanol and methanol esterification, this reaction manifested very low efficiency. The results showed that Starbon was not a good catalyst for a long chain alcohol esterification. Shorter chain on alcohol could lead to faster reaction rate.

3.3 DMAP/EDC Esterification

Data was collected from experiment 2.1.4

Acid	Mass (g)	Alcohol	Mass (g)	EDC （g）	DMAP (g)	Reaction Time(h)	Yield	Code
Trans-4-ethyl-cyclohexanecarboxylic acid，n=2	0.5	4-cyanophenol	0.3	0.5	0.1	3h	72%	LC CN C2
Trans-4-propyl-cyclohexanecarboxylic acid，n=3	0.5	4-cyanophenol	0.3	0.5	0.1	3h	66%	LC CN C3
Trans-4-butyl-cyclohexanecarboxylic acid，n=4	0.5	4-cyanophenol	0.3	0.5	0.1	3h	74%	LC CN C4
Trans-4-pentyl-cyclohexanecarboxylic acid，n=5	0.5	4-cyanophenol	0.3	0.5	0.1	3h	68%	LC CN C5

Table 3.2 Reaction conditions of synthesis of *trans*-4-alkyl-cyclohexane carboxylic acid 4-cyanophenol ester

3.3.1 Green metric

3.3.1.1 PMI of column purification

Process Mass Intensity (PMI) = [total mass used in process or process step]/ [mass of product]

= [CH_2Cl_2 (134 g) + petroleum ether (64 g) + 4-pentyl cyclohexane carboxylic acid (1.0g) + 4-cyano phenol (0.6 g) + EDC (1 g) + DMAP (0.1 g) + silica gel (20 g)]/product LC CN C5 (1.07 g)

= 206.2

In this processing, the material mass for reaction was 11.3 g. In this 11.3g material, 8.9 g CPME was recyclable after reaction. Only 2.4 g of materials was used in this

reaction. But 218 g materials were used for column purification. Materials for purification were the biggest factor.

3.3.1.2 PMI of washing purification

Process Mass Intensity of LC CN C5:

Process Mass Intensity (PMI) = [total mass used in process or process step]/ [mass of product]

= [0.1M NaOH (52 g) + 0.1M HCl (25.9 g) + 4-pentyl cyclohexane carboxylic acid (1.0g) + 4-cyano phenol (0.6 g) + EDC (1 g) + DMAP (0.01 g) + NaCl (saturated) (33.25 g) + $MgSO_4$ (4 g)]/ product LC CN C5 (1.04 g)

= 113.2

Process Mass Intensity of LC CN C4:

Process Mass Intensity (PMI) = [total mass used in process or process step]/ [mass of product]

= [0.1M NaOH (52 g) + 0.1M HCl (25.9 g) + 4-pentyl cyclohexane carboxylic acid (1.0g) + 4-cyano phenol (0.6 g) + EDC (1 g) + DMAP (0.01 g) + NaCl (saturated) (33.25 g) + $MgSO_4$ (4 g)]/ product LC CN C4 (0.98 g)

= 120.2

Process Mass Intensity of LC CN C3:

Process Mass Intensity (PMI) = [total mass used in process or process step]/ [mass of product]

= [0.1M NaOH (52 g) + 0.1M HCl (25.9 g) + 4-pentyl cyclohexane carboxylic acid (1.0g) + 4-cyano phenol (0.6 g) + EDC (1 g) + DMAP (0.01 g) + NaCl (saturated) (33.25 g) + $MgSO_4$ (4 g)]/ product LC CN C3 (1.1 g)

= 107.1

Process Mass Intensity of LC CN C2:

Process Mass Intensity (PMI) = [total mass used in process or process step]/ [mass of product]

= [0.1M NaOH (20.8 g) + 0.1M HCl (10.36 g) + 4-pentyl cyclohexane carboxylic acid (1.0g) + 4-cyano phenol (0.6 g) + EDC (1 g) + DMAP (0.01 g) + NaCl (saturated) (13.3 g) + $MgSO_4$ (4 g)]/ product LC CN C2 (1.12 g)

= 45.6

Because the molecule weight of EDC hydrochloride (191.7 g/mol) and DCC (206.18 g/mol) were so close, using EDC replace for DCC would not have too much improved on atom economy. Even though on atom economy this change did not afford big improvements, it had a great improvement on saving of purification. Because of water solubility of the by-product, a column was not necessary in purification. Product from EDC reaction could be purified by washing with different solvent and drying with $MgSO_4$. Only about 133 g of materials were used for purification. In those 133 g materials, 21.9 g diethyl ether was recyclable. Comparing with column purification, usage of purification materials and PMI was half as much as before. (Showed at figure 3.5.1.1) Another benefit was that the reaction solvent could be changed to CPME. It was recyclable and much greener than CH_2Cl_2. In all these products, 4-ethyl cyclohexane carboxylic acid 4-cyanophenol ester did not need to redisslove in diethyl ether. That meant it could be washed with small amounts of solvent, lowing the PMI.

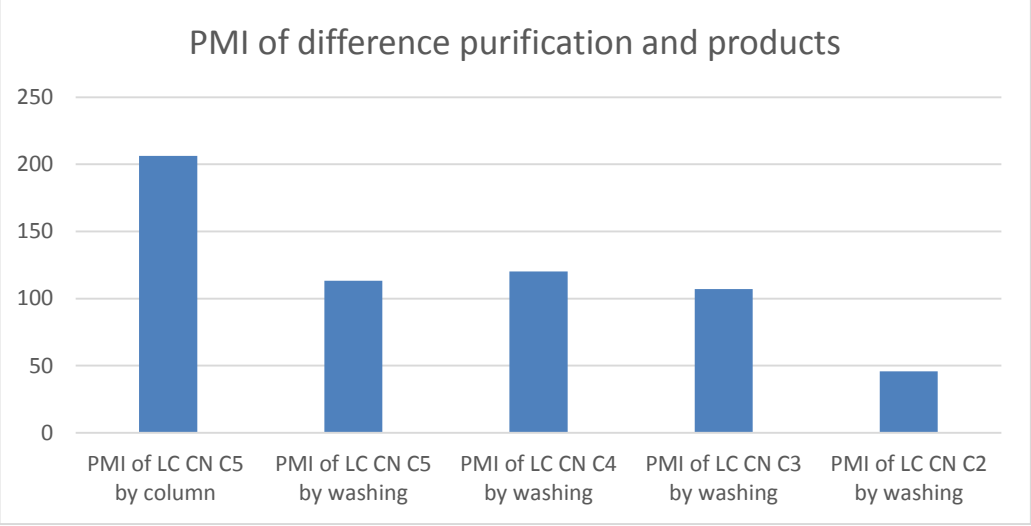


Figure 3.20 PMI of difference purification and products

3.3.2. Microwave irradiation

Figure 3.21 showed different GC results of a series of reactions which were heated by microwave at 100 ℃, 300 W。

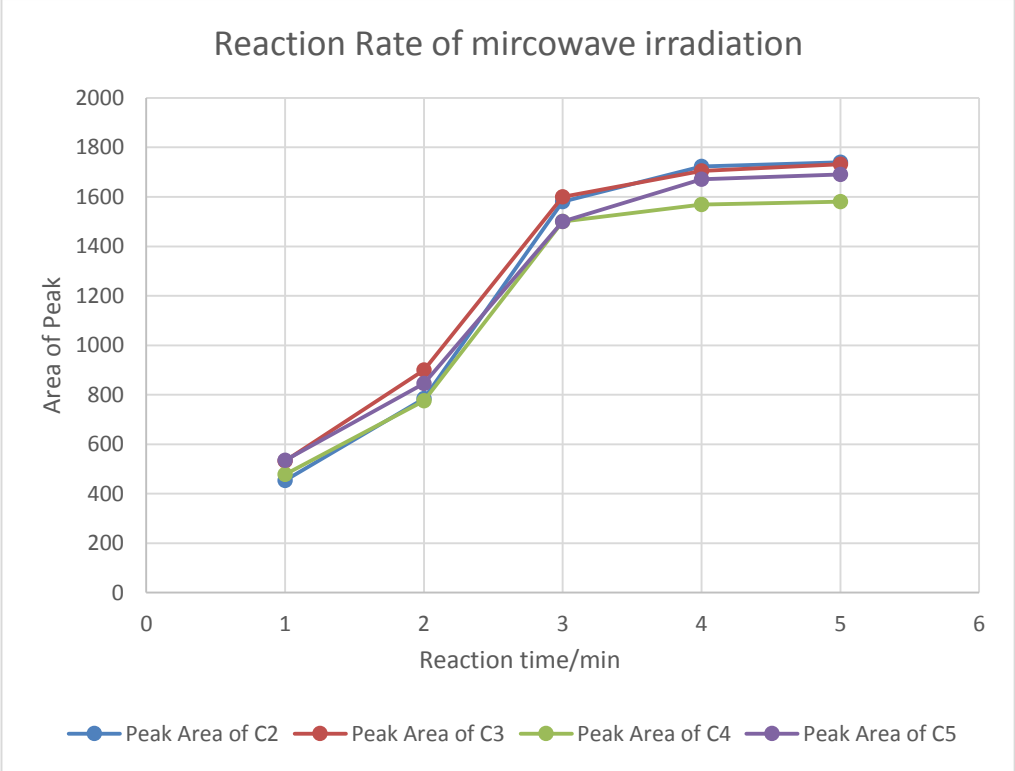
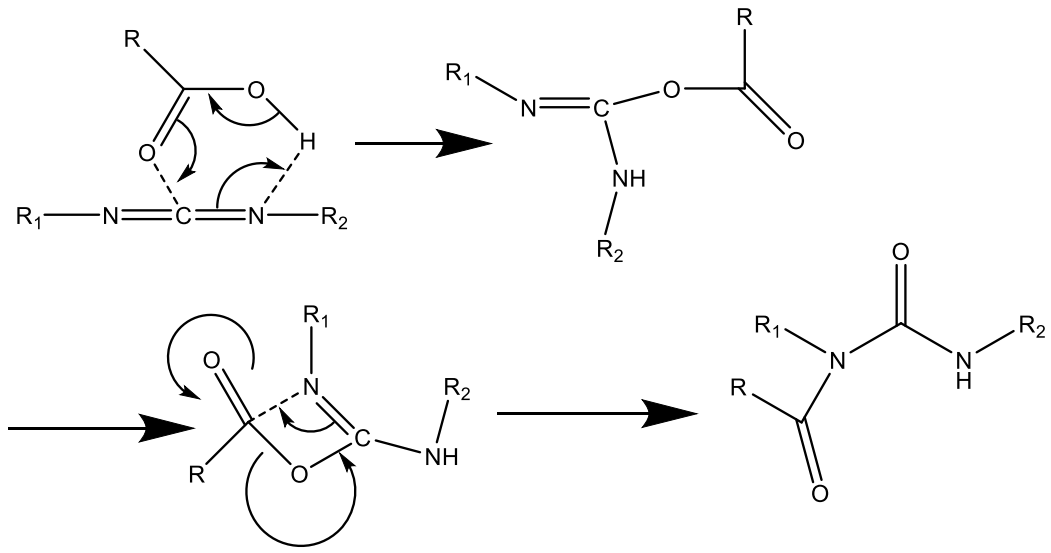


Figure 3.21 Reaction rate of microwave irradiation

(C2:4-ethyl cyclohexane carboxylic acid 4-cyanophenol ester; C3: 4-propyl cyclohexane carboxylic acid 4-cyanophenol ester; C4: 4-butyl cyclohexane carboxylic acid 4-cyanophenol ester; C5: 4-pentyl cyclohexane carboxylic acid 4-cyanophenol ester.)

The figure 3.21 shows that products of reaction did not increase from 4 min to 5 min. It meant that with microwave irradiation reaction can be finished in around 4 min saving a lot of time on reaction instead of stirring at room temperature. Figures from 3.22 to 3.25 displayed comparison of GC results between room temperature and microwave irradiation at different time for 4-ethyl cyclohexane carboxylic acid 4-cyanophenol ester, 4-propyl cyclohexane carboxylic acid 4-cyanophenol ester, 4-butyl cyclohexane carboxylic acid 4-cyanophenol ester and 4-pentyl

cyclohexane carboxylic acid 4-cyanophenol ester. According to those results, the reaction with microwave irradiation had a faster reactive rate, but the reaction at room temperature had about 5% more products. In this kind of reaction, no matter using EDC or DCC, the O-acyl intermediate would have a side-reaction which was 1, 3-rearrangement.(Scheme 20)[55] O-acyl intermediate would rearrange to an N-acyl urea, which was unable to react with alcohol further. The catalyst DMPA acted as an acyl transfer-reagent to make the O-acyl intermediate easier to react with alcohol and the reaction was able to occur at low temperature by reducing the 1, 3-rearrangement of O-acyl intermediate. This type of reaction is usually carried out at 0 ℃ at room temperature.[55] High temperature would cause more side-reactions and lower the yield of the final product. Microwave irradiation in this type of reaction was a conflict. On one side, it could save tons of reaction time. On the other side, it slightly reduces the final yield of products.



Scheme 20 1, 3-rearrangement of O-acyl intermediate

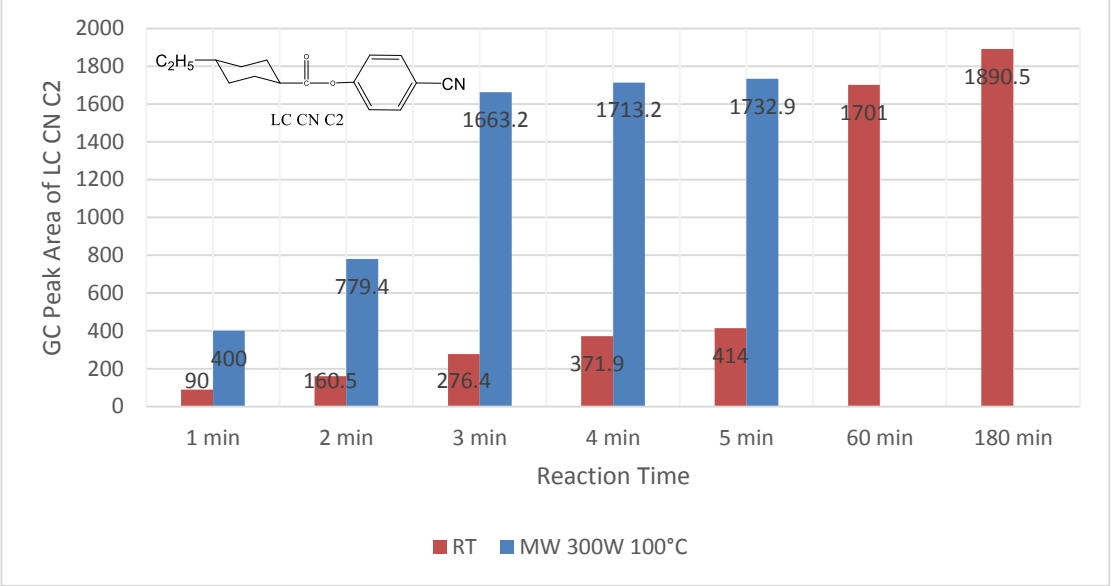


Figure 3.22 GC peak area of 4-ethyl cyclohexane carboxylic acid 4-cyanophenol ester at different time

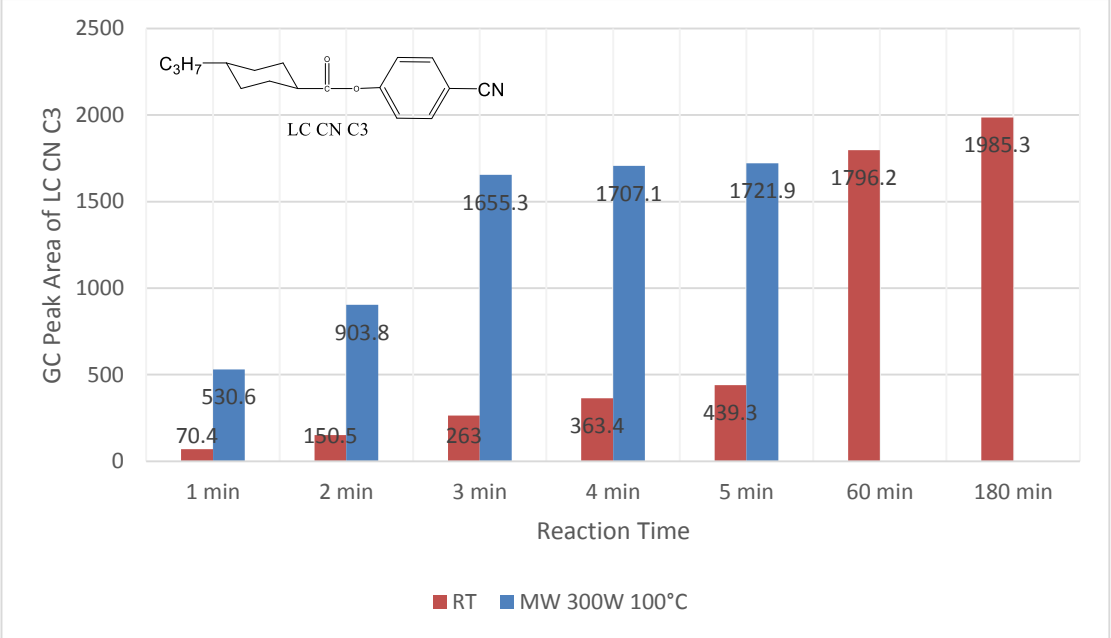


Figure 3.23 GC peak area of 4-propyl cyclohexane carboxylic acid 4-cyanophenol ester at different time

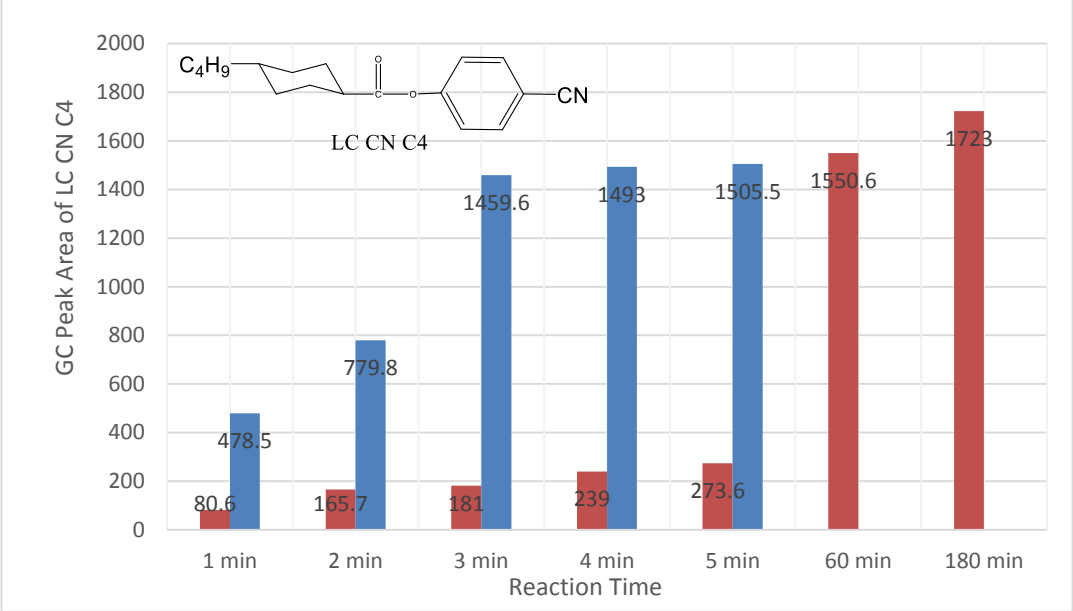


Figure 3.24 GC peak area of 4-butyl cyclohexane carboxylic acid 4-cyanophenol ester at different time

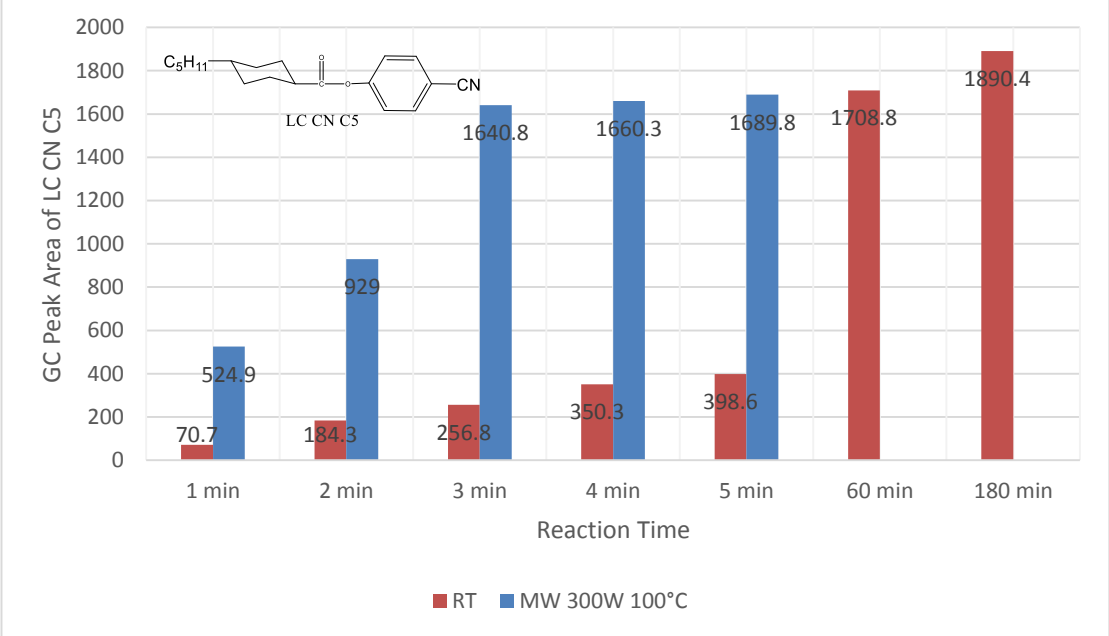


Figure 3.25 GC peak area of 4-pentyl cyclohexane carboxylic acid 4-cyanophenol ester at different time

3.3.3 Liquid Crystal Phase

Products from microwave assisted reactions were analysed by DSC and polarized microscope. Only 4 products were found to have a nematic phase. Their relationship between length of alkyl groups and liquid crystal transition temperature is shown in Figure 3.26. And their nematic phase textures were shown in Figure 3.27. The transition temperatures were fitted to the reference values.[98] *Trans*-4-pentyl-cyclohexane carboxylic acid 4-cyanophenol ester had widest temperature range of liquid crystal phase. The molecules from microwave irradiation do not have any difference on liquid crystal phase and properties. Enthalpy change of liquid crystal phase transition was very small comparing with melting and crystallization.

ΔH/ (KJ/mol)	MW LC CN C2	MW LC CN C3	MW LC CN C4	MW LC CN C5
ΔH_m	14.57	20.12	19.18	13.84
ΔH_{LC}	0.64	0.61	0.78	0.79
ΔH_r	9.87	19.11	15.01	20.82

Table 3.3 Enthalpy change of phase transition

(ΔH_m: Enthalpy change of melting, ΔH_{LC} Enthalpy change of liquid crystal phase, ΔH_r: Enthalpy change of Crystallization)

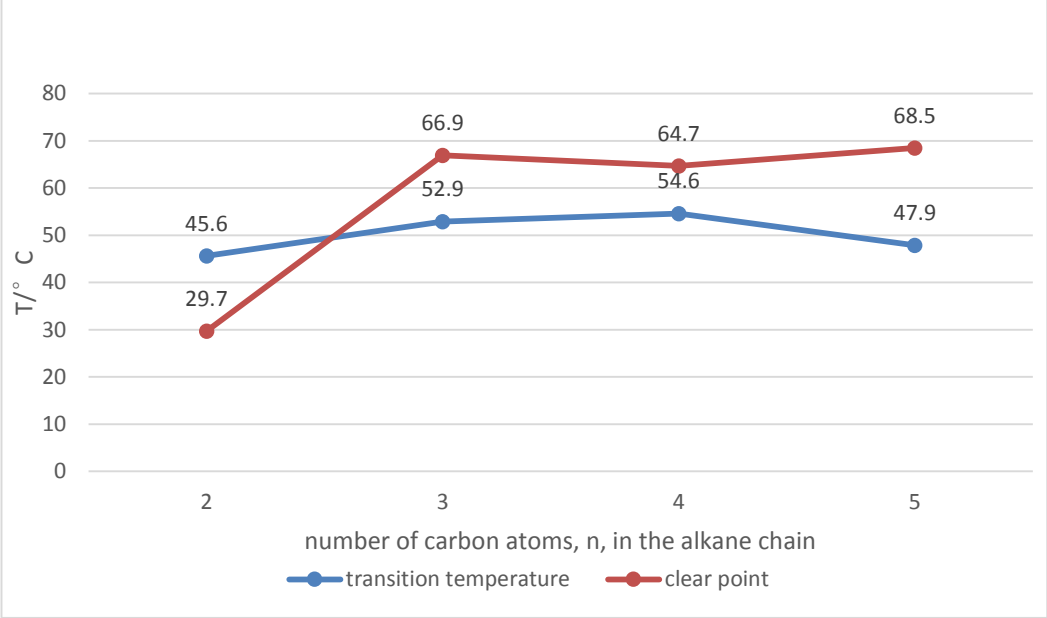


Figure 3.26 Transition temperature of MW LC CN C2-C5

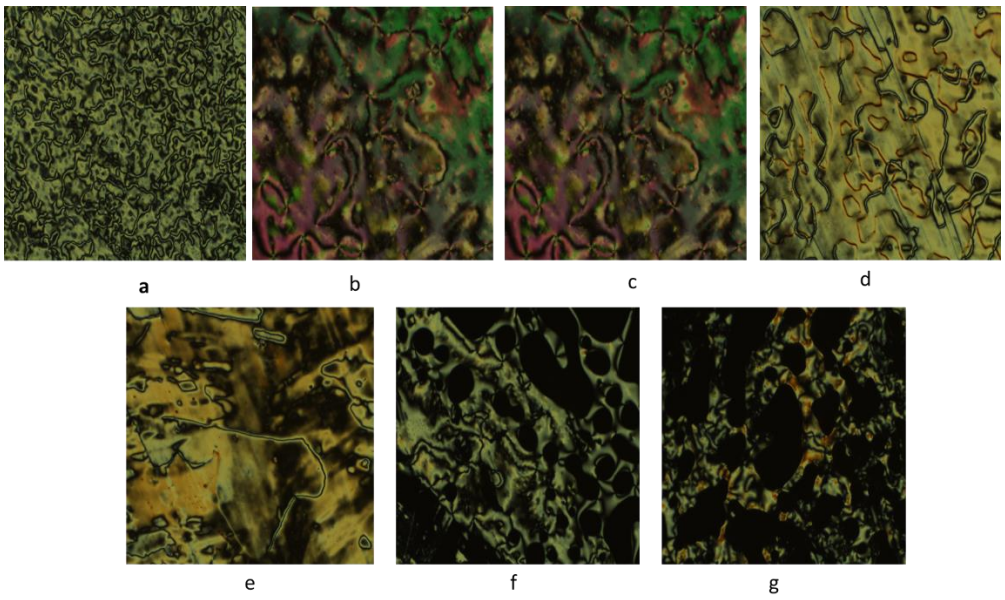
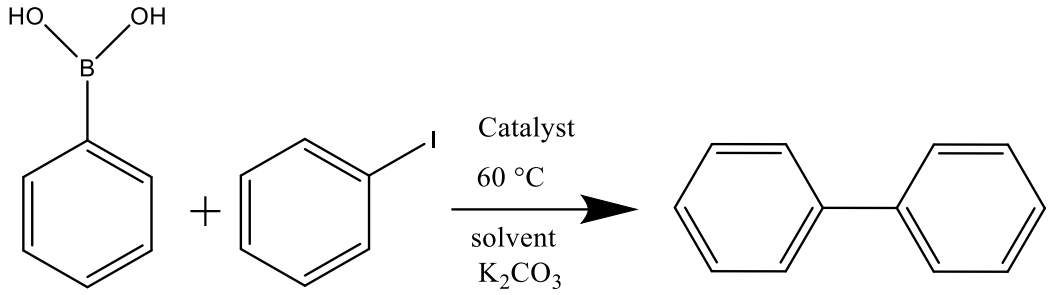


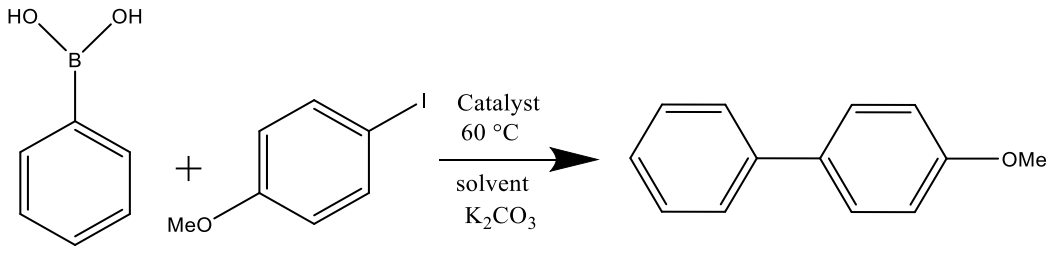
Figure 3.27 nematic phase textures of MW LC CN C2-C5

(**a**: MW LC CN C2 cooling 35 ℃, **b**: MW LC CN C3 cooling 50 ℃, **c**: MW LC CN C3 heating 58.4 ℃, **d**: MW LC CN C4 cooling 59.9 ℃, **e**: MW LC CN C4 heating 58.2 ℃, **f**: MW LC CN C5 heating 61.8 ℃, **g**: MW LC CN C5 heating 65.7 ℃).

3.4 Suzuki Reaction



Scheme 21 Reaction between iodobenzene and Phenylboronic acid



Scheme 22 Reaction between 4-iodoanisole and Phenylboronic acid

3.4.1 Water/ Ethanol Solvent System

Ethanol: Water (v/v)	Catalyst	Reaction time	Yield (3h)	Yield (6h)	Conversion* (6h)	Selectivity*
5:5	$Pd(PPh_3)_4$	3h, 6h	6.3%	10.0%	70.4%	14.2%
6:4	$Pd(PPh_3)_4$	3h, 6h	12.7%	14.1%	99.5%	14.2%
7:3	$Pd(PPh_3)_4$	3h, 6h	29.0%	39.6%	100.0%	39.6%
8:2	$Pd(PPh_3)_4$	3h, 6h	43.2%	66.0%	98.0%	67.3%
9:1	$Pd(PPh_3)_4$	3h, 6h	93.8%	93.8%	100.0%	93.8%
10:0	$Pd(PPh_3)_4$	3h, 6h	41.8%	86.4%	88.7%	97.4%
9:1	S300-Pd	3h, 6h	88.0%	95.3%	98.6%	96.6%
9:1	S350-Pd	3h, 6h	88.1%	93.8%	98.2%	95.5%
9:1	S400-Pd	3h, 6h	89.3%	97.1%	97.6%	99.5%
9:1	S450-Pd	3h, 6h	85.5%	94.5%	98.1%	96.3%
9:1	S500-Pd	3h, 6h	88.9%	94.8%	96.2%	98.5%
9:1	S600-Pd	3h, 6h	96.8%	100.1%	98.4%	101.7%

Table 3.4 Reaction conditions of iodobenzene with ethanol/water solvent system

*Selectivity and conversion was based on Iodobenzene

Water and ethanol mixed solution was a good solvent for polar starting materials. When Iodobenzene and Phenylboronic acid was employed as starting materials, 9:1=ethanol: water (V/V) was the best solution for this reaction. Yield of the product was much higher than other ratio of solutions. Reaction only needed 3h at 60 ℃ to complete. In this condition, all six different Starbon-Pd catalysts had very

good catalytic activity. Yields of products were above 85% and selectivity of reaction were above 95%. Basically, no side-reactions occurred. Starbon S600-Pd had best activity. Yields of products which was catalysed by Starbon S600-Pd was about 10% higher than others and 3% higher than yield of product which was catalysed by reference catalyst $Pd(PPh_3)_4$.

Ethanol: Water (v/v)	Catalyst	Reaction time	Yield	Conversion*	Selectivity*
5:5	$Pd(PPh_3)_4$	2h	98.4%	100.0%	98.4%
6:4	$Pd(PPh_3)_4$	2h	96.6%	100.0%	96.6%
7:3	$Pd(PPh_3)_4$	2h	88.3%	100.0%	88.3%
8:2	$Pd(PPh_3)_4$	2h	85.4%	95.4%	89.5%
9:1	$Pd(PPh_3)_4$	2h	78.5%	80.8%	97.2%
10:0	$Pd(PPh_3)_4$	2h	72.7%	76.6%	94.9%
9:1	S600-Pd	2h	67.5%	80.0%	84.4%
9:1	S500-Pd	2h	86.9%	90.6%	95.9%
9:1	S450-Pd	2h	83.6%	89.8%	93.0%
9:1	S400-Pd	2h	75.5%	87.0%	86.8%
9:1	S350-Pd	2h	71.0%	87.5%	81.2%
9:1	S300-Pd	2h	72.1%	91.6%	78.7%

Table 3.5 Reaction conditions of 4-iodoanisole with ethanol/water system

*Selectivity and conversion was based on 4-iodoanisole

When starting material was change to 4-Iodoanisole and Phenylboronic acid. The best solution condition was change to 5:5=ethanol: water (V/V). Reactions were faster than the last reaction due to methoxy group on para position had a lone pair of electrons. This lone pair of electrons created a *p*-π system with benzene ring. Electrons were able to transmit in this system. This conjugative effect would stabilize the benzene ring and make -I on para position easier to react. Reaction time for this starting material was only 2h at 60 ℃ in best solution ratio. With 4-Iodoanisole and Phenylboronic acid as starting material and same condition, Starbon S500-Pd and Starbon S450-Pd showed the best performance as a catalyst. Yield of products which were catalysed by Starbon S500-Pd and Starbon S450-Pd were around 85% which were 10% to 20% higher than others.

3.4.2 CPME/ Water Solvent System

CPME: Water (v/v)	Catalyst	Reaction time	Yield (3h)	Yield (6h)	Yield (12h)	Conversion* (12h)	Selectivity*
5:5	$Pd(PPh_3)_4$	3h, 6h, 12h	15.9%	28.7%	90.9%	88.6%	97.5%
6:4	$Pd(PPh_3)_4$	3h, 6h, 12h	18.9%	33.3%	82.3%	83.6%	98.4%
7:3	$Pd(PPh_3)_4$	3h, 6h, 12h	29.1%	45.3%	86.9%	84.9%	97.7%
8:2	$Pd(PPh_3)_4$	3h, 6h, 12h	38.2%	53.2%	87.7%	87.5%	99.8%
9:1	$Pd(PPh_3)_4$	3h, 6h, 12h	48.0%	66.9%	100.4%	98.2%	97.8%
10:0	$Pd(PPh_3)_4$	3h, 6h, 12h	0	0	0	0	0
CPME: Water (v/v)	Catalyst	Reaction time	Yield (3h)	Yield (6h)	Yield (12h)	Conversion (6h)	Selectivity*
9:1	S600-Pd	3h, 6h, 12h		6.7%		5.1%	76.1%
9:1	S500-Pd	3h, 6h, 12h		58.3%		53.5%	91.8%
9:1	S450-Pd	3h, 6h, 12h		9.6%		7.2%	75.0%
9:1	S400-Pd	3h, 6h, 12h		6.8%		5.6%	82.4%
9:1	S350-Pd	3h, 6h, 12h		7.7%		5.1%	66.2%
9:1	S300-Pd	3h, 6h, 12h		6.9%			

Table 3.6 Reaction conditions of iodobenzene with CPME/water

*Selectivity was based on biphenyl and conversion was based on Iodobenzene

Water and CPME mixed solution was an alternative solvent for non-polar starting materials. When Iodobenzene and Phenylboronic acid was employed as the starting material, 9:1= ethanol: water (V/V) was still the best solution for this reaction. Yield of the product was much higher than other ratio of solutions. But

reaction need 12h at 60 ℃ to complete which was much slower than water/ ethanol system and in this system, reaction could not occur without water. In this system, only Starbon S500-Pd catalyst had catalytic activity. Yield of products were above 58.3% at 6h and selectivity of reaction were over 91.8%. In this reaction side-reaction was self-coupling of phenylboronic acid which would create the same product as main reaction. Starbon S500-Pd had best activity and selectivity in all the Starbon-Pd catalysts for this reaction. Yield of product which was catalyzed by Starbon S500-Pd was about 58.3% at 6h. The rest of Starbon-Pd catalysts produced small amount products which was less than 10% of theoretical value.

CPME: Water (v/v)	Catalyst	Reaction time	Yield	Conversion* (4-iodoanisole)	Selectivity*
5:5	$Pd(PPh_3)_4$	8h	91.8%	95.1%	96.6%
6:4	$Pd(PPh_3)_4$	8h	72.1%	83.4%	86.4%
7:3	$Pd(PPh_3)_4$	8h	73.0%	77.7%	94.0%
8:2	$Pd(PPh_3)_4$	8h	77.9%	85.6%	91.0%
9:1	$Pd(PPh_3)_4$	8h	78.8%	86.1%	91.5%
10:0	$Pd(PPh_3)_4$	8h	10.1%	14.7%	68.5%
5:5	S300-Pd	8h	6.1%	7.5%	81.5%
5:5	S350-Pd	8h	2.4%	2.5%	97.3%
5:5	S400-Pd	8h	3.2%	3.7%	88.0%
5:5	S450-Pd	8h	2.3%	3.4%	68.2%
5:5	S500-Pd	8h	4.1%	4.5%	92.4%
5:5	S600-Pd	8h	0.9%	5.1%	17.9%

Table 3.7 Reaction conditions of 4-iodoanisole with CPME/water

*Selectivity and conversion was based on 4-iodoanisole

When the starting materials were changed to 4-iodoanisole and phenylboronic acid, the best solution condition was changed to 5:5=ethanol: water (V/V) like water/ethanol system. Reactions were faster as well. It looked like that the ratio of water was only relevant to the starting material. The reaction time for this starting material was 8h at 60 ℃ in best solution ratio. With 4-iodoanisole and phenylboronic acid as starting material none of Starbon-Pd showed a good catalytic activity. All yields of products which were catalysed by Starbon-Pd were lower than 7%. THF was tested as references. In same condition for this reaction,

yield of products were 10% to 20% lower than they were in CPME/ water system. This result showed CPME not only greener than THF but also had higher efficiency for the reaction. It also proved that CPME was a better replacement for THF in Suzuki reaction.

THF: Water (v/v)	Catalyst	Reaction time	Yield	Conversion* (4-Iodoanisole)	Selectivity*
5:5	$Pd(PPh_3)_4$	8h	73.0%	79.5%	91.9%
6:4	$Pd(PPh_3)_4$	8h	57.9%	72.6%	79.8%
7:3	$Pd(PPh_3)_4$	8h	60.5%	63.7%	95.0%
8:2	$Pd(PPh_3)_4$	8h	42.0%	41.7%	100.7%
9:1	$Pd(PPh_3)_4$	8h	14.0%	13.9%	100.2%
10:0	$Pd(PPh_3)_4$	8h	0.0%	0.1%	0.0%

Table 3.8 Reactions of 4-iodoanisole with THF/water system

*Selectivity and conversion was based on 4-iodoanisole

3.4.3 Recycling of Starbon-Pd Catalyst

Figure 3.28 showed the results of GC analysis for recycling of Starbon S500-Pd.

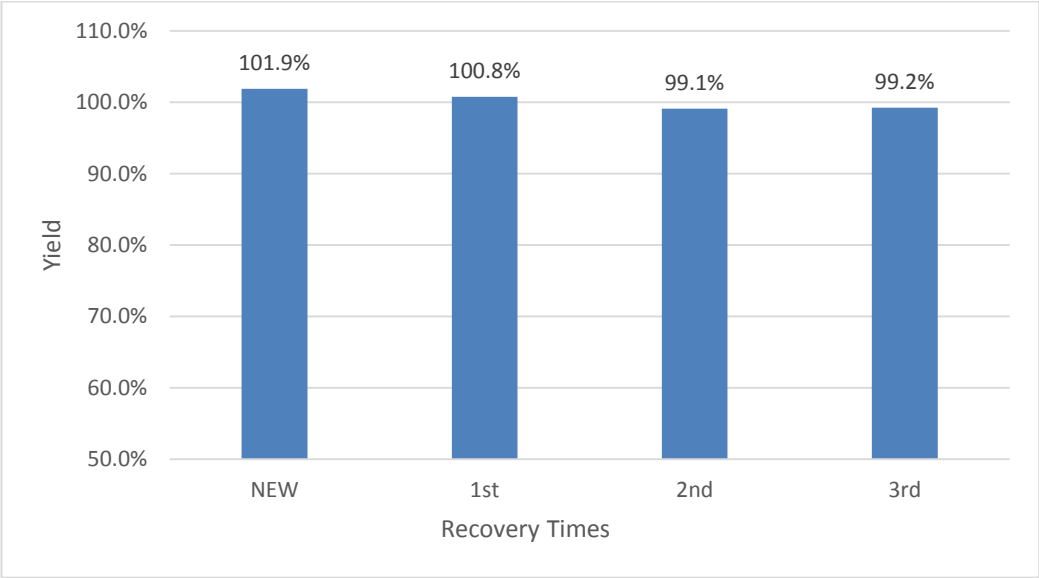
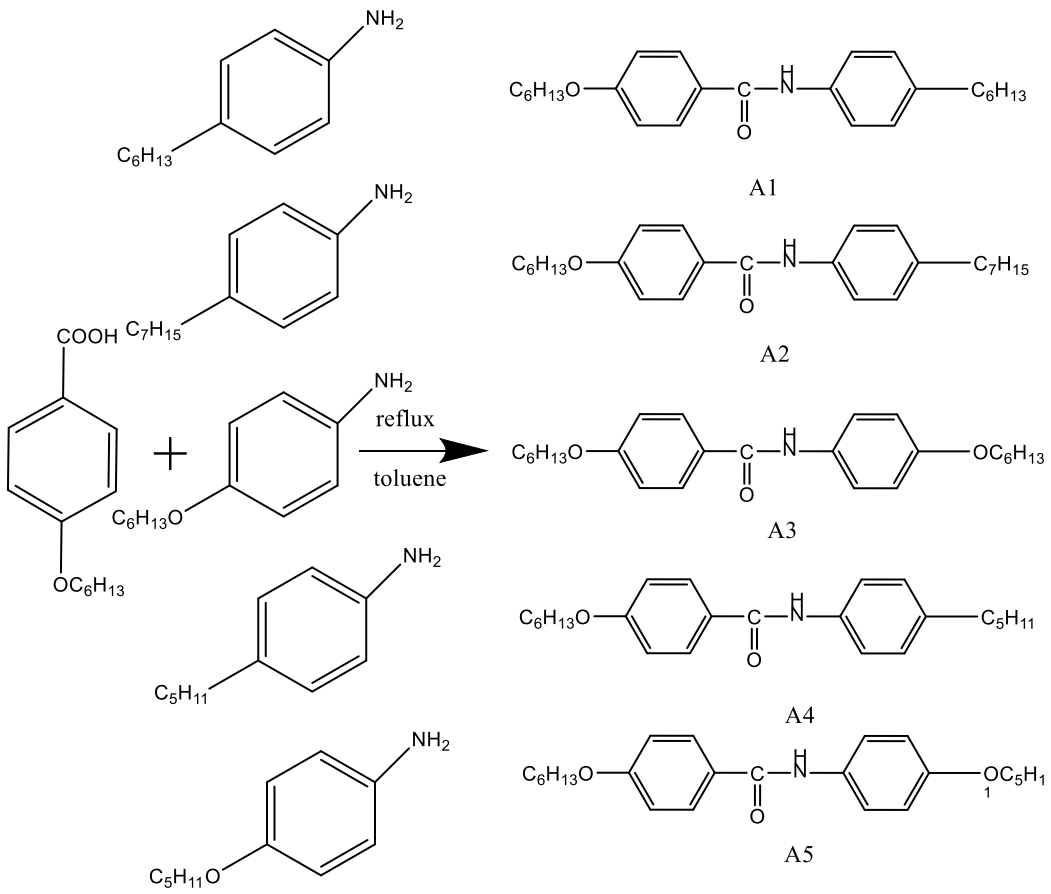


Figure 3.28 Results of GC analysis for recycling of Starbon S500-Pd

According to the results, Starbon S500-Pd still had a good activity after being recovered 3 times.

3.5 Amidation



Scheme 23 Amidation reaction

Activated SiO_2 catalyst was able to convert benzoic acid and aniline to N-phenyl benzamide. Conversion was better with alkoxy groups than alkyl groups. Activated SiO_2 catalyst works with both long chain and short chain substituent group. It is a green reaction which had strong potential on synthesis of liquid crystals with amide groups. Even though compound A1-A5 were fitted to general molecular structure of rod-like liquid crystal, they did not have liquid crystal phase due to hydrogen bond between molecular. In order to obtain liquid crystal phase, molecular with amide group should be designed to have at least three rigid cores, polymer or designed to discotic liquid crystal.

Acid	Mass (g)	Amine	Mass (g)	Reaction Time	Product (g)	Yield
4-hexyloxy benzoic acid	0.5	4-hexylaniline	0.40	24 h	0.45	52.4%
4-hexyloxy benzoic acid	0.5	4-heptylaniline	0.43	24 h	0.49	55.1%
4-hexyloxy benzoic acid	0.5	4-hexyloxyaniline	0.44	24 h	0.62	69.3%
4-hexyloxy benzoic acid	0.5	4-pentylaniline	0.37	24 h	0.36	43.5%
4-hexyloxy benzoic acid	0.5	4-pentyloxyaniline	0.40	24 h	0.54	62.8%

Table 3.9 Reaction conditions and results of amidation

CHAPTER 4 CONCLUSIONS and FURTHER WORK

In esterification, sulfonated Starbon had a good activity with short chain alcohols. It is a green choice for ester terminal group in synthesis of liquid crystals. For ester bridging groups, using EDC as dehydrating agent, CPME as solvent and microwave irradiation were able to save a lot of time on reaction and a number of materials and labour on purification. The products had same liquid crystal phase and properties as reference. With C-C linkage, ethanol/water and CPME/water are two kinds of green solvents for Suzuki reaction with different starting materials. Besides that, Starbon palladium is a highly activity recyclable catalyst in Suzuki reaction, able to replace $Pd(PPh_3)_4$. This improvement is able to save palladium which is an expensive and rare metal. In synthesis of liquid crystals with amide group, Activated SiO_2 catalyst is an easy to obtain catalyst and purification of the reactions involving Activated SiO_2 catalyst is very easy.

In this research, only some one step reactions were carried to create liquid crystal. In further work, those one step reactions will be combined to synthesize complex liquid crystal molecule. Multi-steps synthetic route will be green base on those green technologies.

REFERENCES

1. P. Anastas and N. Eghbali, *Chemical Society Reviews*, 2010, **39**, 301-312.
2. P. T. Anastas and J. C. Warner, *Green chemistry: theory and practice*, Oxford University Press, 2000.
3. V. Budarin, J. H. Clark, J. J. E. Hardy, R. Luque, K. Milkowski, S. J. Tavener and A. J. Wilson, *Angewandte Chemie*, 2006, **118**, 3866-3870.
4. V. L. Budarin, J. H. Clark, R. Luque, D. J. Macquarrie, A. Koutinas and C. Webb, *Green Chemistry*, 2007, **9**, 992.
5. A. Aldana-Pérez, L. Lartundo-Rojas, R. Gómez and M. E. Niño-Gómez, *Fuel*, 2012, **100**, 128-138.
6. R. Luque, V. Budarin, J. H. Clark, P. Shuttleworth and R. J. White, *Catalysis Communications*, 2011, **12**, 1471-1476.
7. V. L. Budarin, J. H. Clark, R. Luque and D. J. Macquarrie, *Chem Commun (Camb)*, 2007, 634-636.
8. R. Luque, V. Budarin, J. H. Clark and D. J. Macquarrie, *Applied Catalysis B: Environmental*, 2008, **82**, 157-162.
9. A. Barau, V. Budarin, A. Caragheorgheopol, R. Luque, D. J. Macquarrie, A. Prelle, V. S. Teodorescu and M. Zaharescu, *Catalysis Letters*, 2008, **124**, 204-214.
10. N. Miyaura, K. Yamada and A. Suzuki, *Tetrahedron Letters*, 1979, **20**, 3437-3440.
11. V. Antonucci, J. Coleman, J. B. Ferry, N. Johnson, M. Mathe, J. P. Scott and J. Xu, *Organic Process Research & Development*, 2011, **15**, 939-941.
12. K. Watanabe, N. Yamagiwa and Y. Torisawa, *Organic process research & development*, 2007, **11**, 251-258.
13. K. Watanabe, N. Kogoshi, H. Miki and Y. Torisawa, *Synthetic Communications®*, 2009, **39**, 2008-2013.
14. S. Kobayashi, H. Kuroda, Y. Ohtsuka, T. Kashihara, A. Masuyama and K. Watanabe, *Tetrahedron*, 2013, **69**, 2251-2259.
15. R. Schmitt, *Electromagnetics explained: a handbook for wireless/RF, EMC, and high-speed electronics*, Newnes, 2002.
16. R. Gedye, F. Smith, K. Westaway, H. Ali, L. Baldisera, L. Laberge and J. Rousell, *Tetrahedron letters*, 1986, **27**, 279-282.
17. R. J. Giguere, T. L. Bray, S. M. Duncan and G. Majetich, *Tetrahedron letters*, 1986, **27**, 4945-4948.
18. A. Loupy, A. Petit, M. Ramdani, C. Yvanaeff, M. Majdoub, B. Labiad and D. Villemin, *Canadian journal of chemistry*, 1993, **71**, 90-95.
19. O. Orliac and F. Silvestre, *Bioresource technology*, 2003, **87**, 63-68.
20. F. Bonnaterre, M. Bois-Choussy and J. Zhu, *Organic letters*, 2006, **8**, 4351-4354.
21. C. Ferroud, M. Godart, S. Ung, H. Borderies and A. Guy, *Tetrahedron Letters*, 2008, **49**, 3004-3008.
22. I. R. Baxendale, C. M. Griffiths‐Jones, S. V. Ley and G. K. Tranmer, *Chemistry-A European Journal*, 2006, **12**, 4407-4416.
23. M. Larhed, G. Lindeberg and A. Hallberg, *Tetrahedron letters*, 1996, **37**, 8219-8222.
24. B. M. Savall and J. R. Fontimayor, *Tetrahedron Letters*, 2008, **49**, 6667-6669.
25. V. V. Namboodiri and R. S. Varma, *Green Chem.*, 2001, **3**, 146-148.

26. A. A. Kiryanov, P. Sampson and A. J. Seed, *The Journal of organic chemistry*, 2001, **66**, 7925-7929.
27. R. S. Varma and R. Dahiya, *Tetrahedron letters*, 1997, **38**, 2043-2044.
28. P. Lidström, J. Tierney, B. Wathey and J. Westman, *Tetrahedron*, 2001, **57**, 9225-9283.
29. M. A. Surati, S. Jauhari and K. Desai, *Archives of Applied Science Research*, 2012, **4**, 645-661.
30. C. O. Kappe, *Angewandte Chemie International Edition*, 2004, **43**, 6250-6284.
31. N. S. Wilson, C. R. Sarko and G. P. Roth, *Organic process research & development*, 2004, **8**, 535-538.
32. D. J. C. Constable, A. D. Curzons and V. L. Cunningham, *Green Chemistry*, 2002, **4**, 521-527.
33. R. A. Sheldon, *Pure and applied chemistry*, 2000, **72**, 1233-1246.
34. R. A. Sheldon, *Chemical Society Reviews*, 2012, **41**, 1437-1451.
35. C. Jimenez-Gonzalez, C. S. Ponder, Q. B. Broxterman and J. B. Manley, *Organic Process Research & Development*, 2011, **15**, 912-917.
36. J. P. F. Lagerwall and G. Scalia, *Current Applied Physics*, 2012, **12**, 1387-1412.
37. R. Templer and G. Attard, *New Sci*, 1991, **25**, 1767.
38. S. Chandrasekhar, *Press, Cambridge*, 1992, **168**.
39. B. Bahadur and M. Tilton, *Liquid crystals: applications and uses*, World Scientific, 1992.
40. P. J. Collings and M. Hird, *Introduction to liquid crystals: chemistry and physics*, CRC Press, 1997.
41. D. Vorländer, *Kristallinisch-flüssige substanzen*, Enke, 1908.
42. G. Friedel, *Ann. phys*, 1922, **18**, 273-474.
43. T. J. Sluckin, D. A. Dunmur and H. Stegemeyer, *Liquid Crystals Series Taylor & Francis: London*, 2004.
44. G. W. Gray, *Molecular structure and the properties of liquid crystals*, Academic press, 1962.
45. G. H. Heilmeier, L. A. Zanoni and L. A. Barton, *Proceedings of the IEEE*, 1968, **56**, 1162-1171.
46. M. Schadt and W. Helfrich, *Applied Physics Letters*, 1971, **18**, 127-128.
47. T. Scheffer and J. Nehring, *Applied Physics Letters*, 1984, **45**, 1021-1023.
48. M. Katayama, *Thin Solid Films*, 1999, **341**, 140-147.
49. T. Urabe, T. Sasaoka, K. Tatsuki and J. Takaki, 13.1: Invited Paper: Technological Evolution for Large Screen Size Active Matrix OLED Display, 2007.
50. K. Inukai, H. Kimura, M. Mizukami, J. Maruyama, S. Murakami, J. Koyama, T. Konuma and S. Yamazaki, 36.4 L: Late‐News Paper: 4.0‐in. TFT‐OLED Displays and a Novel Digital Driving Method, 2000.
51. E. Dalcanale, *Seminars In Organic Synthesis*, 1993, 267-291.
52. R. C. Maze, E. P. Oppenheim and R. M. Reynolds, Google Patents, 1979.
53. R. Hikmet, J. Lub and A. Tol, *Macromolecules*, 1995, **28**, 3313-3327.
54. Y. Hirai, US Patent 20,150,029,446, 2015.
55. B. Neises and W. Steglich, *Angewandte Chemie International Edition in English*, 1978, **17**, 522-524.
56. S. Xu, I. Held, B. Kempf, H. Mayr, W. Steglich and H. Zipse, *Chemistry*, 2005, **11**, 4751-4757.

57. Y. M. Angell, C. García-Echeverría and D. H. Rich, *Tetrahedron letters*, 1994, **35**, 5981-5984.
58. I. Surh, M. Behl, S. A. Elmore and R. S. Chhabra, *Cutaneous and ocular toxicology*, 2012, **31**, 177-187.
59. J. P. López-Alonso, F. Diez-García, J. Font, M. Ribó, M. Vilanova, J. M. Scholtz, C. González, F. Vottariello, G. Gotte and M. Libonati, *Bioconjugate chemistry*, 2009, **20**, 1459-1473.
60. L. O. Damink, P. Dijkstra, M. Van Luyn, P. Van Wachem, P. Nieuwenhuis and J. Feijen, *Biomaterials*, 1996, **17**, 765-773.
61. H. Kono and T. Teshirogi, *International journal of biological macromolecules*, 2015, **72**, 299-308.
62. Y.-A. Lin, A. G. Cheetham, P. Zhang, Y.-C. Ou, Y. Li, G. Liu, D. Hermida-Merino, I. W. Hamley and H. Cui, *ACS nano*, 2014, **8**, 12690-12700.
63. A. Tanaka, Y. Fukuoka, Y. Morimoto, T. Honjo, D. Koda, M. Goto and T. Maruyama, *Journal of the American Chemical Society*, 2014.
64. B. Falkiewicz, Comparison of the efficiency of various coupling systems in the acylation of model secondary amines with thymin-1-ylacetic acid, 1999.
65. S. Gan, A. Yuvaraj, M. Lutfor, M. Mashitah and H. Gurumurthy, *RSC Advances*, 2015, **5**, 6279-6285.
66. B. G. R. SCHEME, 2010.
67. R. Jothiramalingam and M. K. Wang, *Industrial & Engineering Chemistry Research*, 2009, **48**, 6162-6172.
68. K. Nakajima, I. Tomita, M. Hara, S. Hayashi, K. Domen and J. N. Kondo, *Advanced Materials*, 2005, **17**, 1839-1842.
69. A. Takagaki, M. Toda, M. Okamura, J. N. Kondo, S. Hayashi, K. Domen and M. Hara, *Catalysis Today*, 2006, **116**, 157-161.
70. N. Miyaura and A. Suzuki, *Chemical reviews*, 1995, **95**, 2457-2483.
71. N. Miyaura, T. Yanagi and A. Suzuki, *Synthetic Communications*, 1981, **11**, 513-519.
72. K. Matos and J. A. Soderquist, *The Journal of organic chemistry*, 1998, **63**, 461-470.
73. G. B. Smith, G. C. Dezeny, D. L. Hughes, A. O. King and T. R. Verhoeven, *The Journal of Organic Chemistry*, 1994, **59**, 8151-8156.
74. C. Amatore, A. Jutand and G. Le Duc, *Chemistry-A European Journal*, 2011, **17**, 2492-2503.
75. S. Wei, Z. Ma, P. Wang, Z. Dong and J. Ma, *Journal of Molecular Catalysis A: Chemical*, 2013, **370**, 175-181.
76. C. J. Li, *Angewandte Chemie International Edition*, 2003, **42**, 4856-4858.
77. L. Liu, Y. Zhang and B. Xin, *The Journal of organic chemistry*, 2006, **71**, 3994-3997.
78. B. Bandgar, S. V. Bettigeri and J. Phopase, *Tetrahedron letters*, 2004, **45**, 6959-6962.
79. D. Saha, K. Chattopadhyay and B. C. Ranu, *Tetrahedron Letters*, 2009, **50**, 1003-1006.
80. W. Han, C. Liu and Z.-L. Jin, *Organic letters*, 2007, **9**, 4005-4007.
81. K.-i. Shimizu, S. Koizumi, T. Hatamachi, H. Yoshida, S. Komai, T. Kodama and Y. Kitayama, *Journal of Catalysis*, 2004, **228**, 141-151.
82. V. L. Budarin, J. H. Clark, R. Luque, D. J. Macquarrie and R. J. White, *Green Chemistry*, 2008, **10**, 382.

83. T. Kato, J. M. Frechet, P. G. Wilson, T. Saito, T. Uryu, A. Fujishima, C. Jin and F. Kaneuchi, *Chemistry of materials*, 1993, **5**, 1094-1100.
84. H. Kawada and Y. Matsunaga, *Bulletin of the Chemical Society of Japan*, 1988, **61**, 3083-3085.
85. Y. Matsunaga, N. Miyajima, Y. Nakayasu, S. Sakai and M. Yonenaga, *Bulletin of the Chemical Society of Japan*, 1988, **61**, 207-210.
86. D. Zhang, Q. F. Zhou, Y. G. Ma, X. H. Wan and X. D. Feng, *Polymers for Advanced Technologies*, 1997, **8**, 227-233.
87. W. Jackson and H. Kuhfuss, *Journal of Applied Polymer Science*, 1980, **25**, 1685-1694.
88. M. L. Bushey, T. Q. Nguyen, W. Zhang, D. Horoszewski and C. Nuckolls, *Angewandte Chemie International Edition*, 2004, **43**, 5446-5453.
89. M. L. Bushey, A. Hwang, P. W. Stephens and C. Nuckolls, *Angewandte Chemie International Edition*, 2002, **41**, 2828-2831.
90. M. L. Bushey, T.-Q. Nguyen and C. Nuckolls, *Journal of the American Chemical Society*, 2003, **125**, 8264-8269.
91. T.-Q. Nguyen, M. L. Bushey, L. E. Brus and C. Nuckolls, *Journal of the American Chemical Society*, 2002, **124**, 15051-15054.
92. A. Klapars, J. C. Antilla, X. Huang and S. L. Buchwald, *Journal of the American Chemical Society*, 2001, **123**, 7727-7729.
93. V. K. Das, R. R. Devi and A. J. Thakur, *Applied Catalysis A: General*, 2013, **456**, 118-125.
94. J. W. Comerford, T. J. Farmer, D. J. Macquarrie, S. W. Breeden and J. H. Clark, *ARKIVOC*, 2012, **7**, 282-293.
95. X.-D. Yang, X.-H. Zeng, Y.-H. Zhao, X.-Q. Wang, Z.-Q. Pan, L. Li and H.-B. Zhang, *Journal of combinatorial chemistry*, 2010, **12**, 307-310.
96. N. B. Chapman, A. Ehsan, J. Shorter and K. J. Toyne, *Journal Of the Chemical Society B-Physical Organic*, 1967, 570-&.
97. E. L. Eliel, S. H. Schroeter, T. J. Brett, F. J. Biros and J.-C. Richer, *Journal of the American Chemical Society*, 1966, **88**, 3327-3334.
98. M. Takahashi, S. Mita and S. Kondo, *Molecular crystals and liquid crystals*, 1986, **132**, 53-64.