การสังเคราะห์อนุพันธ์แอริลอีไทน์ที่มีหมู่ไตรโพดัลแอมีนและการประยุกต์ในอิเล็กโทรดเมมเบรน
ที่คาดว่าจำเพาะต่อคอปเปอร์(II) และแคดเมียม(II) ไอออน

นายวีระพล ศรีโนนม่วง

วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาวิทยาศาสตรมหาบัณฑิต
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ปีการศึกษา 2558
ลิขสิทธิ์ของจุฬาลงกรณ์มหาวิทยาลัย

SYNTHESIS OF ARYL ETHYNE DERIVATIVES CONTAINING TRIPODAL
AMINE GROUPS AND APPLICATION IN PROSPECTIVE COPPER(II) AND
CADMIUM(II) ION SELECTIVE MEMBRANE ELECTRODES

Mr. Weerapol Srinonmuang
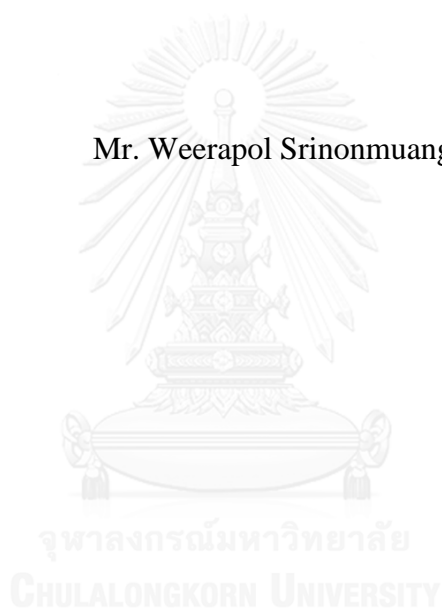
A Thesis Submitted in Partial Fulfillment of the Requirements
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Department of Chemistry
Faculty of Science
Chulalongkorn University
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Thesis Title	SYNTHESIS OF ARYL ETHYNE DERIVATIVES CONTAINING TRIPODAL AMINE GROUPS AND APPLICATION IN PROSPECTIVE COPPER(II) AND CADMIUM(II) ION SELECTIVE MEMBRANE ELECTRODES
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วีระพล ศรีโนนม่วง : การสังเคราะห์อนุพันธ์แอริลอีไทน์ที่มีหมู่ไตรโพดัลแอมีนและการประยุกต์ใน
อิเล็กโทรดเมมเบรนที่คาดว่าจำเพาะต่อคอปเปอร์(II) และแคดเมียม(II) ไอออน (SYNTHESIS OF
ARYL ETHYNE DERIVATIVES CONTAINING TRIPODAL AMINE GROUPS AND
APPLICATION IN PROSPECTIVE COPPER(II) AND CADMIUM(II) ION SELECTIVE
MEMBRANE ELECTRODES) อ.ที่ปรึกษาวิทยานิพนธ์หลัก: ศ. ดร. ธวัชชัย ตันฑุลานิ, 73 หน้า.

พีวีซีเมมเบรนสำหรับอิเล็กโทรดแบบเลือกจำเพาะต่อแคดเมียมไอออน (Cd-ISEs) เตรียมได้จากไอโอ
โนฟอร์ที่ต่างชนิดกัน ไอโอโนฟอร์ I และ II สังเคราะห์จากอนุพันธ์เอริลอีไทน์เป็นโครงสร้างฐาน ผลการ
สังเคราะห์ได้ไอโอโนฟอร์ I และ II คิดเป็นร้อยละของผลิตภัณฑ์ 11 และ 40 ตามลำดับ ในส่วนของไอโอโน
ฟอร์ III มีคาลิกซ์[4]เอรีนเป็นโครงสร้างฐาน ไอโอโนฟอร์ทั้งสามชนิดได้ยึดติดกับหมู่ไตรโพดัลแอมีน:ซึ่งเป็น
ดอนเนอร์อะตอมสำหรับไอออนโลหะโดยเฉพาะอย่างยิ่งแคดเมียมไอออน ไอโอโนฟอร์ II และ III สามารถใช้
เป็นตัวพาไอออนได้อย่างมีประสิทธิภาพในเมมเบรนอิเล็กโทรดสำหรับไอออนโลหะ ในขณะที่ไอโอโนฟอร์ I
ไม่สามารถใช้ได้เนื่องจากการสลายตัว ได้ทำศึกษาองค์ประกอบที่เหมาะสมของเมมเบรนที่ประกอบไปด้วยไอโอ
โนฟอร์ II และ III สำหรับตรวจวัดแคดเมียมไอออน โดยใช้ความเข้มข้นของไอโอโนฟอร์คงที่และได้
ปรับเปลี่ยนปริมาณของไอออนิกแอดดิทีฟและพลาสติไซเซอร์ ซึ่งองค์ประกอบที่เหมาะสมของเมมเบรนจะศึกษา
ในเชิงของการตอบสนองทางโพเทนชิโอเมทริก การผันกลับได้ ความไวและความเลือกจำเพาะต่อแคดเมียม
ไอออนและขีดจำกัดในการตรวจวัดของอิเล็กโทรด ลักษณะที่ดีที่สุดของอิเล็กโทรดแบบเลือกจำเพาะต่อแคดเมียม
ไอออนเตรียมได้จาก 10 มิลลิโมลต่อกิโลกรัมของไอโอโนฟอร์ II และ III และไอออนิกแอดดิทีฟ KTpClPB
(75 เปอร์เซ็นต์โดยโมลสัมพันธ์กับปริมาณไอโอโนฟอร์) ร่วมกับ o-NPOE พลาสติไซเซอร์พีวีซีเมมเบรน (พีวีซี:
o-NPOE เป็น 1:2 โดยมวล) โดยเมมเบรนที่ประกอบไปด้วยไอโอโนฟอร์ II และ III ในอัตราส่วนดังกล่าวแสดง
การตอบสนองต่อแคดเมียมไอออนแบบเนินสต์ที่ช่วงความเข้มข้น 10^{-5} - 10^{-2} โมลาร์ ซึ่งได้ความชันเท่ากับ 26.6
± 0.2 และ 30.7 ± 0.1 มิลลิโวลต์ต่อดีเคด ตามลำดับ โดยทั้งสองอิเล็กโทรดที่ประกอบด้วยไอโอโนฟอร์ II และ
III แสดงเวลาการตอบสนองอย่างรวดเร็วน้อยกว่า 5 วินาที และขีดจำกัดในการตรวจวัดของสองอิเล็กโทรด คือ
$4.75x10^{-6}$ และ $3.95x10^{-6}$ โมลาร์ ตามลำดับ อิเล็กโทรดที่เตรียมขึ้นแสดงความเลือกจำเพาะต่อแคดเมียมไอออน
ได้มากกว่าไอออนโลหะตัวอื่นๆ รวมถึงโลหะแอลคาไล โลหะแอลคาไลน์เอิร์ทและโลหะทรานซิชัน อย่างไรก็
ตามพบว่า Fe^{3+} Cr^{3+} Pb^{2+} เป็นไอออนรบกวนอย่างมากสำหรับไอโอโนฟอร์ II ในขณะที่ Fe^{3+} และ Zn^{2+} เป็น
ไอออนรบกวนที่สำคัญสำหรับไอโอโนฟอร์ III อิเล็กโทรดที่เตรียมขึ้นดังกล่าวสามารถตรวจวัดแคดเมียมไอออน
ได้ในช่วงพีเอช 4.5-6.0 และแสดงการผันกลับได้อย่างเป็นที่น่าพอใจ

ภาควิชา   เคมี   ลายมือชื่อนิสิต _____

สาขาวิชา   เคมี   ลายมือชื่อ อ.ที่ปรึกษาหลัก _____

ปีการศึกษา 2558

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KEYWORDS: ARYL ETHYNE / CALIX[4]ARENE / TRIPODAL AMINE / IONOPHORE / ION SELECTIVE ELECTRODE

WEERAPOL SRINONMUANG: SYNTHESIS OF ARYL ETHYNE DERIVATIVES CONTAINING TRIPODAL AMINE GROUPS AND APPLICATION IN PROSPECTIVE COPPER(II) AND CADMIUM(II) ION SELECTIVE MEMBRANE ELECTRODES. ADVISOR: PROF. THAWATCHAI TUNTULANI, Ph.D., 73 pp.

PVC membranes for cadmium ion selective electrodes (Cd-ISEs) have been prepared from different types of ionophores. Ionophores I and II obtained from aryl ethyne derivatives as building block have been designed and synthesized in 11% and 40% yields, respectively. Ionophores III contains a calix[4]arene framework. Three ionophores were attached to a number of tripodal amine groups as donor atoms for cation ions, especially cadmium ion. Ionophores II and III can be used as effective ion carriers in membrane electrodes for cations while ionophores I cannot be used due to its decomposition. Compositions of the membranes containing ionophores II and III are optimized by using a constant concentration of the ionophores and varying the amount of ionic additives and plasticizers. The optimized membrane compositions are studied in terms of potentiometric responses, reproducibility, sensitivity and selectivity toward Cd^{2+} and the detection limit of electrodes. The best characteristics of Cd-ISEs using ionophores II and III were obtained from membrane compositions having 10 mmol kg^{-1} of ionophores and ionic additive KTpClPB (75 mol% related to the ionophore) incorporating with o-NPOE plasticized PVC membrane (1:2; PVC: o-NPOE by weight). The membranes containing ionophores II and III exhibited a Nernstain response to Cd^{2+} over a working concentration range of 10^{-5}-10^{-2} M with a slope of 26.6 ± 0.2 and 30.7 ± 0.1 mV decade^{-1}, respectively. Electrodes containing II and III displayed fast response time in less than 5 seconds and the detection limits were 4.75×10^{-6} and 3.95×10^{-6} M, respectively. In addition, the prepared Cd-ISEs showed selectivity toward Cd^{2+} over other metal ions including of alkali alkaline earth and transition metals. Fe^{3+}, Cr^{3+} and Pb^{2+} were found to be strong interfering ions for ionophore II while Fe^{3+} and Zn^{2+} were main interfering ions for ionophore III. In addition, the prepared Cd-ISEs can be used to detect Cd^{2+} in the pH range 4.5-6.0 and gave satisfactory reversibility.

Department:	Chemistry	Student's Signature	....
Field of Study:	Chemistry	Advisor's Signature	....
Academic Year:	2015		

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^{13}C NMR	Carbon nuclear magnetic resonance
^{o}C	Degree Celsius
$Cd(NO_3)_2$	Cadmium nitrate
$CdCl_2$	Cadmium chloride
CH_2Cl_2	Dichloromethane
$CDCl_3$	Deuterated chloroform
CH_3CN	Acetonitrile
DOS	Bis(2-ethylhexyl) sebacate
d	Doublet (^1H NMR spectrum)
EMF	Electromotive force
g	Gram
^1H NMR	Proton nuclear magnetic resonance
h	Hour
HCl	Hydrochloric acid
HNO_3	Nitric acid
Hz	Hertz
ISE	Ion selective electrode
J	Coupling constant
K_2CO_3	Potassium carbonate
KF	Potassium iodide
KTpClPB	Potassium tetrakis(4-chlorophenyl) borate
$MgSO_4$	Magnesium sulfate

m	Multiplet (^{1}H NMR spectrum)
M	Molar
mg	Milligram
mL	Milliliter
mV decade^{-1}	Millivolt per decade
mmol kg^{-1}	Millimole per kilogram
mol%	Mole percentage
m/z	Mass per charge ratio
NaBH$_4$	Sodium borohydride
Na BH(OAc)$_3$	Sodium triacetoxy borohydride
NaHCO$_3$	Sodium bicarbonate
NaOH	Sodium hydroxide
NaTFPB	Sodium tetrakis[3,5-bis(trifluoromethyl)phenyl] borate
NO$_3^-$	Nitrate
o-NPOE	2-Nitrophenyl octyl ether
ppm	Part per million
PVC	Poly(vinyl chloride)
s	Singlet (^{1}H NMR spectrum)
SSM	Separate solution method
t	Triplet (^{1}H NMR spectrum)
THF	Tetrahydrofuran
v/v	Volume by volume
wt.%	Percentage by weight
δ	Chemical shift

CHAPTER I

INTRODUCTION

The development of artificial receptors or chemical sensors for heavy metal ions is still very important [1, 2] due to their impact on human health and environmental systems [3]. Cadmium is one of the most toxic heavy metals to human health because it can cause adverse effects on metabolic processes of human beings [4, 5] and destruction of red blood cells [6-8]. Cadmium was contaminated through wastes from industry such as paints, batteries, mining and alloys industry [11]. Nowadays, several methods for determination of cadmium ion have been reported [12-17]. Potentiometric method based on ion selective electrodes (ISEs) is one of the most important methods for determination of metal ions, due to simple fabrication, low cost, good selectivity and sensitivity, fast response, nondestructive analysis and low detection limit [8, 18]. In recent year, a number of ion selective electrodes for cadmium sensors have been reported in the literature [21-27]. However, most of these electrodes suffered from one or more of the following drawbacks: lack of stability and selectivity, limited concentration range and narrow range of working pH and considerable interferences from other cations such as Ag^+, Zn^{2+}, Cu^{2+}, Pb^{2+} and Hg^{2+}. Many researchers are interested in the development of ion selective electrodes by the design and synthesis of novel neutral ionophores.

Calix[4]arene derivatives are very often used as a framework for building a variety of new complexing agents that are selective towards various metal ions [2, 6, 28-30]. Such compounds may find applications in separation, membrane transport, chromatography, and extraction method [32]. Their selectivity depends on the kind of substituents added on the calix[4]arene framework. High lipophilicity of *p-tert-*butylcalix[4]arene substituted at the lower or upper rim makes calix[4]arene as a superb ionophore in ion selective membrane electrodes. Recently, calix[4]arene frameworks were successfully functionalized with tripodal amine (TPA) as neutral ionophore in ion selective membrane electrodes [33, 34].

Furthermore, aryl ethyne derivatives were widely used as building blocks for molecular recognition due to their linear, rigidity, delocalized π-electrons, simple functionalization, providing photophysical properties and lipophilicity of the unsaturated backbones [36-41]. However, aryl ethyne derivatives never be used as an ionophore in ion selective membrane electrodes.

In this research, we have synthesized an aryl ethyne scaffold attaching mono- and di- tripodal amine moieties as neutral ionophores for the construction of novel cadmium ion selective membrane electrodes and compared the cation sensing ability with calix[4]arene based ionophores containing tripodal amine groups.

1.1 Research objective

1. Synthesis of aryl ethyne derivatives containing a number of the tripodal amine groups as neutral ionophores.

2. Preparation of cadmium ion selective membrane electrodes (Cd-ISEs) from the aryl ethyne and calix[4]arene based ionophores containing tripodal amine groups and study of the selectivity and the other characteristics of the electrodes prepared from the synthesized ionophores.

1.2 Scope of the research

The aryl ethyne framework with tripodal amine groups is synthesized. The aryl ethyne and calix[4]arene based ionophores (Figure 1.1) are then incorporated into PVC membranes to prepare electrode which were comparatively evaluated for cadmium detection. The lipophilic building blocks of ionophores **I** - **III** may form stable complexes with Cd^{2+} and retaining the stability of ionophores in the membrane phase. The membrane compositions are optimized by using a constant concentration of ionophores, varying amount of ionic additives (KTpClPB and NaTFPB) and also fixing the ratio of PVC and plasticizers (o-NPOE and DOS) at 1:2 by weight. The characteristics of the electrodes are fully examined: potentiometric response, linear range, detection limit, selectivity coefficient, response time, working pH range and reversibility.

1.3 Benefits of the research

We expect to obtain a polymeric membrane electrode for cadmium determination with a low detection limit.
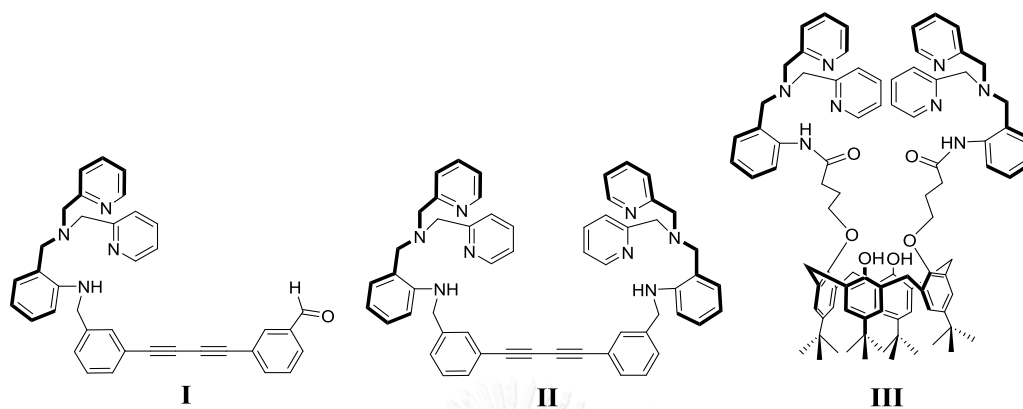
Figure 1.1 Chemical structures of ionophores (**I-III**)

CHAPTER II
LITERATURE REVIEW

2.1 Literature reviews

2.1.1 The design of cation sensing receptors

Currently, the design and synthesis of receptors for cation sensing have attracted chemists' attention. In order to develop a receptor that is selective toward cations, various interactions between hosts and guests in a complementary fashion have been investigated. Several strategies have been used to design a receptor with a good selectivity toward a target cation [43, 44]. Most receptors may contain a variety of functional groups, which must be organized to complement the size and shape of cations. Tripodal amine is one of the most popular receptors widely used to attach onto artificial receptors for cation recognition via non-covalent interactions [45] because this ligand contains chelating donor atoms that can strongly interact with cations. Moreover, the rigidity of the receptor is also important to succeed high binding affinity and good selectivity. Calix[4]arene and aryl ethyne frameworks are extremely interesting molecular scaffolds in the design of artificial receptors because of its rigid and stability. In addition, aryl ethyne contains π-conjugated skeleton and can act as a chromophore or fluorophore for signal transduction [46, 47].

2.1.2 Cation sensing based on tripodal amine (TPA) receptors

Tripodal amine receptor is a tetradentate ligand consisting of a central nitrogen donor connected to three arms, and each arm contains methylene or ethylene linkage and a nitrogen donor as binding sites for metal ions. Tripodal amine ligand has been extensively used as a metal binding receptor in supramolecular chemistry due to their enhanced chelating effect, often bind to metal ions very strongly and the bulkiness of tripodal ligands is highly tunable allowing for controlling interaction with metal ions. In addition, the selectivity of a tripodal amine receptor depends on the rigidity of its arms and its cavity size [48-50]. Many researchers used tripodal amine as receptors for cations, including transition and heavy metal ions.

Mohamadou and co-worker [51] have reported a synthesis of two tripodal heptadentate ligands based on tris[2-(2-pyridylmethyl)aminoethyl]amine **2.1** and tris[2-picolinamidoethyl]amine **2.2** and their interactions with Zn^{2+}. The stability constants of the chelates Zn^{2+} with these ligands were determined by potentiometry and UV spectrometry. Choi at el. [52] have reported a preparation of metal ion complexes of the tripodal amine ligand from bz_3tren **2.3**. The ligand formed stable complexes with Hg^{2+}, Cd^{2+} and Ag^+. These complexes were characterized by X-ray crystral structures. Nolan et al. [53] have designed and synthesized a new unsymmetrical fluorescein sensor containing di-(2-picolyl)amine-based Zinpyr (ZP) family of cation selective sensors **2.4**. This sensor give a positive fluorescence response upon addition of Zn^{2+} or Cd^{2+}. A 5-fold fluorescent enhancement is observed under physiological conditions corresponding to the binding of the Zn^{2+} to the sensor, which inhibits a photoinduced electron transfer (PET) quenching pathway. Ibrahim et al.[54] have reported a synthesis and charecterization of zinc complexes based on tripodal ligands from tris(2-benzimidazolylmethyl)amine **2.5** and methylated derivatives tris(N-methyl-2-benzimidazolylmethyl)amine **2.6** and their applications toward CO_2 hydrations. These complexes reacted with CO_2 in the presense of triethylamine as a base to give bicarbonate complexes.Watchasit and co-worker [55] have synthesized the dinuclear Zn^{2+} complex of anthracene based tripodal tetramine **2.7** as anion sensor using the indicator displacement assay (IDA) approach. In addition, Khamjumphol et al. [33] have synthesized anthracene scaffold connecting to a tripodal amine unit **2.8** as neutral ionophore and used as cation carriers incorporating in PVC membrane electrodes. The result was unsatisfied because the anthracene based ionophore had poor lipophilicity and not able to form stay in the membrane phase. Thus far, cation sensing based on tripodal amine receptors are widely reported in optical sensor but the application in ion selective electrodes are rarely seen.

2.1

2.2

2.3

2.4

R
2.5 = H
2.6 = CH₃

2.7

2.8
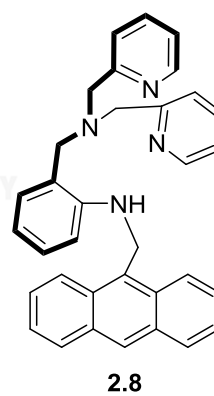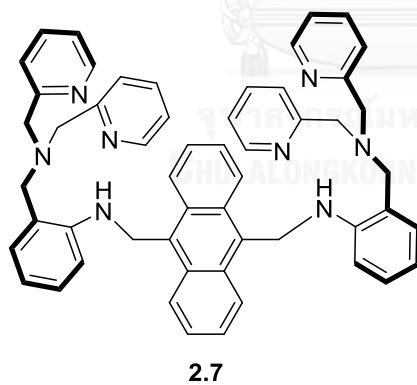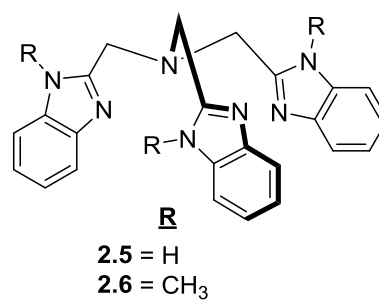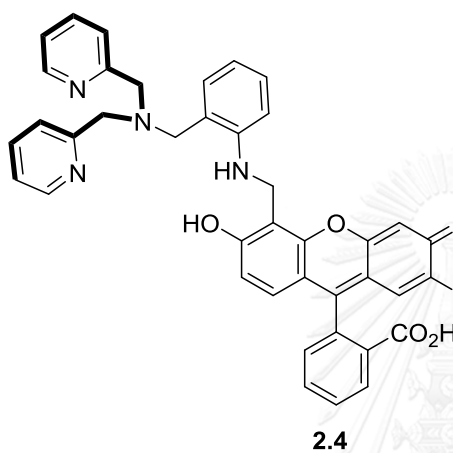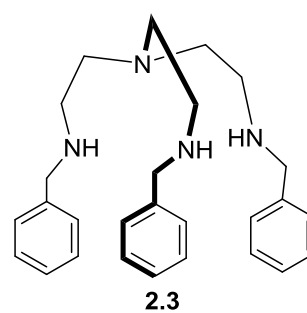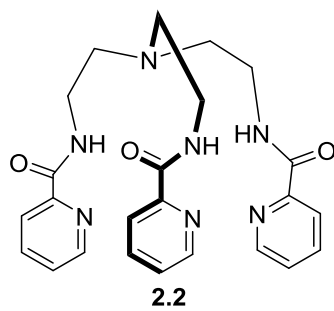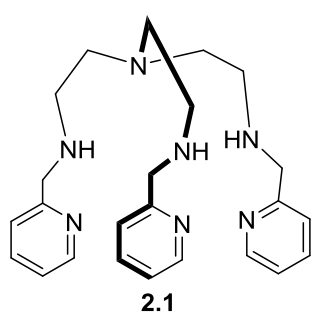
2.1.3 Cation ions sensing based on calix[4]arene building blocks

Calix[4]arene are macrocyclic compounds from the condensation of formaldehyde and phenol groups [56]. Nowadays, calix[4]arenes are considered to be extremely useful for molecular recognition due to their preorganized cavity and facile modification in the rims (both upper rim and lower rims) of the calix[4]arene frameworks. Chawla et al. [28] have synthesized a novel calix[4]arene derivative with appended coumarin moiety for selective recognition of Cu^{2+} ions. A new bis-calix[4]arene platform formed by upper rim–upper rim linking of two calixarene units has been obtained by condensation of diformyl calixarene with carbohydrazide. The synthesized bis-calixarene has been found to selectively detect Fe^{3+} without interference ions [29]. Rusu et al. [30] have reported the synthesis of *p-tert-*butylcalix[4]arenes bearing substituted triazoles at the lower rim were uising click chemistry. The results showed that the product exhibited pronounced selectivity towards Hg^{2+}. A novel anthraquinonoidal calix[4]arene derivatives which preferential recognition toward biologically Zn^{2+} has been reported by Chawla et al [57].

One of the successful applications of calix[4]arenes is in ion selective electrodes due to their hydrophobic, stable, unique three-dimensional and tunable structures [58]. Moreover, the calix[4]arene scaffold can also act as a neutral organic molecules for ion selective electrode. Park et al. [2] have reported the synthesis of five ionophores for transition metal ion selective polymeric membrane electrodes based on 1,3-alternate calix[4]azacrown ethers having 2-picolyl, 3-picolyl, and benzyl unit **2.9-2.13**. The electrodes based on 2-picolyl attached 1,3-alternate calix[4]azacrown ether **2.13** exhibited Nernstian response toward Cu^{2+} ion compared to other electrodes.

R

2.9

2.10

2.11

2.12

2.13
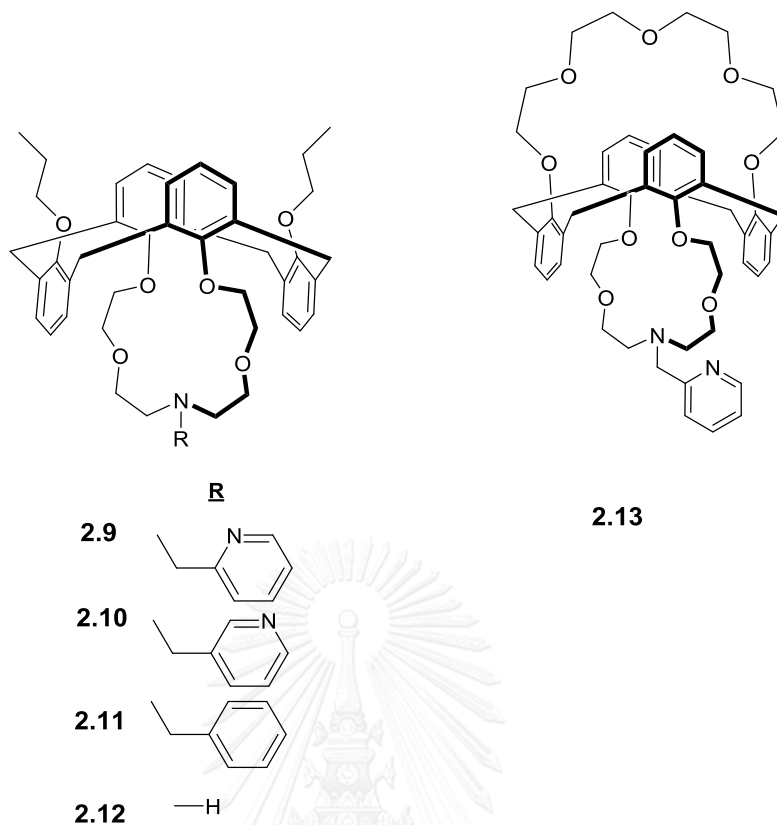
Chen and co-worker [6] have prepared polymeric membranes based on pyridine containing calix[4]arene derivatives **2.14-2.16**. There electrodes gave a good Nernstian response 49-53 mV decade^{-1} for Ag$^+$ and exhibited high selectivity towards Ag$^+$ over a number of alkali, alkaline earth and transition metal ions.

2.14   **2.15**   **2.16**
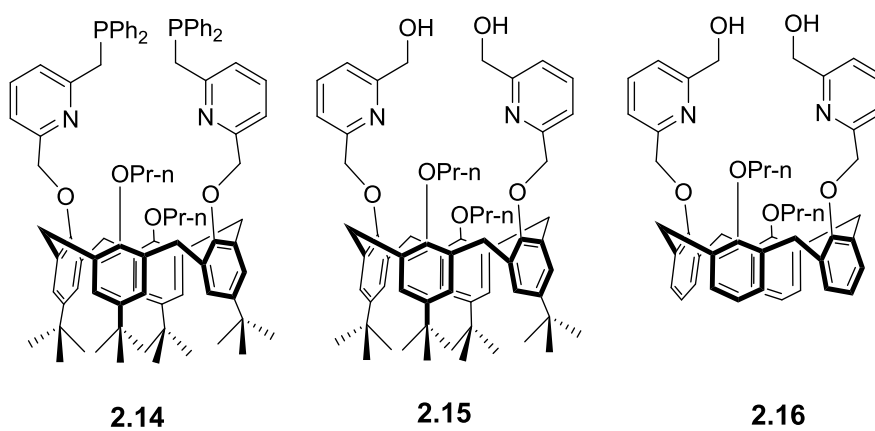
Moreover, a heterocycle functionalized *p*-tert-butylcalix[4]arene **2.17** has been synthesized and explored as an ionophores for polymeric membrane Ag$^+$ ion selective electrode. The electrode containing DOP plasticizer and KT*p*ClPB as ionic additive exhibited a Nernstian response slope of 59.8 mV decade^{-1} in a working concentration range of 5.0×10^{-7} to 1.0×10^{-3} M for Ag$^+$ ions. In addition, the proposed electrode has been successfully used for the determination of Ag$^+$ and Cl$^-$ ions in water samples and in vitamin B$_6$ tablets [9].

2.17
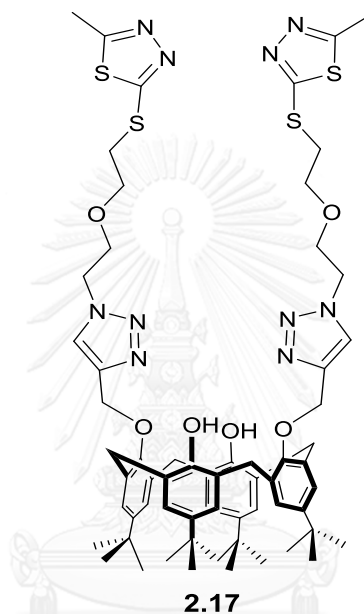
Janrungroatsakul et al. [20] have synthesized four calix[4]arene derivatives containing different donor atoms and chemical structures **2.18**-**2.21** and used as neutral ionophores to prepare Ag$^+$ ion selective electrodes. In this study, the ionophore **2.19** calix[4]arene attaching with two nitrogen and two sulfur donating atoms displayed stronger interactions with Ag$^+$ compared to other ionophores. Moreover, the simple potentiometric method based on polymeric membrane silver ion selective microelectrode (Ag-ISμE) can detect DNA hybridization with the natural PNA probe using silver nanoparticles as redox markers.
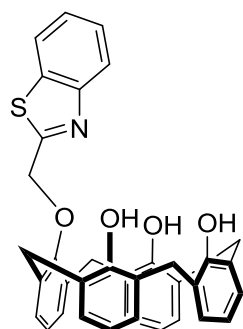
2.18
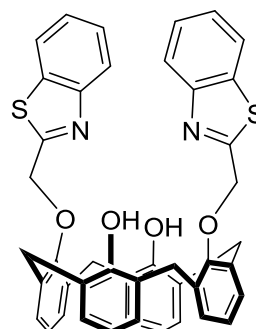
2.19
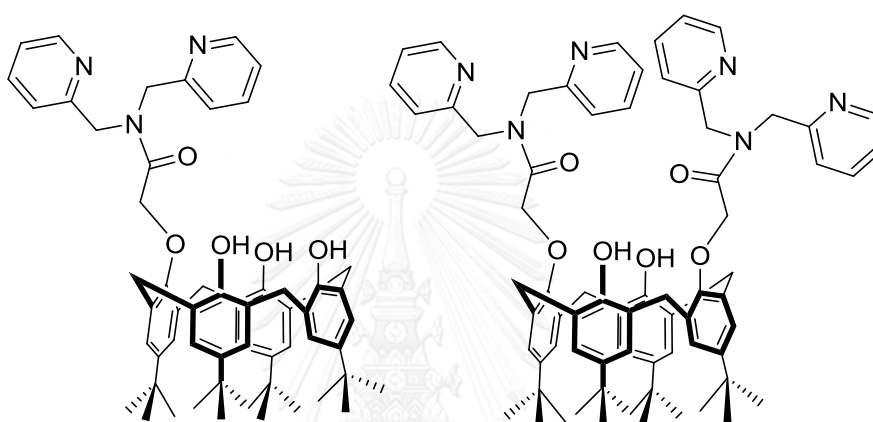
2.20

2.21

Kamel and co-worker [31] have studied response characteristic of a Cu^{2+} ion selective polymer membrane electrode based on macrocyclic calix[4]arene derivatives **2.22** as a neutral ionophore. The membrane electrode formulated with the ionophore and appropriate anionic additive exhibited enhanced potentiometric response toward Cu^{2+} over a concentration range from 8.1×10^{-6} to 1.0×10^{-2} M with a slope of 34.2 ± 0.4 mV decade^{-1}.
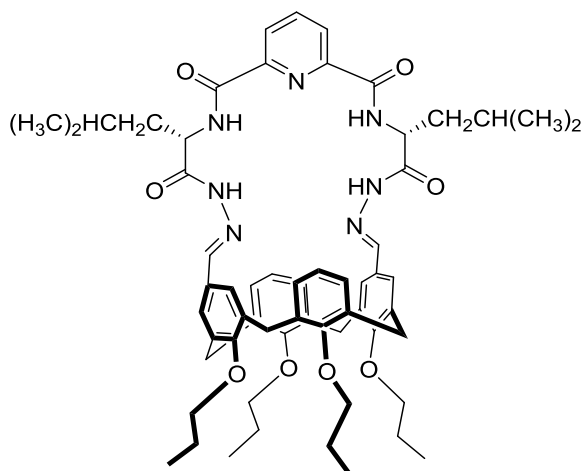
2.22

Bochenska and co-worker [35] have reported five neutral ionophores based on *p-tert*-butylcalix[4]arene connecting with thioamides **2.23**-**2.27**. These ionophores were applied in ISEs and showed Nernstian responses. The compounds were found to have high selectivity towards Pb^{2+} over other investigated cations. The complex stability constants were also determined proving high affinity towards Pb^{2+} for ionophores **2.23** and **2.24**. On the other hand, ionophores **2.25**-**2.27** are not quite stable in the membrane phase. Their lifetimes are shorter (2 – 3 weeks).

2.23 **2.24**

2.25   **2.26**

2.27
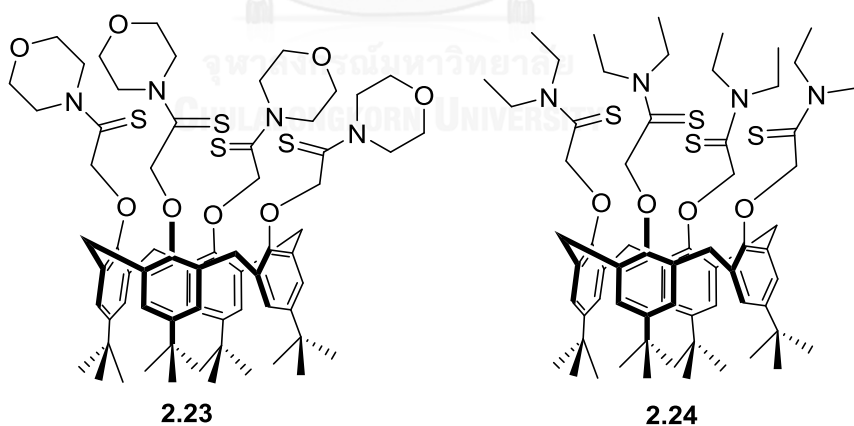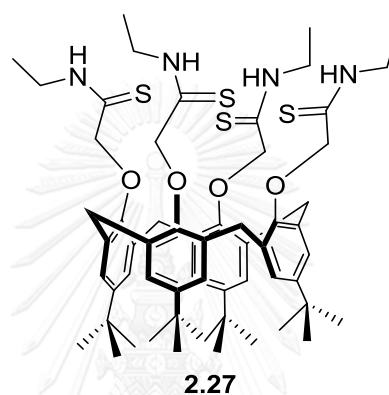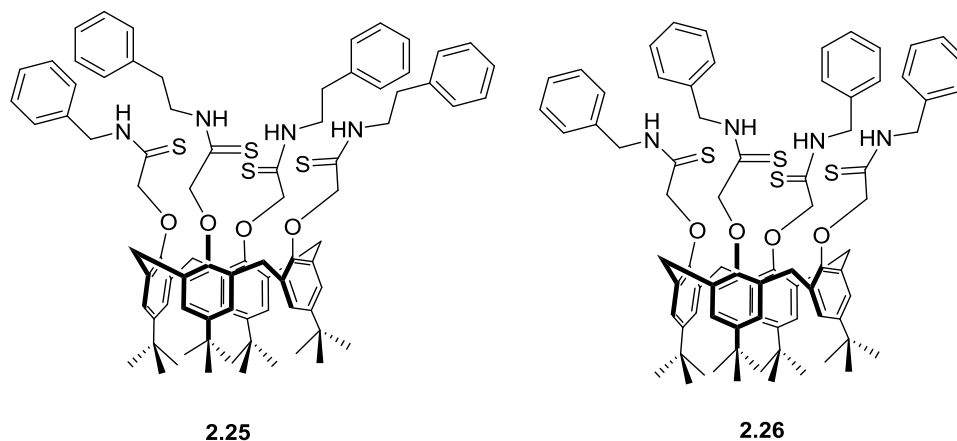
Gupta et al. [42] have demonstrated the use of PVC-based electrodes fabricated from *t*-butyl thiacalix[4]arene (**2.28**) and thiacalix[4]arene (**2.29**) as ionophores for quantification of cadmium ions. It was found that the best performance was obtained for the membrane using the ratio of ionophore **2.29**: PVC: NaTPB: *o*-NPOE, 5:120:3:150. This electrode showed a linear potential response for Cd^{2+} over a wide concentration range, 3.2×10^{-6} to 1.0×10^{-1} M, with Nernstian's slope, 29.5 mV decade^{-1}. Moreover, this electrode has been used in the potentiometric titration of Cd^{2+} with EDTA and successfully used for the quantification of cadmium in river water samples.

2.28

2.29
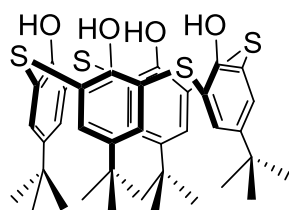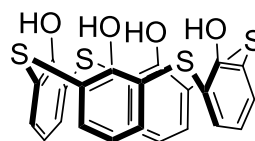
Khamjumphol et al. have reported of the PVC membrane electrodes incorporating with four natural ionophores for Cd^{2+}. Three of them were modified tripodal amine attaching with *p-tert*-butylcalix[4]arene frameworks **2.30**-**2.32**. The result showed that the prepared Cd-ISE from ionophore **2.32** (10.2 mmol kg^{-1}) with KTpClPB (50.1 mol% related to ionophores) as ionic additives in DOS plasticized PVC membrane exhibited a Nernstian response of 29.4 ± 0.6 mV decade^{-1} for Cd^{2+} and a working concentration range of 1.6×10^{-6}–1.0×10^{-2} M. In addition, the fabricated electrode was employed as a probe for detection Cd^{2+} from oxidation of CdS QDs solution and real waste water sample. The response characteristics of the aforementioned literature reviews about the PVC membrane electrode response toward cations based on neutral ionophores are summarized in Table 2.1
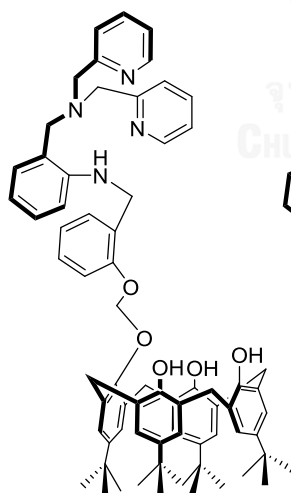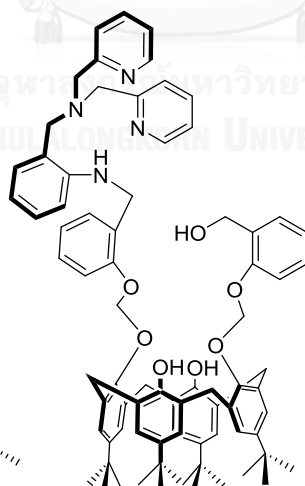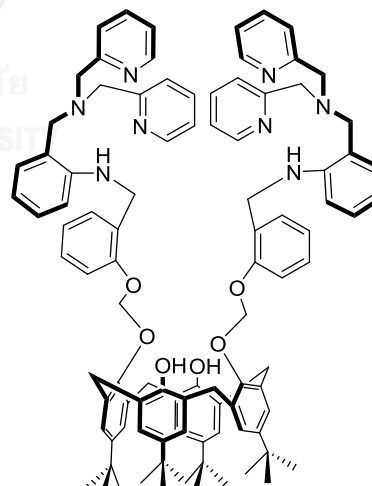
2.30   **2.31**   **2.32**

Table 2.1 General characteristics of some potentiometric cations selective membrane electrodes based on neutral ionophores

Ionophores	Cations	Linear range (M)	Slope (mV decade^{-1})	Response time (s)	pH range	Detection limit (M)	References
2.13	Cu^{2+}	$10^{-4.5} - 10^{-2.5}$	30.2	–	7.0	$1.0{\times}10^{-5}$	[2]
2.14	Ag^+	$5{\times}10^{-6} - 5{\times}10^{-2}$	52.0 ± 2.0	<10	$2.5 - 7.0$	$1.0{\times}10^{-5}$	[6]
2.17	Ag^+	$5.0{\times}10^{-7} - 1.0{\times}10^{-3}$	59.8	<10	$2.2 - 11.4$	$1.0{\times}10^{-7}$	[9]
2.19	Ag^+	$10^{-6} - 10^{-2}$	58.8 ± 0.6	–	–	$4.8{\times}10^{-7}$	[20]
2.22	Cu^{2+}	$8.0{\times}10^{-7} - 1.0{\times}10^{-2}$	34.2 ± 0.4	<20	5.0	$1.8{\times}10^{-9}$	[31]
2.24	Pb^{2+}	$10^{-6} - 10^{-1}$	32.6 ± 2.0	<10	4.0	–	[35]
2.29	Cd^{2+}	$3.2{\times}10^{-6} - 1.0{\times}10^{-2}$	29.5	8	$4.5 - 6.5$	–	[42]
2.32	Cd^{2+}	$1.6{\times}10^{-6} - 1.0{\times}10^{-2}$	29.4 ± 0.6	10	6.0-9.0	1.6×10^{-6}	[33]

2.1.4 Cation ions sensing based on aryl ethyne building blocks

Aryl ethyne derivatives can be conveniently synthesized by coupling of aryl halides with terminal alkyne in the presence of palladium and CuI as a catalyst under basic conditions to construct sp^2- sp C-C bonds, commonly termed as Sonogashira coupling reaction [59]. The general representation of Pd/Cu-catalyzed Sonogashira coupling reaction was shown in Scheme 2.1. Its applications include pharmaceuticals [60], natural products [61], organic materials, nanomaterials, molecular electronics and conjugated polymers [36, 62]. In recent years, aryl ethyne was widely used as building blocks for molecular recognition due to their linear, rigidity in conjugated π-systems, simple functionalization, optical properties and lipophilicity of the arylethynyl linkage [36-40].

$$R^1\!\!-\!\!X \quad + \quad R^2\!\!-\!\!\equiv\!\!-H \quad \xrightarrow[\text{base}]{\text{Pd, CuI catalyst}} \quad R^1\!\!-\!\!\equiv\!\!-R^2$$

R^1 = aryl
R^2 = aryl, alkyl
X = halide
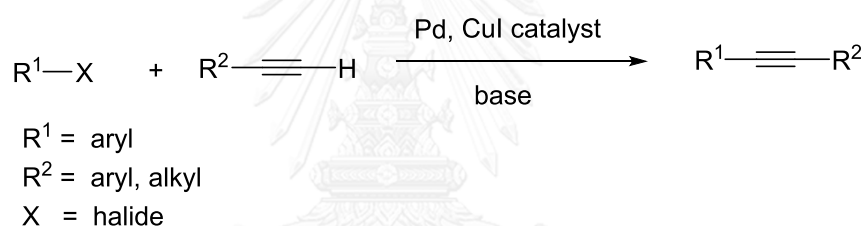
Scheme 2.1 General representation of Pd/Cu-catalyzed Sonogashira coupling reaction

McFarland et al. [63] have reported a synthesis of diphehyl ethyne derivatives **2.33-2.37**. These compounds are able to recognize cations, especially alkali metals (Li^+) in CH_3CN.

2.33   **2.34**   **2.35**, n = 1
                                     2.36, n = 2
                                     2.37, n = 3

Wu and co-worker [39] have reported a design and synthesis of polymer-based fluorescence sensors incorporating triazole unit with π-conjugted backbones **2.38** for Hg^{2+} detection in aqueous solution compared with othor metal ions such as Co^{2+}, Ni^{2+}, Na^+, Ag^+, K^+, Cr^{3+}, Mg^{2+}, Al^{3+}, Ca^{2+}, Pb^{2+}, Fe^{3+}, Cd^{2+}, Cu^{2+} and Zn^{2+}. The results shown that the polymer sensor can exhibit the most pronounced fluorescence quenching response to Hg^{2+} with high selectivity and sensitivity because the triazole unit as the metal recognition unit only interacted with Hg^{2+}.

R = $(CH_2CH_2O)_2CH_3$ Polymer sensor **2.38**

Gomila and co-worker [64] have designed and synthetized a novel chelating ligand based on two tripodal tris(2-pyridylmethyl)amine (TMPA) units linked by unsaturated rigid spacers mono **2.39** and di-alkyne **2.40**. These ligands strongly interacted with Cu^{2+} and used to prepare an electrochemical sensor of dioxygen.

2.39   **2.40**

There are several research studies on using the tripodal amine unit as a receptor for cations recognition and many literature reviews on using ionophores based on calix[4]arene building blocks as ion carriers in ion selective electrodes while aryl ethyne derivatives are frequently used in the design and synthesize for cation sensing in term of optical sensors. However, the aryl ethyne derivatives have been rarely reported as ionophores for cation detection in the field of ion selective electrodes. Therefore, we have designed ionophores containing aryl ethyne and calix[4]arene skeletons connected a number of the tripodal amine groups. We expect that these ionophores can be incorporated in PVC membrane electrodes and give excellent cation sensing electrodes.

CHAPTER III

EXPERIMENTAL

3.1 Instruments and materials

3.1.1 Instruments

^{1}H and ^{13}C NMR spectra were recorded on a Varian Mercury 400 NMR and a Bruker Avance 400 NMR spectrometer. Chemical shifts were reported in part per million (ppm) using deuterated $CDCl_3$. MALDI-TOF mass spectra were recorded on a Biflex Bruker Mass spectrometer using 2-cyano-4-hydroxycinnamic acid (CCA) as a matrix. The purity of the products was investigated by CHNS/O analyzer (Perkin Elmer PE2400 series II). EMF values of membrane electrodes were recorded by an EMF 16-channel potentiometer (Lawson Labs Inc., Malvern, PA 19355, USA). A reference electrode Ag/AgCl (Metrohm 6.0276.100) was used with 1M LiOAc and 3M KCl solutions as salt bridge electrolyte and internal reference electrode, respectively. The pH values were recorded by an Orion 2-star Benchtop pH meter (Thermo Fisher Scientific).

3.1.2 Materials

Ionophore **III** was synthesized by the previously published procedure [34]. All chemical reagents for synthesis employed reagent grade chemicals. Solvents were standard analytical grade purchased from Fluka, Aldrich, Carlo Erba, Merck or Lab scan. Dichloromethane and acetonitrile were distilled in the presence of calcium hydride as drying agent under nitrogen before use. Tetrahydrofuran (THF) was distilled over sodium and benzophenone. Column chromatography was carried out using silica gel (Kieselgel 60, 0.063 0.200 mm, Merck) and aluminum oxide (aluminum oxide 90 standardized, 0.063-0.200 mm, Merck). Thin layer chromatography (TLC) was performed on silica gel plates (Kieselgel 60, F_{254}, 1mm). Potassium tetrakis(p-chlorophenyl)borate (KT*p*ClPB), sodium tetrakis[3,5-bis(trifluoromethyl)phenyl]borate (NaTFPB), poly(vinyl chloride) (PVC), *o*-nitrophenyl octyl ether (*o*-NPOE), bis(2-ethylhexyl) sebacate (DOS) and tetrahydrofuran (THF) were purchased from Fluka. Nitrate, chloride and hydroxide

salts of cations were obtained from BHD, Fluka, Carlo Erba, and Merck. All solutions were prepared with ultrapure Milli-Q water.

3.2 Synthesis

3.2.1 Synthesis of the aryl di-ethyne building blocks (1)
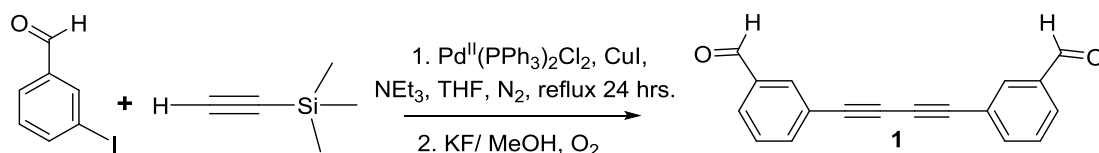
A mixture of 3-iodobenzaldehyde (0.46 g, 4.29 mmol), Pd(Ph$_3$)$_2$Cl$_2$ (2.80 mg, 0.04 mmol) and CuI (0.16 g, 0.08 mmol) were dissolved in dry THF (10.00 mL). Then, trimethylsilylacetylene (TMSA) (0.43 mL, 3.00 mmol) and triethylamine (0.55 mL, 4.00 mmol) were added to the mixture. The solution was stirred and refluxed overnight. KF (0.23 g, 4.00 mmol) and methanol (10 mL) were added, and the reaction mixture was stirred in air overnight. The reaction was filtered and the solvent was removed in vacuo. The residue was purified by column chromatography (SiO$_2$) with hexane: dichloromethane (20:80 v/v) as eluent. Compound **1** was obtained as white powders (0.19 g, 48%).

Characterization data for compound 1

^{1}H NMR (CDCl$_3$, 400 MHz, ppm): δ 10.01 (s, 2H, CHO), 8.03 (s, 2H, ArH), 7.90 (d, 2H, J=8.0 Hz, ArH), 7.78 (d, 2H, J=7.6 Hz, ArH), 7.54 (t, 2H, 7.6 Hz, ArH).

^{13}C NMR (CDCl$_3$, 400 MHz, ppm): δ 191.02, 137.87, 136.61, 133.87, 129.95, 129.30, 122.84, 80.60, 74.98.

Elemental analysis for C$_{18}$H$_{10}$O$_2$

Calculated**:** C, 83.71%; H, 3.90%

Found**:** C, 83.20%; H, 4.04%.

3.2.2 Synthesis of the aryl mono-ethyne building blocks (2)

A mixture of CuI (0.02 g, 0.12 mmol), Pd(OAc)$_2$ (0.04, 0.18 mmol), and triphenylphosphine (0.05, 0.21 mmol) in 10.00 mL of acetonitrile. The solution was degassed with N$_2$ for 30 min. Then, triethylamine (0.07 g, 0.72 mmol), 3-iodobenzaldehyde (0.50 g, 2.15 mmol) and calcium carbide (0.41, 6.39 mmol) in 30.00 mL of acetonitrile were added. The mixture was stirred and refluxed under N$_2$ atmosphere overnight. The reaction mixture was filtered and then evaporated to dryness under vacuum. The crude product was isolated by column chromatography (SiO$_2$) with hexane: dichloromethane (30:70 v/v) as eluent to give compound 2 as a white solid (0.20 g, 39%).

Characterization data for compound 2

^{1}H NMR (CDCl$_3$, 400 MHz, ppm): δ 9.92 (s, 2H, CHO), 7.94 (d, 2H, J=0.8 Hz, ArH), 7.77(s, 2H, ArH), 7.68 (m, 2H, ArH), 7.45 (t, 2H, 7.6 Hz, ArH).

^{13}C NMR (CDCl$_3$, 400 MHz, ppm): δ 191.44, 137.22, 136.69, 133.03, 129.49, 129.32, 124.03, 89.42.

MS (MALDI-TOF): calcd for [M] m/z, 234.07 found 234.15.

3.2.2 Synthesis of tripodal amine moiety

3.2.2.1 Synthesis of bis(pyridin-2-ylmethyl)amine (1a)
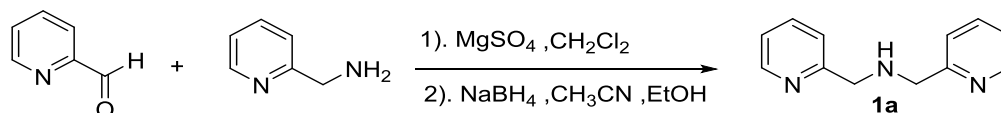
A solution of 2-pyridinecarboxaldehyde (0.50 g, 4.62 mmol) was dried using anhydrous $MgSO_4$ (2.78 mg, 4.62 mmol). Then, 2-(aminomethyl) pyridine (0.50 g, 4.66 mmol) in CH_2Cl_2 (30 mL) was added, and the solution was stirred under N_2 atmosphere for 3 h at room temperature. The suspension was filtered, washed with CH_2Cl_2 (200 mL), and the solvent was removed under vacuum. The crude product was dissolved in CH_3CN (15 mL) and was cooled to $-$ 5 ^{o}C. Then CH_3COOH (0.40 mL, 6.67 mmol) was added in one portion. A suspension of $NaBH_4$ (1.04 g, 27.45 mmol) in absolute ethanol (200 mL) was added to the clear yellow solution. The color of the solution changed from yellow to bright red by the end of addition. After stirring for 18 h at room temperature, the reaction was added 12 M HCl (5 mL, 136.98 mmol), and heated at 60 ^{o}C for 2 h. The solution was filtered and concentrated in vacuo, then dissolved in water (70 mL). The resulting yellow aqueous solution was basified by addition of NaOH pellets. Then, the solution was extracted with diethylether (3×200 mL). The organic layer was dried over anhydrous $MgSO_4$ and the solvent was evaporated. The product 1a was obtained as a yellow oil (4.00 g, 78%).

Characterization data for compound 1a

^{1}H NMR (CDCl$_3$, 400 MHz, ppm): δ 8.54 (d, 2H, J=4.0 Hz, ArH), 7.63 (m, 2H, ArH), 7.34 (d, 2H, J=8.0 Hz, ArH), 7.15 (m, 2H, ArH), 3.99 (s, 4H, -CH$_2$-), 3.03 (s, 1H, -NH-).

^{13}C NMR (CDCl$_3$, 400 MHz, ppm): δ 159.23, 149.26, 136.49, 122.34, 122.06, 54.62.

MS (MALDI-TOF): calcd for [M]$^+$ m/z, 199.25 found 198.97.

3.2.2.2 Synthesis of 2-((bis(pyridin-2-ylmethyl)amino)methyl)aniline (1b)
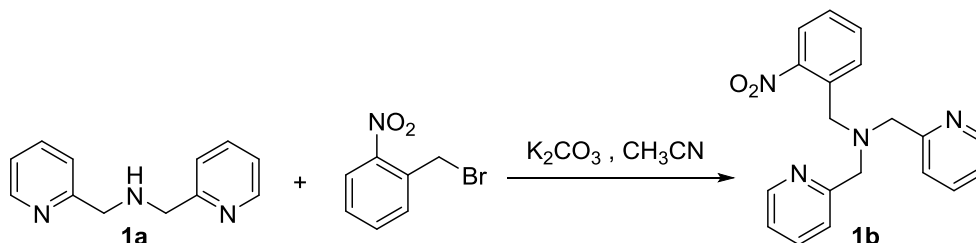
Compound **1a** (1.00 g, 5.07 mmol), K_2CO_3 (5.60 g, 40.51 mmol) and 2-nitrobenzylbromide (9, 980 mg, 4.54 mmol) were combined in 20 mL of CH_3CN and stirred for 12 h under N_2 atmosphere. The crude reaction was filtered through celite to give a brown oil after solvent removal. The product **1b** was obtained as a brown oil (2.74g, 81 % yield).

Characterization data for compound 1b

^{1}H NMR (CDCl3, 400 MHz, ppm): δ 8.34 (d, 2H, J=4.8 Hz, ArH), 7.57 (m, 1H, ArH), 7.49 (m, 2H, ArH), 7.33 (t, 1H, J= 7.46, ArH), 7.24 (s, 1H, ArH), 7.18 (t, 2H, J=7.6 Hz, ArH), 7.12 (s, 1H, ArH), 6.99 (t, 2H, J=6.4 Hz, ArH), 3.94 (s, 2H, -CH2-), 3.66 (s, 4H, -CH2-).

^{13}C NMR (CDCl3, 400 MHz, ppm): δ 158.19, 149.77, 148.46, 136.52, 133.96, 132.19, 131.30, 127.80, 124.11, 123.24, 122.08, 60.02, 55.72.

MS (MALDI-TOF): calcd for [M][+] m/z, 334.14 found 332.06.

3.2.2.3 Synthesis of tripodal amine (TPA)
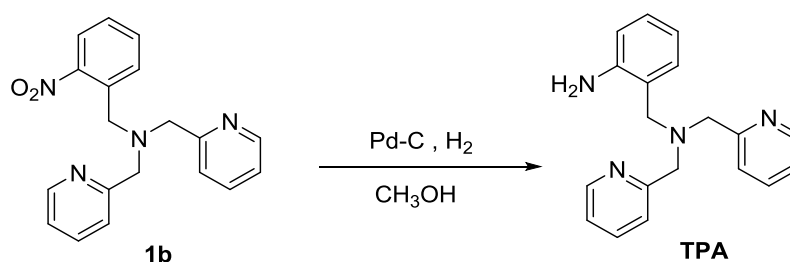
Compound **1b** (2.74 g, 8.20 mmol) and Pd-C (0.30 g, 10% activated) were mixed in 150 mL of CH_3OH and stirred under a hydrogen atmosphere for 24 h. The reaction mixture was filtered through celite to give a dark yellow oil after solvent removal. The product **1b** was obtained as a dark yellow oil (2.02g, 81 %).

Characterization data for TPA

^{1}H NMR (CDCl$_3$, 400 MHz, ppm): δ 8.53 (d, 2H, J=4.8 Hz, ArH), 7.63 (d, 2H, J=2.0 Hz, ArH), 7.61 (d, 1H, J=1.6 Hz, ArH), 7.59 (d, 1H, J=1.6 Hz, ArH), 7.36 (d, 1H, J=7.6, ArH), 7.13 (m, 2H, ArH), 7.04 (t, 1H, J=6.0, ArH), 6.64 (d, 2H, J=5.6 Hz, ArH), 3.78 (s, 4H, -CH$_2$-), 3.65 (s, 2H, -CH$_2$-).

^{13}C NMR (CDCl$_3$, 400 MHz, ppm): δ 159.26, 149.03, 146.99, 136.129, 131.18, 128.45, 123.43, 122.33, 121.96, 117.22, 115.41, 60.15, 57.89.

MS (MALDI-TOF): calcd for [M] m/z, 304.17 found 304.23.

3.2.3 Synthesis of aryl di-ethyne derivatives containing tripodal amine moieties (I and II)
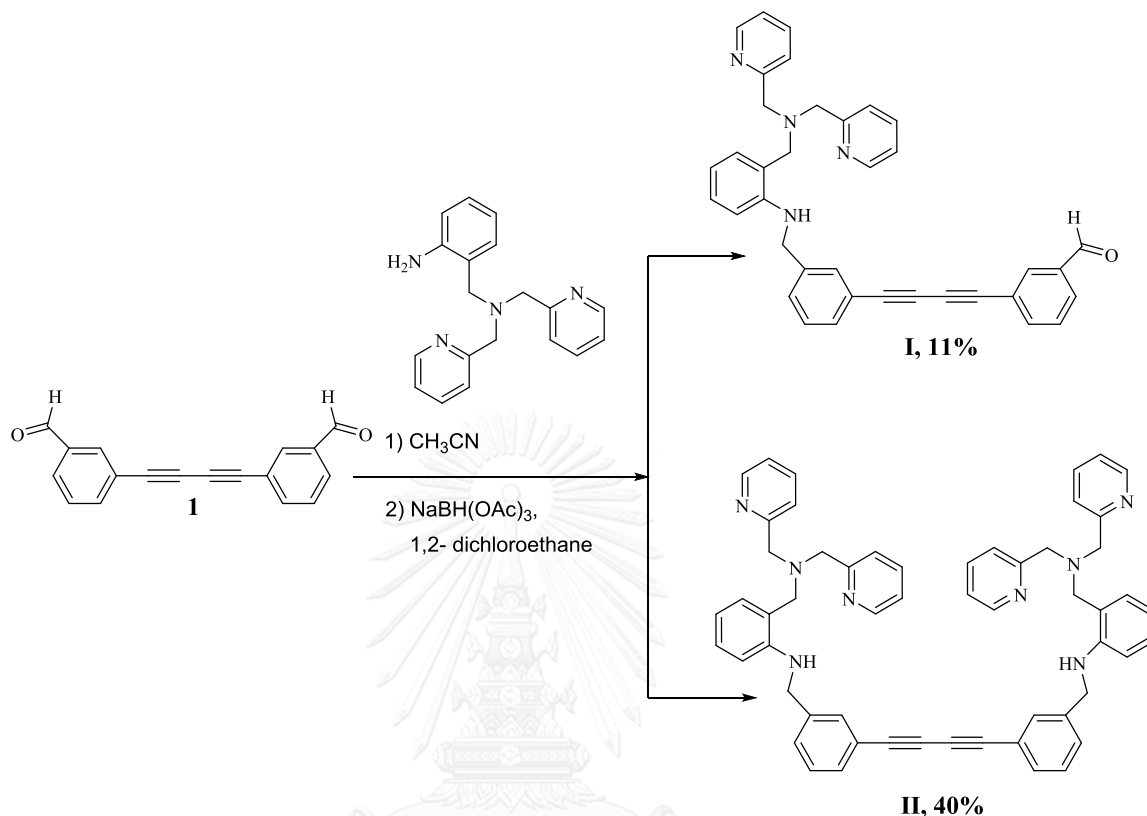
Compound 1 (0.28 g, 1.08 mmol) in 10 mL of CH_3CN was added dropwise to tripodal amine (TPA) (0.72 g, 2.38 mmol). The resulting mixture was stirred and refluxed under nitrogen atmosphere for 48 h. After cooling to room temperature, the solvent was evaporated under vacuum. The residue was dissolved in 1,2-dichloroethane (10 mL) and subsequently $NaBH(OAc)_3$ (1.14 g, 5.40 mmol) was added. The reaction mixture was stirred and refluxed under nitrogen atmosphere overnight. The solution was extracted with saturated $NaHCO_3$ (2x50 mL) and washed with deionized water (2x100 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was then evaporated. The purification was conducted on column chromatography (alumina/CH_2Cl_2) to obtain a major product **II** as a pale yellow solid (0.39 g, 40%) and a minor product **I** as a yellow oil in (0.06 g, 11%).

Characterization data for I

^{1}H NMR (CDCl$_3$, 400 MHz, ppm): δ 9.97 (s, 1H, -CHO-), 8.45 (t, 6H, J=4.8, Hz, ArH), 8.00 (s, 2H, ArH), 7.86 (m, 1H, ArH), 7.74 (m, 2H, ArH), 7.54 (m, 2H, ArH), 7.42 (m, 1H, ArH), 7.26 (s, 2H, ArH), 7.09 (m, 1H, ArH), 6.58 (t, 2H, J=7.2, ArH), 6.46 (m, 1H, ArH), 4.39 (s, 2H, -CH$_2$-), 3.79(d, 4H, J=5.2 Hz, -CH$_2$-), 3.68 (d, 2H, J=3.2 Hz, -CH$_2$-).

MS (MALDI-TOF): calcd for [M] m/z, 546.24 found 546.36.

Characterization data for II

^{1}H NMR (CDCl$_3$, 400 MHz, ppm): δ 8.45 (d, 4H, J= 4.8 Hz, ArH), 7.55 (m, 6H, ArH), 7.42 (t, 4H, J= 7.6 Hz, ArH), 7.38 (s, 4H, ArH), 7.27 (m, 6H, ArH), 7.10 (d, 2H, J=4.8 Hz, ArH), 7.07 (m, 2H, ArH), 6.58 (s, 2H, ArH), 6.45 (d, 2H, J=8.4 Hz, ArH), 4.39 (t, 4H, J=1.2 Hz, CH$_2$-), 3.78(s, 8H, -CH$_2$-), 3.68 (s, 4H, -CH$_2$-).

^{13}C NMR (CDCl$_3$, 400 MHz, ppm): δ 159.19, 149.10, 148.96, 147.89, 141.04, 136.35, 131.48, 131.07, 128.72, 128.52, 123.23, 122.70, 121.97, 121.90, 116.02, 110.03, 81.80, 74.02, 60.15, 58.53, 47.23.

Elemental analysis for C$_{56}$H$_{50}$N$_8$ .H$_2$O

Calculated: C, 78.84%; H, 6.14%; N, 13.14%

Found: C, 78.98%; H, 6.25%; N, 12.34%

MS (MALDI-TOF): calcd for [M]$^+$ m/z, 834.42 found 833.16.

3.2.4 Attempts to synthesize aryl mono-ethyne derivatives containing tripodal amine moieties (IIa)
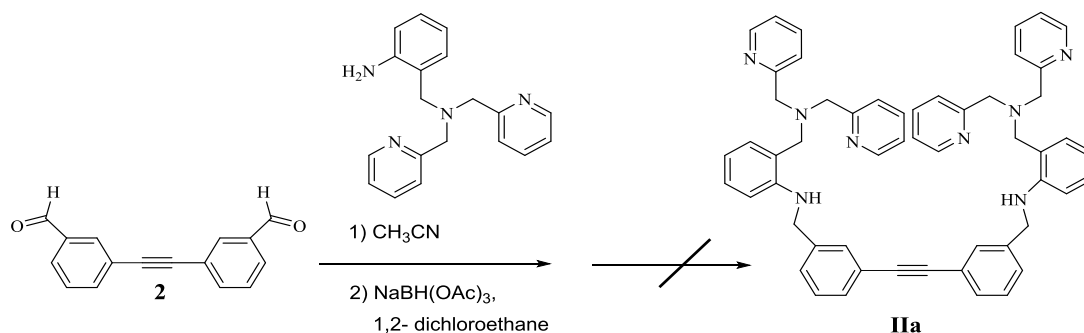
Compound **IIa** was synthesized following a procedure in the synthesis of **I** and **II**. Compound **2** (0.15 g, 0.64 mmol) in CH_3CN (10 mL) was added to tripodal amine (TPA) (0.44 g, 1.47 mmol). The solution was mixed and refluxed under N_2 atmosphere 48h. The reaction mixture was then cooled to room temperature and the solvent was removed under vacuum. 1,2-Dichloroethane (10 mL) and $NaBH(OAc)_3$ (0.67 g, 3.20 mmol) was subsequently added. Then, the solution was stirred and refluxed under N_2 atmosphere 24h. The crude product was extracted and washed by saturated $NaHCO_3$ (2x50 mL) deionized water (2x100 mL), respectively. The organic layer was dried use anhydrous $MgSO_4$, filtered and the solvent was then evaporated. The residue was isolated by column chromatography (alumina) with CH_2Cl_2 as eluent to obtain products as a dark yellow oil and a white solid. These products were characterized by ^{1}H NMR spectroscopy. The results suggested that a dark yellow oil and a white solid products were the starting materials: tripodal amine (TPA) and compound **2**.

3.3 Ion selective electrode studies

3.3.1 Preparation of the membrane electrode

The membrane was prepared as described previously [33, 34]. Ionophores (10 mmol kg^{-1}), various amount of the ionic additives, KTpClPB or NaTFPB (25, 50 and 75 mol % relative to the ionophore) were mixed with o-NPOE or DOS plasticized PVC (PVC: Plasticizers, 1:2 w/w) in 2 mL of THF. The mixture was dispensed as a thin film on a glass slide. The membrane was dried at room temperature for 1 d. Before use, the membrane was conditioned in 0.01 M solution of cations (nitrate salts). The inner filling solution (IFS) was 0.01 M cations (chloride salts) solutions. The composition of membrane electrodes were summarized in Table 4.1 and 4.2.

3.3.2 The EMF measurement

Potentiometric responses of membrane electrodes were investigated by a EMF 16-channel potentiometer (Lawson Lab Inc., Malvern, PA 19355, USA) at ambient temperature. The reference electrode Ag/AgCl with double junction was used (type 6.0726.100, Metrohm AG, CH-9010 Herisau, Switzerland). The activity values were calculated according to the Debye – Hückel procedure [65]. The potentiometric measurements were made with the following electrochemical cell:

Ag, AgCl / 3M KCl // 1 M LiOAc // sample (aq) / membrane / IFS / AgCl, Ag
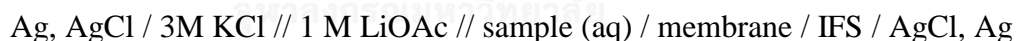
Performance of the electrode was investigated by measuring the potential of Cd^{2+} solutions with concentrations ranging from 10^{-7} to 10^{-2} M by dilution series of the 10^{-4}, 10^{-2} and 1M cations (nitrate salts) stock solutions. The solutions were stirred and potential readings were recorded when they reached stable values. The detection limit was measured from the intersection of two extrapolated segments of calibration curves [66].

3.3.3 Selectivity measurement

The selectivity coefficients explaining the preference of the membrane for interfering ions relative to Cd^{2+} were determined by the separate solution method (SSM) as recommended by the IUPAC [67]. The SSM was the measurement of two

separate solutions, both containing calibration curves of interfering and primary ions at the concentration range from 10^{-7} to 10^{-2} M. The selectivity coefficients were calculated from the observed EMF values and equation 3.1. The interfering ions studied were alkali, alkaline earth and transition metals (Na^+, K^+, Mg^{2+}, Ca^{2+}, Cr^{3+}, Fe^{3+}, Ni^{2+}, Cu^{2+}, Zn^{2+}, Cd^{2+} and Pb^{2+}) as nitrate salts. In addition, for Pb^{2+} solution pH was adjusted to pH 4 by adding 1% HNO_3 before determination [68]. All the experiments were repeated there times (SD, n=3).

$$\log K_{I, J}^{pot} = \frac{Z_I F \{E(J) - E(I)\}}{2.303RT} + \log \left[\frac{a_I(I)}{a_J(J)^{Z_I/Z_J}} \right] \tag{3.1}$$

Where E(I), E(J) and Z_I, Z_J and $a_I(I)$ and $a_J(J)$ are measured potentials, charges, and the activity value of primary ion and interfering ions in separate solution, respectively. R, T, and F are gas constant (8.314 J K^{-1} mol^{-1}), temperature (K), Faraday constant (9.6847 C mol^{-1}), respectively.

3.3.4 Effect of pH

The effect of pH on the response of the electrodes was investigated over the pH range of 2.0–10.0 for 10^{-4}, 10^{-3} and 10^{-2} M of $Cd(NO_3)_2$ solutions. 1% HNO_3 and 1.0 M NaOH were used to adjust the pH solutions.

3.3.5 Reversibility

Measurements of electrode reversibility were performed in the sequential concentration of 10^{-4} and 10^{-3} M of $Cd(NO_3)_2$ solution. The potential values were continually recorded. The electrode was then washed and the measurement was repeated in the same concentrations. The measurement was replicated for five times.

3.4 Analytical applications in real samples

The fabricated Cd-ISE was applied to determine Cd^{2+} in real water samples (mineré, nestle and singha brands) and tap water. The samples were treated with standard cadmium solution at the concentration 4.0×10^{-5} and 1.0×10^{-4} M. and then the percentage recoveries were calculated from the observed EMF values

CHAPTER IV
RESULTS AND DISCUSSION

4.1. Design and synthesis of ionophores

In this work, we have designed three ionophores containing a different number of the tripodal amine groups and lipophilicity of the building blocks. Ionophores **I** and **II** contained mono and di-substituted tripodal amine groups attached to the aryl ethyne skeletons, respectively. Ionophore **III** had two tripodal amine groups connecting to the calix[4]arene scaffold. The relationship between the structure of the ionophores and cation sensing abilities were fully compared and examined by potentiometric measurements.
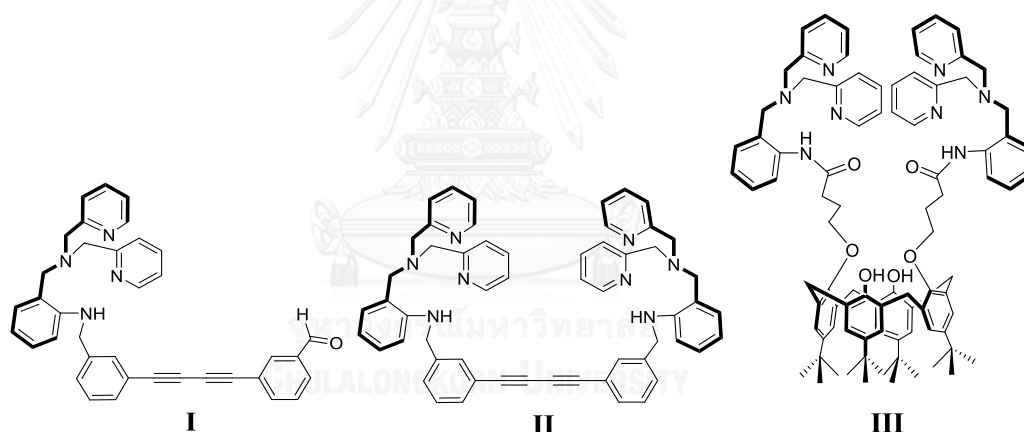
Figure 4.1 Structure of ionophores (**I-III**)

4.1.1 Synthesis of ionophores I and II

The synthetic pathway of ionophores **I** and **II** is shown in Scheme 4.1. Compound **1** has been successfully synthesized using the Sonogashira coupling in a one pot fashion [39]. 3-Iodobenzaldehyde reacted with trimethylsilylacetylene under Sonogashira conditions using $PdCl_2(PPh_3)_2$ and CuI as catalyst and NEt_3 as base to form the trimethyl(phenylethynyl)silane product. KF and methanol were then added to cleave the TMS protecting group. The crude product was purified by column chromatography to obtain the compound **1** in 48% yield. Compound **1** was then used

for coupling with tripodal amine (TPA) in acetonitrile under N_2 atmosphere to form shift base compounds. Subsequently, the shift base compounds were reduced to generate amine compounds using $NaBH(OAc)_3$ as a reducing agent. The crude product was isolated by column chromatography to give mono-substituted tripodal amine product **I** in 11% yield as a minor product and di-substituted tripodal amine product **II** as a major product in 40% yield. The desired ionophores were obtained in low yield possibly due to the steric hindrance of the aryl ethyne backbones led to the encumbrance of nucleophilic addition of the aryl ethyne dicarboxaldehyde and the tripodal amine moieties. In addition, the partial of the yield may be lost in the chromatography column.

4.1.2 Characterization of ionophores I and II

The structures of ionophores **I** and **II** were fully characterized by ^1H and ^{13}C NMR, mass spectroscopy and elemental analysis. The ^1H NMR spectrum of ionophore **I** displayed the proton of carboxaldehyde peak at 9.97 ppm. The characteristic of the aromatic proton groups and proton peaks of tripodal amine moiety were found in the region of 8.45 - 6.46 ppm. All the methylene linked protons showed at 4.39, 3.79 and 3.68 ppm. In addition, the MALDI-TOF mass spectrum confirmed the structure of this ionophore by showing a peak at 546.24 m/z corresponding to the molecular structure of **I** $[C_{34}H_3N_4O]$.

The ^1H NMR spectrum of ionophore **II** showed characteristic proton peaks of tripodal amine moiety and the aryl groups in the region of 8.45 - 6.45 ppm. All the methylene protons appeared at 4.39, 3.78 and 3.65 ppm. For The ^{13}C NMR spectrum, the signals of carbon-carbon triple bond were appeared at 81.80 and 74.02 ppm [39, 69]. The MALDI-TOF mass spectrum confirmed the structure of this ionophore by showing a parent peak at 833.16 m/z corresponding to the molecular structure of **II** $[C_{56}H_{50}N_8]^+$. Elemental analysis confirmed the purity of this compound.

The cation sensing abilities of ionophores **I** was not examined due to its low yield and stability. Compound **I** changed from a yellow to brown oil upon storing, indicating decomposition.
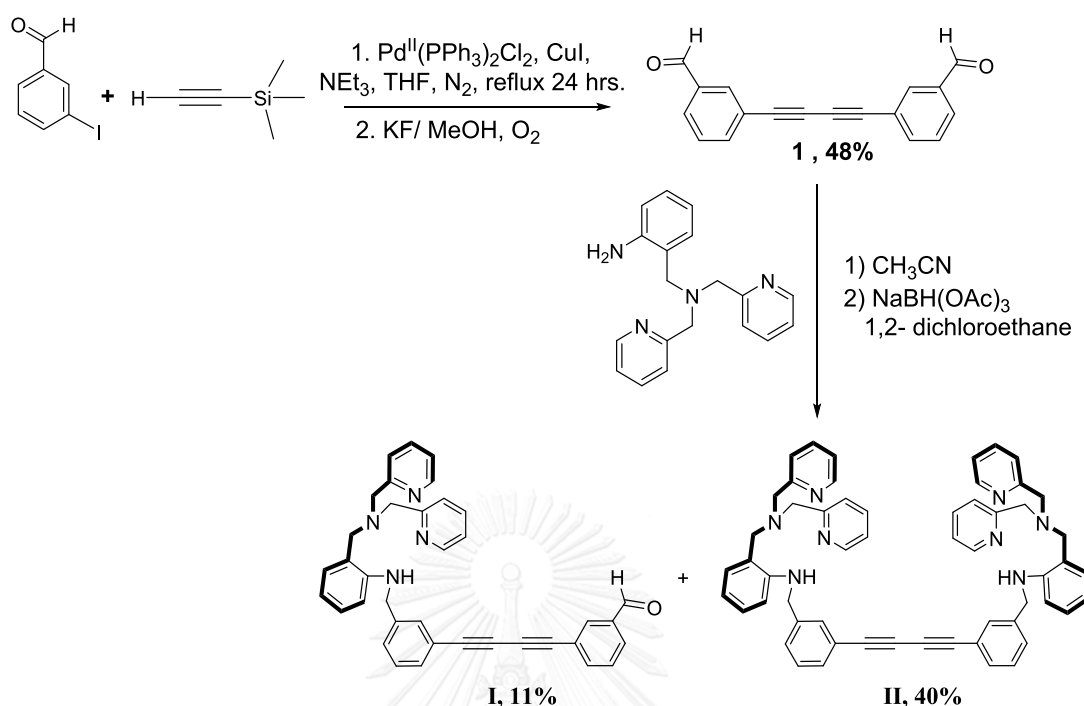
Scheme 4.1 Synthetic pathway of ionophore I and II

4.2 Preparation of the membranes from ionophores II and III

The PVC-based membrane electrodes have been prepared by incorporating appropriate amounts of ionophores **II** and **III** at ca.10 mmol kg^{-1}, various amounts of the ionic additives KTpClPB and NaTFPB (25, 50 and 75 mol % corresponded to the mole of the ionophores), plasticizers (o-NPOE and DOS) and PVC polymer (in the ratio of 1:2; PVC: plasticizers) in THF 2 mL. The components were added in terms of weight percentages (in the total weight of 220 mg). The prepared membrane was conditioned in a 0.01 M of the primary ion overnight prior to use. The characteristic sensors of the membranes were fully examined: the potentiometric response, working concentration range, selectivity, response time, working pH range and reversibility of membrane electrodes. All the experiments were replicated in three times.

4.2.1 Potentiometric cations responses

The PVC membrane electrodes were prepared from ionophores **II** and **III** (ca. 10 mmol kg^{-1}) in the presence of 75 mol% KT*p*ClPB (related to ionophore) in *o*-NPOE plasticized PVC membranes. A comparative study of cation sensing abilities of the both ionophores as cation carriers in PVC membranes was investigated by the potentiometric response toward a diversity of cation ions, including alkali, alkaline earth and transition metal ions (Na^+, K^+, Mg^{2+}, Ca^{2+}, Cr^{3+}, Fe^{3+}, Ni^{2+}, Cu^{2+}, Zn^{2+}, Cd^{2+} and Pb^{2+}) as nitrate salts at the concentration range 10^{-7} to 10^{-2} M of cation ions. The potentiometric cation responses have been considered in terms of a slope near Nernstian's equation (29.2 mV decade^{-1}) and a working concentration range. The responses of membranes containing **II** and **III** were shown in Figure 4.2 and 4.3. Both electrodes from ionophores **II** and **III** showed good responses to Cd^{2+} compared to other cation ions because ionophores **II** and **III** possessing two tripodal amine receptors that can accommodate Cd^{2+} ions [51, 53, 70-72]. The results of the potentiometric responses indicated that the fabricated PVC membranes from **II** and **III** have a selective response to Cd^{2+} over other cations, resulting in a Nernstian characteristic response in a wide concentration range, while membrane prepared from **II** and **III** displays responses towards cations which give responses characteristics non Nernstian's slope as illustrated in Appendix B (Table A1 and A2). In the case of Cu^{2+}, the membranes from **II** and **III** gave the negative EMF response after electrode contacted with a Cu^{2+} solution. This phenomenon is call Donnan exclusion failure [73] due to the ionophore formed strong and non-reversible complexes with Cu^{2+} resulting in changes of the permselectivity of the membranes. Then the membrane responded to NO_3^- from $Cu(NO_3)_2$ or other anions to give a negative EMF value. The data are shown in Figure 4.2 and 4.3 for both electrodes fabricated from **II** and **III**. In the previous work, tripodal amine moieties were successfully modified on calix[4]arene and anthrancene scaffold and used as neutral ionophores towards anions from Donnan failure in ion selective electrode induced by Cu^{2+} [33, 34]. Therefore, these ionophores were not suitable to fabricate membrane electrodes for Cu^{2+} detection.
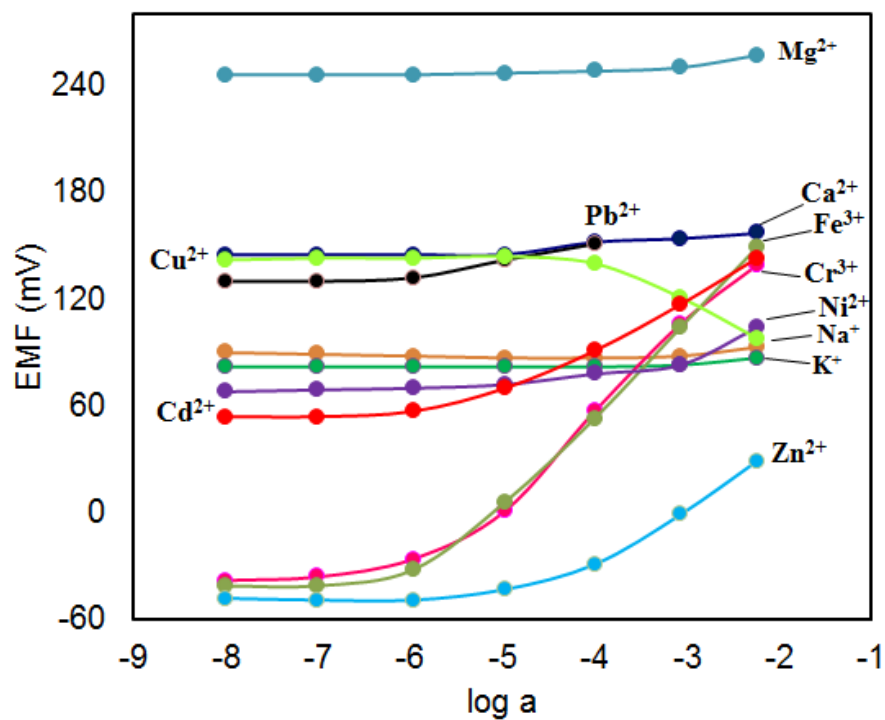
Figure 4.2 Potentiometric cations response of membranes containing **II** in the presence of 75 mol% KT*p*ClPB.
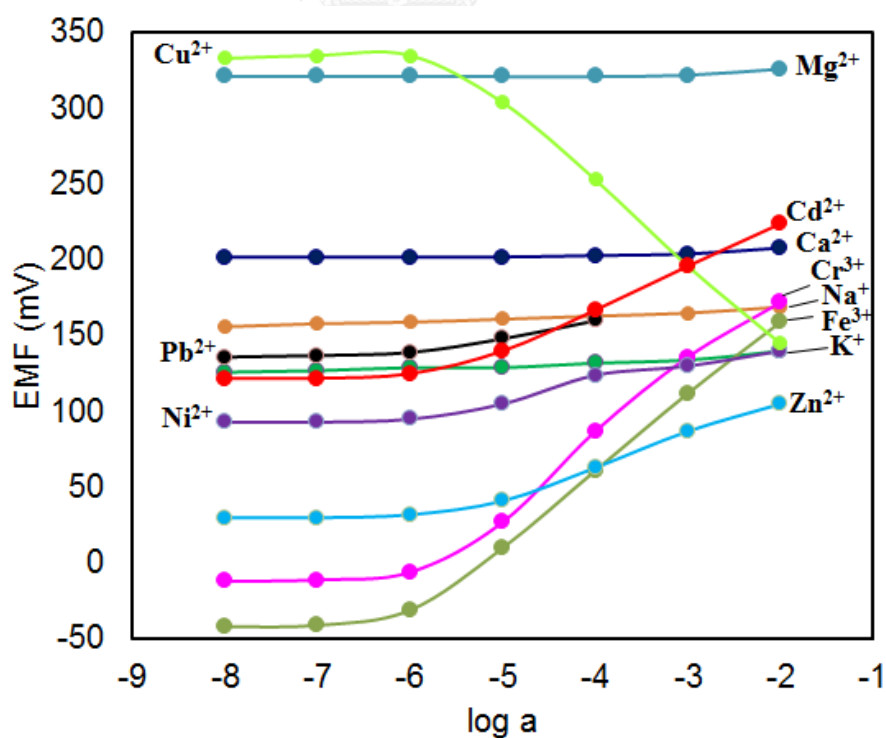
Figure 4.3 Potentiometric cations response of membranes containing **III** in the presence of 75 mol% KT*p*ClPB.

4.2.2 Optimization of membrane compositions

Besides the important role of the ion carrier in preparing membrane electrodes, some important features of the PVC membrane, such as the amount of ionophores, nature of plasticizers and especially the ionic additives used, significantly influenced the sensitivity and selectivity. It is well known that the sensitivity and selectivity obtained for a given ion selective electrode not only depends on the nature of ionophore but also significantly on the membrane composition and the properties of the plasticizer employed [74]. Thus, the effects of the membrane composition and the nature of plasticizer on the response characteristics of Cd-ISEs based on **II** and **III** were investigated and the results are summarized in Tables 4.1 and 4.2. The optimal compositions were considered from the response slope to the theoretical Nernstian's equation (29.6 mV decade^{-1}) and the lower detection limit toward Cd^{2+}. Moreover, the working concentration range and reproducibility of electrode (standard deviations in triplicate experiments) were also significant characteristics to be investigated.

Commonly used plasticizers include *o*-NPOE and DOS [75], while the ionic additives are assisted to balance charge between inside and outside in the membrane and reducing resistance of the membrane [76]. The ionophores were incorporated into two different ionic additives namely KT*p*ClPB and NaTFPB as ionic exchangers and different plasticizers *o*-NPOE and DOS in PVC membranes. The compositions of the membranes were optimized by using a constant amount of ionophores (ca. 10 mmol.kg^{-1}) and varying mol% of ionic additives (25, 50 and 75 mol% relate to the ionophores) and keeping ratios of PVC: plasticizers (1:2 by weight).

The membrane compositions and characteristics of electrodes from ionophores **II** are shown in Table 4.1 (entries 1-12). The potential responses of membrane are illustrated in Figure 4.4. Figure 4.4a show the response characteristics of *o*-NPOE membrane in the presence of 25 and 50 mol% KT*p*ClPB these membranes illustrating a lower than Nernstain's slope (23.1 ± 0.1 and 22.1 ± 0.1 mV dacade^{-1}, respectively). However, when the ionic additive was increased to 75 mol% KT*p*ClPB, the membrane response was found with a slope of 26.6 ± 0.2 mV decade^{-1} at the concentration ranges 10^{-5}- 10^{-2} M and gave the lower detection limit of 4.75x10^{-6} M.

The results are showed in Table 4.1 (entries 1-3). On the other hand, DOS-plasticized PVC membranes incorporated with 25, 50 and 75 mol% KTpClPB (Table 4.3, entries 4-6) showed nonlinearity response in the working concentrations, especially at the concentration 10^{-2} M as illustrated in Figure 4.4b.

For the membrane using **II** incorporated in NaTFPB as ionic additives in the presence of o-NPOE and DOS plasticized PVC membranes, it was found that o-NPOE plasticized PVC membranes in the presence 25 mol% NaTFPB (entry 7) showed closes to Nernst equation (30.7 ± 0.1 mV decade^{-1}). However, this composition was not suitable composition due to the unstability of response potentials upon repeating experiments. The result was shown in Appendix B (A22). Upon the increase amount of ionic additives to 50 and 75 mol% NaTFPB (entries 8-9), the membranes exhibited under- Nernstian slope (25.5 ± 0.6 and 23.6 ± 0.4 mV dacade^{-1}, respectively) as illustrated in Figure 4.4c. Membrane electrode prepared with DOS plasticized PVC membranes showed a super-Nernstian slope (44.5 ± 0.4 mV decade^{-1}) at the concentration range 10^{-5}-10^{-2} M for membrane in the presence of 25% NaTFPB, while 50 and 75 mol% NaTFPB displayed narrow concentration range and showed non Nernstain responses (Figure 4.4d). The results are summarized in Table 4.1 (entries 10-12).

The results of Table 4.1 showed that most compositions using for membranes **II** were inappropriate for preparing Cd-ISEs because they have no appropiate to the EMF measurements. Only the prepared Cd-ISE from ionophores **II** using 75 mol% KTpClPB and o-NPOE plasticized PVC membrane (entry 3) showed the best composition that given the best characteristic response in terms of slope, working concentration range, reproducibility (repeated three experiments) and lower detection limit. However, the ionophore **II** gave a under-Nernstian slope (26.6 ± 0.2 mV decade^{-1}), possibly due to the leaching of ionophores II from the organic phase to the aqueous phase.

Furthermore, the characteristics of membrane electrodes based on ionophore **III** at the same compositions with **II** are summarize in Table 4.2 (entries 13-24) and the potential responses are shown in Figure 4.5. It was found that the *o*-NPOE plasticized polymeric membrane in the presence of 25 mol% KT*p*ClPB (entry 13) showed a narrow working concentration range, while membrane containing 50 mol% KT*p*ClPB (entry 14) gave a slope of 31.0 ± 0.1 mV decade^{-1}, but cannot reproducible measurements when examining three times. The result was shown in Appendix B (A23). On the other hand, when changing the amount of KT*p*ClPB to 75 mol% (entry. 15), the potential response exhibited good characteristic Nernstian response slope of 30.7 ± 0.1 mV decade^{-1}. This electrode showed a working concentration range of 10^{-5} to 10^{-2} M and the detection limit of 3.95×10^{-6} M. In the case of *o*-NPOE plasticized PVC membrane incorporated with NaTFPB as ionic additive, the membranes containing 25, 50 and 75 mol% NaTFPB (entries 19-21) displayed under-Nernstain slope of 23.5 ± 0.3, 22.8 ± 0.3 and 23.5 ± 03 mVdecade^{-1}, respectively. The characteristics responses are shown in Figure 4.5c. For the membranes entries 16-18 and 22-24 gave super-Nernstian slope. The characteristics responses are illustrated in Figure 4.5b and d.

The results from Tables 4.1 and 4.2 indicated that ionophore **III** was more a suitable cation carrier than ionophore **II** in terms of a good response characteristics to Nernstian slope and a lower detection limit, possibly due to the ionophore **III** containing a calix[4]arene building based having more stability in the membrane phase. Moreover, the increased lipophilicity of calix[4]arene frameworks can prevent leaching of the ionophore from the membrane phase better than aryl ethyne based ionophore **II**. Hence, in this work, we have chosen the ionophore **III,** incorporating 75 mol% of KT*p*ClPB as ionic additives and *o*-NPOE plasticized PVC membrane (1:2, PVC: *o*-NPOE) as the optimal composition to the fabrication of membrane and studied Cd^{2+} ion selective electrodes.

Table 4.1 Membrane preparation and electrode response properties of ionophores **II** towards $Cd(NO_3)_2$

Entry	Membrane composition						Slope	Linear	R^2	Detection
	Ionophore **II**	Ionic additives		Plasticizers		PVC	(mVdecade^{-1})	range	(n=3)	limit
	mg (mmol.kg^{-1})	KTpClPB	NaTFPB	o-NPOE	DOS	mg (wt.%)	($\pm$ SD, n=3)	(M)		(M)
		mg (mol %)	mg (mol%)	mg (wt.%)	mg (wt.%)					
1	1.85 (10.0)	0.28 (25.6)		145.30 (66.0)		72.72 (33.0)	23.1 ± 0.1	10^{-5}-10^{-3}	0.9925	4.30 x 10^{-6}
2	1.84 (10.0)	0.56 (50.3)		145.13 (65.9)		72.62 (32.9)	22.1 ± 0.1	10^{-5}-10^{-3}	0.9964	4.06 x 10^{-6}
3	1.90 (10.3)	0.85 (77.9)		144.92 (65.9)		72.53 (32.9)	26.6 ± 0.2	10^{-5}-10^{-2}	0.9933	4.75 x 10^{-6}
4	1.83 (10.0)	0.27 (24.7)			145.33 (66.0)	72.64 (33.0)	50.8 ± 0.3	10^{-5}-10^{-3}	0.9998	1.84 x 10^{-6}
5	1.88 (10.2)	0.54 (49.4)			145.20 (65.9)	72.56 (32.9)	31.0 ± 0.1	10^{-5}-10^{-3}	0.9932	3.36 x 10^{-6}
6	1.83 (10.0)	0.82 (75.1)			144.93 (65.8)	72.50 (32.9)	23.5 ± 0.3	10^{-5}-10^{-3}	0.9967	3.58 x 10^{-6}
7	1.85 (10.0)		0.47 (24.6)	145.20 (65.9)		72.56 (32.9)	30.7 ± 0.1	10^{-5}-10^{-2}	0.9947	6.58 x 10^{-6}
8	1.87 (10.1)		0.99 (51.8)	144.90 (65.7)		72.46 (32.9)	25.5 ± 0.4	10^{-5}-10^{-2}	0.9882	5.25 x 10^{-6}
9	1.83 (10.0)		1.46 (76.5)	144.59 (65.6)		72.25 (32.8)	23.6 ± 0.2	10^{-5}-10^{-2}	0.9927	5.14x 10^{-6}
10	1.87 (10.1)		0.49 (25.6)		145.22 (65.9)	72.60 (32.9)	44.5 ± 0.4	10^{-5}-10^{-2}	0.9952	5.06 x 10^{-6}
11	1.84 (10.0)		0.96 (50.3)		144.85 (65.8)	72.43 (32.9)	26.4 ± 0.3	10^{-5}-10^{-3}	0.9859	2.72 x 10^{-6}
12	1.85 (10.0)		1.48 (77.6)		144.50 (65.6)	72.25 (32.8)	23.3 ± 0.3	10^{-5}-10^{-3}	0.9963	3.67 x 10^{-6}

Figure 4.4 The effect of ionic additives in the presence of different plasticizers of membrane containing **II** response toward Cd^{2+}, (a) and (b) are KTpClPB in o-NPOE and DOS, (c) and (d) are NaTFPB in o-NPOE and DOS, respectively.

Table 4.2 Membrane preparation and electrode response properties of ionophores **III** towards $Cd(NO_3)_2$

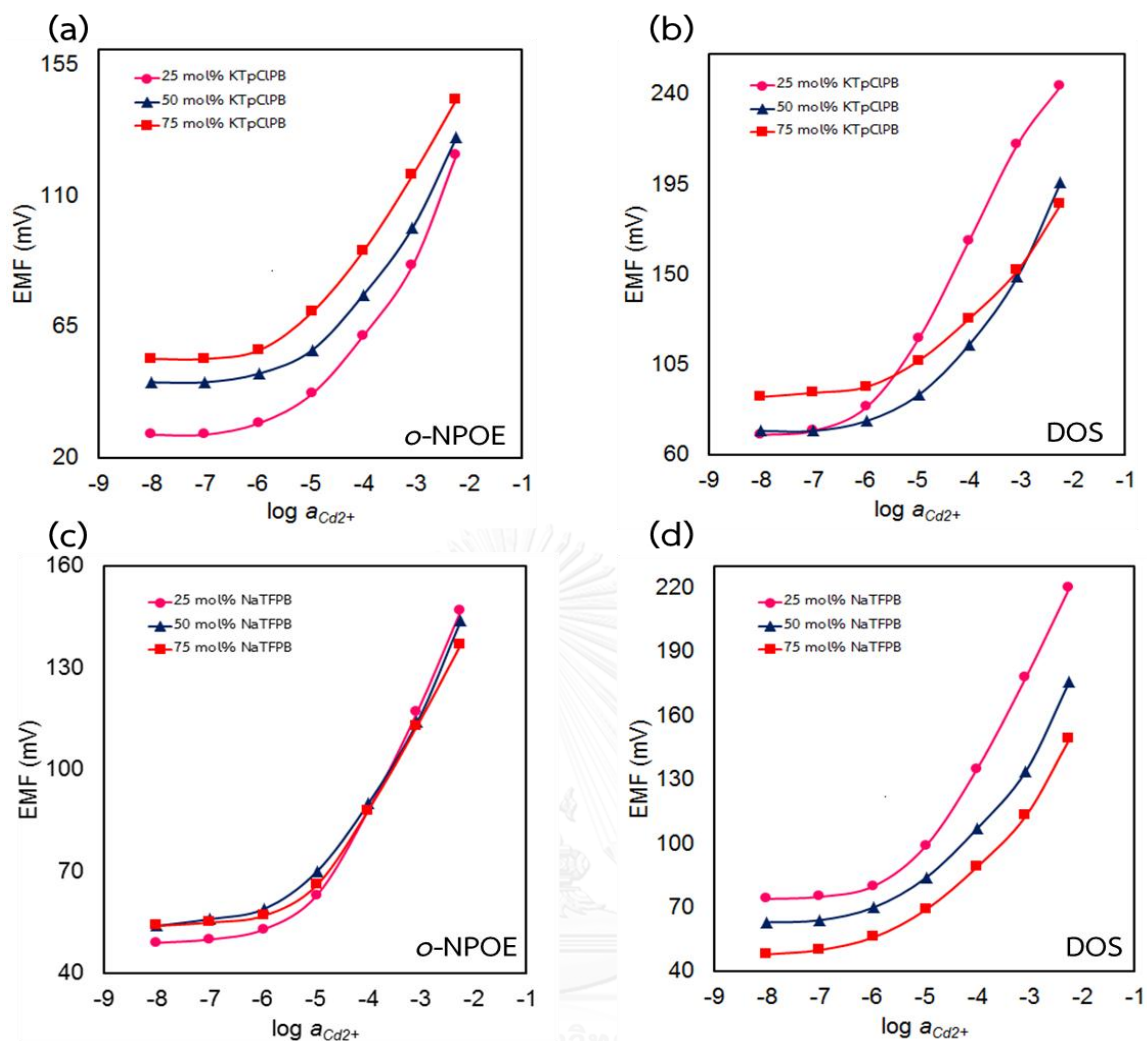| Entry	Ionophore III mg (mmol.kg^{-1})	Ionic additives		Plasticizers		PVC mg (wt.%)	Slope (mVdecade^{-1}) ($\pm$ SD, n=3)	Linear range (M)	R^2 (n=3)	Detection limit (M)
		KTpClPB mg (mol %)	NaTFPB mg (mol%)	o-NPOE mg (wt.%)	DOS mg (wt.%)					
13	3.07 (10.0)	0.28 (25.6)		144.48 (65.6)		72.33 (32.8)	30.4 $\pm$ 0.1	10^{-5}-10^{-3}	0.9808	6.64 x 10^{-6}
14	3.06 (10.0)	0.54 (49.4)		144.29 (65.5)		72.19 (32.8)	31.0 $\pm$ 0.1	10^{-5}-10^{-2}	0.9943	6.36 x 10^{-6}
15	3.07 (10.0)	0.87 (79.6)		144.10 (65.4)		72.12 (32.7)	30.7 $\pm$ 0.1	10^{-5}-10^{-2}	0.9975	3.95 x 10^{-6}
16	3.06 (10.0)	0.29 (26.5)			144.49 (65.6)	72.30 (32.8)	39.0 $\pm$ 0.1	10^{-5}-10^{-2}	0.9908	5.01 x 10^{-6}
17	3.06 (10.0)	0.54 (49.4)			144.32 (65.6)	72.18 (32.8)	34.7 $\pm$ 0.1	10^{-5}-10^{-2}	0.9937	2.65 x 10^{-6}
18	3.09 (10.0)	0.83 (76.0)			144.10 (65.4)	72.07 (32.7)	33.2 $\pm$ 0.1	10^{-5}-10^{-2}	0.9924	4.75 x 10^{-6}
19	3.08 (10.0)		0.48 (24.6)	144.45 (65.6)		72.16 (32.7)	23.5 $\pm$ 0.3	10^{-5}-10^{-3}	0.9846	6.04 x 10^{-6}
20	3.08 (10.0)		0.98 (49.7)	144.02 (65.4)		72.01 (32.7)	22.8 $\pm$ 0.4	10^{-5}-10^{-3}	0.9895	5.22 x 10^{-6}
21	3.10 (10.1)		1.45 (74.3)	143.70 (65.2)		71.88 (32.6)	23.5 $\pm$ 0.3	10^{-5}-10^{-2}	0.9986	2.09 x 10^{-6}
22	3.10 (10.1)		0.49 (25.7)		144.35 (65.6)	72.16 (32.7)	39.4 $\pm$ 0.4	10^{-5}-10^{-2}	0.9993	3.01 x 10^{-6}
23	3.07 (10.0)		0.96 (50.3)		144.12 (65.4)	72.10 (32.7)	35.5 $\pm$ 0.3	10^{-5}-10^{-2}	0.9988	1.96 x 10^{-6}
24	3.05 (9.9)		1.45 (76.0)		143.77 (65.3)	71.89 (32.6)	33.4 $\pm$ 0.1	10^{-5}-10^{-2}	0.9993	3.08 x 10^{-6}
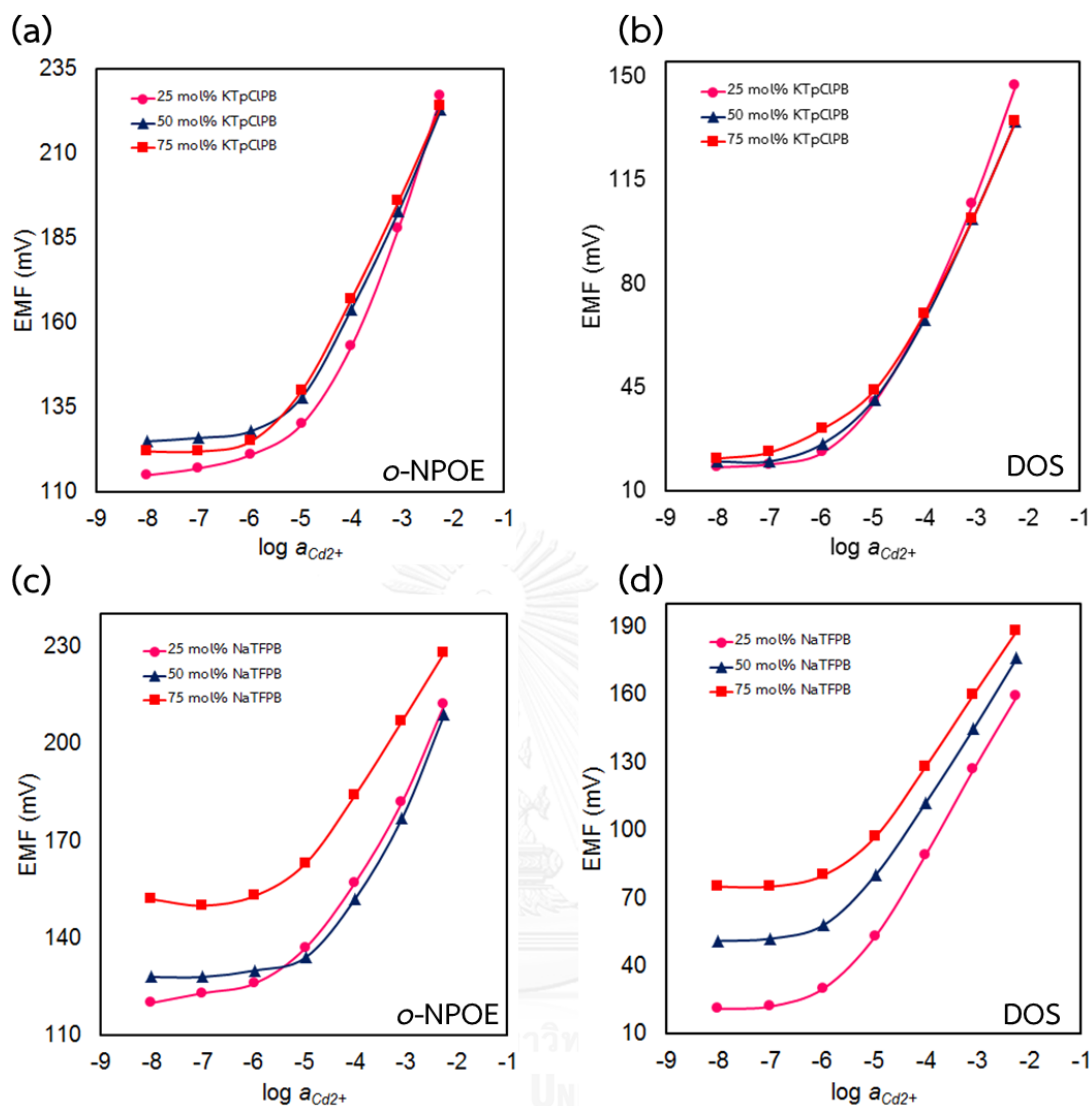
Figure 4.5 The effect of ionic additives in the presence of different plasticizers of membrane containing **III** response toward Cd^{2+}, (a) and (b) are KT*p*ClPB in *o*-NPOE and DOS, (c) and (d) are NaTFPB in *o*-NPOE and DOS, respectively.

4.2.3 Response characteristics of the membrane fabricated from II and III

The optimized membrane compositions from **II** and **III** were used to determine the characteristics response of the electrode performances. As shown in Figure 4.5 and 4.6 for the responses of fabricated Cd-ISEs by using ionophores **II** and **III**, respectively. It was found that, the EMF value increased upon addition of Cd^{2+} solution concentration from 10^{-7} to 10^{-2} M. The response times of the membranes were calculated according to IUPAC recommended. the fabricated membrane

electrode from ionophores **II** and **III** displayed fast response time in less than 5 s before reaching an equilibrium potential value of each the concentration corresponding to the fast exchange of the kinetics when occur complexation and decomplexation of Cd^{2+} and ionophores in membrane phase [77]. The insets displayed calibration curves that provided theoretical predicted Nernstian slopes of 26.6 ± 0.2 and 30.6 ± 0.1 mV decade^{-1} and detection limit of 4.75×10^{-6} and 3.96×10^{-6} M for Cd-ISEs using ionophores **II** and **III**, respectively. The detection limit was measured from the intersection of two extrapolated segments of calibration curves. In addition, both ionophores can determine Cd^{2+} in the concentration range of 10^{-5} to 10^{-2} M. The comparative study of the response characteristics of the membrane fabricated from **II** and **III**, show that III is a more suitable ionophores to prepare Cd^{2+} ion selective electrodes, and pH effect, reversibility and application are further examined.
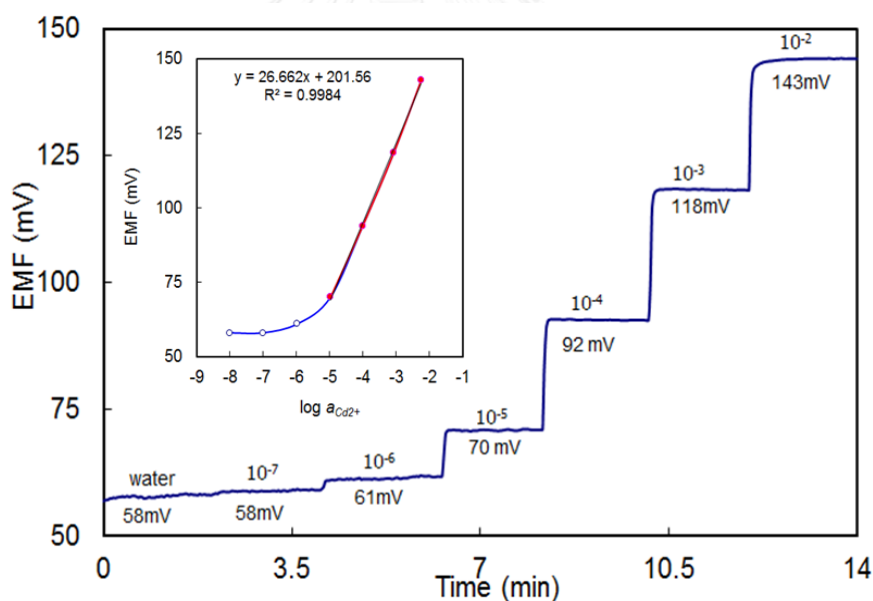

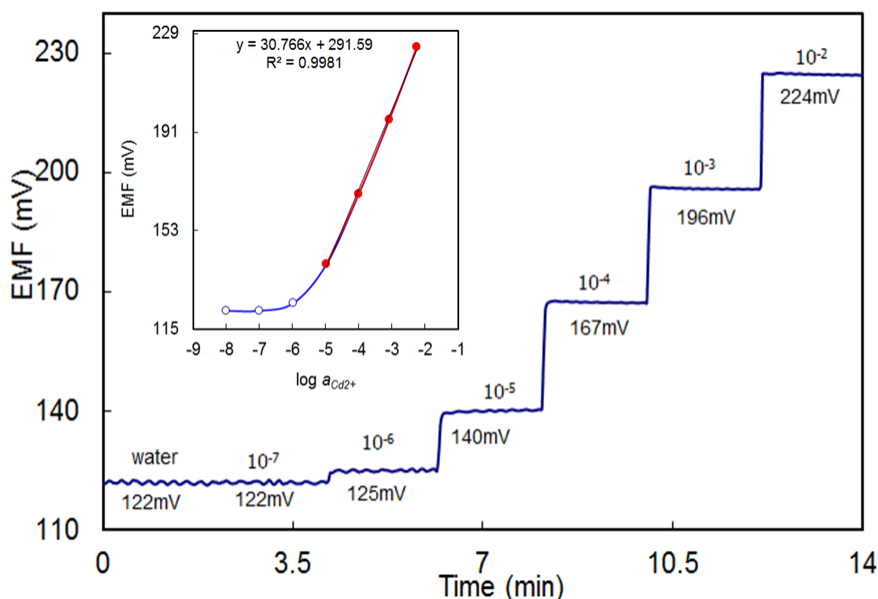**Figure 4.6** Response characteristic of the membranes containing **II** in the presence of 75 mol% KTpClPB toward Cd^{2+}

Figure 4.7 Response characteristic of the membranes containing **III** in the presence of 75 mol% KT*p*ClPB toward Cd^{2+}

4.2.4 Potentiometric selectivity of cadmium electrodes

The potentiometric selectivity coefficient ($\log K^{pot}_{Cd,j}$) is one of the most important characteristics of an ion selective electrode. In this work, the potentiometric responses of the proposed Cd-ISEs relative to a variety of metal ions (Na^+, K^+, Mg^{2+}, Ca^{2+}, Cr^{3+}, Fe^{3+}, Ni^{2+}, Zn^{2+}, Cd^{2+} and Pb^{2+}) were determined by the separation solution method (SSM) as recommended by IUPAC [67]. The potentiometric of electrode comprising an ion selective electrode and a reference electrode is measured with two separate solutions. The selectivity coefficients were calculated from the observed EMF values at the concentration 0.01 M solutions of Cd^{2+} and interfering ions, only Pb^{2+} used in the concentration 10^{-4} M). The resulting logarithimic selectivity coefficients are summarized in Figure 4.8 and in Appendix B (Table A3). This diagram shows selectivity coefficient of the PVC membrane electrodes containing ionophores **II** and **III** in the presence of 75 mol% KT*p*ClPB incorporating in *o*-NPOE plasticized membranes. All the experiments were measured three times. From Figure 4.8, its can be seen that the fabricated Cd-ISE from ionophores **II** showed selectivity toward Cd^{2+} compared to other cations. Most of the interfering ions have selectivity coefficients lower than Cd^{2+} (order of the selectivity of ionophore **II**:

$Cd^{2+} > Zn^{2+} > Na^+ > K^+ > Ni^{2+} > Ca^{2+} > Mg^{2+}$) whereas Fe^{3+}, Cr^{3+} and Pb^{2+} were found to be strong interfering ions. The membrane containing ionophore **III** showed order of selectivity, $Cd^{2+} > Cr^{3+} > Ni^{2+} >> K^+ > Na^+ >> Ca^{2+} > Mg^{2+}$. In addition, the membrane had Fe^{3+} and Zn^{2+} as main interfering ions. The potential interfering ions of both electrodes were transition metals, probably due to hard–soft acid base effect of nitrogen donor and transition metal ions [78]. These interfering ions were commonly found for Cd-ISE. Moreover, alkali and alkaline earth showed more interfering effects in membranes containing ionophore **II** as compared to ionophore **III**. The results implied that ionophores **III** containing calix[4]arene framework possessed a suitable distance between two tripodal amine groups for accommodation of Cd^{2+} ions. Even though Fe^{3+} and Zn^{2+} was found to be main interfering ions for electrodes from ionophores **III**, these interfering ions showed non-Nernstian response as shown in the Figure 4.3. Therefore, electrodes from ionophores **III** can be used to detect Cd^{2+} in the solutions.
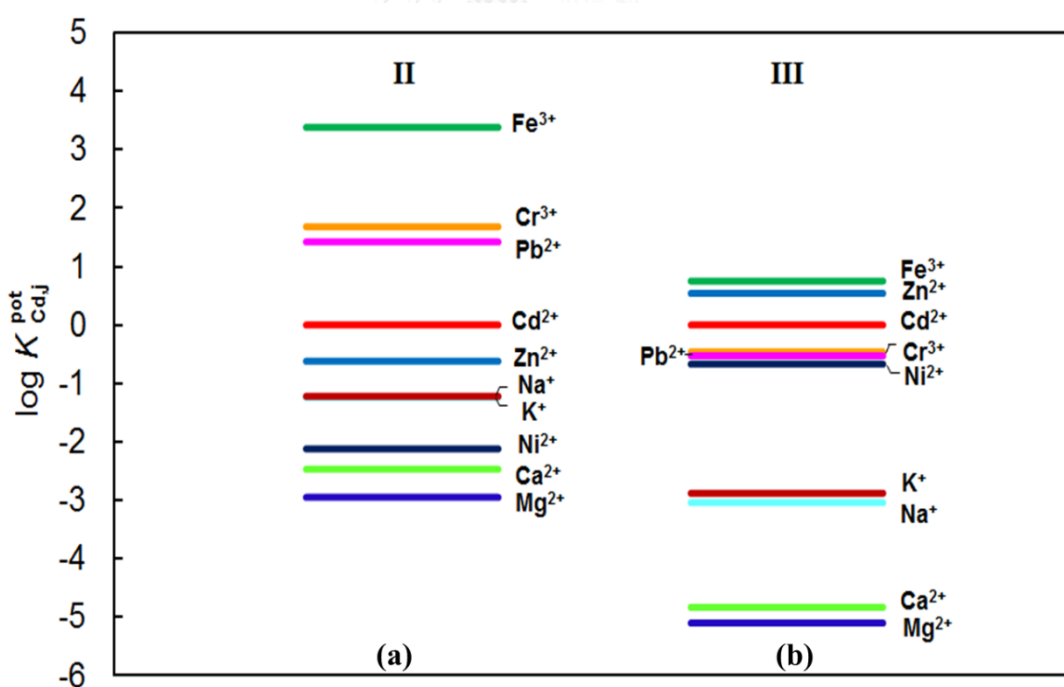

Figure 4.8 A comparison of the selectivity coefficients of the membranes containing (a) **II** and **III** (b) in the presence of 75 mol% KT*p*ClPB

4.2.5 pH effect of the membrane electrode

The effect of pH on the potentiometric response of the electrode containing **III** in the presence 75 mol% KTpClPB in o-NPOE plasticized PVC membrane was investigated at three fixed concentrations (10^{-4}, 10^{-3} and 10^{-2} M) of Cd^{2+} over the pH range between 2.0 and 10.0. The pH of the solution was adjusted by small dropping of 1% HNO_3 followed by 1M NaOH. The results as illustrated in Figure 4.9. It was found that the potentiometric responses remain constant within the pH range 4.5 - 6.0 and hene this was chosen as a working pH range for the Cd-ISEs. From the Figure 4.8, at the high pH (> 6.0) displayed deviations of the potentiometric response signals probably due to the effect of interference hydroxide ion and the formation cadmium hydroxide species in the system [79]. On the other hand, at low pH (< 4.5) the observed increase of the EMF signals due to the protonation of the ionophore in membrane phase and the electrodes responding to H^+ protonation of the nitrogen atoms in the structure of tripodal amine moieties along with the Cd^{2+} [42].
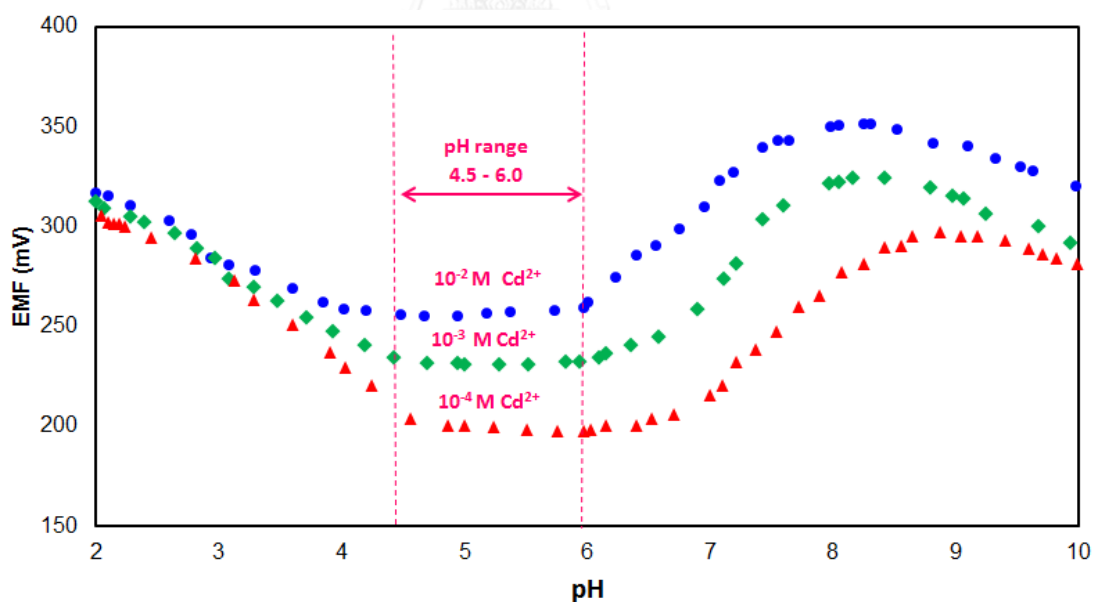
Figure 4.9 The pH effect on potentiometric response of the Cd-ISEs using ionophore **III** at different of the concentration between 10^{-4}, 10^{-3} and 10^{-2} M. Cd^{2+}

4.2.6 Reversibility of the membrane electrode

The reversibility of the membrane electrode containing **III** was investigated by measuring the potentiometric response of Cd^{2+} solution at the concentration 10^{-4} and 10^{-3} M. It can be seen from Figure 4.10. The result shows that, the potential of the electrode was rather stable at each concentration. When solutions of Cd^{2+} were changed from low to high concentration (10^{-4} to 10^{-3} M), the potentiometric responses were restored. The reversibility of electrode can measured over five times with excellent results.
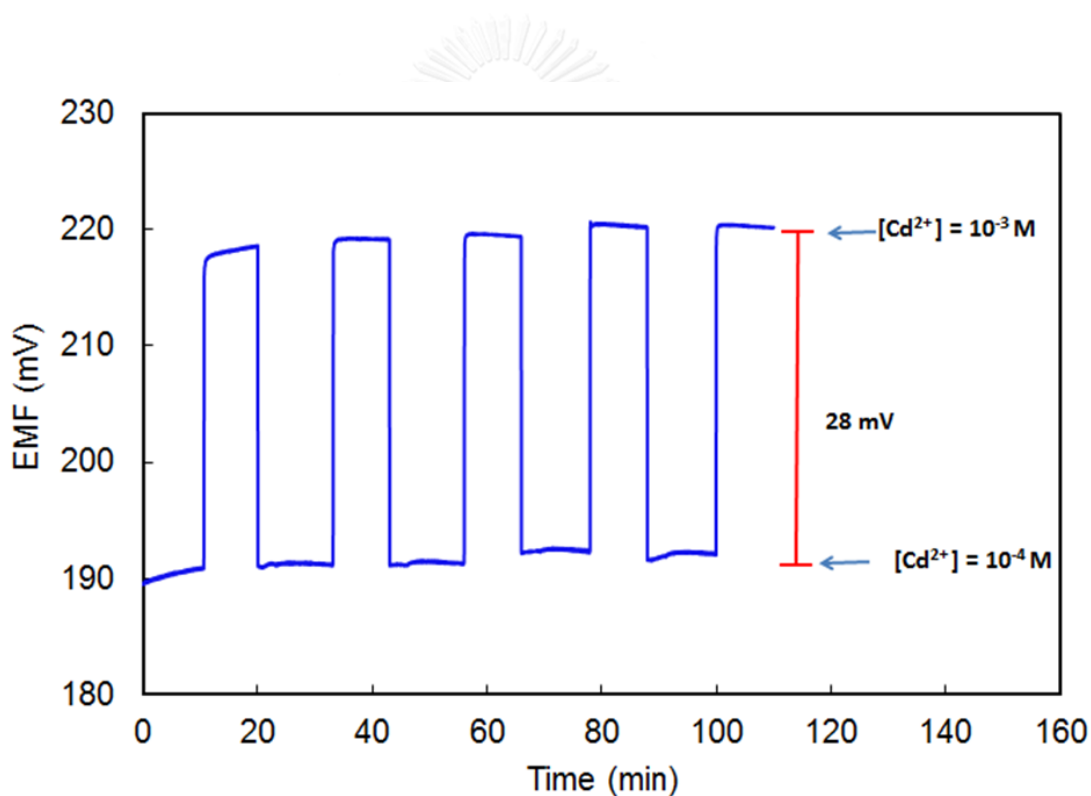
Figure 4.10 The reversibility of the Cd-ISEs using ionophore **III** at different of the concentration between 10^{-4} and 10^{-3} M Cd^{2+}

4.3 Analytical applications in real water samples

The applicability of the fabricated Cd-ISE from ionophore **III** was used for the determination of Cd^{2+} in real water samples such as drinking water (mineré, nestle and singha brands) and tap water. In the case of tap water was filtered through the nylon 0.45 μm membrane prior to use. In the experimental section, the water samples were spiked standard cadmium solution at the concentration 4.0×10^{-5} and 1.0×10^{-4} M into the samples. Unfortunately, the results were unsatisfied possibly due to the water samples contained varieties of the interfering ions that can disturb and decrease the electrode functions.

CHAPTER V
CONCLUSION

The design and synthesis of aryl ethyne building blocks containing a number of tripodal amine groups (ionophore **I** and **II**) has been successfully synthesized by the Sonogashira coupling in a one pot fashion followed by the Schiff-based coupling with tripodal amine (TPA) moieties to obtain desired ionophores **I** (11% yield) as minor product and **II** (40 % yield) as major product. The synthesized ionophores I and **II** were used as cation carriers in ion selective electrodes as well as comparative studies of the electrode characteristics with the ionophore **III** which is a calix[4]arene derivative.
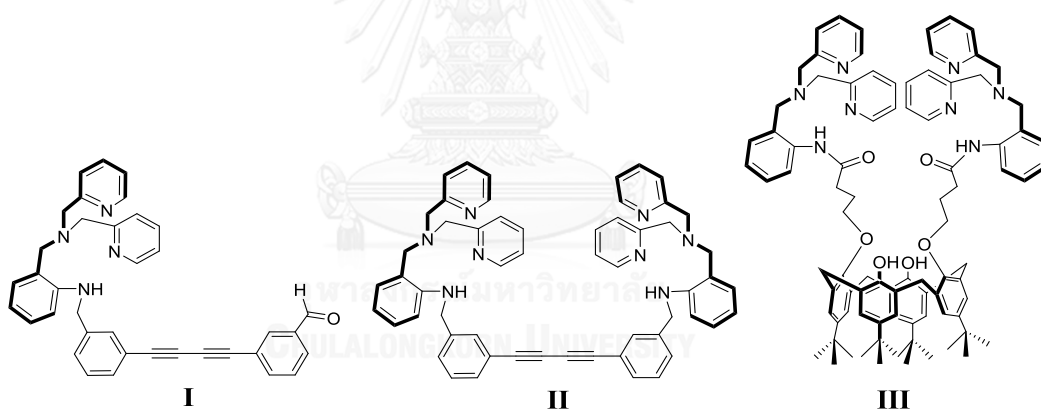
The membrane electrode using aryl ethyne and calix[4] arene building blocks containing tripodal amine donor groups (**II, II** and **III**) as neutral carriers were successfully prepared for Cd^{2+} ion selective electrodes at working concentration $10^{-5}10^{-2}$ M. However, ionophores **I** cannot be used to fabricate membrane electrode due to its instability and decomposition. The membrane using ionophore **II** incorporating with 75 mol% KT*p*ClPB, PVC and *o*-NPOE showed a Nernstian's slope of 26.6 ± 0.2 mV decade^{-1}, while the membrane using ionophore **III** containing at the same compositions with **II** displayed a good characteristic Nernstian's slope with 30.7

$\pm$ 0.1 mV decade^{-1} compared to other compositions. The detection limits of both electrodes containing **II** and **III** were 4.75x10^{-6} M and 3.95x10^{-6} M, respectively. The prepared membrane electrode can be used to detect Cd^{2+} in the pH range 4.5-6.0. Moreover these membrane electrode displayed a satisfactory reversibility and fast response time in less than ca. (<5s). In addition, the selectivity investigations of the fabricated Cd-ISEs show selectivity toward Cd^{2+} over a number of interfering ions. However, Fe^{3+}, Cr^{3+} and Pb^{2+} were found to be strong interfering ions to Cd^{2+} for ionophore **II** while membrane containing ionophore **III** had Fe^{3+} and Zn^{2+} as main interfering ions. Therefore, the fabricated Cd-ISEs also cannot be applied effectively to detect Cd^{2+} in real samples probably due to an effect of strong interfering ions in real samples.

Suggestion and future work

The main problem of this research is that the fabricated electrodes cannot be applied to determine cadmium in real samples due to many interfering ions. For ionophore **II** containing aryl ethyne building blocks, the ionophore is not lipophilic enough. This ionophore was leached from the organic phase into the aqueous phase. We suggest the synthesis of new ionophores having more lipophilic groups such as the alkyl chain connecting to the aryl ethyne building block. For ionophore **III** containing oxygen and nitrogen donor sites that can coordinate with various interfering ions, we suggest the synthesis of new ionophore by changing from the carbonyl groups to nitrogen donor sites in order to avoid binding to many non-targeting ions.

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APPENDIX

APPENDIX A
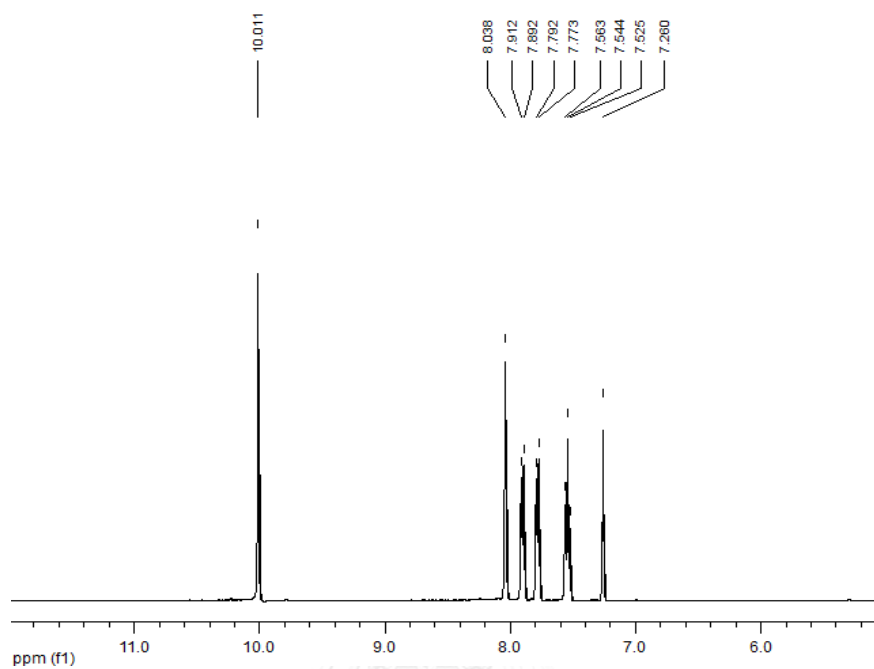
Figure A1 ^{1}H NMR spectrum of **1** in CDCl$_3$
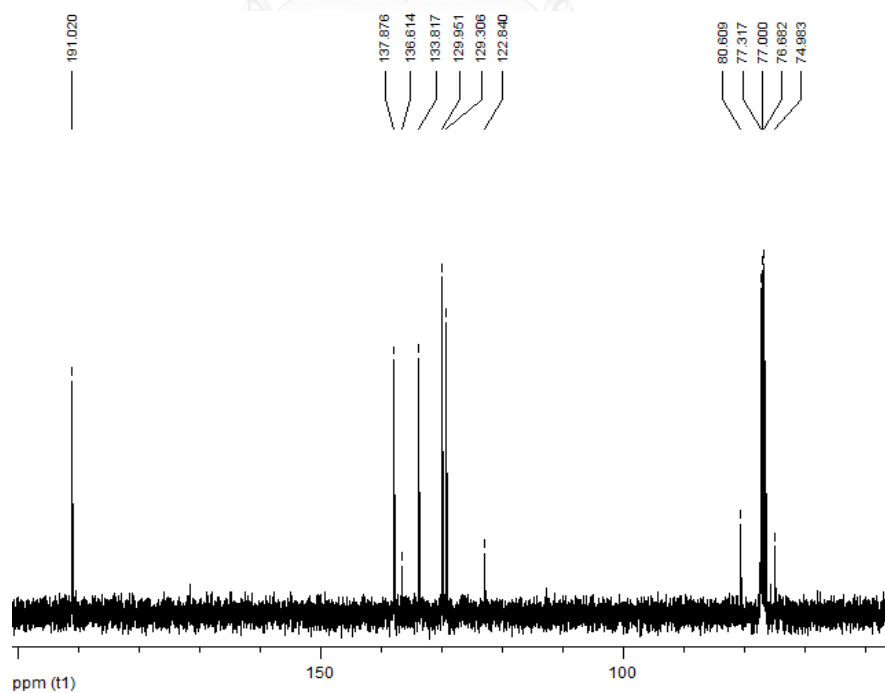
Figure A2 ^{13}C NMR spectrum of **1** in CDCl$_3$
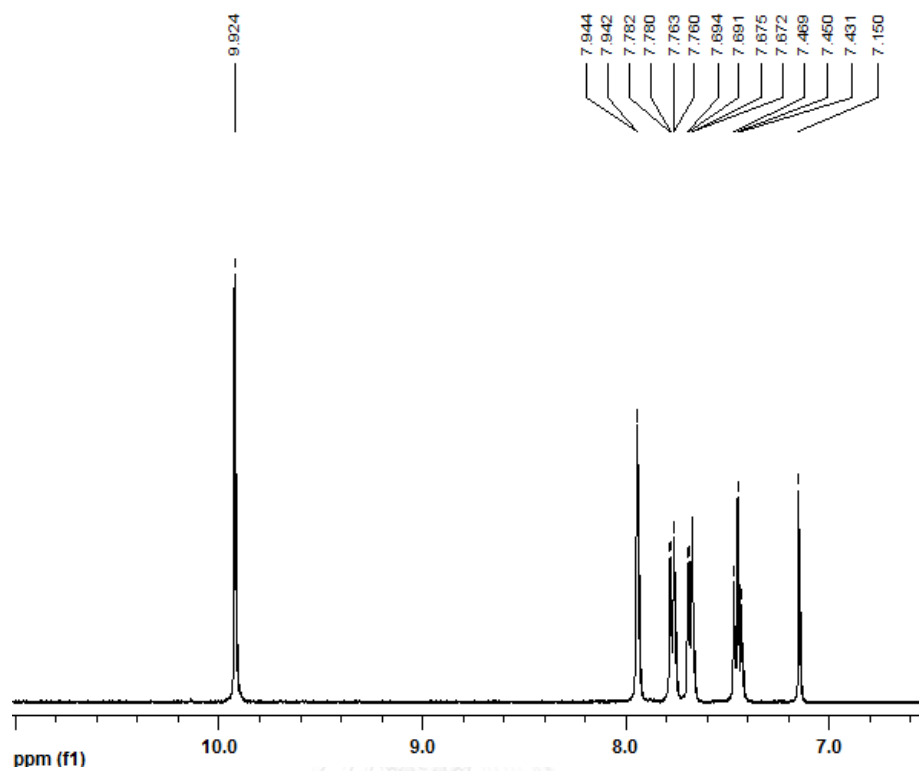
Figure A3 ^{1}H NMR spectrum of **2** in CDCl$_3$
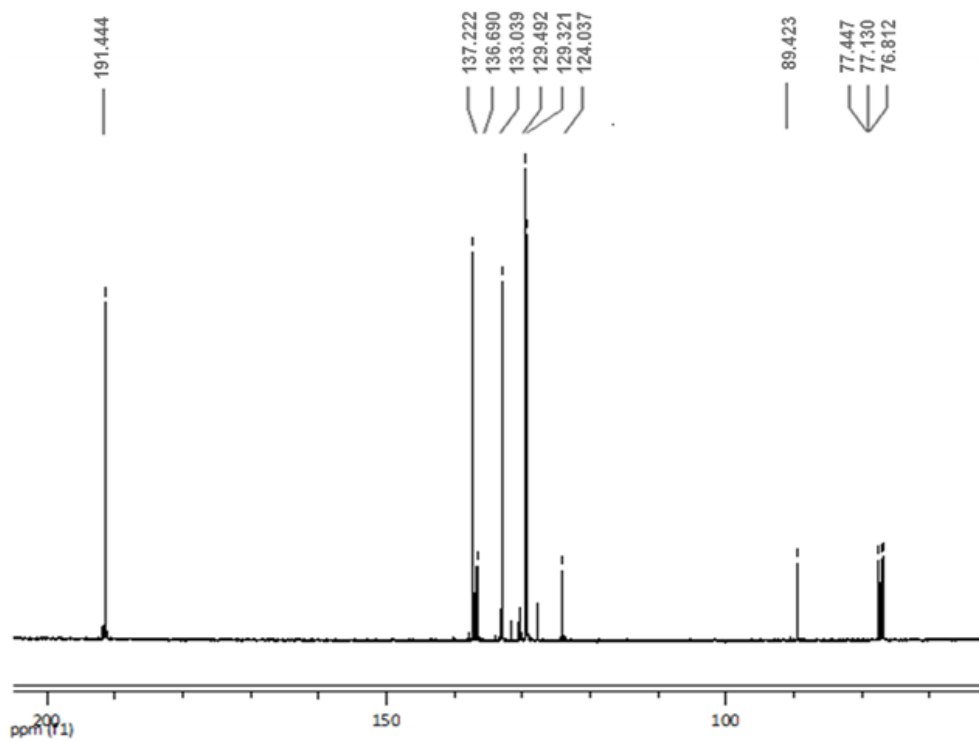

Figure A4 ^{13}C NMR spectrum of **2** in CDCl$_3$
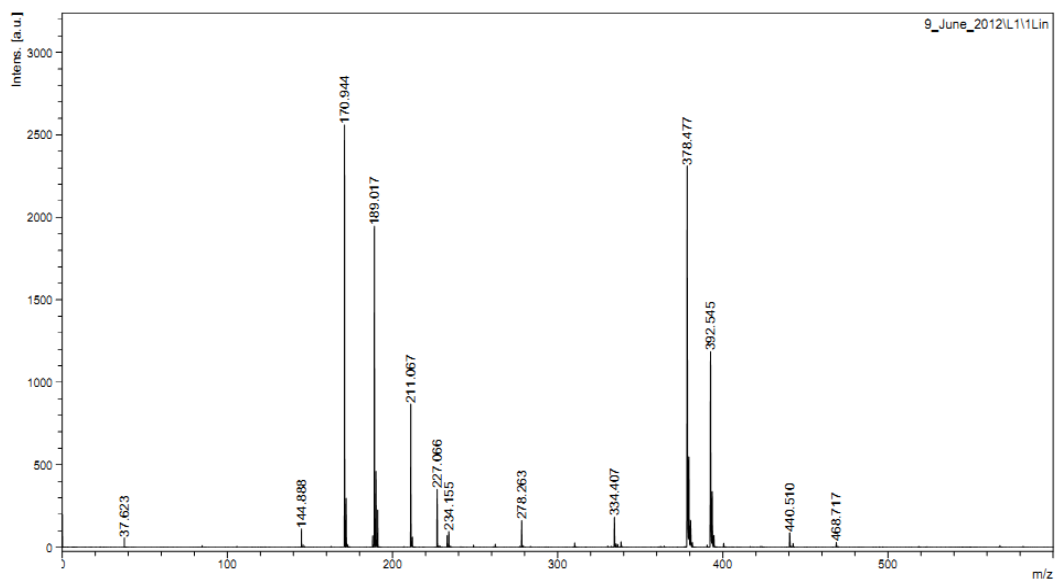
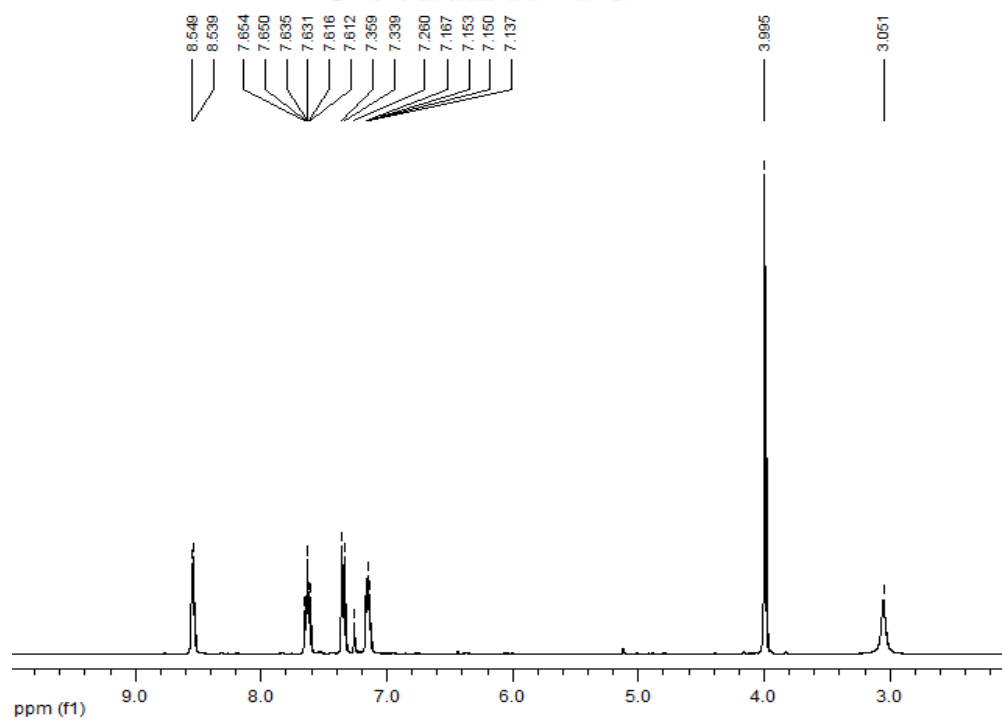**Figure A5** MALDI-TOF mass spectrum of **2**

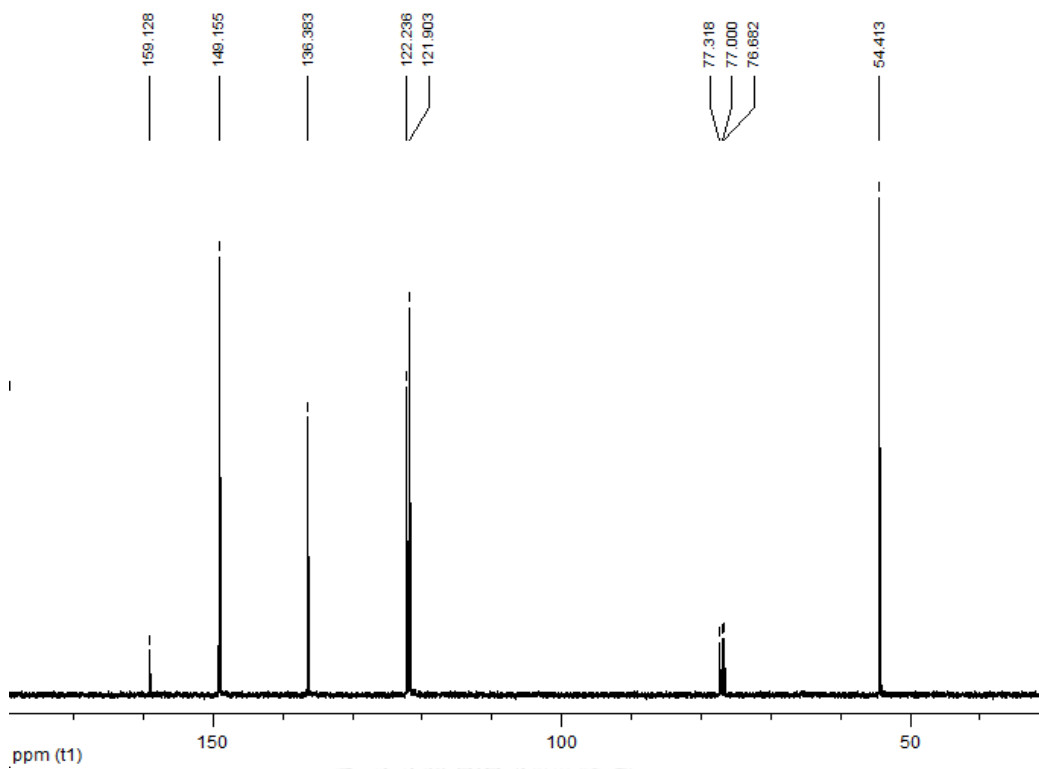**Figure A6** ^{1}H NMR spectrum of **1a** in CDCl$_3$

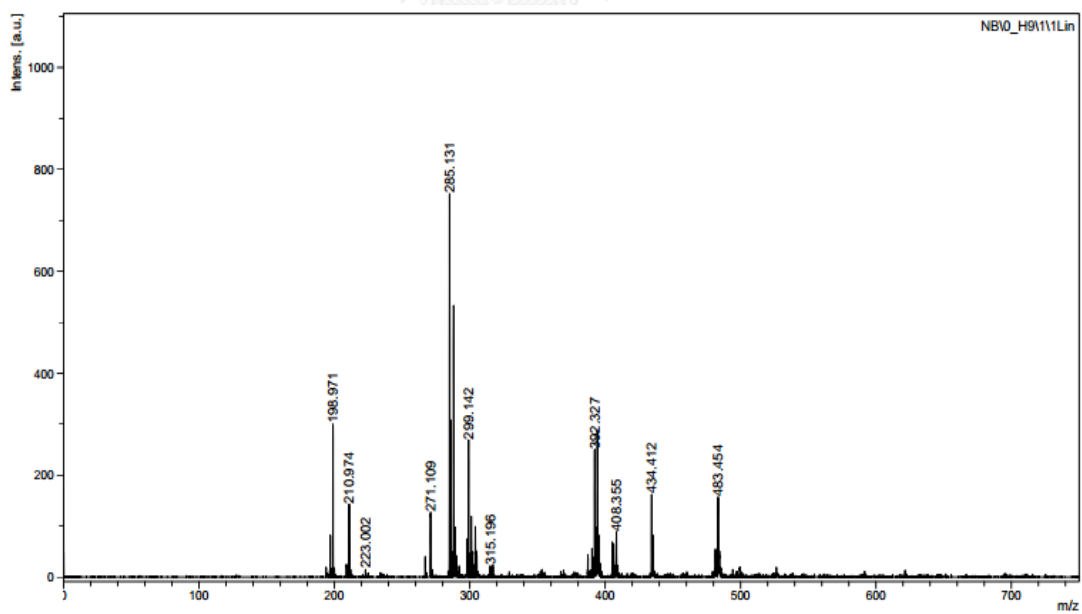**Figure A7** ^{13}C NMR spectrum of **1a** in CDCl$_3$

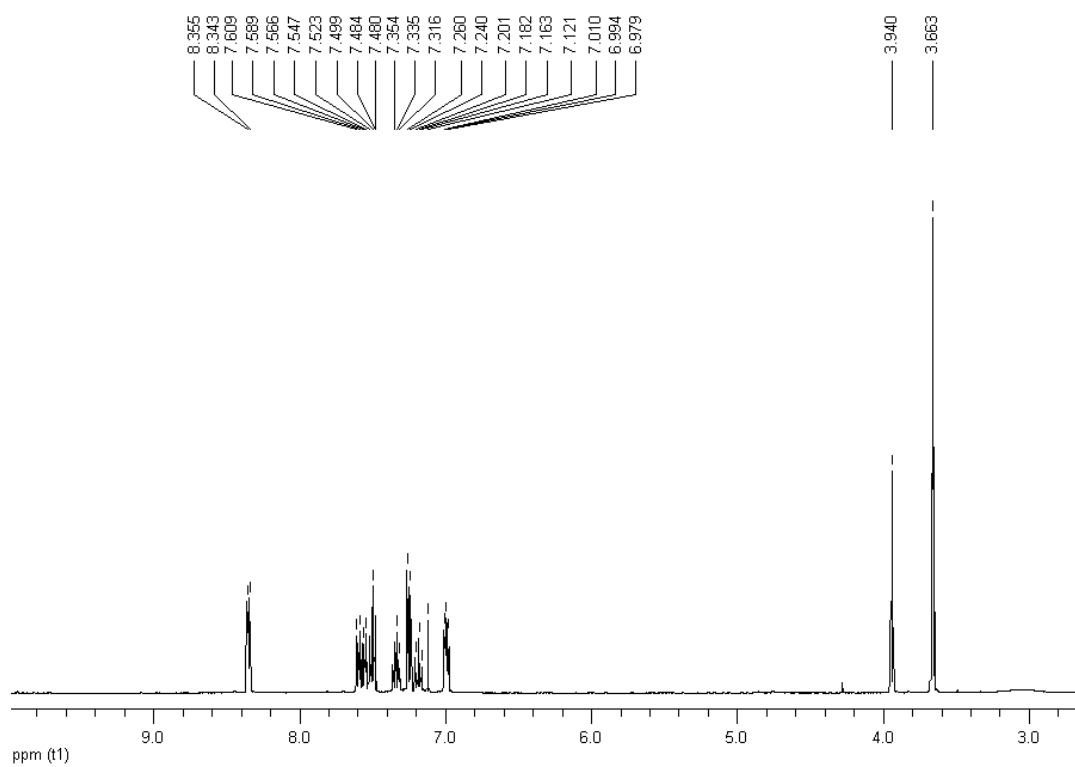**Figure A8** MALDI-TOF mass spectrum of **1a**

Figure A9 ^{1}H NMR spectrum of **1b** in CDCl$_3$
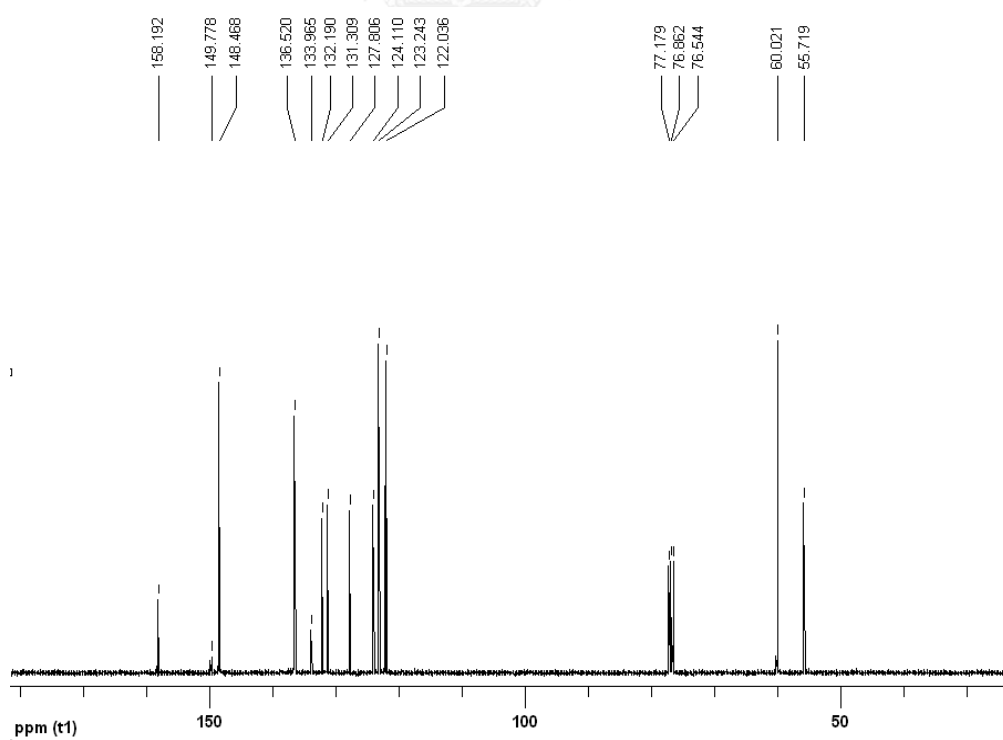

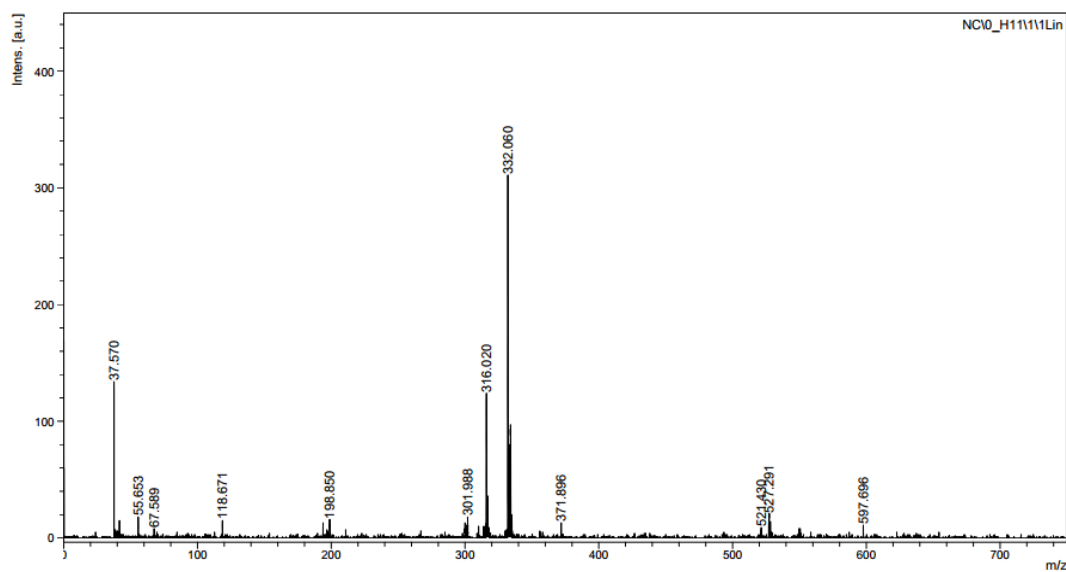**Figure A10** ^{13}C NMR spectrum of **1b** in CDCl$_3$

Figure A11 MALDI-TOF mass spectrum of **1b**
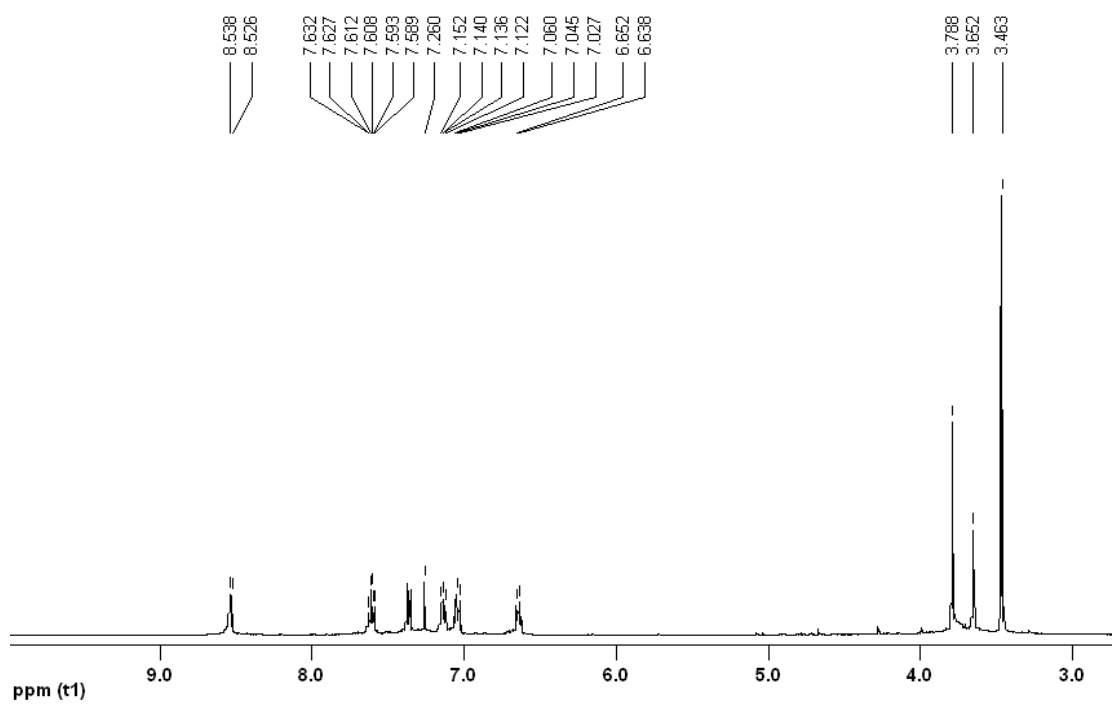

Figure A12 ^{1}H NMR spectrum of **TPA** in CDCl$_3$
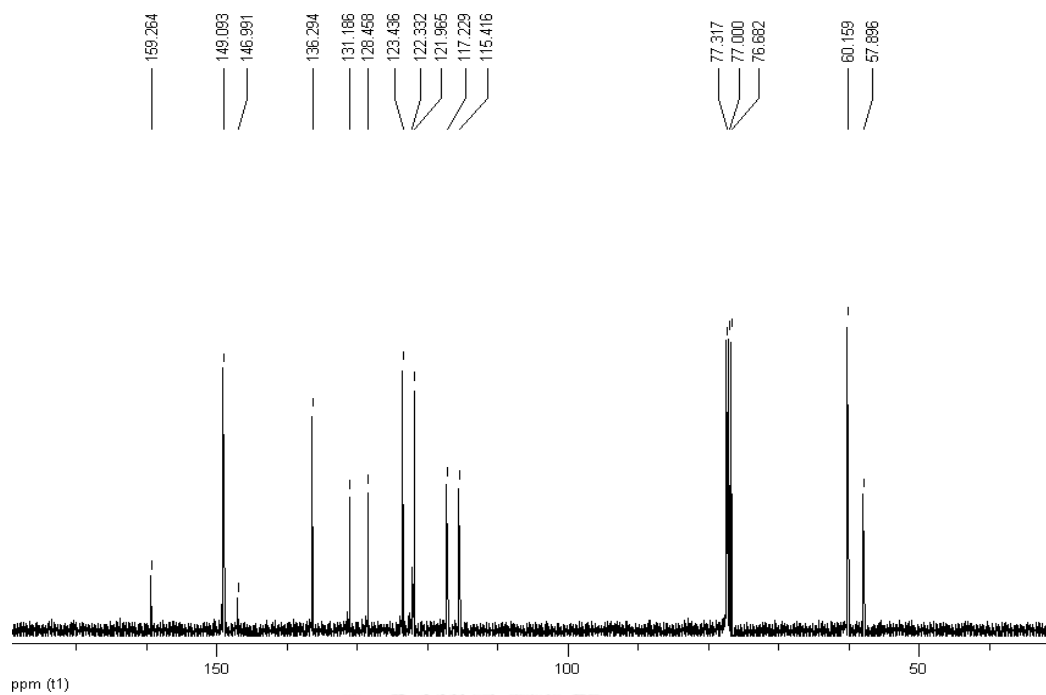
Figure A13 ^{13}C NMR spectrum of TPA in CDCl$_3$
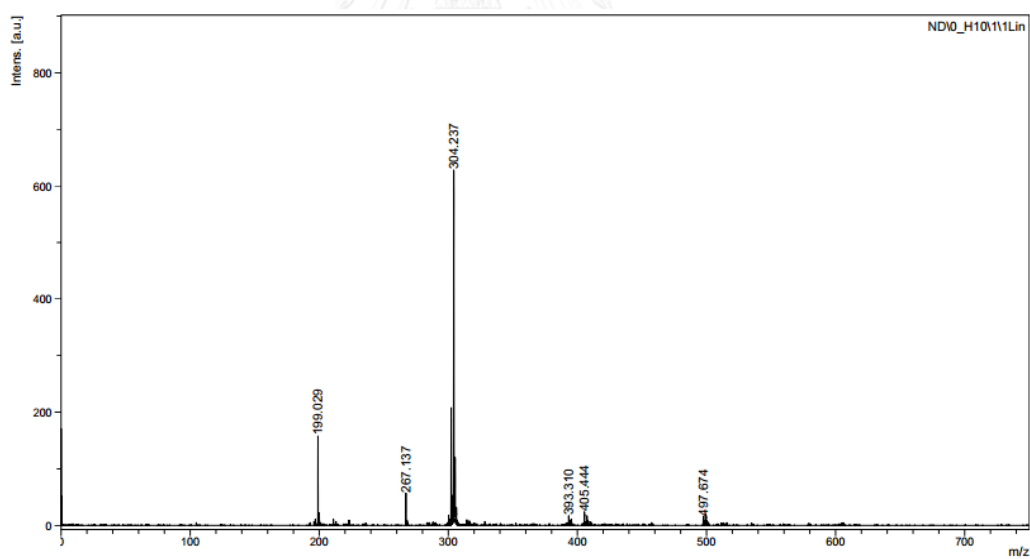
Figure A14 MALDI-TOF mass spectrum of TPA

9.982 8.471 8.459 8.439 8.004 7.873 7.854 7.735 7.562 7.544 7.427 7.414 7.395 7.380 7.286 7.268 7.260 7.113 7.101 7.084 7.073 7.067 6.606 6.588 6.570 6.461 6.440 4.393 3.798 3.785 3.689 3.682

Figure A15 ^{1}H NMR spectrum of ionophore **I** in CDCl$_3$

Figure A16 MALDI-TOF mass spectrum of ionophore **I**

Figure A17 ^{1}H NMR spectrum of ionophore **II** in CDCl$_3$

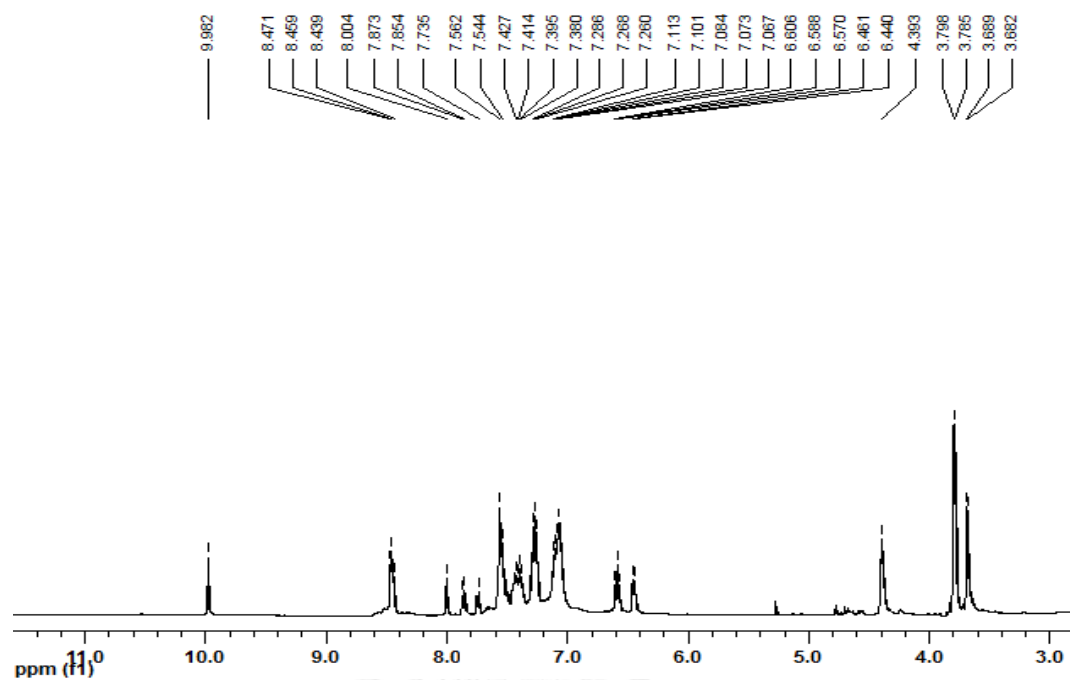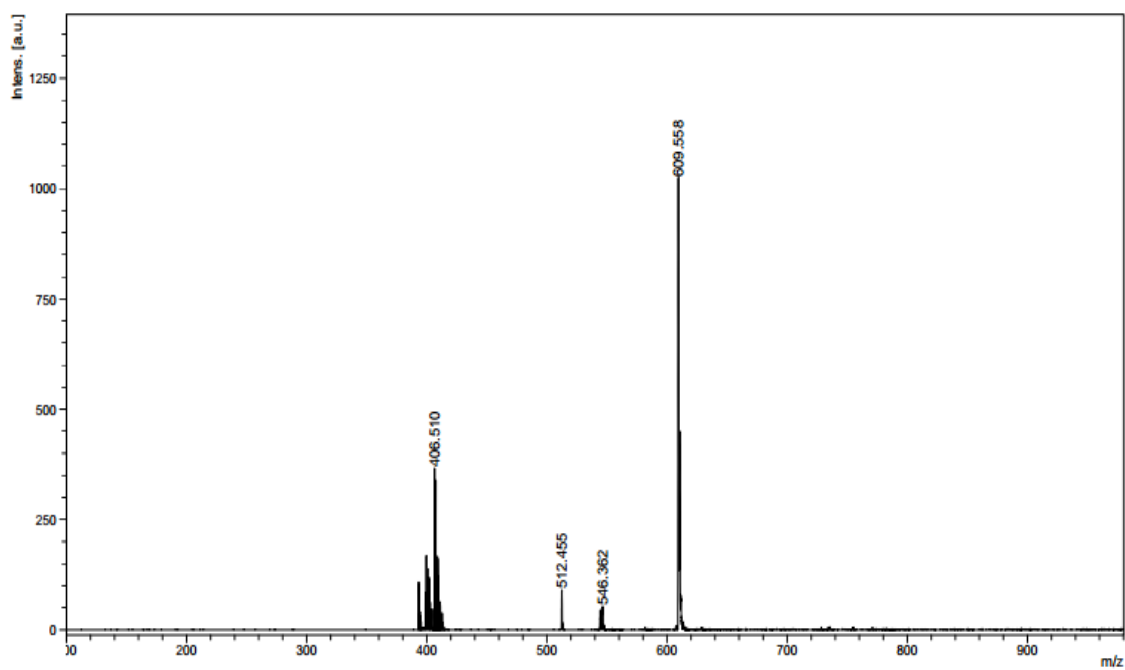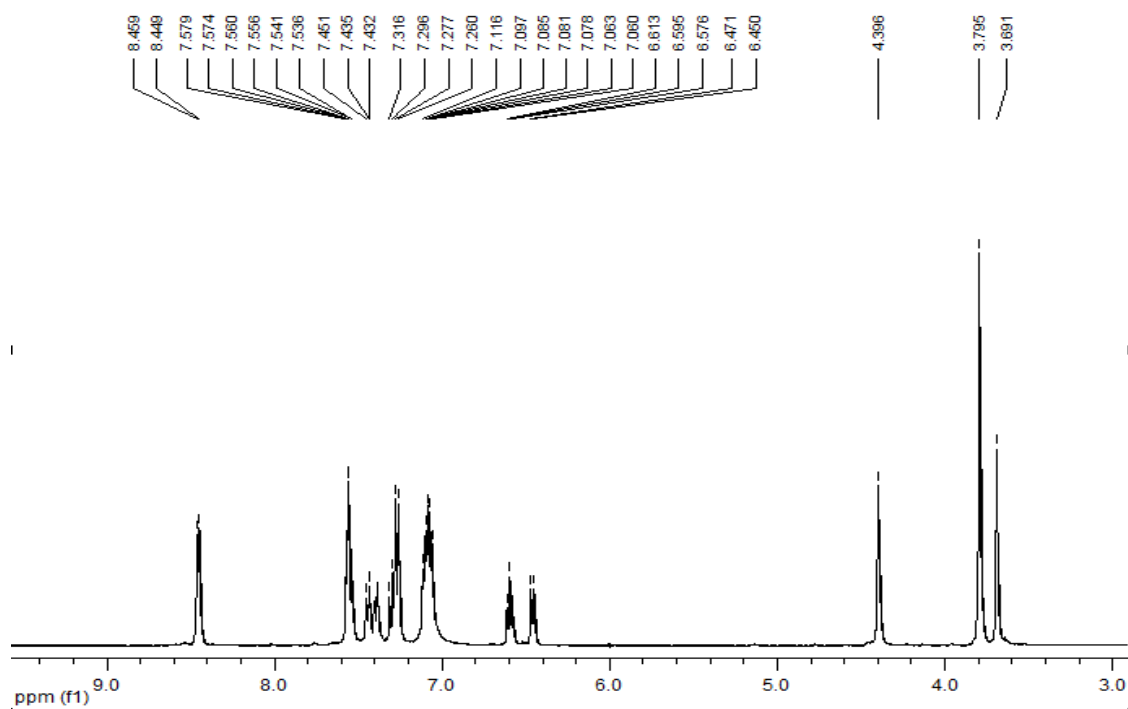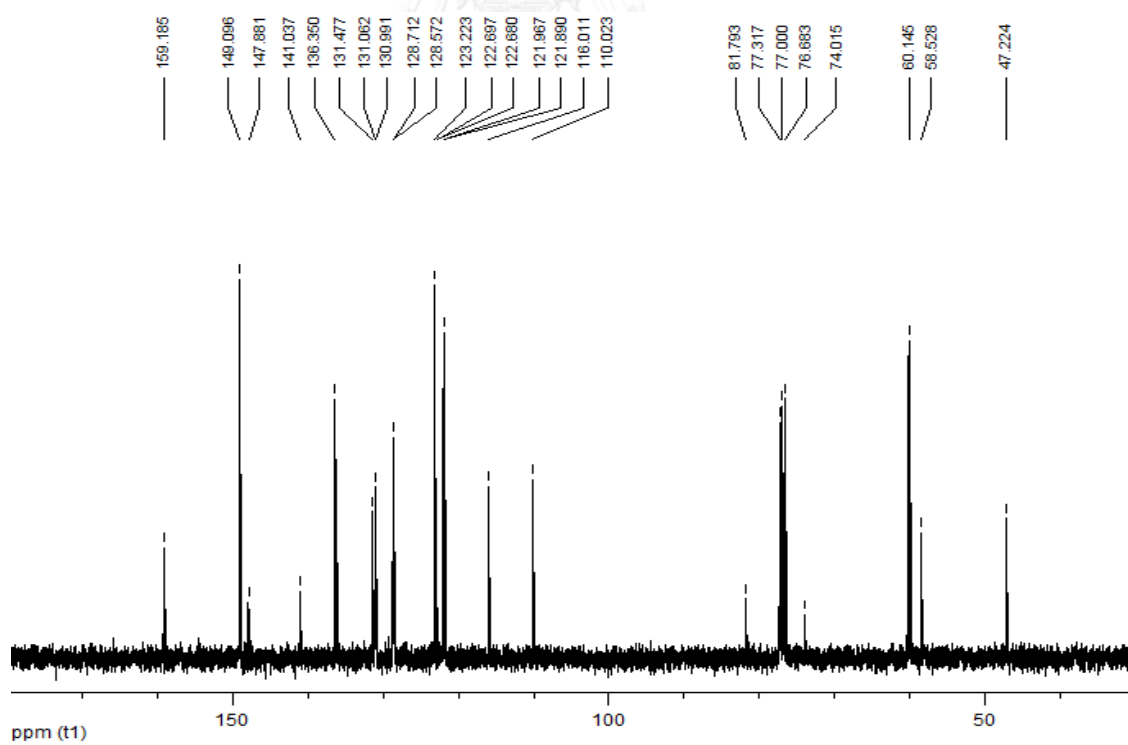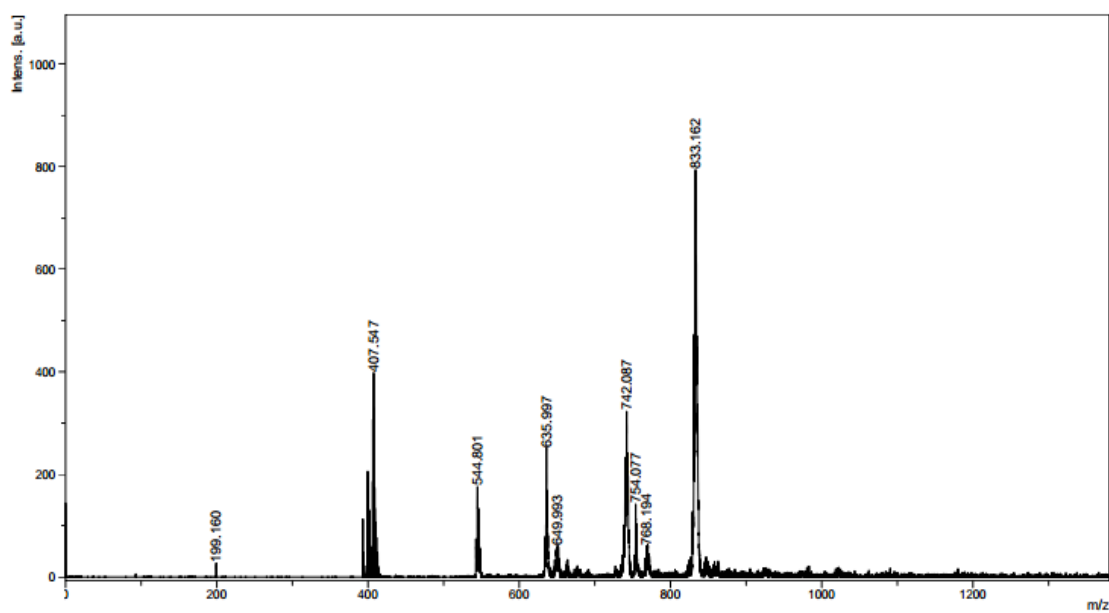**Figure A18** ^{13}C NMR spectrum of ionophore **II** in CDCl$_3$

Figure A19 MALDI-TOF mass spectrum of ionophore **II**

APPENDIX B

Table A1 Potentiometric response of membranes containing **II** in the presence of 75 mol% of the ionic additive KTpClPB toward cations

Cations	Preconditioned (0.01 M)	Inner filling solution (0.01 M)	Slope (mV decade^{-1}) ($\pm$ S, n=3)	Linear range (M)
NaNO$_3$	NaNO$_3$	NaCl	6.2 ± 0.8	10^{-3}-10^{-2}
KNO$_3$	KNO$_3$	KCl	4.5 ± 0.5	10^{-3}-10^{-2}
Mg(NO$_3$)$_2$	Mg(NO$_3$)$_2$	MgCl$_2$	5.9 ± 2.0	10^{-3}-10^{-2}
Ca(NO$_3$)$_2$	Ca(NO$_3$)$_2$	CaCl$_2$	4.8 ± 1.0	10^{-3}-10^{-2}
Cr(NO$_3$)$_3$	Cr(NO$_3$)$_3$	CrCl$_3$	49.2 ± 1.3	10^{-4}-10^{-2}
Fe(NO$_3$)$_3$	Fe(NO$_3$)$_3$	FeCl$_3$	53.9 ± 0.8	10^{-5}-10^{-2}
Ni(NO$_3$)$_2$	Ni(NO$_3$)$_2$	NiCl$_2$	22.3 ± 2.3	10^{-3}-10^{-2}
Cu(NO$_3$)$_2$	Cu(NO$_3$)$_2$	CuCl$_2$	-20.4 ± 0.1	10^{-4}-10^{-2}
Zn(NO$_3$)$_2$	Zn(NO$_3$)$_2$	ZnCl$_2$	33.0 ± 1.5	10^{-4}-10^{-2}
Cd(NO$_3$)$_2$	Cd(NO$_3$)$_2$	CdCl$_2$	26.6 ± 0.2	10^{-5}-10^{-2}
Pb(NO$_3$)$_2$	Pb(NO$_3$)$_2$	PbCl$_2$	10.5 ± 0.1	10^{-5}-10^{-3}

The ratio of PVC: o-NPOE at 1:2 wt.%

Table A2 Potentiometric response of membranes containing **III** in the presence of 75 mol% of the ionic additive KTpClPB toward cations

| Cations	Preconditioned (0.01 M)	Inner filling solution (0.01 M)	Slope (mV decade^{-1}) ($\pm$ S, n=3)	Linear range (M)
NaNO$_3$	NaNO$_3$	NaCl	4.8 ± 0.5	10^{-3}-10^{-2}
KNO$_3$	KNO$_3$	KCl	5.9 ± 1.3	10^{-3}-10^{-2}
Mg(NO$_3$)$_2$	Mg(NO$_3$)$_2$	MgCl$_2$	5.2 ± 2.2	10^{-3}-10^{-2}
Ca(NO$_3$)$_2$	Ca(NO$_3$)$_2$	CaCl$_2$	5.2 ± 0.6	10^{-3}-10^{-2}
Cr(NO$_3$)$_3$	Cr(NO$_3$)$_3$	CrCl$_3$	51.7 ± 1.2	10^{-5}-10^{-2}
Fe(NO$_3$)$_3$	Fe(NO$_3$)$_3$	FeCl$_3$	55.6 ± 0.7	10^{-5}-10^{-2}
Ni(NO$_3$)$_2$	Ni(NO$_3$)$_2$	NiCl$_2$	14.6 ± 2.0	10^{-3}-10^{-2}
Cu(NO$_3$)$_2$	Cu(NO$_3$)$_2$	CuCl$_2$	-59.3 ± 0.1	10^{-5}-10^{-2}
Zn(NO$_3$)$_2$	Zn(NO$_3$)$_2$	ZnCl$_2$	22.2 ± 1.4	10^{-4}-10^{-2}
Cd(NO$_3$)$_2$	Cd(NO$_3$)$_2$	CdCl$_2$	30.7 ± 0.1	10^{-5}-10^{-2}
Pb(NO$_3$)$_2$	Pb(NO$_3$)$_2$	PbCl$_2$	10.4 ± 0.3	10^{-5}-10^{-3}

The ratio of PVC: o-NPOE at 1:2 wt.%
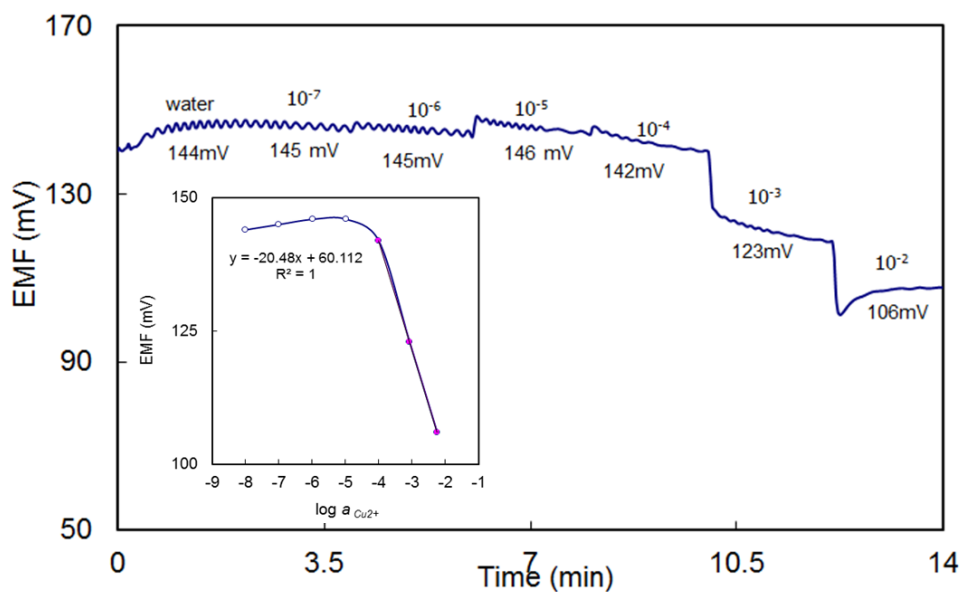
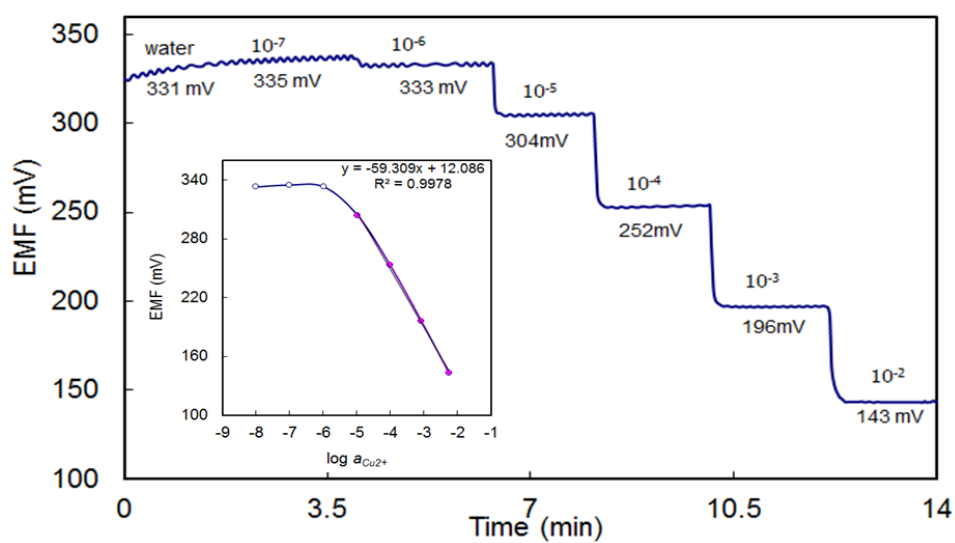**Figure A20** Response characteristic of the membranes containing **II** in the presence of 75 mol% KTpClPB toward Cu^{2+}.

Figure A21 Response characteristic of the membranes containing **III** in the presence of 75 mol% KTpClPB toward Cu^{2+}.
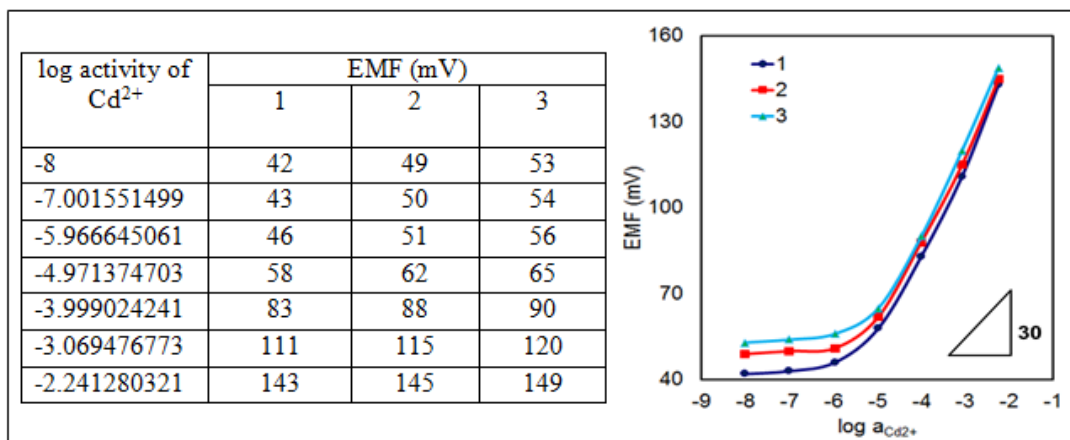
log activity of Cd^{2+}	EMF (mV)		
	1	2	3
-8	42	49	53
-7.001551499	43	50	54
-5.966645061	46	51	56
-4.971374703	58	62	65
-3.999024241	83	88	90
-3.069476773	111	115	120
-2.241280321	143	145	149

Figure A22 Response characteristic of the membranes containing **II** in the presence of 75 mol% KTpClPB toward Cd^{2+} (repeated three experiments).

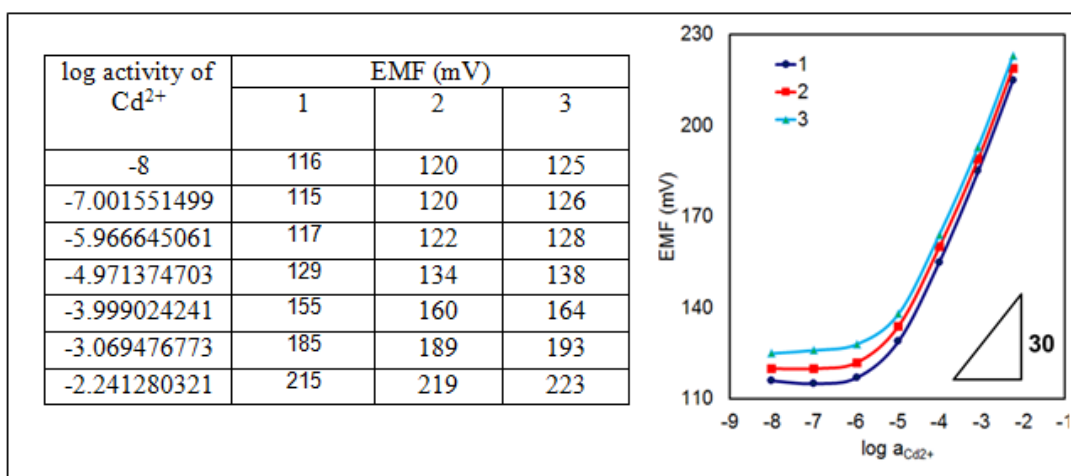| log activity of Cd^{2+}	EMF (mV)		
	1	2	3
-8	116	120	125
-7.001551499	115	120	126
-5.966645061	117	122	128
-4.971374703	129	134	138
-3.999024241	155	160	164
-3.069476773	185	189	193
-2.241280321	215	219	223

Figure A23 Response characteristic of the membranes containing **III** in the presence of 75 mol% KTpClPB toward Cd^{2+} (repeated three experiments)

Table A3 Selectivity coefficients values observed for Cd^{2+} selective electrode for various interfering ions using separate solution method.

Interfering ions	Selectivity coefficients ($\log K_{Cd,j}^{pot}$)	
	Ionophore **I**	Ionophore **II**
Na^+	-1.24	-3.04
K^+	-1.22	-2.88
Mg^{2+}	-2.95	-5.10
Ca^{2+}	-2.47	-4.83
Cr^{3+}	1.68	-0.46
Fe^{3+}	3.38	0.75
Ni^{2+}	-2.12	-0.67
Zn^{2+}	-0.62	0.54
Pb^{2+}	1.42	-0.53

VITA

Mr. Weerapol Srinonmuang was born December 10, 1989 in Roi-Et, Thailand. He received the Bachelor's degree of Science in Chemistry from Mahasarakham University in 2012. After that, he entered the graduate student at Department of Chemistry, Faculty of Science, Chulalongkorn University, then become a member of Supramolecular Chemistry Research Unit (SCRU) and worked under supervision of Professor Dr. Thawatchai Tuntulani.