พอลิเมอร์ลอกแบบโมเลกุลของพอลิ(3,4-เอทิลีนไดออกซีไทโอฟีน) จากปฏิกิริยาพอลิเมอไรเซชันในสถานะของแข็ง

Molecularly Imprinted Poly(3,4-ethylenedioxythiophene) From Solid State Polymerization

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MOLECULARLY IMPRINTED POLY(3,4-ETHYLENEDIOXYTHIOPHENE) FROM SOLID STATE POLYMERIZATION

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Submitted to the Department of Chemistry, Chulalongkorn University

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Title Molecularly Imprinted Poly(3,4-Ethylenedioxythiophene) From Solid State Polymerization

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Abstract

Molecularly imprinted polymers (MIPs), specialized materials employed to create artificial receptors with a predetermined specificity and selectivity for a given template, were prepared from the monomer 3,4-ethylenedioxythiophene (EDOT). Its polymer, poly(3,4-ethylenedioxythiophene) (PEDOT), was obtained through the solid state polymerization (SSP) in the presence of the selected template molecules, *p*-nitrophenol (PNP) and pyrene. The resulting conjugated MIPs, monitored by UV-Vis spectroscopy, exhibit the recognition toward their template molecules compared to non-imprinted polymers (NIPs) in the binding process. The results show that the specific adsorption values (△Q) of PNP and pyrene molecules bound to the MIPs were 300.71 and 12.73 μmol/g, respectively. The rebinding capacities of the PNP-MIPs were 73.44%, while only 8.68% was obtained for pyrene-MIPs. These values indicated that the MIP prepared from SSP-PEDOT could be specifically imprinted with the relatively polar PNP template, but was not successful with the non-polar pyrene. The robustness, ease of preparation and low cost provide great promise to develop this material for on-site molecule-specific sensors.

Keywords: Molecularly imprinted polymer, Solid-state polymerization, PEDOT

ชื่อโครงการ พอลิเมอร์ลอกแบบโมเลกุลของพอลิ(3,4-เอทิลีนไดออกซีไทโอฟีน)จากปฏิกิริยาพอลิเมอไรเซชันในสถานะของแข็ง

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บทคัดย่อ

พอลิเมอร์ลอกแบบโมเลกุล (MIP) เป็นวัสดุพิเศษที่ใช้ในการสร้างตัวรับสังเคราะห์ ที่มีความจำเพาะต่อโมเลกุลที่ถูกลอกแบบ โดยจะนำมอนอเมอร์ 3,4-เอทิลีนไดออกซีไทโอฟีน (EDOT) มาผ่านปฏิกิริยาพอลิเมอไรเซชันในสถานะของแข็ง (SSP) ที่มีโมเลกุลแม่แบบ คือ พาราไนโตรฟีนอล หรือไพรีนปนอยู่ เพื่อให้ได้พอลิ(3,4-เอทิลีนไดออกซีไทโอฟีน) (PEDOT) ที่ลอกแบบโมเลกุลแม่แบบทั้งสอง โดยจะติดตามสมบัติการจดจำโมเลกุลแม่แบบนี้ด้วยเทคนิคยูวี-วิสิเบิลสเปกโทรสโกปีของโมเลกุลแม่แบบ เทียบกับพอลิเมอร์ที่ไม่ได้ลอกแบบไว้ (NIP) ผลการศึกษายืนยันว่าพอลิเมอร์ดังกล่าวมีความจำเพาะเจาะจงในการเลือกจับโมเลกุลที่ลอกแบบมาและพบว่าพอลิเมอร์ลอกแบบโมเลกุลมีค่าการดูดซับจำเพาะ (△Q) สำหรับโมเลกุลพาราไนโตรฟีนอลเท่ากับ 300.71 μmol/g และสำหรับโมเลกุลไพรีนเท่ากับ 12.73 μmol/g นอกจากนี้ยังพบว่าพอลิเมอร์ลอกแบบโมเลกุลมีความสามารถในการจับยึดพาราไนโตรฟีนอล และ ไพรีนเท่ากับ 73.44% และ 8.68% ตามลำดับ จากผลการทดลองสามารถสรุปได้ว่าพอลิเมอร์ PEDOT ที่เตรียมจากกระบวนการ SSP สามารถลอกแบบโมเลกุลแม่แบบที่ค่อนข้างมีขั้วอย่างพาราไนโตรฟีนอลได้อย่างจำเพาะ แต่ไม่ประสบผลสำเร็จนักกับโมเลกุลแม่แบบที่ไม่มีขั้วอย่างไพรีน สามารถพัฒนาวัสดุนี้เพื่อใช้เป็นเซ็นเซอร์สำหรับการตรวจวัดทางเคมีที่จำเพาะสำหรับสารบางชนิดได้ เนื่องจากความคงทน ขั้นตอนการสังเคราะห์ที่ไม่ซับซ้อนและมีราคาสูง

คำสำคัญ: พอลิเมอร์ลอกแบบโมเลกุล, พอลิเมอไรเซชันในสถานะของแข็ง, พอลิ(3,4-เอทิลีนไดออกซีไทโอฟีน)

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LIST OF ABBREVIATIONS

cm^{-1}	: Unit of wavenumber (IR)
^{13}C NMR	: Carbon-13 nuclear magnetic resonance spectroscopy
^{o}C	: Degree Celsius
$CDCl_3$	: Deuterated chloroform
d	: Doublet (NMR)
EDOT	: 3,4-ethylenedioxythiophene
Equiv	: Equivalent
EtOAc	: Ethyl acetate
g	: Gram
^{1}H NMR	: Proton nuclear magnetic resonance spectroscopy
h	: Hour
Hz	: Hertz
IR	: Infrared spectroscopy
J	: Coupling constant
m	: Multiplet (NMR)
min	: Minute
mg	: Milligram
mL	: Milliliter
M	: Molar
mM	: Millimolar
mmol	: Millimole
m.p.	: Melting point
MeOH	: Methanol
MIPs	: Molecularly imprinted polymers

NaOH	: Sodium hydroxide
NIPs	: Non-imprinted polymers
nm	: Nanometer
NBS	: N-bromosuccinimide
PEDOT	: Poly(3,4-ethylenedioxythiophene)
PNP	: p-nitrophenol
ppm	: Parts per million
Q	: The amount of template molecules bound to polymers
Q_{MIPs}	: The amount of template molecules bound to imprinted polymers
Q_{NIPs}	: The amount of template molecules bound to non-imprinted polymers
q	: Quartet (NMR)
RT. rt	: Room temperature
SSP	: Solid-state polymerization
s	: Singlet (NMR)
st	: Stretching vibration
t	: Triplet (NMR)
TLC	: Thin layer chromatography
UV-Vis	: Ultra-violet and visible spectroscopy
V	: Volume (ml)
μmol	: Micromole
δ	: Chemical shift
λ_{max}	: Maximum wavelength

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Chapter I

Introduction

1.1 A Brief History of Molecularly Imprinted Polymers

Over recent years, molecularly imprinted polymers (MIPs) have shown great potential in numerous applications in pharmaceutics, biological technology, sensor technology and so forth. Although there has been substantial research during the past years, increased motivation to assess the true potential of molecularly imprinted polymers is still in demand for modern chemistry.

From Wulff's seminal work [1] in 1973, the notion of molecularly imprinted polymers was developed and intensively studied. They were among the early group to synthesize molecularly imprinted polymers, employing a covalent approach for resolving the racemic mixture of glyceric acid. Elsewhere, Mosbach and coworkers [2] were the first group to introduce molecularly imprinted polymers using a non-covalent approach in order to mimic antibody combining sites. The simplicity of their method allowed it to be vastly used to create the later-generation of imprinted polymers.

1.2 Fundamental Principle of Molecularly Imprinting Technique

Molecularly imprinted polymers have experienced much attention due to their versatile synthetic approach for preparing highly cross-linked polymer matrix with recognition sites that are solely specific to certain templates e.g. an atom, ion, molecule, complex or a molecular, ionic or a molecular assembly, including micro-organisms [3]. The preparation of molecularly imprinted polymers commences with the assembling of functional monomers surrounding our interest templates. This process is analogous to a theory originating in biochemistry which is called lock-and-key mechanism, explaining the interaction between enzyme and substrate [4].

Subsequently, the recognition site with high selectivity is formed during the interaction between functional groups on the template and monomer through a polymerization process. Then the template is removed from the site by a certain condition, leaving it with a cavity that resembles both size and shape of the template. The obtained cavity, which occurs inside the synthetic polymer, demonstrates an excellent sensitivity and selectivity toward specific template molecule (Figure 1.1) [5].

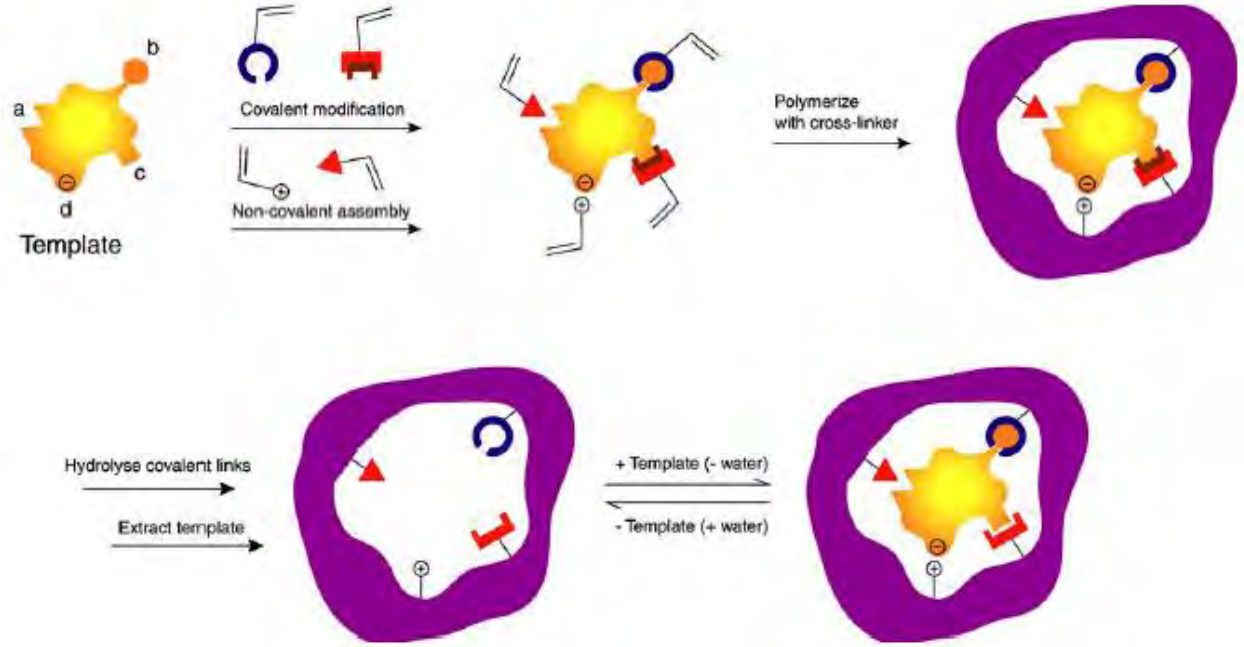


Figure 1.1 Schematic illustration of the imprinting process [5].

The classification of molecularly imprinted polymers depends on several factors, but the interactions between templates and functional monomers are one-way to indicate the types of molecularly imprinted polymers. As mentioned earlier, there are two approaches which have been commonly employed: covalent (including metal-coordination) and non-covalent bond. Nonetheless, the more popular approach, which was extensively used for synthesizing molecularly imprinted polymers, is the non-covalent method due to the following reasons: [4]

- The interactions between functional monomers and templates are easy to design and obtain.
- Extraction procedure of templates requires unsophisticated technique, normally accomplished by exhaustive extraction.
- Greater possibility of various functional groups can be employed to interact with the templates in the molecularly imprinted polymer.
- Molecularly imprinted polymer can be retained for years without degrading its efficiency.

1.3 Approach for Selective Binding Sites

1.3.1) Covalent Imprinting Approach

Covalent imprinting was the first strategies that were employed in the molecularly imprinted polymer. The covalent imprinting approach is discriminated by mean of which one or more functional units and the templates are attached through covalent bonds in order to form a template-monomer by a chemical step independent of polymer formation. After polymerization process, the templates are extracted from the imprinted polymer matrix, leaving the unpaired functional groups in the binding sites and these sites are capable of binding specific target molecule by re-establishment of the covalent bond. The classical methods of covalent imprinting implicate readily reversible condensation reactions such as ketal/acetal, boronate ester and Schiff's base formation to prepare template-monomers [3, 5].

The boronic acids, which are somewhat suitable for covalent binding with diol-containing templates, are often employed as binding sites, and their formation and dissociation process are swift and facile. Boronic acids consist of five-membered cyclic structures in which the rigidity is sufficient to fix the covalent linkages for a desired conformation. The latter procedure involves hydrolysis of boronate ester groups to

remove the template. Thus, the linkages of boronic groups inside the recognition site are arranged orderly for guest binding. The boronic esters approach has been the most successful reversible covalent methods, especially for imprinting of carbohydrate derivatives. The template molecules employed include [5] glyceric acid, derivatives of mannose, galactose, fructose, sialic acid, castasterone and nucleotides. Furthermore, the boronate esters have also been consolidated in molecularly imprinted polymers for fluorescent sensing.

Ketal/acetal formation between a diol and a carbonyl compound has been employed for molecular imprinting protocols. After the extraction of templates, the rebinding process took place by carbonyl chloride with an alcohol reaction or by the displacement of bromide by a carboxylate anion. However, carboxylic acids have limited capability when employed in the fully covalent method owing to their slow rebinding kinetics and the need for activate intermediates. Shea and coworkers [6], who employed a polymerizable diol as the binding group, have been intensively studied mono- and di-ketone templates in particular.

The Schiff's bases are a beneficial approach for the imprinting of either primary amine or carbonyl compound by condensation. The derivatives of amino acid have been prosperously imprinted via this approach, but the rebinding procedure with the resultant enantioselective polymers take a considerable amount of time for many potential applications, such as chromatographic separation [7].

The advantage of the covalent imprinting approach is that the functional group residues are only found in the recognition sites associated with a template, which perhaps useful to lower non-specific interactions. However, the disadvantages of the covalent approach are the need for a sophisticated technique of synthetic chemistry to be fulfilled on the template before the polymerization process and a chemical treatment on the polymer to release the template.

1.3.2) Non-covalent Imprinting Approach

The formation of non-covalent imprinting interactions between functional monomer and template during polymerization are similar to those interactions between polymer and template in the rebinding process. The interactions are based on typical non-covalent forces such as hydrogen bonding, ionic interactions, electrostatic interactions, van der Waals forces and hydrophobic forces [8]. This approach has been vastly employed because it provides more flexibility in terms of the functionalities on a desirable template. Additionally, the synthesis process requires much less complicated procedure than the pre-synthesis of covalent adducts. On the other hand, those imprinted polymers, which employed the covalent approach, were obtained in situ simply by conglomerating the functional monomers and templates in the form of polymerization mixtures while the non-covalent imprinting was spontaneously formed. After the polymerization, the removal of the template can be facilely done by simple extraction of polymer with suitable solvents.

1.3.2.1) Functional Monomer

The selected monomer is a crucial factor in order to synthesize unique recognition sites designed for a specific template. A wide variety of commercially available functional monomer enables researchers to take advantage of distinct kinds of intermolecular interactions. Typical functional monomers (Figure 1.2) [9] are carboxylic acids (acrylic acid, methacrylic acid, vinylbenzoic acid), sulphonic acids (2-acrylamindo-2-methylpropane sulphonic acid), heteroaromatic bases (vinylpyridine, vinylimidazole).

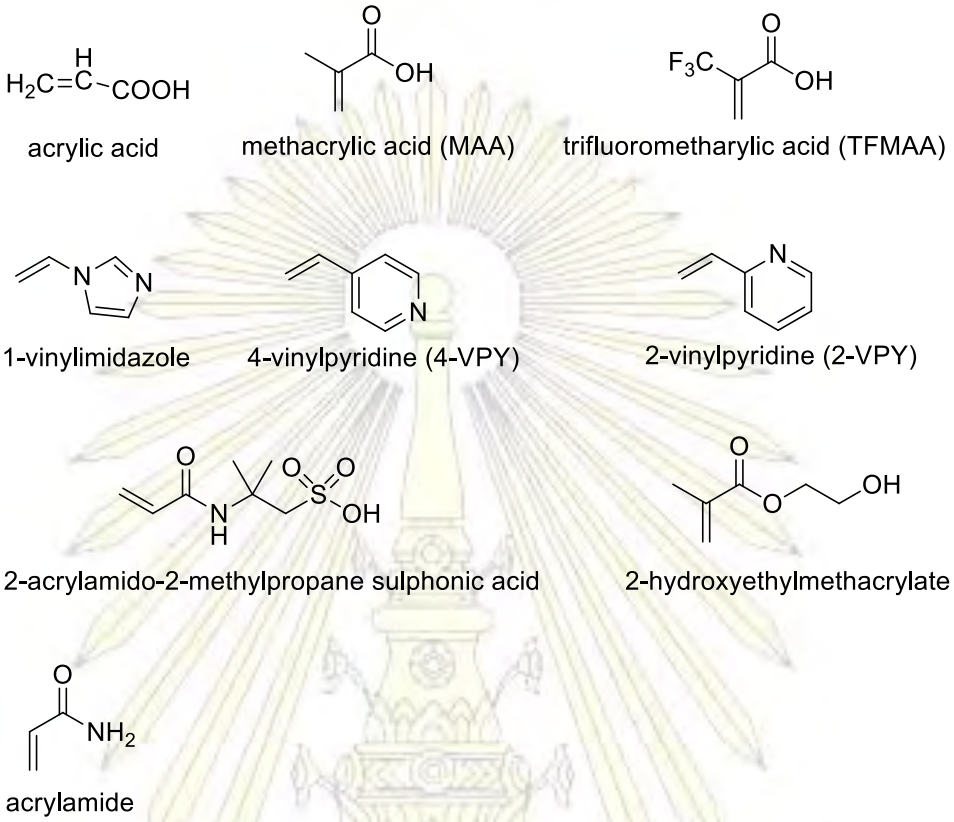


Figure 1.2 Structures of the most common monomers employed for imprinting.

In general, the monomer is selected due to its functional group must complement to those found on the template molecule. For instance, if our interested template consists of either carboxylic or sulfonic acid groups, the possibility of selected functional monomer should contain an amine group. The reason is that they can both form strong ionic interactions between one another. In addition, functional monomers are selected considering strength and nature between template and monomer.

Methacrylic acid (MAA) [10] has been extensively used as the most common functional monomer for the variety of template molecules such as nucleotides, drugs, peptides, herbicides, biologically active substance, environmental contamination and so forth. Furthermore, methacrylic acid, consisting of carboxyl group that act both as

hydrogen bond donor and acceptor, has the capability to interact with a basic functional group on a template molecule. Recently, new functional monomers, trifluoromethacrylic acid (TFMAA), have been developed because it is a stronger acid due to the effect of electronegativity. Thus, trifluoromethacrylic acid is competent in forming stronger ionic interactions. The function monomers, consisting of amidine and urea, have been developed for the purpose of the stoichiometrically imprinted polymeric receptor of β-lactam antibiotics, abating non-specific adsorption [11].

1.3.2.2) Cross-linkers

In imprinted polymer synthesis, cross-linker also implements vital functions, for instance, controlling the morphology of the polymer matrix, stabilizing the imprinted binding sites and imparting mechanical stability to the polymer matrix in order to maintain its molecular recognition capability [12]. Varieties of cross-linkers have been employed as shown in Figure 1.3 [9].

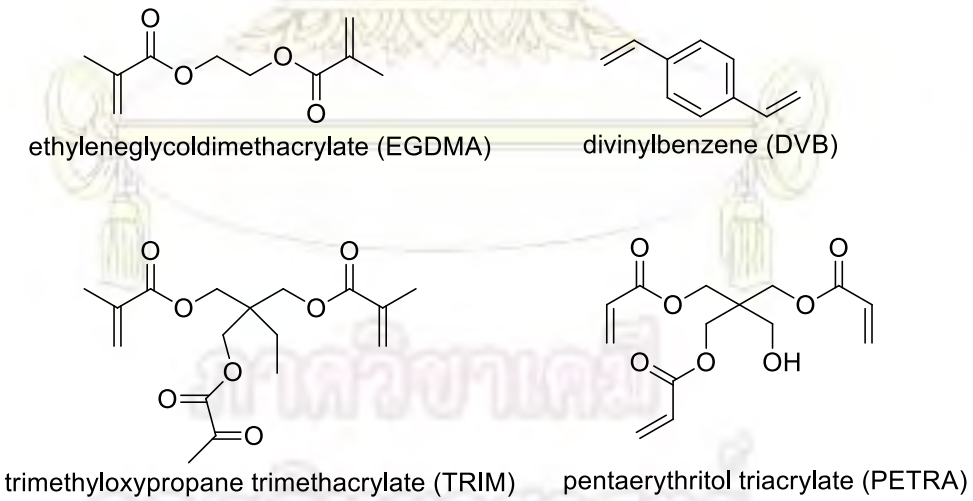


Figure 1.3 Structures of the most common cross-linkers employed for molecular imprinting.

High cross-link ratios are normally employed in order to access permanently porous (macroporous) materials with a sufficient mechanical stability. The most widely utilizable cross-linkers are ethylene glycol dimethacrylate (EGDMA) and trimethyloxypropane trimethacrylate (TRIM). Furthermore, the capability of cross-linkers also depends on the templates and solvent in the reaction mixtures. Trimethyloxypropane trimethacrylate as a cross-linker provides more rigidity, structure order and effective binding sites in comparison with ethylene glycol dimethacrylate.

1.3.2.3) Solvents

Selecting a suitable solvent has been a crucial factor in achieving a satisfactory imprinting and successful rebinding results. Commonly, the solvents generally employed for molecularly imprinted polymers synthesis are toluene, chloroform, dichloromethane or acetonitrile. The solvent serves as aiding substance in order to bring all the components (monomer, template, initiator and cross-linker) into a single phase in the polymerization process and responsible for creating pores within a macroporous polymer. Large size of pores will assure good flow through the resultant molecularly imprinted polymer. The choice of solvents depends on its role toward which type of imprinting approach. The selection of solvents for the non-covalent imprinting approach is more significant in order to promote the formation of non-covalent interactions among the functional monomer and template and, therefore, enhance the imprinting efficiency [13].

Generally, the non-covalent imprinting approach is less complicated to achieve and applicable to a variety of template molecules than the covalent imprinting approach. During the polymerization process, the covalent linkage between template and monomer is needless and the condition of polymerization has to be cautiously chosen to maximize the formation of non-covalent interaction in the mixture. Additionally, the removal of template molecules can be facilely occurred from the polymer matrix by exhaustive extraction with appropriate solvents due to its weakly interact by non-covalent linkages. On the contrary, the covalent imprinting interaction between template and monomer requires stability and specific geometry. In some condition, the imprinting effect is decreased in the extraction procedure, which requires rather severe conditions for cleavage of covalent linkages. Selection of the imprinting approach in accordance with a desirable selectivity for the analyzed template molecules should be carefully considered.

1.4 Applications of the Molecularly Imprinted Polymers

The unique properties of molecularly imprinted polymers have made them an intriguing method for variety of applications including [9]:

- Molecularly imprinting chromatographic techniques:

  One of the most traditional applications is the molecularly imprinting chromatography, particularly for liquid chromatography (LC) using molecularly imprinted polymers. They are employed as a stationary phase for the separation, which were generally synthesized through bulk polymerization, ground, sieved mechanically and subsequently packed into a chromatographic column. Furthermore, the focused analysis is mainly the separation of template molecules with closely related structures such as

different kinds of steroids, various herbicides, and structures that are not amino acid derivatives.

- Solid-phase extraction and by-product removal:

  Another important field of molecularly imprinted polymers in analytical chemistry is solid-phase extraction (SPE). In this case, molecular imprinting polymer particles, employed as selective sorbent materials, are packed in a high-performance liquid chromatography (HPLC) column for SPE and purifying analyzed molecules from the complex matrices. This application has been adapted to extract several compounds in different sample matrices, for instance, clinical samples, environmental samples, food analysis and so forth.

- Molecularly imprinted polymers as chemical sensors and biosensors:

  The applications of molecularly imprinted polymers, based on sensing, are capable of identifying and binding target molecules with related specificity and selectivity to their natural analogues. Recently, there has been prosperously employed with different kinds of transducers, for instance, the integration of molecularly imprinted polymers with sensors using either a photochemical or thermal initiator, and by surface grafting with chemical or UV initiation. The latter approach has a possibility to control modification of inert electrode surfaces with thin films of specific polymers which are an advantage comparing to the previous approach. In addition, the molecularly imprinted polymer can be electropolymerized on the surface of transduction platform.

- Molecularly imprinted polymers in catalysis and drug delivery

  The usage of molecularly imprinted polymer for catalytic purposes is an important aspect of modern chemistry because they have the ability to mimic the selectivity and stereospecificity of the binding domains of antibodies and enzymes which are normally utilized as catalysts in some reactions [9]. Molecularly imprinted polymers for drug delivery applications have been considered a great challenge over the past few

years owing to unique characteristics: the polymer matrix should be stable to maintain the conformation in the absence of the template; they should be capable of resisting enzymatic, chemical interference and mechanical stress that can be found in biological fluids.

1.5 Conducting Polymers

Conducting polymers (CPs) are known to possess many intriguing features. These polymers, which contain π-conjugated structures, are characterized by a high conductivity, and a good electrochemical reversibility that justifies their use as transducers in the fabrication of efficient electrochemical sensors. Furthermore, conducting polymers are able to functionalize with different functional groups, which can be selected as tags for their ability to recognize biological or chemical target molecules [14]. Therefore, the field of conducting polymers has been intensively studied by thousands of researchers and they are striving to develop the materials that are application stable in the conducting state, facilely process, and cost effective technique.

1.6 Poly(3,4-ethylenedioxythiophene) (PEDOT)

Over the past two decades, varieties of conducting polymers have been developed, particularly those based on polypyrroles, polyanilines, polyphenylenes, poly(p-phenylene vinylene)s and polythiophenes have attracted the most attention, especially the polyaniline has shown the most promising potential among others such as forming conductive structures at relatively low cost and in bulk amounts. Unfortunately, there is a possible presence of benzidine moieties in the polymer backbone, which might yield toxic products upon degradation and cause carcinogenic.

A new polythiophene derivative, poly(3,4-ethylenedioxythiophene) (PEDOT), has been one of the most industrially essential conjugated polymer owing to its excellent electronic properties and remarkable stability. The backbone structure of this polymer is shown in Figure 1.4 [15].

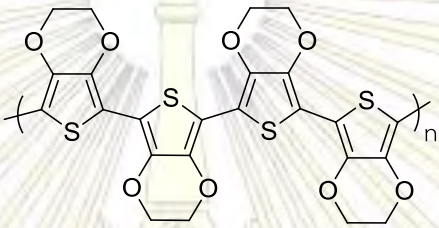


Figure 1.4 The structure of poly(3,4-ethylenedioxythiophene) (PEDOT).

Originally, this polymer was prepared by employing either standard oxidative chemical or electrochemical polymerization methods. Since the preparation of a coated-polymer was conducted on the anode surface during electrochemical polymerization, the obtained polymers are not easily processed after the formation of polymers. The yields of prepared polymers from this method are relatively low, and the polymers often do not have a stable structure.

In addition, the traditional oxidative polymerization with $FeCl_3$ in organic solvents provides relatively high yields in comparison with the electrochemical polymerization method and the final product, which the researchers obtain, has a characteristic of an insoluble blue-black doped polymer powder, the use of a water-soluble electrolyte [polystyrene sulfonic acid (PSS)] as a charge-balancing dopant during polymerization, gives a polymer solution which is capable of processing and forms semitransparent conducting films upon spin-casting. In order to obtain the neutral polymer, a nickel(0) complex-promoted polycondensation of 2,5-dihalo-3,4-ethylenedioxythiophenes has been employed [16]. However, the limitations of this method can cause a severe problem for poly(3,4-ethylenedioxythiophene) applications as well as for in-

depth investigation of molecular order in this conducting polymer. In truth, there is no possibility to obtain a well-defined polymer structure, except the synthesis of conducting polymers is conducted via pure chemical polymerization ways, without the addition of catalysts.

1.7 Solid State Polymerization (SSP) of PEDOT

A reasonable solution for the problems of methods for preparing poly(3,4-ethylenedioxythiophene) lies in a solid-state polymerization of a structurally pre-organized crystalline monomer. The notion of solid-state polymerization was first realized in the 1960s and 1970s with polydiacetylenes. Subsequently, this technique has attracted a substantial group of research due to several advantages, including low operating temperatures, which control byproducts and thermal degradation of the reaction, required-inexpensive equipment, less complicate procedures, and environmental-friendly process [27].

Meng and co-workers [16] have discovered by coincidence that as a result of prolonged storage (2 years) of the monomer at room temperature or heated approximately 50-80 $^{\circ}$C has led to the solid-state polymerization of 2,5-dibromo-3,4-ethylenedioxythiophene (DBEDOT) (Figure 1.5).

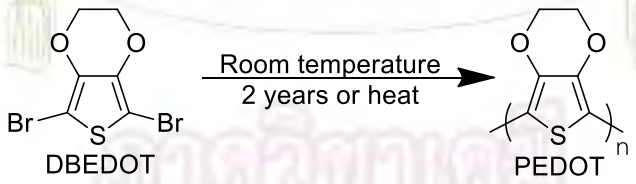


Figure 1.5 Solid-state polymerization of DBEDOT.

Time is an important factor which influences the transformation of colorless crystalline 2,5-dibromo-3,4-ethylenedioxythiophene into black blue substance without evident change of morphology. Astonishingly, the conductivity of this decomposition product seemed to be very high for an organic solid, approximately up to 80 S/cm. Furthermore, the reaction time can be reduced by increasing the temperature to the melting point (97 ^{o}C).

The solid-state polymerization of 2,5-dibromo-3,4-ethylenedioxythiophene at the lowest temperature and longest duration of the reaction time provides the highest conductivity, which perhaps reflects the achievement of a higher degree of order. It is apparent that heating monomer above its melting point results in a significant decreased of conductivity by 0.1 S/cm, which increased to 5.8 S/cm. after doping with iodine, approaching the value of a $FeCl_3$-synthesized PEDOT (7.6 S/cm). Not very significant, but a certain rise in conductivity of SSP-PEDOT about 2 times was found on exposing a sample to iodine vapor.

Poly(3,4-ethylenedioxythiophene) had attracted considerable interests attribute to its low band gap, high electrical conductivity, stable morphology, and excellent optical transparency in the visible region; additionally, it also possesses many practical applications, for instance, all-organic light-emitting diodes, polymer field-effect transistors and so forth. The ether groups at the position of ß and ß$'$ in poly(3,4-ethylenedioxythiophene) help avoiding the formation of α-ß$'$ linkages defect during the polymerization. Therefore, the thiophene ring, which acquires from other substituents such as polyether or alkoxy groups at the ß positions, has the possibility of higher solubility and better physical and chemical properties.

In 2013, Yin and coworkers [17] have conducted a synthesizing of poly(3,4-ethylenedioxythiophene) (PEDOT) by acid-assisted polycondensation based on 2-bromo-3,4-ethylenedioxy thiophene (BEDOT). Under the exposure to ambient atmosphere, the formation of poly(3,4-ethylenedioxythiophene) is in a doped state to some extent, revealing a lack of conductivity at 10^{-6} S/cm while improved to 0.3 S/cm along with further iodine doping. Such

discovering provides an alternative way for the synthesis of conjugated polymers by simple acid-assisted polycondensation due to the formation of a neutral polymer (Figure 1.6).

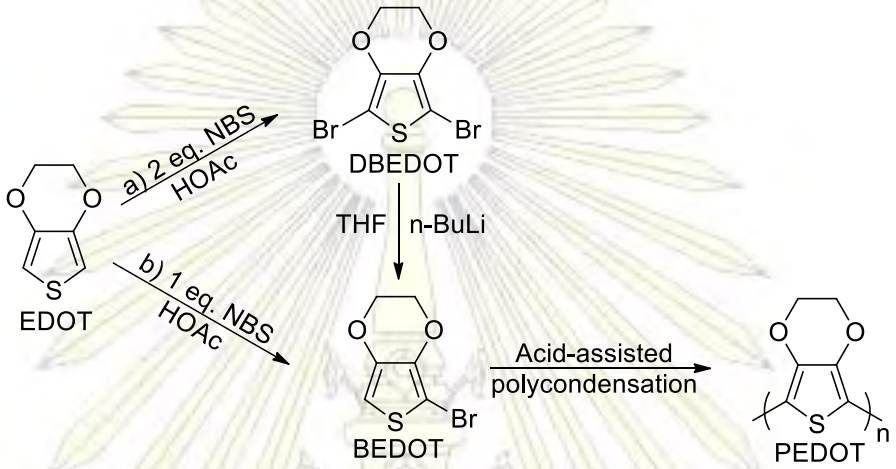


Figure 1.6 Synthesis of PEDOT through acid-assisted polycondensation.

1.8 Literature Reviews

Kubo and coworkers [18] have prepared a cyclobarbital-selective molecularly imprinted polymer using 2-acrylamidoquinline as a fluorescent functional monomer. This molecular imprinting polymer was polymerized through self-assembly of template molecules with functional monomers followed by co-polymerization with a cross-linker. The resultant imprinted polymer exhibited an improvement in fluorescence intensity when target compounds were bound. This sensing approach employing fluorescent imprinted polymers as signaling receptors would be beneficial for the quantitation of non-fluorescent analytes.

Pardieu and coworkers [14] have prepared an electrochemical sensor that consolidates the selectivity demonstrated by molecular imprinting polymers, with the sensitivity and the immediate detection offered by the use of an electrochemical transduction. Furthermore, it is capable of recognizing pesticide molecules, atrazine. The poly(3,4-ethylenedioxythiophene-co-thiophene-acetic acid), poly(EDOT-co-AAT), has been fabricated, in the presence of atrazine, on

a platinum electrode by electrochemical polymerization. From this research, the AAT monomers are capable of interact with atrazine through hydrogen bonds in which EDOT monomers are polymerized in order to stabilize and homogenize the film. The further extracting process of atrazine creates highly specific recognition sites towards newly added atrazine. In addition, the sensor showed promising results: selectivity towards triazinic groups, a large range of detection 10^{-9}mol L^{-1} to 1.5×10^{-2}mol L^{-1} in atrazine and low detection limit at 10^{-7}mol L^{-1}.

Ho and coworkers [19] have deposited poly(3,4-ethylenedioxythiophene) on an indium tin oxide electrode (ITO) for the amperometric detection of morphine which this electrode displays a satisfied electrocatalyst for morphine oxidation. Furthermore, the MIP-PEDOT modified electrode is prepared through electropolymerized 3,4-ethylenedioxythiophene (EDOT) onto an indium tin oxide electrode (ITO) in an electrolytic solution containing morphine (Figure 1.7). By applying a fixed potential to the MIP-PEDOT modified electrode at 0.75 V, a satisfied linear relationship between the current density and morphine concentration, ranging from 0.1 to 1 mM, was achieved. Additionally, a sensitivity of 91.86 μA/cm^2 per mM morphine is obtained and the detection limit was calculated as 0.2 mM (57.0 μg/mL) at a signal-to-noise ratio of 3. As a result, the researcher is able to fabricate a modified electrode which exhibits satisfied sensitivity, selectivity, and reproducibility for morphine detection.

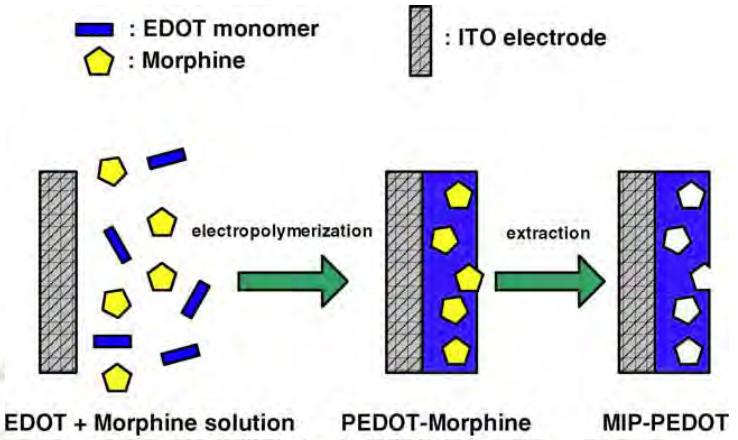


Figure 1.7 Schematic for the preparation of a MIP-PEDOT modified electrode.

Chen and coworkers [20] have successfully prepared a conductive polymer of poly(3,4-ethylenedioxythiophene) by solid-state polymerization and used as a counter electrode in the liquid dye-sensitized solar cell. The experiment results shown that the performance of poly(3,4-ethylenedioxythiophene) is comparable with traditional Pt in a dye-sensitized solar cell when it employed as the counter electrode. This indicates that solid-state polymerization is a versatile preparation method owing to its ease preparation, simple coating, and heating processes; additionally, this method may have more advantages over other traditional methods of the large scale fabrication of poly(3,4-ethylenedioxythiophene) counter electrode for dye-sensitized solar cell (Figure 1.8).

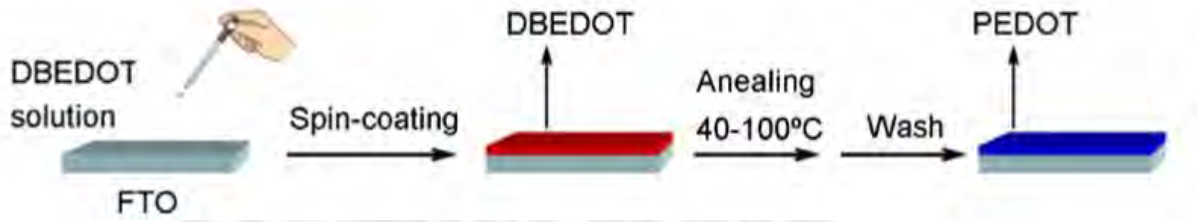


Figure 1.8 The preparation of poly(3,4-ethylenedioxythiophene) counter electrode under solid state polymerization.

Guo and coworkers [21] have successfully coupled molecularly imprinted polymers (MIPs) with electrochemical sensor based on gold nanoparticles (AuNPs), to form a microporous-metal-organic film (MMOF), in order to improve selectivity. The MMOF was deposited on a gold electrode by electropolymerization of p-aminothiophenol (PATP) functionalized-AuNPs in the presence of TNT as a template (Figure 1.9) [22]. This sensor provided a minimal detection limit of TNT that equals to 0.04 fM which was obtained from a calibration curve of TNT, within the range of 4.4 fM – 44 nM. To conclude, the MIP-hybrid sensor has provided many advantages such as highly sensitive, inexpensive and facile for onsite detection of TNT.

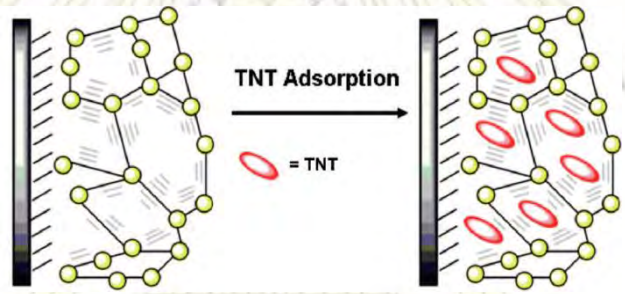


Figure 1.9 Illustration of microporous metal organic sensor and TNT as template.

In conclusion, the molecular imprinting technology can be applied to create recognition sites that determined selectivity properties. The molecularly imprinted polymers are obtained through polymerization in the presence of a template molecule. The solid-state polymerization could also result in another stable polymer structures without adding any catalysts. Therefore, highly specific cavities are generated in the polymeric matrix. After the extraction of target molecules, molecularly imprinted polymers display interesting recognition properties towards the template, originating from a shape and chemical functionality considerations in the cavities present in the polymer matrix. Hence, the objective of high specificity together with high sensitivity can be realized by combining the concept of molecularly imprinted polymers with the use of conducting polymers.

1.9 Objectives

The objectives of this research are to employ the solid-state polymerization of 2,5-dibromo-3,4-ethylenedioxythiophene (DBEDOT) monomers surrounding selected template molecules, to provide imprinted poly(3,4-ethylenedioxythiophene) (PEDOT). The resulting molecular imprinted conjugated PEDOT would consist of cavities that have selectivity and specificity towards the template molecules, in which the binding property of the imprinted polymer can be monitored by the altered concentration of the template solution in comparison to the non-imprinted polymers.

Chapter II

Experiments

2.1) Chemicals

Thin layer chromatography (TLC) was performed on aluminum sheets precoated with silica gel (Merck Kieselgel 60 F_{254}, Merck KGaA, Darmstadt, Germany). Column chromatography was performed using 0.063-0.200 mm or 70-230 mesh ASTM silica gel 60 (Merck Kieselgel 60 G, Merck KGaA, Darmstadt, Germany). Solvents employed in synthesis were reagent or analytical grades. Solvents used in column chromatography were distilled from commercial grade prior to use. Other reagents were purchased from the following venders:

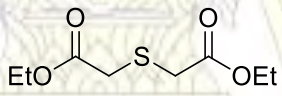
- RCI labscan (Bangkok, Thailand): acetone, dichloromethane, chloroform
- Acrös Organics (New Jersey, USA): N-bromosuccinimide (NBS)
- Fluka Chemical (Buchs, Switzerland): sodium metal
- Merck Co. (Darmstadt, Germany): sodium hydroxide (NaOH), concentrated hydrochloric acid, diethyl ether (Et_2O), ethanol absolute (EtOH)
- Ajax Finechem Pty (Auckland, New Zealand): calcium chloride
- Cambridge Isotope Laboratories (USA): deuterated chloroform ($CDCl_3$)
- Aldrich (USA): diethyl oxalate $(CO_2Et)_2$, 3,4-ethylenedioxythiophene (EDOT), anhydrous magnesium sulfate ($MgSO_4$)

2.2) Instruments and Equipment

The ^{1}H and ^{13}C NMR spectra were obtained from samples dissolved in deuterated chloroform ($CDCl_3$) measured with Varian Mercury NMR spectrometer operated at 400.00 MHz for ^{1}H and 100.00 MHz for ^{13}C nuclei (Varian Company, USA). Samples, weighed by PB403-S Mettler Toledo, were dissolved in EtOAc, MeOH, acetone or water to record their UV-Vis absorption spectra using Agilent 8453E UV-Visible spectrometer. The FT-IR spectra were recorded on a Nicolet 6700 FT-IR spectrometer. Melting points were determined with a Stuart Scientific Melting Point SMP10 (Bibby Sterlin Ltd., Staffordshire, UK).

2.3) Monomer Synthesis

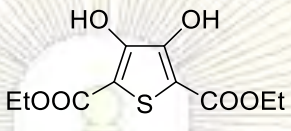
2.3.1) Diethyl thiodiglycolate (1)



(1)

A solution of sodium sulfide nonahydrate ($Na_2S.9H_2O$, 12.0 g, 50 mmol) in water (30 ml) was added dropwise to the solution of ethyl chloroacetate (13.24 g, 55 mmol) in acetone (50 mL). Then the reaction was refluxed under nitrogen atmosphere for approximately 3 h. The cooled reaction mixture was extracted by diethyl ether three times. The separated organic layer was dried over anhydrous $MgSO_4$ and was evaporated by a rotary evaporator to give compound (1) as a yellow liquid (8.549 g, 64%) ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 4.19 (q, J = 7.1 Hz, 4H), 3.37 (s, 4H), 1.28 (t, J = 7.2 Hz, 6H) (Figure A.1, Appendix A). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 169.5, 61.1, 33.3, 13.9 (Figure A.2, Appendix A).

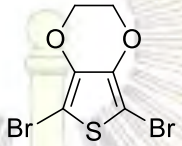
2.3.2) Diethyl 3,4-dihydroxythiophene-2,5-dicarboxylate (2)



(2)

Sodium metal (2.4 g, 0.21 mol) was dissolved in ethanol (75 mL). Subsequently, this solution was added dropwise to a mixture of compound (1) (2 g, 0.010 mol) and diethyl oxalate (4.5 g, 0.03 mol) for 30 mins in an ice bath. Then the reaction was refluxed (70-80 ^{o}C) under nitrogen atmosphere for additional 2 h and 30 mins. After the refluxed process, the reaction was cooled to room temperature, poured distilled water (400 mL) to dissolve the remaining residues, and acidified by concentrated hydrochloric acid (10 mL) to obtain a yellow precipitate. The filtered solid was recrystallized from methanol, resulted in white needle crystals of compound (2) (1.242 g, 61%), m.p. 134-135 ^{o}C, ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 9.36 (s, 2H), 4.39 (q, J = 7.1 Hz, 4H), 1.38 (t, J = 7.1 Hz, 6H) (Figure A.3, Appendix A). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 165.5, 151.6, 107.1, 61.7, 14.0 (Figure A.4, Appendix A). IR (ATR, cm^{-1}): 3305 (-OH st), 2981 (-CH st), 1690 (C=O st), 1663 (C=C st) (Figure A.5, Appendix A).

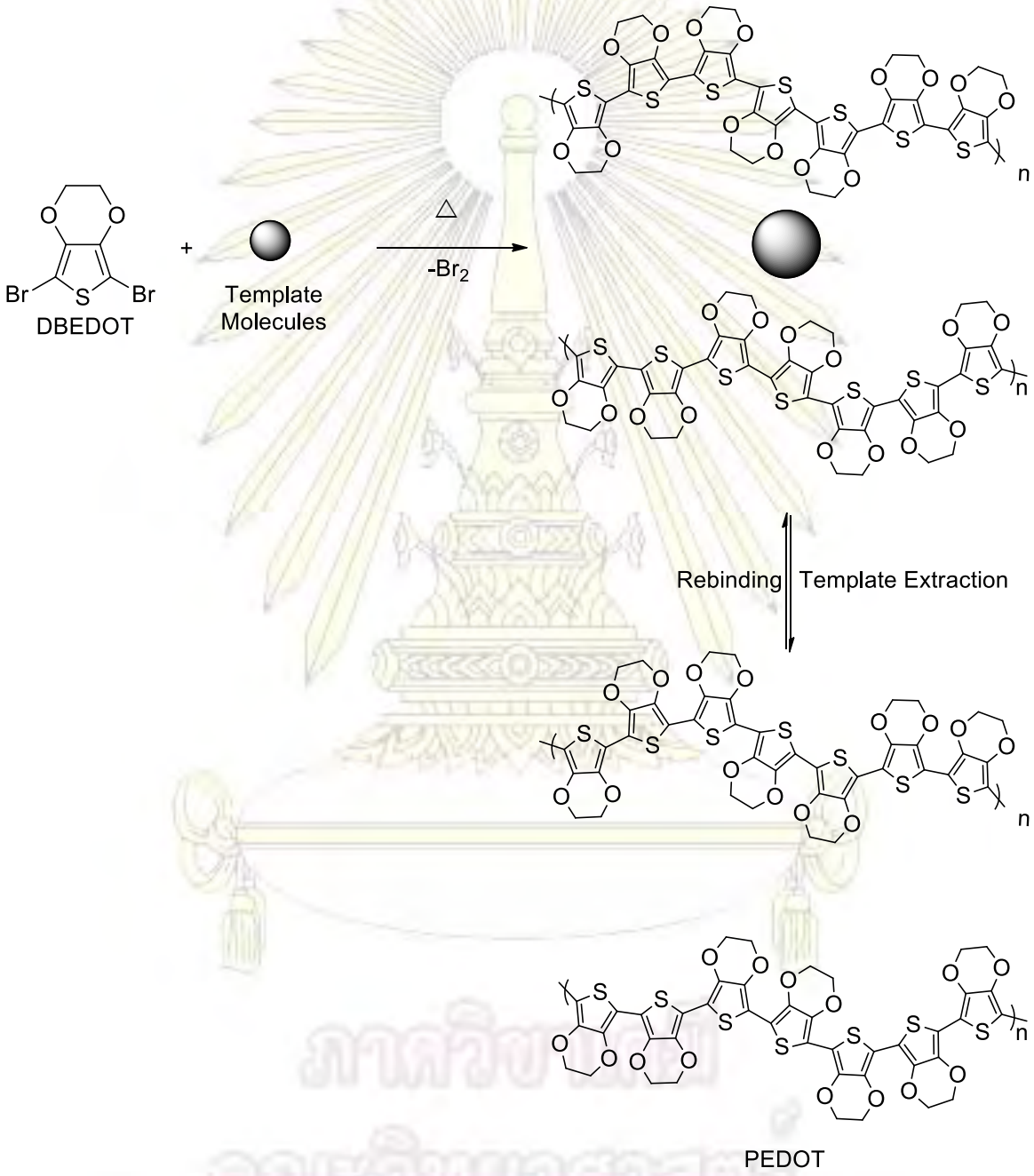
2.3.3) 2,5-Dibromo-3,4-ethylenedioxythiophene (3)



(3)

3,4–Ethylenedioxythiophene (EDOT) (0.142 g, 1.0 mmol) was combined with both N-bromosuccinamide (NBS) (0.4450 g, 2.5 mmol) and chloroform (10 mL), and stirred for 1-2 min. Subsequently, the crude mixture was quenched with saturated Na_2CO_3 and NaOH (2M). Then it was purified by column chromatography, eluted with 3:2 mixture of hexane and ethyl acetate to get a pale yellow solid of compound (3) (0.290 g, 98%), m.p. 96-97 $^{\circ}$C, ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 4.27 (s, 4H) (Figure A.6, Appendix A). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 139.7, 85.5, 64.9 (Figure A.7, Appendix A). IR (ATR, cm^{-1}): 2923 (-CH st), 1505 (C=O st), 1080 (-C-O st) (Figure A.8, Appendix A).

2.4) Preparation of Molecularly Imprinted Polymers (MIPs)



Scheme 2.1 Imprinting template molecules through SSP process

1000 ppm (0.014 g, 0.101 mmol) of p-nitrophenol (PNP) was added to 10 mL ethyl acetate solution of compound (3) (0.108 g, 0.360 mmol). The rotary evaporator was used to remove the homogeneous mixture, resulting in a white solid substance. Subsequently, the obtained product was heated at 85°C for 72 h. During the heating process, the solid turned into dark blue with slight appearance of brown bromine vapor. After the heating, the resulting dark blue solid was allowed to cool to room temperature in a desiccator as the *p*-nitrophenol-imprinted polymers (PNP-MIPs). The process of preparing molecularly imprinted polymers was repeated with pyrene (0.013 g, 0.064 mmol). In order to compare the abilities of MIPs, non-imprinted polymers (NIPs) were prepared similar to MIPs in parallel, but in the absence of the template molecules.

After the polymerization process, both MIPs and NIPs samples were exhaustively extracted by soxhlet extraction with methanol (250 mL) for approximately 16 h or until no template molecules and leftover monomers were detected by TLC and UV-Vis spectroscopy. The template-vacant polymer samples were kept dry in desiccator overnight.

2.5) Binding Experiments

Five exact concentrations of the template solutions were prepared and their UV-Visible absorptions were used to create a calibration curve (Appendix B). Then 50 mL of 1000 ppm of the template solution was added to each of the corresponding MIP and NIP samples. The mixtures of MIP and NIP were stirred at room temperature. Then at every hour, 20 μL from each aliquant was diluted to an appropriate concentration before being measured the absorbance. The absorbance was monitored until the value reached the equilibrium and remained constant. The amount of binding capacities of the MIP was examined by extracting out the bound template molecules from the equilibrated MIP and NIP samples by repeating the soxhlet extraction with methanol for 8 h.

The amount of template molecules bound to the imprinted polymer (Q) was calculated by subtracting the amount of unbound substrate from its initial concentration. To compare the imprinting effect, the specific adsorption values, $\triangle Q = |Q_{MIPs} - Q_{NIPs}|$ where Q_{MIPs} and Q_{NIPs} are the amount of bound template molecules on the imprinted and non-imprinted polymers at equilibrium, respectively, were used. The average of triplicate independent experiments was employed for the analysis and discussion [23, 24].

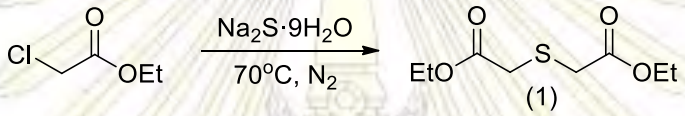
The binding process was monitored by UV-Vis spectroscopy, measuring at the λ_{max} at 306 nm and 273 nm for PNP and pyrene templates, respectively. Calibration curves of the templates were prepared and measured by plotting a graph between absorbance and concentrations of template solution (Figure B.1 for PNP and Figure B.2 for pyrene Appendix B); a linear relationship was obtained and employed for calculation of $\triangle Q$, Q_{MIPs}, and Q_{NIPs} values.

Chapter III

Results and Discussion

3.1) Monomer Synthesis

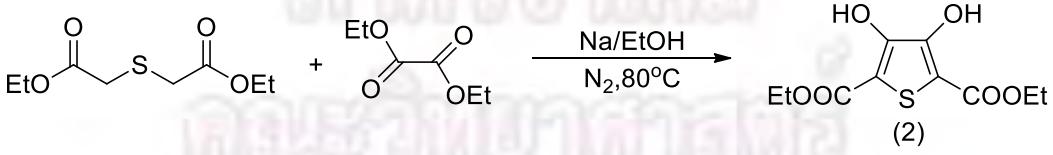
3.1.1) Diethyl Thioglycolate (1)



Scheme 3.1 Synthesis of diethyl thiodiglycolate.

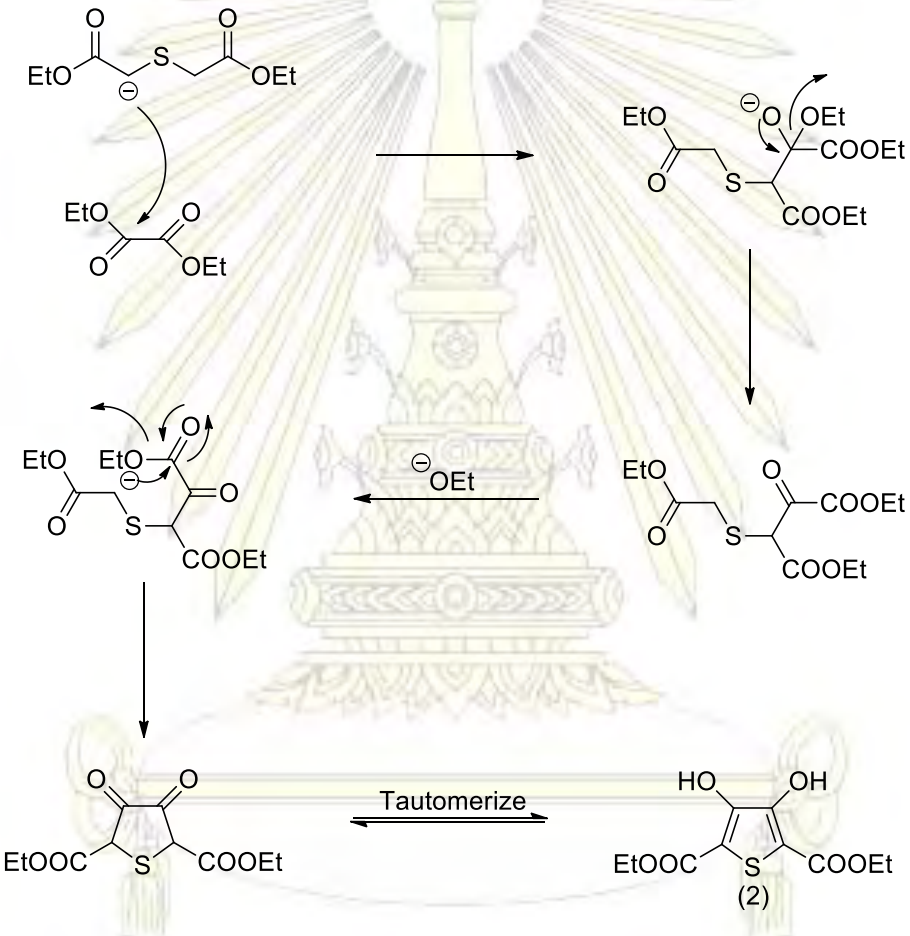
The solution of ethyl chloroacetate in acetone was treated by double S_N2 reaction with sodium sulfide, resulting in the formation of compound (1). The physical appearance of compound (1) was a yellow liquid and the yield was obtained at 64%. Additionally, the ^{1}H NMR spectrum exhibited methylene peak at 3.37 ppm, the quartet and triplet signals of the ethyl group at 4.19 and 1.28 ppm, respectively (Figure A.1, Appendix A). The ^{13}C NMR spectrum displayed a carbonyl carbon at 169.5 ppm (Figure A.2, Appendix A).

3.1.2) Diethyl 3,4-dihydroxythiophene-2,5-dicarboxylate (2)



Scheme 3.2 Synthesis of diethyl 3,4-dihydroxythiophene-2,5-dicarboxylate (2).

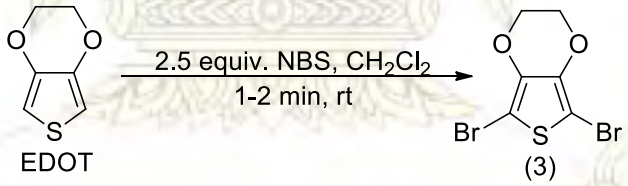
Hinsberg reaction [25], a condensation between compound (1) and diethyl oxalate under basic condensation, was employed to synthesize compound (2). The mechanism is the consecutive condensations of Claisen reactions to produce a diketone intermediate, which tautomerizes to the corresponding dihydroxythiophene (Scheme 3.3)



Scheme 3.3 Illustration of the mechanism of Hinsberg reaction.

The physical appearance of the obtained compound (2) was white needle crystals with 61% yield after recrystallization in methanol. The ^{1}H NMR displayed a broad singlet –OH peak at 9.36 ppm (Figure A.3, Appendix A). The ^{13}C NMR spectrum showed a peak of the carbonyl carbon at 165.5 ppm, and the two carbons of the thiophene ring appeared at 107.1 and 151.6 ppm (Figure A.4, Appendix A). Additionally, the IR spectrum exhibited a significantly strong broad –OH stretching at 3305 cm^{-1}, and the aromatic double bond region at 1690 and 1663 cm^{-1} (Figure A.5, Appendix A). This intermediate (2) was originally planned to be used in a subsequent 3-step synthesis of 3,4-ethylenedioxythiophene (EDOT). However, due to the time limit, the planned synthesis has never been carried out. Instead, the commercially available EDOT was used for further reactions and preparations of the derived polymers in the rest of this work.

3.1.3) Brominations of Thiophene Derivatives



Scheme 3.4 Synthesis of 2,5-dibromo-3,4-ethylenedioxythiophene (3)

Commonly, the α-positions of thiophene ring are reactive towards electrophiles or radicals, particularly the electron-rich thiophenes. 3,4–ethylenedioxythiophene (EDOT) was brominated at room temperature employing N-bromosuccinimide (NBS), resulting in the formation of compound (3), which required only 1-2 min in accordance with the Scheme 3.4.

Furthermore, treating NBS in a halogenated solvent (CH_2Cl_2) at room temperature and ambient atmosphere provided the most promising yields of bromination at 98%. The extended time of this reaction was found to result in degrading of the product and lower yields were obtained [26].

The product was characterized by ^{1}H NMR spectrum with the absence of the signal at $\delta\sim$6.32 ppm which corresponds to the α-hydrogen signal used to be other characterizations matched well with those of previous report [26] on the thiophene ring before the bromination reaction (Figure A.6, Appendix A).

3.2 Preparation of Molecularly Imprinted Polymers (MIPs)

Solid state polymerization (SSP) approach provided readily-doped poly(3,4-ethylenedioxythiophene) (PEDOT), a solid substance with a dark blue color, from heating of the corresponding dibromo derivatives of EDOT. The resulted PEDOT, an insoluble polymer, became an ideal framework for molecular imprinting. Subsequently, suitable template molecules were encapsulated within the recognition sites and formed specific cavities that were proper to the trapped templates during the SSP approach. After the binding process, the template molecules were extracted by exhaustive soxhlet extraction with methanol, resulting in an imprinted polymer with supposedly vacant specific cavities imprinted by the removed template. The SSP method was expected to stabilize the arrangement of the cavities in the polymeric matrices. Then the MIPs were dried and immersed again in template solution to test the rebinding process which was monitored by UV-Vis spectroscopy. Non-imprinted polymers (NIPs), which were repeated prepared following the preceding experiment without the template molecules, were employed in parallel experiment in comparison with MIPs. The amount of template molecules that were bound to the polymers provided the specific absorption values ($\triangle$Q), at various sampling times of MIPs and NIPs, which could be calculated to compare any differential imprinting effects between them.

3.2.1) P-nitrophenol-molecularly Imprinted Polymers (PNP-MIPs)

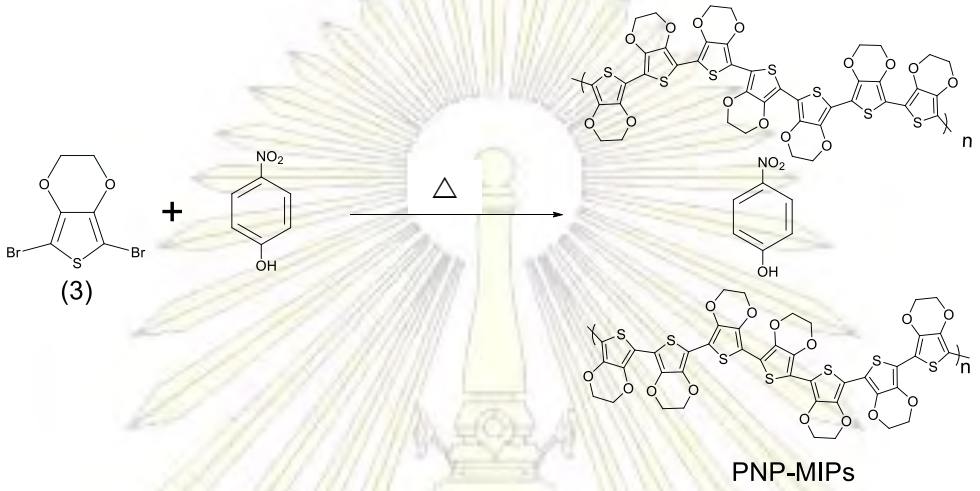


Figure 3.1 Synthesis of MIPs with PNP as a template molecule.

The binding process was carried out to investigate the imprinting effect, using PNP as template molecules. As shown in Figure 3.2, the concentration of PNP solution in ethyl acetate with MIPs constantly declined from the beginning and became stable from 6 h onward until the end of the experiment. In contrast, the concentration of PNP solution in ethyl acetate with NIPs remained relatively constant throughout the binding process with some fluctuations within a narrow range. The difference in concentrations of PNP between the two solutions after reaching equilibriums indicated the presence of differential absorption of PNP into the polymer potentially induced from the inherent imprinting property of MIP.

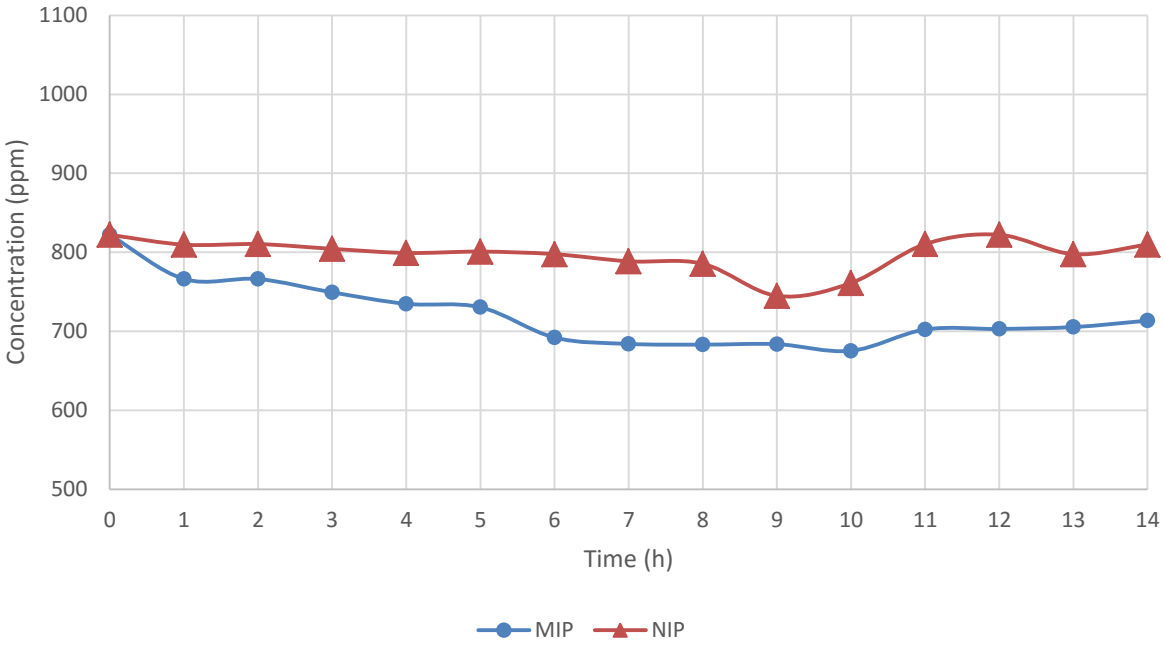


Figure 3.2 The concentrations of PNP solutions in ethyl acetate during binding process between PNP-MIPs and NIPs at various sampling times.

In order to obtain the quantitative imprinting effect, the specific adsorption values (△Q) were defined as:

$$\triangle Q = |Q_{MIPs} - Q_{NIPs}| \qquad (1)$$

$$Q\,(\mu mol/g) = \left(\frac{Ci - Ce}{W \times MW}\right) \times V \qquad (2)$$

Where C_i, the initially measured concentration, and C_e, the equilibrium concentration, can be acquired from the binding experiment. V (mL) is the volume of the solution and W (g) is the weight of the dried polymer, MIPs or NIPs, and MW stands for the molecular weight of the template molecules.

In accordance with the current experiment with PNP, the C_e value was taken from the average of those sampling values from 6 h to 14 h which were regarded as the equilibrium region for the PNP-MIPs binding experiment, which were the same region as NIPs. The calculation yielded the specific adsorption value (△Q) of PNP molecules bound to the MIPs to be 523.25 μmol/g, indicating that the specific recognition sites were formed. Noted that the higher the specific adsorption value, the better the imprinting process.

MIPs

The weight of dried PNP-MIPs was 0.108 g.

From equation (2); Q_{MIPs} (μmol/g) $= \left(\frac{Ci-Ce}{W \times MW}\right) \times V$

$$= \left(\frac{822.10-693.57}{0.108 \times 139.11}\right) \times 50\ mL$$

= 427.76 μmol/g

NIPs

The weight of dried NIPs was 0.106 g.

$$= \left(\frac{822.10-784.63}{0.106 \times 139.11}\right) \times 50\ mL$$

= 127.05 μmol/g

From equation (1); $\triangle Q = |Q_{MIPs} - Q_{NIPs}|$

= 427.76 – 127.05

= 300.71 μmol/g

The attractive interactions between the template molecules (PNP), and the polymers, are strong enough to create such specific cavities. The rigid polymeric structure could also be maintained throughout the extraction process and remain effective for the binding of template. In other words, the template molecules were successfully imprinted into the polymeric structure of MIPs derived from SSP-PEDOT comparing to the non-specific background binding of NIPs.

3.2.2) Pyrene-molecularly Imprinted Polymers (Pyrene-MIPs)

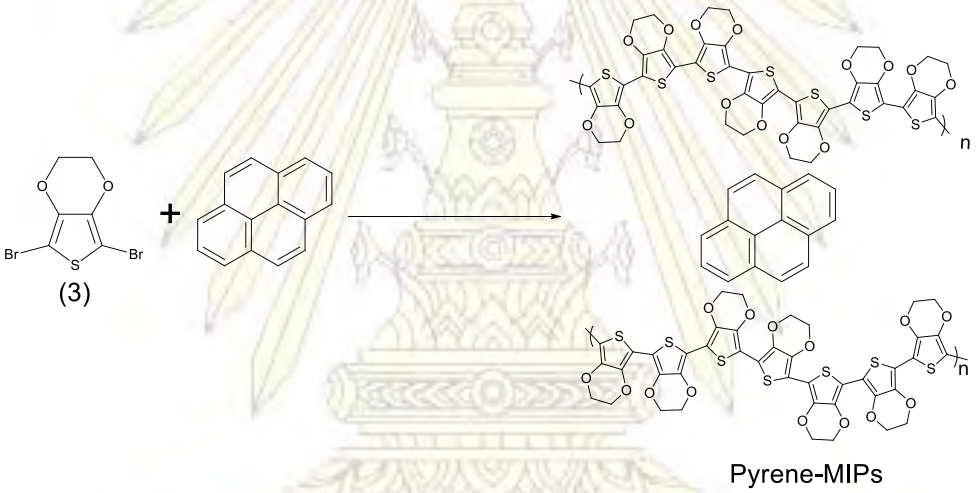


Figure 3.3 Synthesis of MIPs with pyrene as a template molecule.

The binding process was similarly performed as the preceding 3.2.1 using pyrene as the template. The results for pyrene-MIPs were disappointedly not as pronounce as the previous one. The concentrations of pyrene in ethyl acetate for MIPs only slightly declined at the beginning and largely remained quite constant after 2 h. The NIPs were also steady with slightly increase in later samplings, perhaps due to handling errors from the evaporation of the solvent.

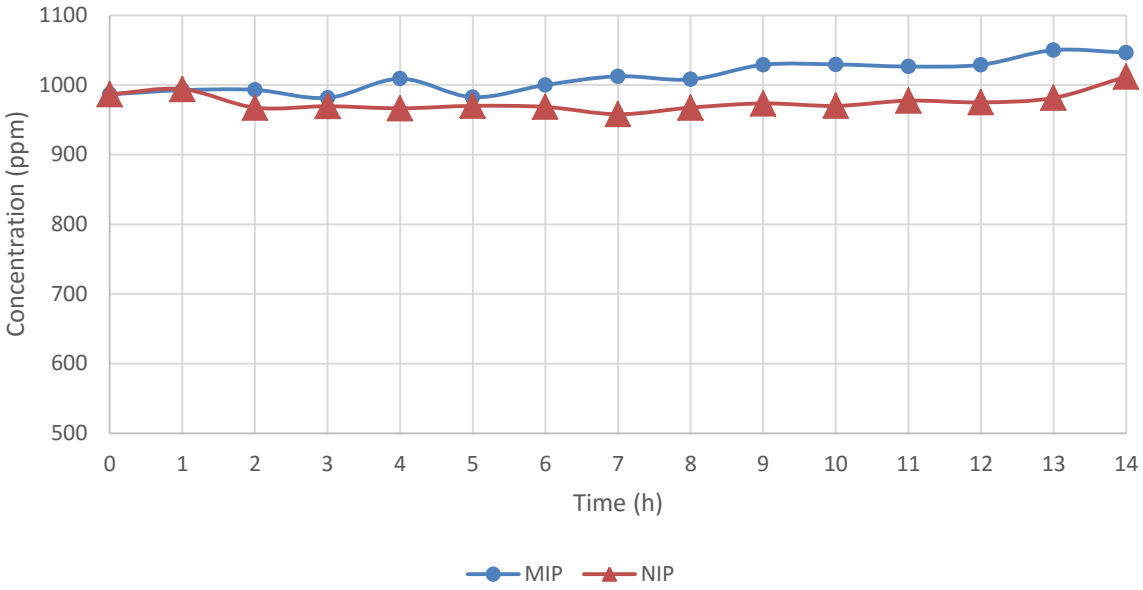


Figure 3.4 The concentrations of pyrene solutions in ethyl acetate during binding process between pyrene-MIPs and NIPs at various sampling times.

According to the current experiment with pyrene, the C_e value was taken from the average of those sampling values from 2 h to 8 h which were regarded as the equilibrium region for the pyrene-MIPs binding experiment, which were the same region as NIPs. The suspected data after 8 h were omitted. The calculation yielded the $\triangle Q$ value or the specific adsorption value of pyrene molecules bound to the MIPs to be 12.73 μmol/g, which is relatively low comparing to the preceding PNP binding experiment, suggesting that pyrene, which is relatively non-polar, poorly interacted with the polymer and did not well distributed. Thus, the cavities were not sufficiently created during the MIPs preparation. The merely van der Waals force among template molecules and the monomers was relatively weak compared to stronger polar interactions including hydrogen bonds associated with the previous PNP-MIP.

MIPs

The weight of dried pyrene-MIPs was 0.323 g.

From equation (2); Q_{MIPs} (μmol/g) = $\left(\frac{Ci-Ce}{W \times MW}\right) \times V$

$$= \left(\frac{959.70-952.18}{0.323 \times 202.25}\right) \times 50\ mL$$

= 5.75 μmol/g

NIPs

The weight of dried NIPs was 0.325 g.

$$= \left(\frac{959.70-935.41}{0.325 \times 202.25}\right) \times 50\ mL$$

= 18.48 μmol/g

From equation (1); $\triangle Q = |Q_{MIPs} - Q_{NIPs}|$

= 5.75 – 18.48

= 12.73 μmol/g

An alternative route to determine the binding capacities of the MIPs was to estimate the percentage of specific adsorption values from the template extraction at the end of the binding experiment, compared to the initial amount of the template used to prepare the MIPs.

❖ The calculation of binding capacities of PNP-MIPs

The initial amount of *p*-nitrophenol (PNP) in ethyl acetate solution used to prepare MIPs before the binding experiment was 822.10 ppm.

The amount of *p*-nitrophenol in ethyl acetate solution obtained from exhaustive extraction with methanol at the end of the binding process was 603.75 ppm.

The binding capacities of PNP-MIPs $= \left(\frac{603.75}{822.10}\right) \times 100$

$= 73.44\ \%$

❖ The calculation of binding capacities of pyrene-MIPs

The initial amount of pyrene in ethyl acetate solution used to prepare MIPs before the binding experiment was 959.70 ppm.

The amount of pyrene in ethyl acetate solution obtained from exhaustive extraction with methanol at the end of the binding process was 83.27 ppm.

Therefore, The binding capacities of pyrene-MIPs $= \left(\frac{83.27}{959.70}\right) \times 100$

$= 8.68\ \%$

The calculated binding capacities of the MIPs were 73.44% for PNP and 8.68% for pyrene. This large difference well supports the preferential imprinting of polar template molecules as observed in the preceding $\triangle Q$ calculation. Other general factors that could attribute to a low percentage of these values could be from incomplete extraction of the bound template molecules from the inaccessible parts of the polymers; the excessive initial concentrations of the templates employed for preparing MIPs were perhaps much higher than the actual binding capacities; and solvent evaporation during samplings in order to monitor the binding process that leads to handling errors and fluctuations of data.

Chapter IV

Conclusion

Some precursors for monomer synthesis have been synthesized. Diethyl thioglycolate (1) was prepared from substitutions of ethyl chloroacetate with sodium sulfide (Na_2S) in 64% yield. Compound (1) was reacted with diethyl oxalate through Hinsberg reaction, resulting in the formation of diethyl 3,4-dihydroxythiophene-2,5-dicarboxylate (2) in 61% yield. Unfortunately due to time limit, the subsequent synthesis from this route was discontinued. Instead, the commercially available EDOT was brominated with N-bromosuccinamide to provide the desired 2,5-dibromo-3,4-ethylenedioxythiophene (3) in superb yield of 98%.

The facile solid state polymerization (SSP) processes of monomer (3) surrounding the template molecules, PNP or pyrene, to obtain unprecedented imprinted PEDOTs have been achieved. After template removals, the binding experiments of these MIPs monitored by UV-Vis spectroscopy were accomplished by attempted these rebinding of template molecules. The results exhibited that the specific adsorption values ($\triangle Q$) that reflect the imprinting effect for PNP-MIPs and pyrene-MIPs were 300.71 μmol/g and -12.73 μmol/g, respectively comparing to NIPs. After another soxhlet extractions, the rebinding capacities of the PNP-MIPs and pyrene-MIPs were calculated to be 73.44% and 8.68%, respectively. The results indicated that PEDOT prepared by SSP could be imprinted and recognized its template molecules with high capacity for the relatively polar template PNP, which exhibited more promising sensitivity and specificity in template detection than MIPs of non-polar pyrene. These results suggested that SSP-PEDOT could be developed further into specific sensors for given template molecules.

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APPENDICES

Appendix A

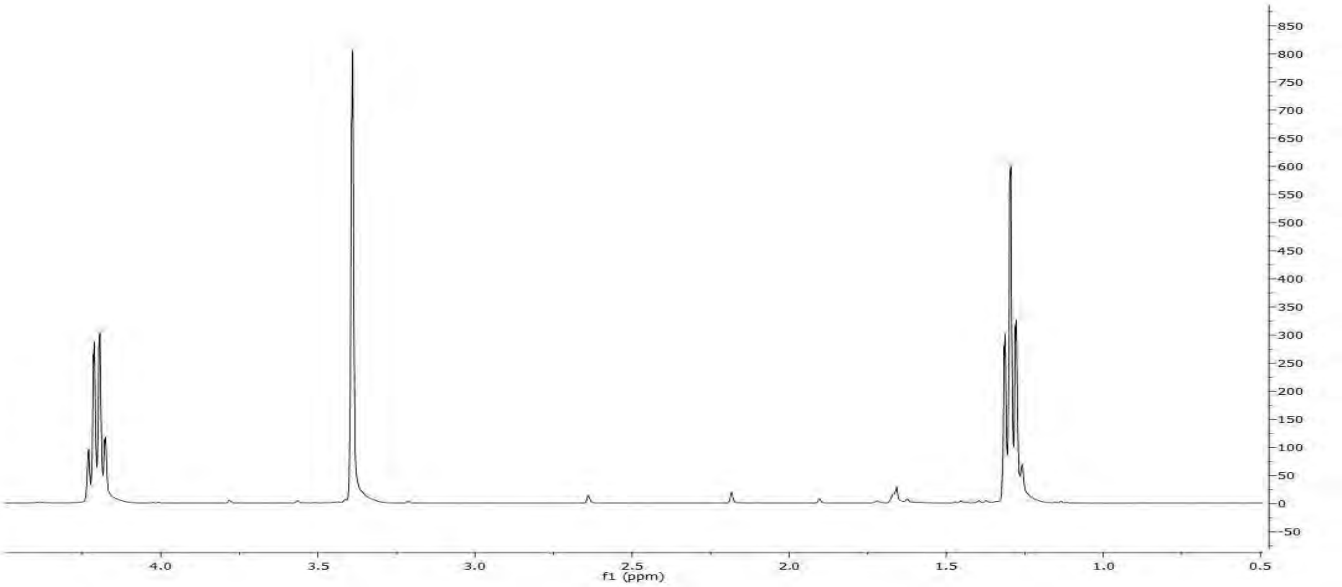

Figure A.1 ^{1}H NMR ($CDCl_3$) spectrum of compound 1

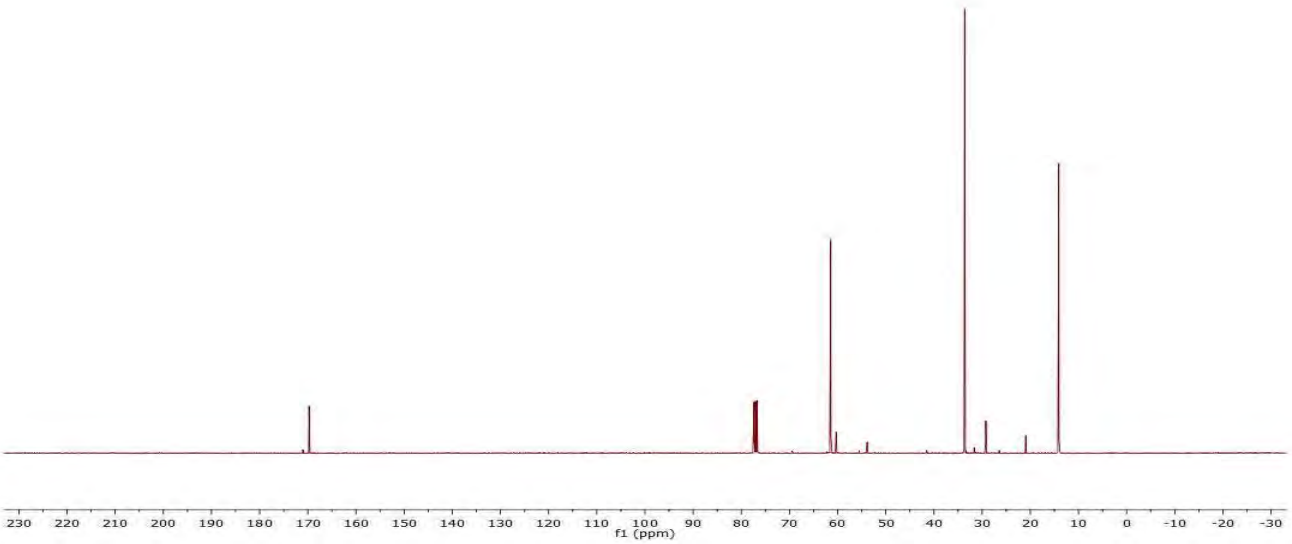

Figure A.2 ^{13}C NMR ($CDCl_3$) spectrum of compound 1

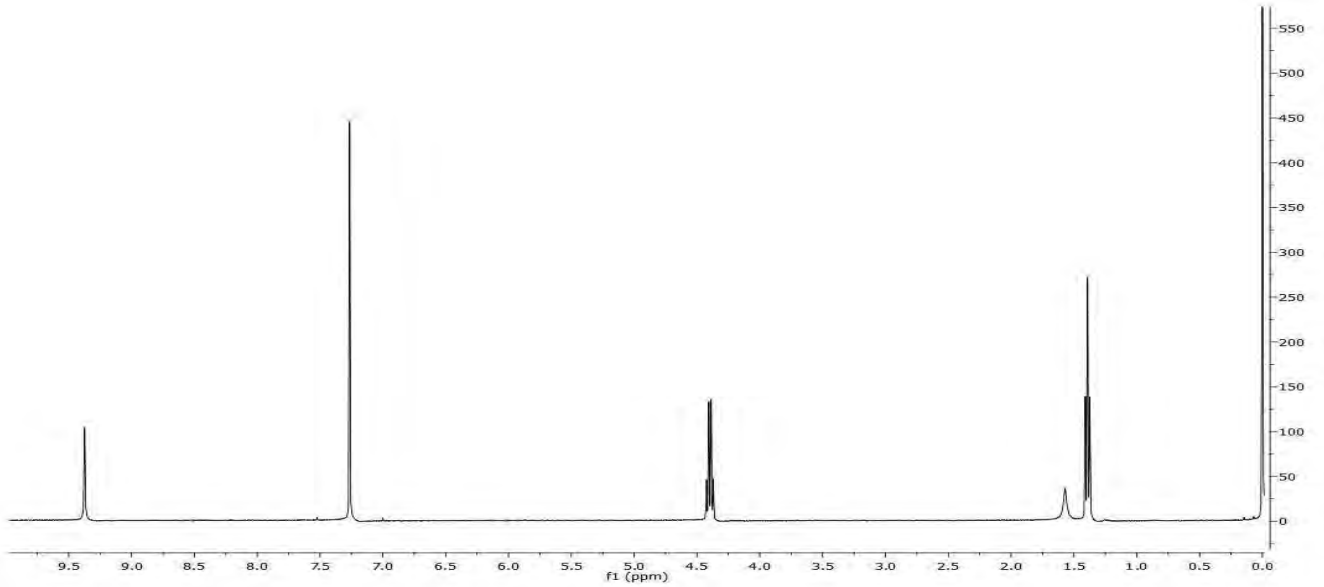

Figure A.3 ^{1}H NMR ($CDCl_3$) spectrum of compound 2

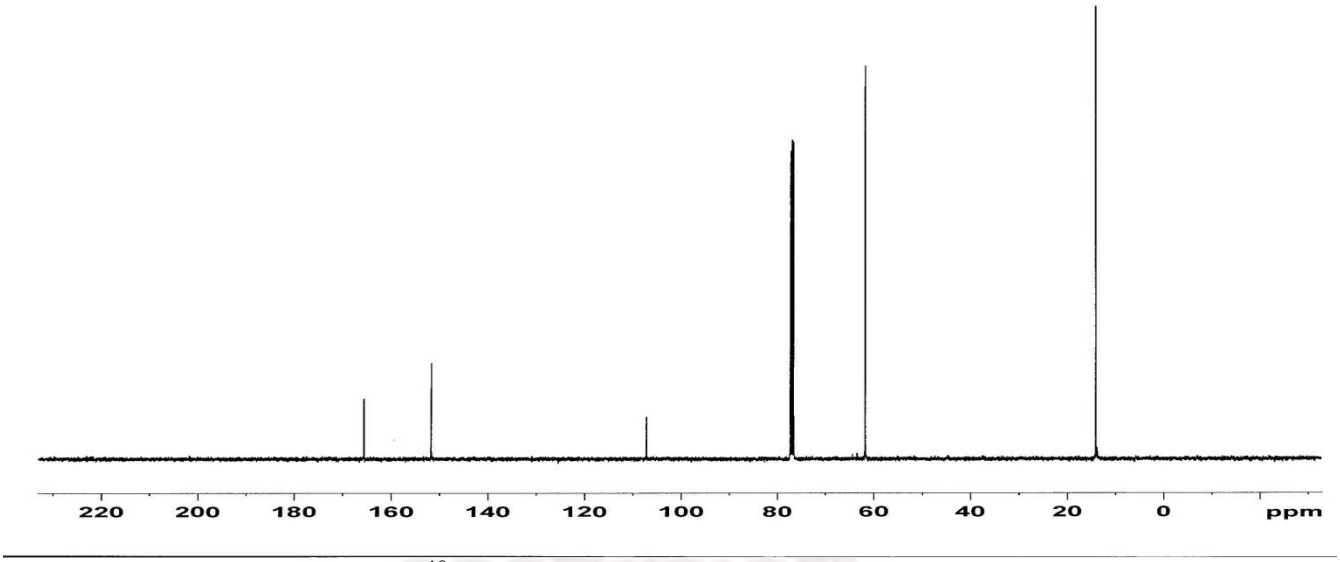

Figure A.4 ^{13}C NMR ($CDCl_3$) spectrum of compound 2

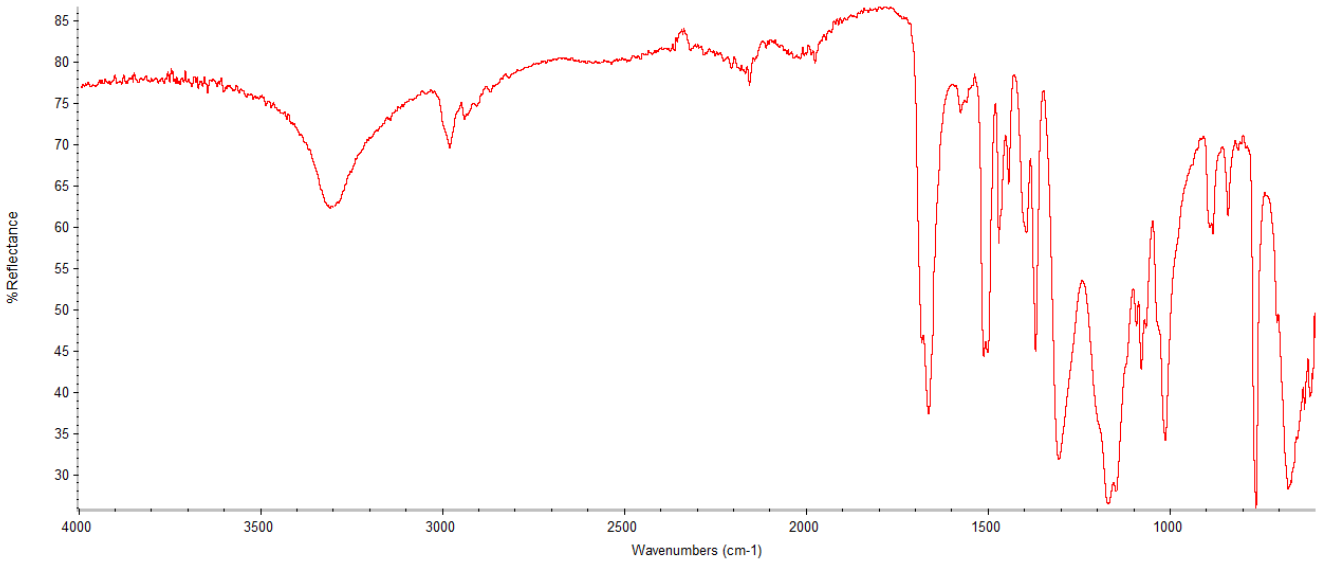

Figure A.5 IR spectrum of compound 2

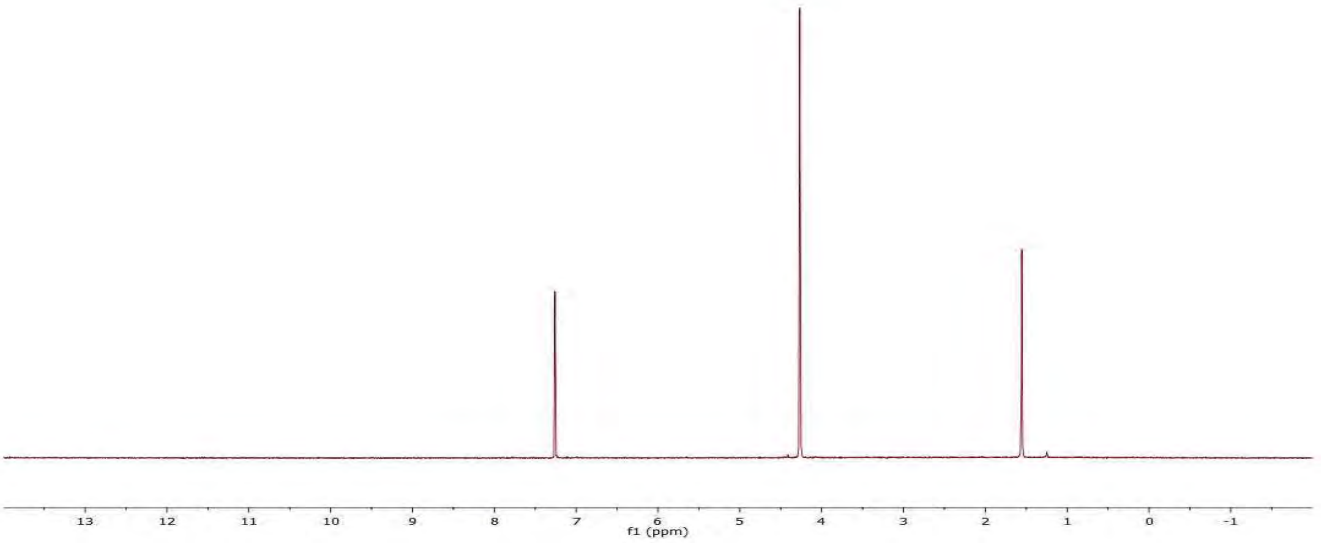

Figure A.6 ^{1}H NMR ($CDCl_3$) spectrum of compound 3

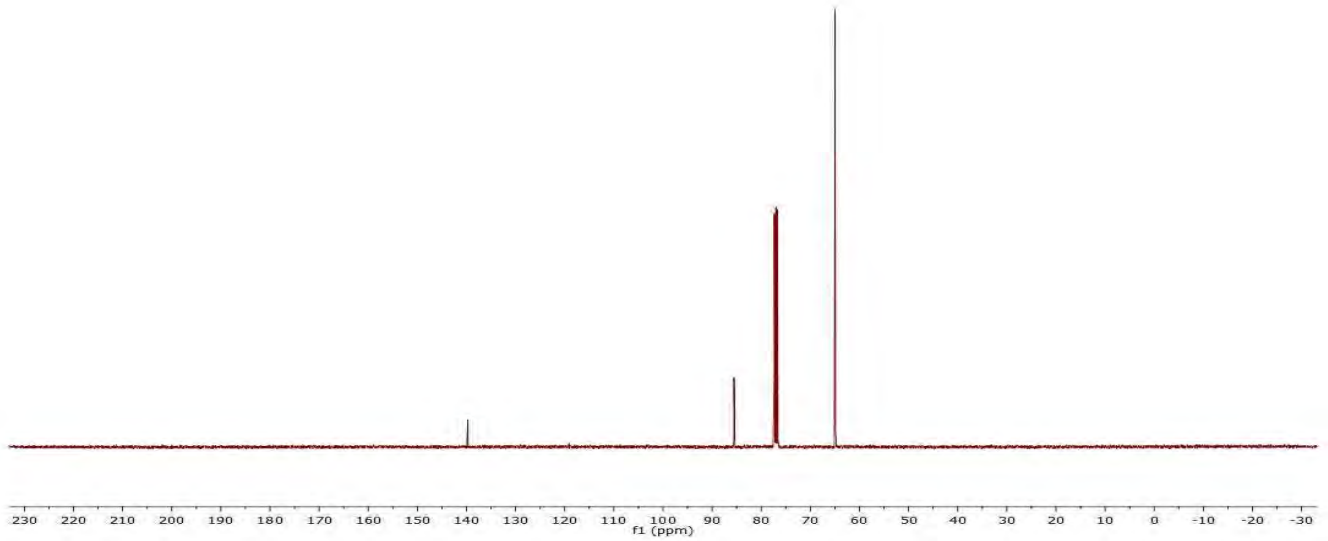

Figure A.7 ^{13}C NMR ($CDCl_3$) spectrum of compound 3

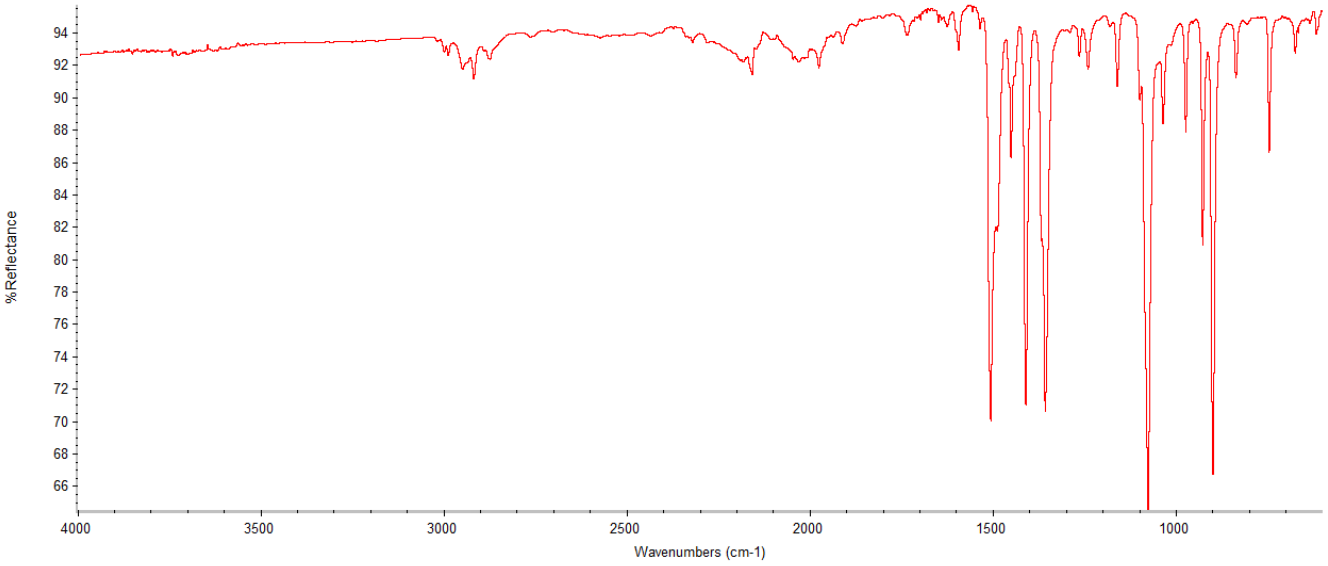

Figure A.8 IR spectrum of compound 3

Appendix B

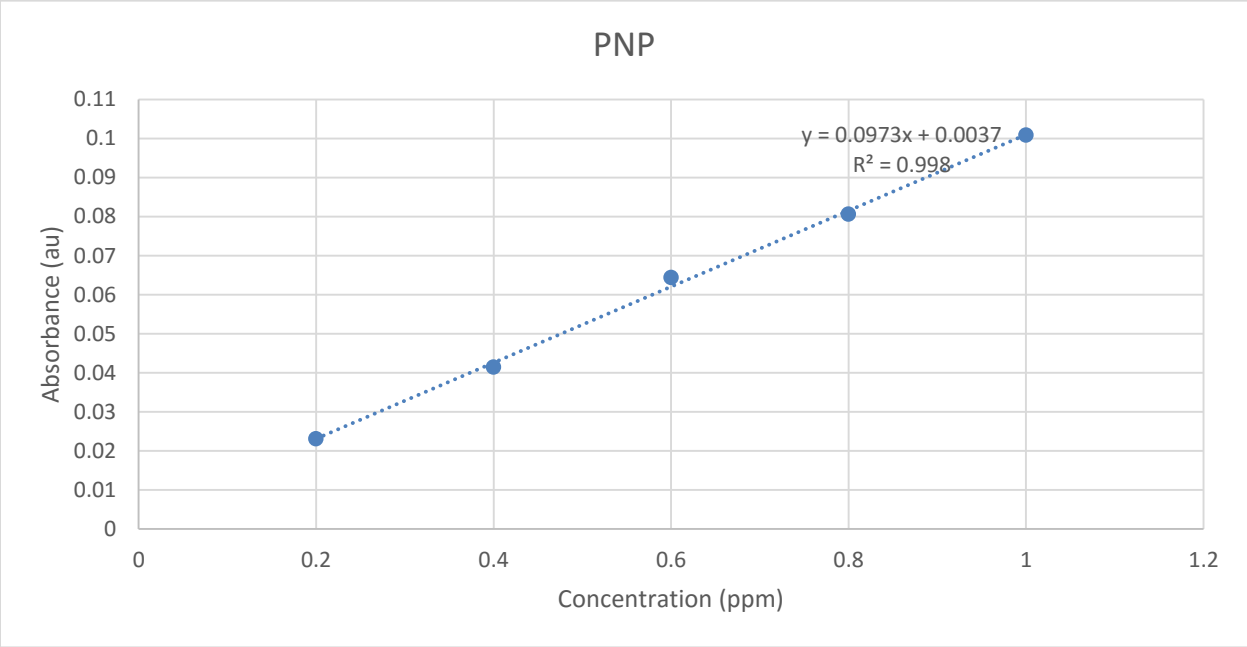

Figure B.1 Calibration curve of *p*-nitrophenol (PNP) in ethyl acetate

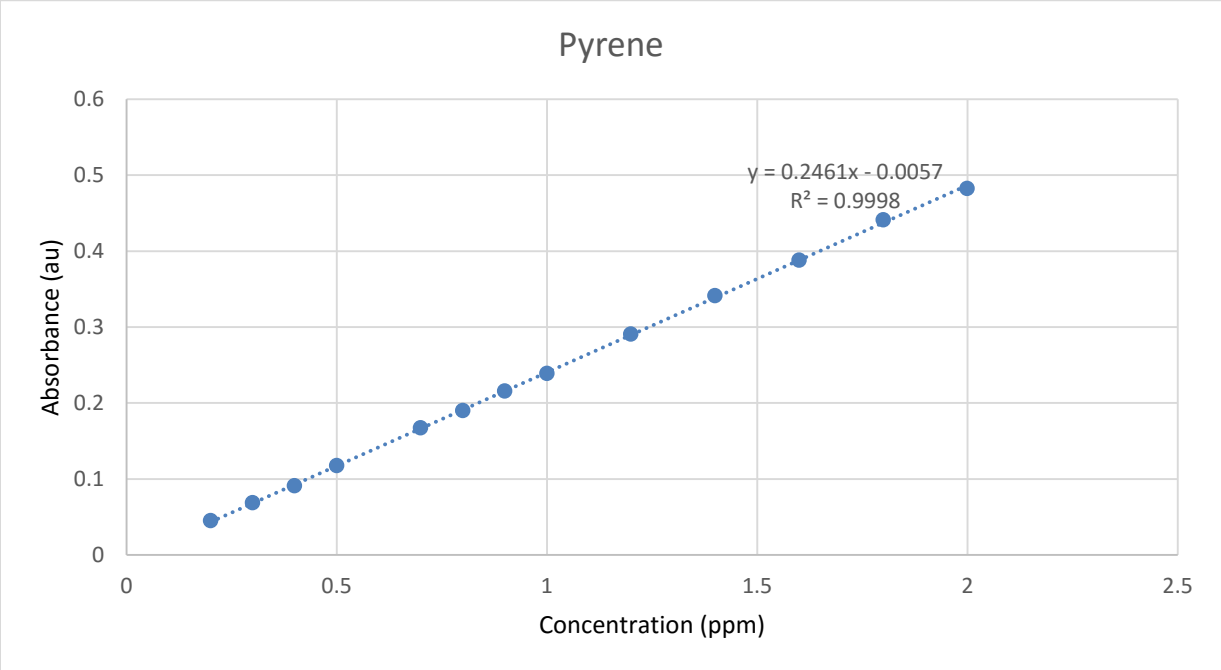

Figure B.2 Calibration curve of pyrene in ethyl acetate

Curriculum Vitae

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