SYNTHESIS, CHARACTERIZATION AND PHOTOPHYSICAL STUDIES ON CHALCONE-BASED CHEMOSENSORS FOR THE DETECTION OF ALUMINIUM AND FLUORIDE IONS

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2018

SYNTHESIS, CHARACTERIZATION AND PHOTOPHYSICAL STUDIES ON CHALCONE-BASED CHEMOSENSORS FOR THE DETECTION OF ALUMINIUM AND FLUORIDE IONS

by

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Thesis submitted in fulfilment of the requirements
for the degree of
Master of Science

August 2018

ACKNOWLEDGEMENT

First of all, I would like to express my sincere gratitude to my main supervisor, Professor Yeap Guan Yeow for giving me an opportunity to conduct this project under his supervision. His support, immense knowledge and advice throughout the research project are greatly appreciated. I would also like to thank Dr. Elango Hrishikesan for his technical support. I am grateful to the School of Chemical Sciences for allowing me to access to the research facilities and thankful to all the technical staff from this school for the assistance.

I wish to gratefully acknowledge Malaysian Ministry of Higher Education (MOHE) for funding this project through FRGS Grant No.203/PKIMIA/6711422 and MyBrain15 Postgraduate Scholarship Programme for the financial support in my Master study. I also thank my fellow laboratory mates for giving me their opinions, suggestions, ideas and helps.

Most importantly, none of this could have happened without my family. I would like to thank my parents for their unconditional support and encouragement all this while.

TABLE OF CONTENTS

ACKNOWLEDGEMENT		ii
TABLE OF CONTENTS		iii
LIST OF TABLES		vii
LIST OF FIGURES		viii
LIST OF SYMBOLS AND ABBREVIATIONS		xii
ABSTRAK		xiv
ABSTRACT		xvi
CHAPTER 1 - INTRODUCTION		1
1.1	Sensor	2
1.2	Colorimetric Chemosensors	3
1.3	Fluorometric Chemosensors	4
1.4	Importance of Cations and Anions for Detection	5
1.5	Mechanisms of Sensing	6
1.6	Photoinduced Internal Charge Transfer (PICT)	6
1.7	Photoinduced Electron Transfer (PET)	8
1.8	Fluorescence Resonance Energy Transfer (FRET)	9
1.9	Chemistry of Chalcone	10
1.10	Chalcone in Chemosensor Applications	10
1.11	Chemosensors Design for Ions	13
	1.11.1 Chemosensors Design for Al^{3+} Ion Detection	14
	1.11.2 Chemosensors Design for F^- Ion Detection	17
1.12	Problem Statement	20
1.13	Objectives of Present Research Project	20

CHAPTER 2 - EXPERIMENTAL 21

2.1 Chemicals 21

2.2 Synthesis of Intermediary and Title Compounds 22

2.2.1 Synthetic scheme of receptor (1-[3-(2-Hydroxy-phenyl)-3-oxo-propenyl] -naphthalen-2-yloxy)-acetic acid (**NAC**) 22

2.2.1(a) Synthesis of (1-Formyl-naphthalen-2-yloxy) acetic acid ethyl ester (NAEE) 22

2.2.1(b) Synthesis of (1-[3-(2-Hydroxy-phenyl)-3-oxo-propenyl]-naphthalen-2-yloxy)-acetic acid (**NAC**) 22

2.2.2 Synthetic scheme of receptor (1-[3-Oxo-3-(3-oxo-3H benzo[f]chromen-2-yl)-propenyl]-naphthalen-2-yloxy)-acetic acid (**CAC**) 23

2.2.2(a) Synthesis of (1-Formyl-naphthalen-2-yloxy)-acetic acid ethyl ester (NAEE) 23

2.2.2(b) Synthesis of 2-Acetyl-benzo[f]chromen-3-one (ABCM) 24

2.2.2(c) Synthesis of (1-[3-Oxo-3-(3-oxo-3H-benzo[f]chromen-2-yl)-propenyl]-naphthalen -2-yloxy)-acetic acid (**CAC**) 24

2.2.3 Synthetic scheme of receptor 7-Diethylamino-3-[3-(2-hydroxy-naphthalen-1-yl)-acryloyl]-chromen-2-one (**DNAC**) 25

2.2.3(a) Synthesis of 3-acetyl-7-(diethylamino)-2H-chromen-2-one (ADCM) 25

2.2.3(b) Synthesis of 7-Diethylamino-3-[3-(2-hydroxy-naphthalen-1-yl)-acryloyl]-chromen-2-one (**DNAC**) 26

2.3 Characterization 27

2.3.1 Carbon, Hydrogen and Nitrogen microanalysis (CHN) 27

2.3.2 Fourier transform-infrared spectroscopy (FT-IR) 27

2.3.3 Fourier transform nuclear magnetic resonance spectroscopy (FT-NMR) 27

2.3.4 UV-Visible Spectrophotometer 28

2.3.5 Fluorescence Spectrophotometer 28

2.4 Details of the measurement procedures 29

2.4.1 Details of metal titrations 29

2.4.2 Details of selectivity study 29

2.4.2 Determination of association constants 30

2.4.3 Determination of Stoichiometry 31

2.4.4 Determination of limit of detection 31

CHAPTER 3 - RESULTS AND DISCUSSION 32

3.1 Characterization of Key Intermediates and Receptor Compounds by Spectroscopic Techniques 32

3.1.1 FT-IR 34

3.1.2 ^{1}H-NMR Spectroscopy 39

3.1.3 ^{13}C-NMR Spectroscopy 49

3.2 Spectral and Chemosensing Studies of Chalcone-based Receptor (**NAC**) for Al^{3+} ion 54

3.2.1 Photophysical studies of **NAC** 54

3.2.2 Competition with other cations 63

3.2.3 Determination of stoichiometry between **NAC** and Al^{3+} ions 63

3.2.4 ^{1}H-NMR spectral studies of **NAC**-Al^{3+} complex 63

3.3 Spectral and Chemosensing Studies of Chalcone-based Receptor (**CAC**) for Al^{3+} ion 69

3.3.1 Photophysical studies of **CAC** 69

3.3.2 Competition with other cations 75

3.3.3 Determination of stoichiometry between **CAC** and Al^{3+} ions 75

3.3.4 ^{1}H-NMR spectral studies of **CAC**-Al^{3+} complex 75

3.4 Spectral and Chemosensing Studies of Chalcone-based Receptor (**DNAC**) for F^{-} ion 81

3.4.1 Photophysical studies of **DNAC** 81

3.4.2 Competition with other anions 88

3.4.3 Determination of stoichiometry between **DNAC** and F^{-} ions 88

CHAPTER 4 – CONCLUSION 91

4.1 Scope of future work 94

REFERENCES 95

LIST OF PUBLICATION

LIST OF TABLES

		Page
Table 1.1	Specifications of allowed ion concentration in drinking water	13
Table 3.1	Empirical formulas, molecular weights (MW), percentage yields (%) and CHN microanalytical data of all title compounds	33
Table 3.2	FT-IR absorption frequencies (v/cm^{-1}) of selected functional groups and relative intensities for all title compounds	35
Table 3.3	^{1}H-NMR chemical shifts (δ / ppm) of the intermediate compounds (multiplicity in parentheses)	41
Table 3.4	^{1}H-NMR chemical shifts (δ / ppm) of the receptor compounds (multiplicity in parentheses)	42
Table 3.5	^{13}C-NMR chemical shifts (δ / ppm) of the receptor compounds	50

LIST OF FIGURES

		Page
Figure 1.1	Schematic diagram of a chemical sensor device	3
Figure 1.2	Schematic representation of PICT chemosensor in sensing process	7
Figure 1.3	Molecular orbital diagram and schematic representation of photoinduced electron transfer process (PET)	8
Figure 1.4	Schematic representation of FRET chemosensor in sensing process	9
Figure 2.1	Synthesis of **NAC**	23
Figure 2.2	Synthesis of **CAC**	25
Figure 2.3	Synthesis of **DNAC**	26
Figure 3.1	FT-IR spectrum of receptor **NAC**	36
Figure 3.2	FT-IR spectrum of receptor **CAC**	37
Figure 3.3	FT-IR spectrum of receptor **DNAC**	38
Figure 3.4	^{1}H-NMR spectrum of compound NAEE	43
Figure 3.5	^{1}H-NMR spectrum of compound ABCM	44
Figure 3.6	^{1}H-NMR spectrum of compound ADCM	45
Figure 3.7	^{1}H-NMR spectrum of compound **NAC**	46
Figure 3.8	^{1}H-NMR spectrum of compound **CAC**	47
Figure 3.9	^{1}H-NMR spectrum of compound **DNAC**	48
Figure 3.10	^{13}C-NMR spectrum of compound **NAC**	51
Figure 3.11	^{13}C-NMR spectrum of compound **CAC**	52
Figure 3.12	^{13}C-NMR spectrum of compound **DNAC**	53

Figure 3.13	UV-vis absorption spectra of chemosensor **NAC** (100 μM) in the absence and presence of various metal ions (100μM) in water	56
Figure 3.14	Absorption spectral changes of **NAC** (100 μM) in the presence of different concentrations of Al^{3+} ions in water	57
Figure 3.15	Fluorescence emission spectra of sensor **NAC** (100 μM) in water upon addition of metal perchlorate salts (1 equiv.) such as Ag^{+}, Al^{3+}, Ca^{2+}, Cd^{2+}, Cu^{2+}, Fe^{2+}, Hg^{2+}, K^{+}, Mn^{2+}, Na^{+}, Ni^{2+}, Pb^{2+} and Zn^{2+}	58
Figure 3.16	Fluorescence titration spectra of chemosensor **NAC** (100 μM) upon addition of different concentrations of Al^{3+} ions in water	60
Figure 3.17	A Benesi-Hildebrand plot based on fluorescence intensity of **NAC** with added Al^{3+} concentrations in water	61
Figure 3.18	A plot between the relative fluorescence intensity and the concentration of Al^{3+} ion to determine the detection limit of probe **NAC** towards Al^{3+} ions	62
Figure 3.19	Competitive selectivity of **NAC** towards Al^{3+} in the presence of other metal ions (1 equiv.) in water	65
Figure 3.20	Job's plot for the interaction of **NAC** with Al^{3+} in water indicating 2:1 stoichiometry for **NAC**-Al^{3+} complex	66
Figure 3.21	^{1}H-NMR titration of **NAC** with Al^{3+} ions in D_2O	67
Figure 3.22	The binding structure after the interaction between **NAC** and Al^{3+} ions	68
Figure 3.23	UV-vis absorption spectra of chemosensor **CAC** (100 μM) in the absence and presence of various metal ions (100μM) such as Ag^{+}, Al^{3+}, Ca^{2+}, Cd^{2+}, Cu^{2+}, Fe^{2+}, Hg^{2+}, K^{+}, Mn^{2+}, Na^{+}, Ni^{2+}, Pb^{2+} and Zn^{2+} in water	71

Figure 3.24	Absorption spectral changes of **CAC** (100 μM) in the presence of different concentrations of Al^{3+} ions in water	72
Figure 3.25	A plot between the absorbance and the concentration of Al^{3+} ion to determine the detection limit of probe **CAC** towards Al^{3+} ions	73
Figure 3.26	Benesi-Hildebrant plot based on absorbance intensity of **CAC** with added Al^{3+} ions	74
Figure 3.27	Competitive selectivity of **CAC** towards Al^{3+} in the presence of other metal ions (1 equiv.) in water	77
Figure 3.28	Job's plot for the interaction of **CAC** with Al^{3+} in water indicating 2:1 stoichiometry for **CAC**-Al^{3+} complex	78
Figure 3.29	Stacked ^{1}H-NMR spectra of **CAC** before and after the addition of Al^{3+} in D_2O	79
Figure 3.30	Proposed structure of probe **CAC** before and after the complexation with Al^{3+} ions	80
Figure 3.31	Fluorescence spectra of probe **DNAC** (2.0×10^{-5} M) with different anions (2 eq.)	83
Figure 3.32	Proposed structures relating to the deprotonaton and formation of HF_2^- species	84
Figure 3.33	Fluorescence titration spectra of probe **DNAC** (2.0×10^{-5} M) with F^- ions from 0 to 5 eq.	85
Figure 3.34	Proposed intramolecular charge transfer from naphthol to chalcone core	86
Figure 3.35	A plot between the relative fluorescence intensity and the concentration of F^- ions to determine the detection limit of **DNAC** towards F^- ions.	87
Figure 3.36	Fluorescence response of probe **DNAC** with and without competing anions	89

Figure 3.37 Fluorescence Job's plot for probe **DNAC** with F^- in acetonitrile 90

LIST OF SYMBOLS AND ABBREVIATIONS

α	Alpha
a.u.	Arbitary Unit
°C	Degree Celcius
D_2O	Deuterium Oxide
equiv	Equivalent
g	gram
h	hour
M	Molar
mg	Milligram
mL	Milli Litre
mmol	Millimole
mol	Mole
nm	Nanometer
ppm	Parts per million
%	Percentage
cm^{-1}	Per centimeter
WHO	World Health Organization
β	Beta
λ	Lambda (Wavelength)
μM	Micromolar
π	Pi
σ	Sigma
δ	Delta

K_a	Association constant
LOD	Limit of detection
MOPS	3-(N-morpholino)propanesulfonic acid

SINTESIS, PENCIRIAN DAN KAJIAN FOTOFIZIKAL ATAS KEMOSENSOR YANG BERASASKAN KALKON BAGI PENGESANAN ION ALUMINIUM DAN FLUORIDA

ABSTRAK

Dalam tesis ini, sintesis dan kajian tiga kemosensor berasaskan kalkon yang berbeza untuk mengesan ion Al^{3+} dan F^{-} dengan kaedah mata kasar dan fluorimetrik telah diterangkan. Pencirian struktur bagi sebatian utama telah dijalankan dengan teknik spektroskopi Fourier Transform Inframerah (FT-IR), spektroskopi Proton dan Karbon Resonans Magnetik Nuklear (1H- dan 13C-NMR). Respons molekul penerima terhadap pelbagai ion logam dan anion telah diselidiki dengan kaedah UV-Vis dan spektroskopi pendarfluor dan melalui pemerhatian mata kasar. Kajian mengenai tingkah laku pengikatan kemosensor (1-[3-(2-Hidroksi-fenil)-3-oxo-propenil]-naftalena-2-iloksi)-asid asetik (**NAC**) yang disintesis dengan spektrofotometer UV-Vis menunjukkan kepilihan yang sangat baik dan respons yang pantas terhadap ion Al^{3+}. Peningkatan pendarfluor yang ketara semasa penambahan ion Al^{3+} berbanding dengan ion logam lain menjadikannya kemosensor terpilih yang sesuai bagi ion Al^{3+}. Penerima **NAC** memaparkan perubahan penyerapan dari 399 nm kepada 416 nm kerana pengikatan **NAC** dengan Al^{3+} mencetuskan peningkatan ketegaran sistem melalui operasi pendarfluoran pengkelatan dipertingkat (CHEF) yang tidak berlaku pada kation logam lain. Stoikiometri penerima **NAC** dan ion Al^{3+} didapati sebagai 2:1 dengan menggunakan kaedah Job dengan pemalar pengikatan $K_a = 0.21\times10^2\ M^{-2}$. Anjakan dalam data spektrum FT-NMR mendedahkan bahawa dua atom O kumpulan karboksil dan hidroksil serta atom oksigen kumpulan oksimetilena terlibat dalam koordinasi. Penerima (1-[3-Oxo-3-(3-oxo-3H-benzo[f]kromen-2-il)- propenil]-

naftalena-2-iloksi)-asid asetik (**CAC**) mengesan ion Al^{3+} dalam medium air 100% di mana perubahan warna dari kuning ke sian dapat dilihat melalui mata kasar. Selepas penambahan ion Al^{3+}, mekanisme pemindahan cas dalaman (ICT) dalam kromofor kumarin ditingkatkan dan ia dapat dikenal pasti dengan mata kasar. Stoikiometri 2:1 bagi penerima **CAC**:ion Al^{3+} telah diselidiki oleh plot Job dan pemalar pengikatan didapati sebagai $K_a = 5.91\ M^{-2}$. Tingkah laku penderiaan anion 7-Dietilamino-3-[3-(2-hidroksi-naftalena-1-il) -akrilokil]-kromen-2-on (**DNAC**) telah dikajikan dengan teknik UV-Vis. Pembentukan ikatan hidrogen antara pengesan **DNAC** dan ion F^- menimbulkan peningkatan intensiti pelepasan pengesan pada 524 nm yang boleh dikaitkan dengan pemindahan cas dalaman (ICT) yang dibangunkan oleh deprotonasi OH dari unit naftol ke moieti kalkon dalam pengesan **DNAC**. Tidak terdapat sebarang gangguan oleh anion lain dalam intensiti pendarfluor kompleks semasa pengesanan ion F^- dalam CH_3CN. Plot Job mencadangkan nisbah **DNAC**:ion F^- sebagai 1:1 dengan pemalar pengikatan $K_a = 3.33\times10^{-5}\ M^{-1}$.

SYNTHESIS, CHARACTERIZATION AND PHOTOPHYSICAL STUDIES ON CHALCONE-BASED CHEMOSENSORS FOR THE DETECTION OF ALUMINIUM AND FLUORIDE IONS

ABSTRACT

In this thesis, the syntheses and studies of three different chalcone-based chemosensors for the detection of Al^{3+} and F^{-} ion by naked eye and fluorimetric method have been described. The structure elucidation for the ultimate compounds have been characterized by spectroscopic techniques (FT-IR, ^{1}H- and ^{13}C-NMR). The response of the receptor molecules to various metal ions and anions were investigated by UV-Vis and fluorescence spectroscopy methods and to some extend through naked-eye observations. Study on binding behavior of the synthesized chemosensor (1-[3-(2-Hydroxy-phenyl)-3-oxo-propenyl]-naphthalen-2-yloxy)-acetic acid (**NAC**) by UV-Vis spectrophotometer has shown excellent selectivity and rapid response toward Al^{3+} ion. The obvious fluorescence increment upon the addition of Al^{3+} ion over other metal ions made it a suitable selective chemosensor for Al^{3+} ion. Receptor **NAC** displays a change in absorption from 399 nm to 416 nm as the binding of **NAC** with Al^{3+} triggered the improvement in the rigidity of the system through the operation of chelation enhanced fluorescence (CHEF) which did not happen to other metal cations. The stochiometry of receptor **NAC** and Al^{3+} ion was found to be 2:1 using Job's method with an association constant of $K_a = 0.21 \times 10^2\ M^{-2}$. The shift in FT-NMR spectral data reveals that two O atoms of carboxyl and hydroxyl groups and the oxygen atom of the oxymethylene group involved in coordination. The receptor (1-[3-Oxo-3-(3-oxo-3H-benzo[f]chromen-2-yl)-propenyl] -naphthalen-2-yloxy)-acetic acid (**CAC**) detect Al^{3+} ion in 100% water medium in which a change in colour from yellow to

cyan can be observed by naked eye. After the addition of Al^{3+} ion, the internal charge transfer (ICT) mechanism in coumarin chromophore was enhanced that can clearly be identified by naked eye. The 2:1 stoichiometry of receptor **CAC**:Al^{3+} ion was investigated by Job's plot and the association constant was found to be $K_a = 5.91\ M^{-2}$. The anion sensing behaviours of 7-Diethylamino-3-[3-(2-hydroxy-naphthalen-1-yl)-acryloyl]-chromen-2-one (**DNAC**) were studied by UV-Vis technique. The formation of hydrogen bonding between the probe **DNAC** and F^- ion gave rise to the increase in the emission intensity of probe at 524 nm which can be attributed to the internal charge transfer (ICT) developed by the deprotonation of OH from napthol unit to the chalcone moiety in the probe **DNAC**. There was no interference by other anions in the fluorescence intensity of the complex during the F^- ion detection in CH_3CN. Job's plot suggests the ratio of **DNAC**: F^- ion as 1:1 with an association constant of $K_a=3.33\times10^{-5}\ M^{-1}$.

CHAPTER 1

INTRODUCTION

Cations and anions play an indispensable role in physiology, catalysis, medical diagnostics, chemical, environmental and biological processes such as an ion transport through membranes, enzyme cofactor, maintenance of cell shape and signal transduction [Christianson & Lipscomb 1989, Gloe et al. 1998, Valeur & Leray 2000, Vázquez et al. 2004]. These heavy metals are widely used in mining, extraction, chemical and pharmaceutical industries in a range of different forms. As a result, public health problems such as Parkinson, Alzheimer and Wilson's diseases arose [Bonda et al. 2001, Perl et al. 1982, Pithadia et al. 2012]. Although most of the metals are essential elements for living systems at varying amounts but they are the major pollutants in our environment and have entered into our human body through drinking water and food intake which might cause serious illness at excessive accumulation amount. Not only cations, anions are also highly health hazardous and toxic in nature.

Despite having many methods for the cations and anions detection such as mass spectrometry (MS) [Kriegeskotte et al. 2009], atomic absorption spectrometry (AAS) [Frankowski et al. 2010, Pourreza & Hoveizavi 2005], inductively coupled plasma mass spectroscopy (ICP-MS) [del Castillo Busto et al. 2005] and others, but they do not allow continuous monitoring and expensive. In recent years, the development of chemosensors for the detection of various cations and anions have attracted significant attention because of ease to operate, high sensitivity and selectivity and observed by naked eye without the use of sophisticated instruments.

The recognition of metal ions with non-covalent interactions has reminded us of a Nobel Prize in 1987 which was shared by triad of the scientists – Pedersen, Cram and Lehn for the development of host-guest in the field of supramolecular chemistry

[Pedersen 1967]. A supramolecule consists of two parts, a host and a guest species that interact with one another in a weaker and reversible non-covalent manner such as Van der Waals forces, hydrogen bonding, π-π interactions, metal coordination, hydrophobic forces and electrostatic forces [Gellman 1997]. This chapter deals about the general overview on different type of chemosensors and their advantages, heavy metals and their properties, a short literature review on the mode of sensing and their examples and finally the challenges faced and the objectives of the present research.

1.1 Sensor

Nowadays, sensors are everywhere in our life. A sensor is a device that detects some type of input from the physical environment and produces a human-readable signal in response. For example, thermometers, smoke alarms, pH meter are very common sensors in our daily life. A chemical sensor is a device that transforms chemical information, ranging from the concentration of a specific sample component to total composition analysis, into an analytically useful signal [Hulanicki et al. 1991].

Basically, there are three components that constitute a sensor: A receptor, spacer and an active unit (Figure 1.1). A receptor is responsible for the selective analyte binding. In another word, the selective receptor is capable of identifying analyte of interest. A spacer is a device that is able to convert the energy carrying the chemical information about the recognition element into a measurable signal. As for the active unit, its properties should change upon analyte binding and responsible for reporting the recognition event [Martínez-Máñez & Sancenón 2003].

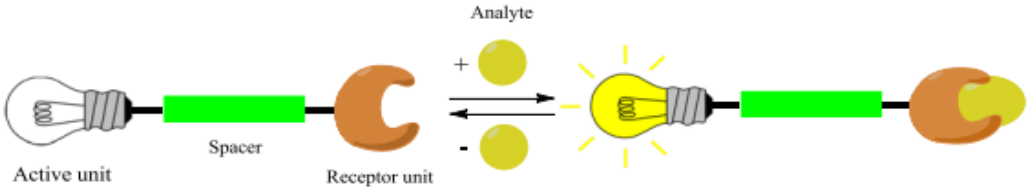


Figure 1.1 Schematic diagram of a chemical sensor device.

In general, the chemosensors can be divided into three types:

- Colorimetric chemosensors
- Fluorometric chemosensors
- Electrochemical chemosensors

A colorimetric chemosensor is a technique in which a change in color occurs due to the interaction between analyte and sensor. For example, litmus paper, where there is a color change with H^+ ion. In fluorescent chemosensor, there is a difference in emission intensity upon analyte binding to the sensor. In electrochemical chemosensor, there is a change in oxidation/reduction potential when analyte bound to the sensor unit. In this research, only colorimetric and fluorometric chemosensors for the detection of cations and anions will be discussed.

1.2 Colorimetric Chemosensors

A colorimetric chemosensor is a method in which a selectively change in color occurs upon interaction between sensor and a particular target analyte, due to their change in absorbance. For examples, litmus paper, where there is a color change with H^+ ions; and phenolphthalein, an acid-base indicator, which is colorless in acidic condition and magenta in alkaline solution.

Colorimetric determination of both cations and anions based on supramolecular ideas had gained the popularity since a long time ago. Among the techniques available for the detection of ions, colorimetric method is the easiest to operate and the cheapest way to offer the qualitative and quantitative information. Cheng and his coworkers had designed a receptor with azobenzene moiety for the recognition of Hg^{2+} ions based on Internal Charge Transfer (ICT) mechanism from light yellow to deep red [Cheng et al. 2011]. An aldazine-based colorimetric chemosensor was reported by Narayanaswamy *et al.* to detect Cu^{2+} and Fe^{3+} from pale yellow to purple color [Narayanaswamy & Govindaraju 2012]. Color change visible by naked eye allows an immediate indication of the presence of the particular analyte without employing any spectroscopic device.

1.3 Fluorometric Chemosensors

The fluorescence detection of specific molecules and ions has attracted considerable interest because it is cheap, highly sensitive, easy to operate and also due to its importance in the field of medicine, analytical, industrial and environmental chemistry.

In a fluorescence sensing approach, usually a fluorophore is non-fluorescent and acts as a signal transducer that converts the information into an optical signal when the analyte molecule is bound to it [Arimori et al. 2002, Guliyev et al. 2009]. For the recognition moiety or ionophore, it determines mainly the interaction selectivity and sensitivity with analytes based on the non-covalent bonding such as hydrogen bonding, metal complexation, π-π stacking, hydrophobic forces and electrostatic interactions. Numerous chemical and biochemical analytes can be detected by fluorescence methods: cations, anions, neutral molecules and gases.

1.4 Importance of Cations and Anions for Detection

Alkali and alkaline earth metal ions are found in the human body and have a great importance owing to their involvement in wide environmental and biological processes. For example, potassium and sodium are two of the most important ions in our human nervous system. As an electrolyte, potassium and sodium transport and maintain electrical impulses of human cells which are vital for human blood, hydration and help to ensure other important body functions [Beer et al. 1997].

The d-block transition metals are found everywhere on earth in various amounts and also found in our bodies. In today's society, transition metals are in high demand and are extensively used in industrial and construction purposes. Besides, many of the transition elements are essential to our human body and play important role in numerous biological processes. In hemoglobin, Fe^{3+} iron is used to transport oxygen throughout the human body in blood. Cu^{2+} copper is used to protect the body from free radicals damage and also work with iron to help the body form red blood cells. However, transition metal ions can become toxic at high concentration. Accumulation of transition metals in human body can cause Alzheimer's disease, infant liver damage and gastrointestinal problems [Bush 2003, Uauy et al. 1998].

Toxic heavy metals such as lead, mercury and cadmium, are highly health hazardous and require sensitive detection in the environment. Lead enters the environment and human body through smoking, automobile emission, mining and pesticide which will cause mental retardation, liver and kidney damage and anemia [Rifai et al. 1993]. Mercury is poisonous in any form and poisoning happen from mercury vapor inhalation, ingestion, injection and absorption through skin [Davidson et al. 1998, Hennrich et al. 1999]. Therefore, selective and sensitive recognition of these metal ions are of great interest to many scientists.

Anions play many roles in chemical and biological processes such as transfer catalysts, redox agents, nucleophiles or bases [Christianson et al. 1989]. Chloride ions are essential element for human health by maintaining metabolism and the acid-base balance in body. Fluoride is used in dental care and for the treatment of osteoporosis but can lead to fluorosis upon excessive exposure [Ayoob & Gupta 2006]. Cyanide ion is highly hazardous to living organisms in any type of release but still in high demand in industrial processes such as gold mining, electroplating and production of polymers. The selective and sensitive detection of all of these ions are very important to ensure human can in a healthy environment.

1.5 Mechanisms of Sensing

There is a variety of different signalling principles that are utilized in fluorescent chemosensors design such as electron transfer, charge transfer, energy transfer, and formation of excimer. The fluorophore that experiences this perturbation of photoinduced processes converts the recognition event into the photophysical changes, such as spectra, fluorescence quantum yield and lifetime.

1.6 Photoinduced Internal Charge Transfer (PICT)

When a sensor design incorporated an electron-donating group and an electron-withdrawing group into the molecule in a manner which allows direct electronic communication between the two components, it undergoes photo-induced internal charge transfer (PICT) by excitation of light as shown in Figure 1.2. Upon excitation of a fluorophore, a redistribution of electron density in both donor and acceptor groups occurs which will then be accompanied by an instantaneous change

in the dipole moment of the fluorophore. As such, it results in a stroke shift in wavelength [Valeur & Leray 2000].

If a cation interacting with the acceptor group, the electron withdrawing nature of that group enhanced resulting in a red shift in absorption spectrum. In contrast, when a cation bound to the donor moiety conjugated to the fluorophore, the electron donating capability of the moiety reduced and a blue shift in absorption spectrum will be observed owing to the reduction in the conjugation of the π system [Loehr & Voegtle 1985].

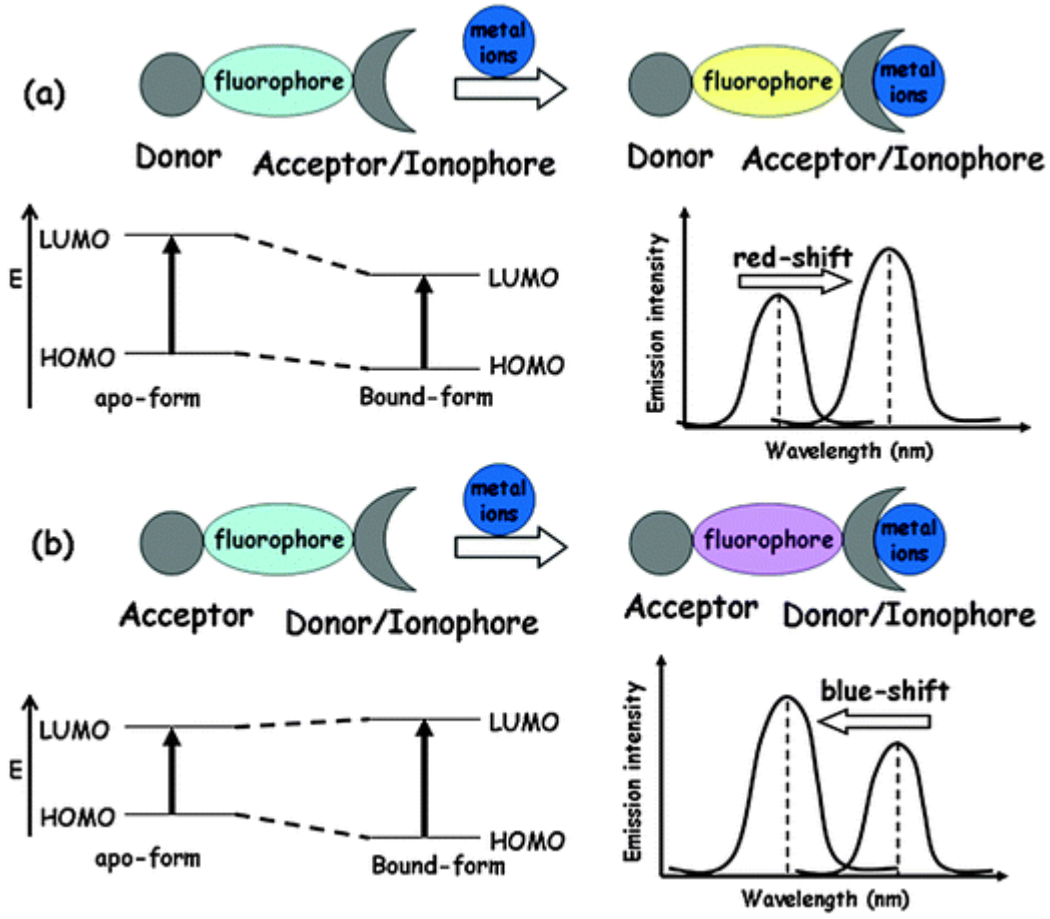


Figure 1.2 Schematic representation of PICT chemosensor in sensing process [Liu et al. 2013].

1.7 Photoinduced Electron Transfer (PET)

Photoinduced electron transfer (PET) is one of the most important mechanisms for fluorescent chemosensors. A numerous fluorescent sensors for cations and anions had been developed based on this principle [Baki & Akkaya 2001, Czarnik 1993, de Silva et al. 1991]. However, in PICT-type chemosensors, a PET system design must incorporate a spacer unit between receptor and fluorophore groups. Upon exposure of fluorophore with light, an electron in highest occupied molecular orbital (HOMO) was excited to lowest unoccupied molecular orbital (LUMO). Before relaxation occurs, a PET take place from an external orbital of this fluoroionphore with energy level between HOMO and LUMO of the fluorophore to the HOMO of the fluorophore resulting in fluorescene quenching [Martínez-Máñez & Sancenón 2003]. However, when binding with a cation, the energy level of external orbital is reduced to lower than that of HOMO of the fluorophore and hence the electron transition become unfavourable which leads to fluorescence enhancement as displayed in Figure 1.3.

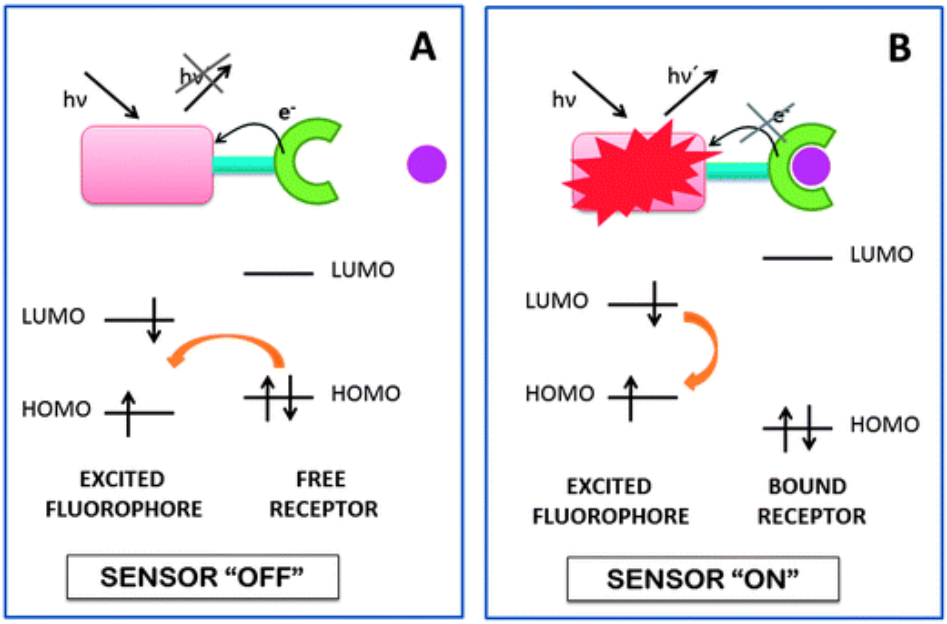


Figure 1.3 Molecular orbital diagram and schematic representation of photoinduced electron transfer process (PET) [Culzoni et al. 2013].

1.8 Fluorescence Resonance Energy Transfer (FRET)

Fluorescence resonance energy transfer (FRET) is another signaling mechanism that can be relied on in fluorometric chemosensor design. It is a non-radiative process in which the energy of an excited state donor (D) is transferred to an adjacent ground state acceptor (A) that allows fluorescence of latter is observed. In other words, energy of the donor (D) at its excited state is used to excite the acceptor (A) through energy transfer as shown in Figure 1.4. The efficiency of energy transfer depends on the distance between D and A, the concentration of A, and the extent of spectral overlap [Harekrushna 2011]. The difference between PET and FRET is that the net result of FRET is a transfer of the excitation energy from a donor to an acceptor, whereas PET took place from the ground state of the donor which initially excites the acceptor and donor is never converted to an excited state.

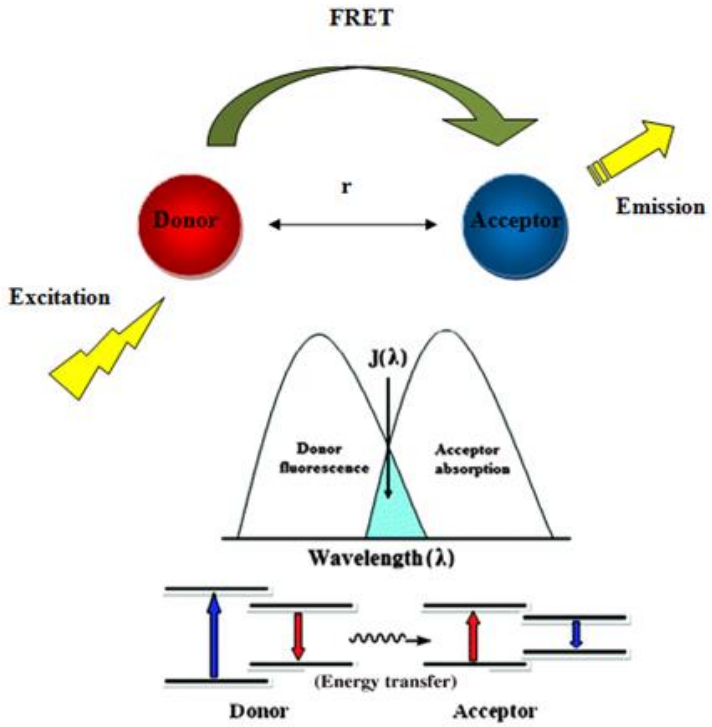


Figure 1.4 Schematic representation of FRET chemosensor in sensing process [Tabassum et al. 2012].

1.9 Chemistry of Chalcone

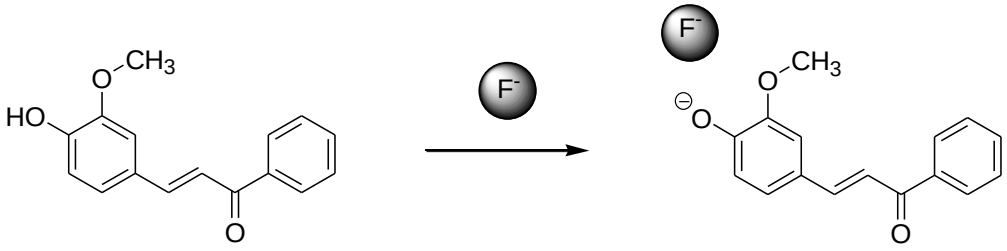
Chalcone is a natural compound bearing the 1,3-diphenyl-2-propen-1-one framework and is one of the most abundant groups of natural products [Tomazela et al. 2000]. In the past few years, chalcone had been recognized as one of the groups that showed prominent result in antimicrobial, antitumor, anti-inflammatory and anticancer activities due to the presence of enone functionality in chalcone moiety [Das & Manna 2016, Fang et al. 2014, Nowakowska 2007, Saydam et al. 2003]. Chalcone was claimed to possess excellent blue light transmittance and remarkable nonlinear optical (NLO) property, which is an essential element for optical application and it has also been served as starting material for the synthesis of a variety of heterocyclic compounds [Denis et al. 1988, Devarajegowda et al. 2001, Zhao et al. 2000].

1.10 Chalcone In Chemosensor Applications

The chalcones and their derivatives are important intermediates in organic synthesis. They possess keto functionality which may interact with cation of particular interest. In addition, the hydroxychalcone derivative can be a promising candidate for anion chemosensor because of its ability for proton donating in hydrogen bonding interaction and its conjugation system through phenol ring and enone group.

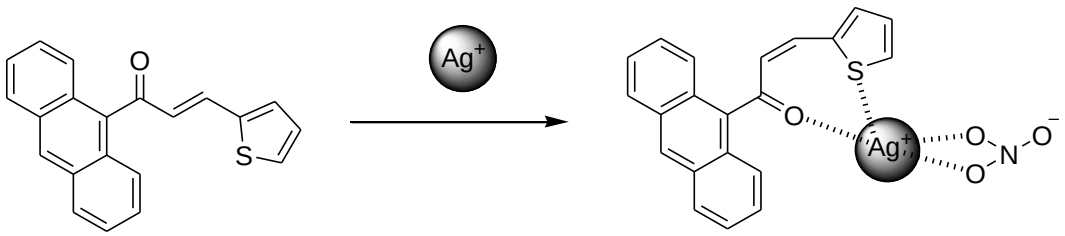
Fitriana et al. (2016) studied a colorimetric detection of F^-, CO_3^{2-}, CN^-, and SO_4^{2-} anions in DMSO system using a chalcone-based receptor **1**. The decrease of absorption band at 367 nm with the appearance of new broad peak at 507 nm was due to the breaking of O-H bond and the formation of deprotonated sensor, which is responsible for the colorimetric signalling. A detectable colour change from yellow to

red was observed upon addition of F^{-}, CO_3^{2-} and CN^{-} to sensor and it became orange in the presence of SO_4^{2-}.



(**1**)

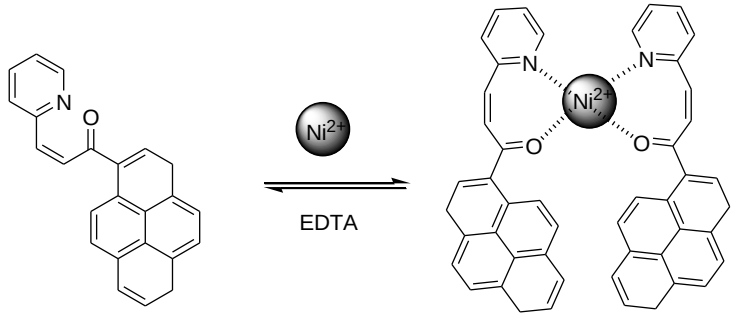
A ratiometric chalcone-based receptor **2** appended by anthracene unit as the fluorophore was designed and developed by Velmurugan et al. (2015) to selectively discriminate Ag^{+} ion over other metal ions tested. The fluorescence intensity of emission band at 415 nm was enhanced by addition of Ag^{+} ion in the aqueous system with a prominent blue shift of the emission maximum of about 10 nm from 415 nm to 405 nm. This is due to the hindrance of photoinduced electron transfer along with the intramolecular charge transfer mechanism.



(**2**)

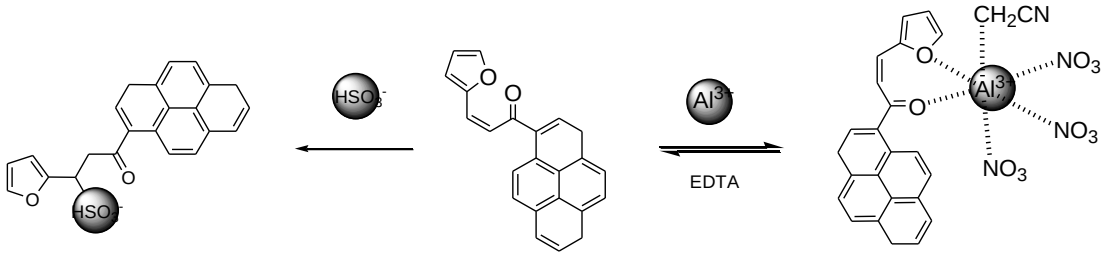
Prabhu et al. (2017) had reported a ratiometric fluorescent chemosensor **3** based on pyrene-conjugated pyridine. Pyrene was chosen as a reporter unit due to its ideal monomer and excimer emissions. Pyridine that behave as a good coordinating ability for metal ion binding sites is covalently linked with π-conjugated C=C bridge. A new intense peak with maximum absorption at 456 nm was observed upon addition of Ni^{2+} to a solution of **3** corresponding to the formation of an excimer. The binding

ratio of receptor **3** with Ni^{2+} ion of 2:1 was further confirmed by Benesi-Hildebrand plot.



(**3**)

Recently, Don et al. (2017) have reported a furan-pyrene conjugated chalcone receptor **4** for selective detection of Al^{3+} and HSO_3^- in aqueous acetonitrile. Addition of Al^{3+} ion to receptor produces a highly intense fluorescence band at 388 nm. The enhancement of emission intensity can be attributed to the suppression of PET process. Reversible binding of receptor **4** with Al^{3+} ion was also examined by addition of EDTA to Al^{3+} bound receptor **4** resulting a decrease in the fluorescence intensity at 388 nm. Interestingly, addition of HSO_3^- caused fluorescence enhancement with a notable red shift from 388 to 394 nm owing to the intramolecular charge transfer process from furan to pyrene rings.



(**4**)

1.11 Chemosensors Design for Ions

Metals are found naturally in the earth's crust and have been used extensively in many different areas for thousands of years owing to their high electrical conductivity, malleability and luster. Toxic metals and anions are well known environmental pollutants and they enter the environment by natural and anthropogenic activities such as mining, industrial discharge, pest control, power generation and a number of others. Accumulation of these hazardous ions in human body can cause serious illness. Therefore, there has been increasing concern about exposures and intakes of toxic ions by humans nowadays. Implementation of restrictive regulations on drinking water was conducted to limit the concentration of toxic ions to enter human body. In order to create a useful chemosensor, the detection limit of a sensor toward ions should be lower than the desirable limit provided in drinking water quality standard as displayed in Table 1.1.

Table 1.1 Specifications of allowed ion concentration in drinking water.

No.	Parameter	Desirable Limit (mg/L)	
		Ministry of Health (MOH)	World Health Organization (WHO)
1	Nickel	0.02	0.02
2	Copper	1.0	1.0
3	Iron	0.3	0.3
4	Aluminium	0.2	0.03
5	Sulphate	250	250
6	Zinc	3	5
7	Chloride	250	250
8	Fluoride	0.4 - 0.6	1.5
9	Manganese	0.1	0.1
10	Cadmium	0.003	0.003
11	Lead	0.01	0.01
12	Arsenic	0.01	0.01
13	Mercury	0.001	0.006
14	Nitrate	10	50

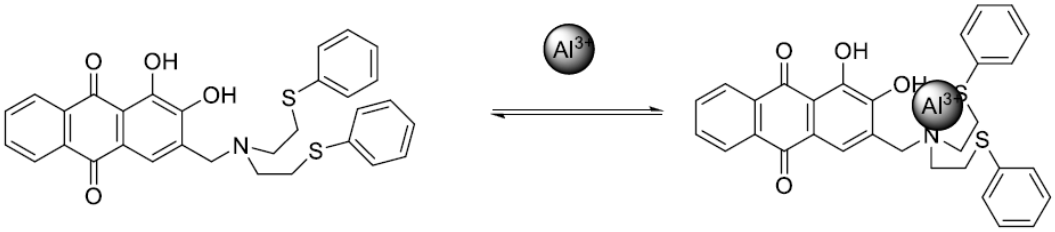
1.11.1 Chemosensors Design for Al^{3+} Ion Detection

Among all the metals as listed in Table 1.1, aluminium is the most abundant metal and the third most abundant element found in the earth's crust after oxygen and silicon. The properties of aluminium include high thermal conductivity, lightweight, high strength, easy to recycle and excellent corrosion resistance that make it attractive to be applied in the textile, transportation, packaging and aerospace industries. Aluminium also can be found in numerous consumer items such as pharmaceutical drugs, cosmetics, food additives, cooking utensils, antiperspirant and water [Jung et al. 2012, Maity & Govindaraju 2010].

Besides, aluminium is a well known non-essential trace element in human body. The World Health Organization (WHO) report had summarized that the maximum intake of aluminum has been prescribed to be around 3-10 mg per day [Lu et al. 2011]. Excessive accumulation of aluminium in body might damage kidney and nervous system causing aluminium-induced disease such as Alzheimer's disease and Parkinson's disease [Ambreen et al. 2017, Chin-Chan et al. 2015, Iglesias-González et al. 2017]. It also impedes plant growth and harm fish in acidified water. Owing to the potential impact of Al^{3+} ion on human and environment, highly sensitive and selective chemosensors is highly required. It is a challenging task to design an aluminium recognition chemosensor because of aluminium's poor coordination ability and lack of spectroscopic properties [Soroka et al. 1987].

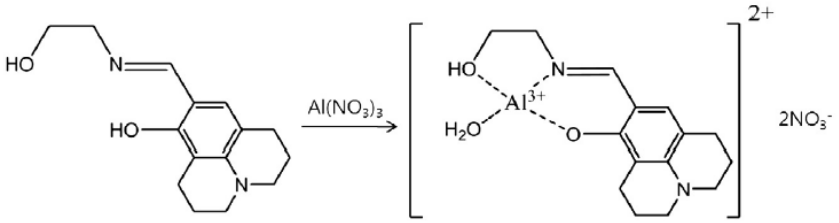
Lu et al. (2011) reported a 1,2-dihydroxyanthraquinone based chemosensor that was designed and synthesized based on PET mechanism. Receptor **5** specifically recognized Al^{3+} ions in aqueous solution by coordinating with S_2N podand moiety and one OH group from 1,2-dihydroxyanthraquinone fluorophore unit that cause a significant enhancement of the emission intensity at 603 nm in the fluorescence

spectrum. This observation can be ascribed to the inhibition of PET processes from both the sulphur and nitrogen donors to the fluorophore.



(**5**)

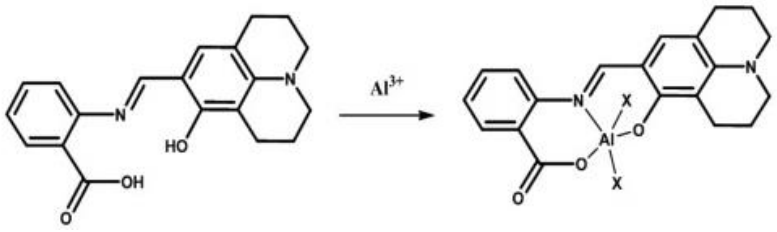
Schiff base colorimetric and fluorescent receptor **6** was designed by combining ethanolamine with 8-hydroxyjulolidine-9-carboxaldehyde and used for studying chemosensing properties Kim et al. (2014) for various metal ions. Upon complexation of Al^{3+} ion with receptor unit induced a red shift of 46 nm in absorption as well as emission spectrum and recorded in DMF/HEPES buffer, thus changing colorless to yellow followed by blue emission. This is attributed to the formation of rigid complex after binding of **6** with Al^{3+} causing the chelation-enhanced fluorescent (CHEF) effect and inhibiting the C=N isomerization.



(**6**)

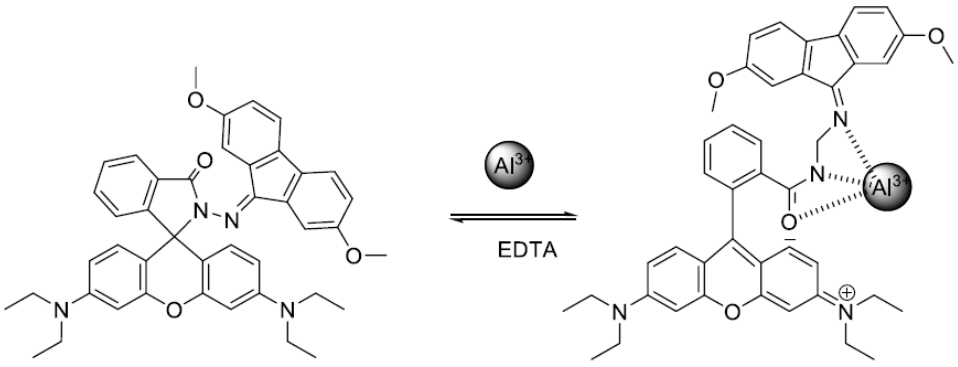
A water-soluble carboxylic functionalized chemosensor **7** reported by Lee et al. (2015) was developed for selective recognition of Al^{3+} ion based on CHEF mechanism. In this process, the Al^{3+} ion was incorporated by coordinating to two OH groups from both julolidine and carboxylate groups and imine nitrogen. It exhibited a highly sensitive and selective "turn-on" fluorescent response toward Al^{3+} ion even at

24 nm level. It was claimed that the presence of carboxylate group as a hard base in a chemosensor make it more selective towards the hard acid, Al^{3+} and increase its water solubility.



(**7**)

Dhara et al. (2013) had developed a new receptor **8** for Al^{3+} ions. The sensing mechanism of receptor based on Al^{3+}-induced reversible ring-opening mechanism of rhodamine spirolactam form. The receptor **8** was designed by combination of 2,7-dimethoxy-9H-fluoren-9-one with rhodamine B. It exhibited a highly sensitive and selective "turn-on" bright orange fluorescent and colorimetric response towards Al^{3+} ion from colourless to purple. Further, sensing ability of receptor was observed to be 2.4 μM level in the fluorescence method. Herein, spirolactam moiety of **8** acted as a signal switcher which was envisioned to turn on when the cation was bound to the rhodamine molecule.



(**8**)

1.11.2 Chemosensors Design for F^- Ion Detection

Being the first anion and the most electronegative element in the periodic table, fluoride ion plays an important role in chemical and biological processes such as treatment of osteoporosis and skeleton fluorosis [Riggs et al. 1990]. It is also able to form hydrogen bond with hydrogen-bond donor. Fluoride released into environment naturally through volcanoes eruption and in marine aerosols. Human activities such as coal combustion and waste from various industrial processes also lead to the release of fluoride into the environment. Besides that, fluoride also present in drinking water for the prevention of dental caries.

However, at high exposure level, intake of fluoride causes skeleton fluorosis, memory loss, kidney failure, gastrointestinal, neurological and urinary problem [Lantz et al. 1987]. The WHO recommended allowed fluoride level in drinking water should not be more than 1.5 μg/L which considered as a limit of health-risk to human being [Kanduti et al. 2016]. Owing to these reasons, selective recognition of fluorine ion is significance. The four main interaction modes between receptor and fluoride ion are as follow:

(1) anion-π interactions,

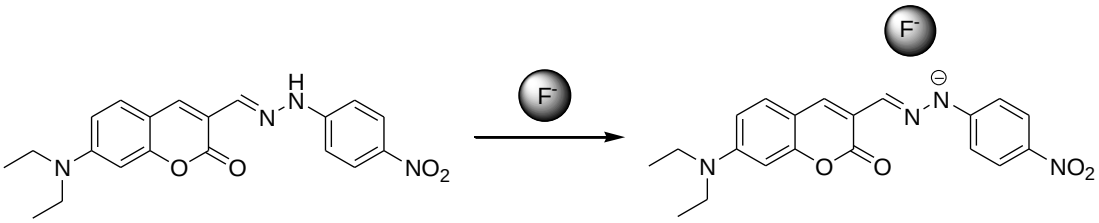
(2) anion sensing through hydrogen bonds between CH, -NH and -OH groups,

(3) Lewis acid-base inter-actions and

(4) anion induced chemical transformation reactions.

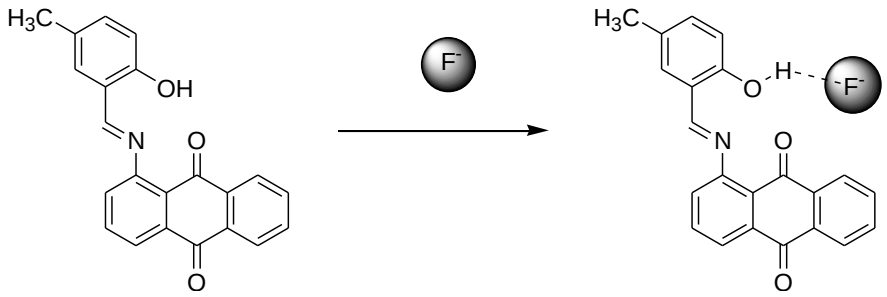
A coumarin-based with Schiff-base as bridge receptor **9** was developed by Zhuang et al. (2011). A high selectivity and sensitivity for F^- ion over other tested anions was rendered by receptor **9** in acetonitrile medium. Addition of F^- ion induced

red shift of absorption spectrum attributed to the intramolecular charge transfer in the whole system via deprotonated form of -NH group in receptor unit. The receptor exhibited a large color changes from yellow to blue and can be clearly visualized by naked eye.



(**9**)

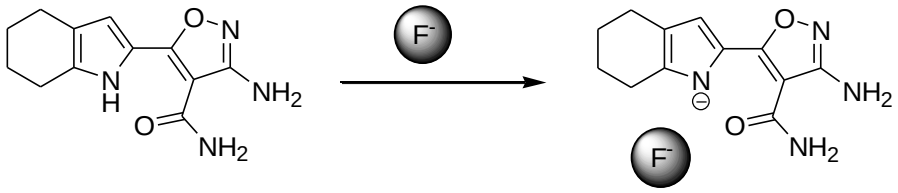
Devaraj et al. (2007) have reported anthraquinone-based receptor **10** as a highly colorimetric and selective fluorescent probe for F^- ion. Receptor **10** possessing a phenolic OH group able to bind fluoride via hydrogen bond interactions produces a dramatic colour changes from light pink to brown. Addition of successive amounts of F^{-} ion results in a reduction of the intensity of the fluorescence emission maximum of receptor **10**.



(**10**)

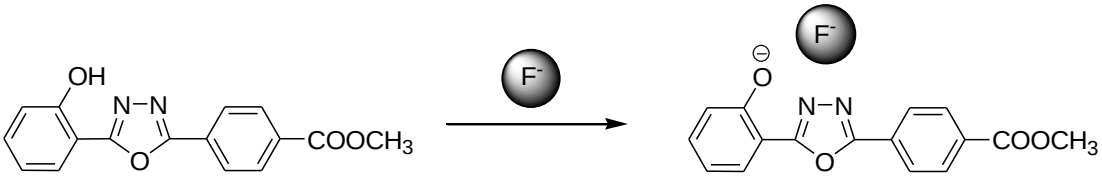
Yang et al. (2011) had synthesized isoxazole derivative composed of pyrrole receptor **11** for F^- ions in CH_3CN medium. Receptor **11** operates via a two-stage deprotonating process in pyrrole moiety leading to a new absorption peak at 375 nm with a clear isosbestic point at 352 nm. The binding behavior of receptor **11** with F^-

was further confirmed by ^{1}H-NMR titration with the disappearance of the pyrrole NH proton. With the increasing concentration of fluoride, the emission maximum was red-shifted and the emission intensity was quenched when F^{-} ion was added.



(**11**)

A novel 1,3,4-oxadiazole based receptor **12** was developed by Ma et al. (2013) containing phenol hydroxyl as the hydrogen-bond donor. Receptor **12** underwent stepwise deprotonating by the influence of F^{-} ion addition, which gave rise to a blue shift of absorption peak from 294 to 272 nm and a new broad absorption band formed at 423 nm. A distinct colour change occurs from colourless to yellow can be clearly identified by naked eye. Fluorescence enhancement and fluorescence colour change from pale blue to green was observed after the addition of F^{-} ion.



(**12**)

1.12 Problem Statements

Although an enormous work on chemosensor had been reported by researchers all over the world since the last two decades, however, there is a limited work focusing on the chalcone-based chemosensors. In addition, the water soluble chalcone-based chemosensor remains rare because of its hydrophobic properties. Hence, the current investigation will place the emphasis on the synthesis and characterization of new chalcone-based chemosensor workable for the selective detection of cations or anions in the aqueous medium through naked eye and the increment of fluorescence intensity. Several chalcone-based molecules incorporated with carboxyl group as chelating units which is hydrophilic in nature will be employed for selective detection of specific cations or anions in water medium.

1.13 Objectives of Present Research Project

The objectives of this research project are:

(a) To synthesize new chalcone derivatives capable to exhibit chemosensing properties particularly for selective detection of cations and anions in the aqueous medium detected by naked eye.

(b) To characterize the synthesized chemosensors in solid state via various spectroscopic techniques.

(c) To investigate the chemosensing behaviour of the synthesized chemosensors by the UV-Vis and fluorescence measurements.

(d) To identify whether a chalcone moiety could be connected to a suitable chelating unit bearing N, O soft donor atoms at various positions and hence induce the chemosensing behaviour of the synthesized receptor.

CHAPTER 2

EXPERIMENTAL WORK

This chapter describes experimental details for the preparation of three different receptor compounds and the recognition studies.

2.1 Chemicals

All the intermediary and the title compounds in this project have been synthesized by using chemicals listed below. These chemicals and solvents were used directly without further purification.

2-hydroxy-1-napthaldehyde, 4-(diethylamino)salicylaldehyde, 2'-hydroxy-1'-acetonaphthone, ethyl acetoacetate, piperidine, 3-(N-morpholino)propanesulfonic acid (MOPS) and the perchlorate salts of all cations used (Ag^{+}, Al^{3+}, Ca^{2+}, Cd^{2+}, Cu^{2+}, Fe^{2+}, Hg^{2+}, K^{+}, Mn^{2+}, Na^{+}, Ni^{2+}, Pb^{2+} and Zn^{2+}) were obtained from Sigma-Aldrich. Ethyl chloroacetate was purchased from Merck. 2'-hydroxyacetophenone and tetrabutylammonium salts of all anions (F^{-}, Cl^{-}, Br^{-}, I^{-} and OH^{-}) used were obtained from Fluka. Potassium carbonate anhydrous was obtained from R & M Chemical. Potassium iodide, sodium hydroxide pellets, sodium sulfate anhydrous, acetone, methanol and ethanol were supplied by QRec. The title compounds were prepared following the procedure as described in section 2.2.

2.2 Synthesis of Intermediary and Title Compounds

2.2.1 Synthetic scheme of receptor {1-[3-(2-Hydroxy-phenyl)-3-oxo-propenyl] -naphthalen-2-yloxy}-acetic acid (NAC)

The synthetic route towards the synthesis of receptor **NAC** is shown in Figure 2.1. Firstly, 2-hydroxy-1-napthaldehyde was alkylated with ethyl chloroacetate which was then subjected to hydrolysis and finally reacted with 2'-hydroxyacetophenone through aldol condensation in a single step to obtain the target receptor **NAC**.

2.2.1(a) Synthesis of (1-Formyl-naphthalen-2-yloxy)-acetic acid ethyl ester (NAEE)

To a solution of 2-hydroxy-1-napthaldehyde (1.0 equiv.) and ethyl chloroacetate (1.0 equiv.) in acetone, potassium carbonate anhydrous (4.0 equiv.) was added followed by a pinch of potassium iodide. After 24 hours reflux, the reaction mixture was filtered off to remove K_2CO_3 and the solvent was left to evaporate. The reaction mixture was treated with water and extracted with diethyl ether and the organic layer was dried on anhydrous Na_2SO_4. The crude product was washed with ethanol to afford a beige solid. Percent yield is 53%.

2.2.1(b) Synthesis of {1-[3-(2-Hydroxy-phenyl)-3-oxo-propenyl]-naphthalen-2-yloxy}-acetic acid (NAC)

Compound **NAEE** (1.0 equiv.) was added to a mixture of 2'-hydroxyacetophenone (1.0 equiv.) in ethanol and stirred for 15 mins. A 10% sodium hydroxide solution was added and stirred for overnight. The precipitate thus formed was filtered and dried. The product was washed with acetonitrile to get a yellow solid, **NAC**. Percent yield is 78%.

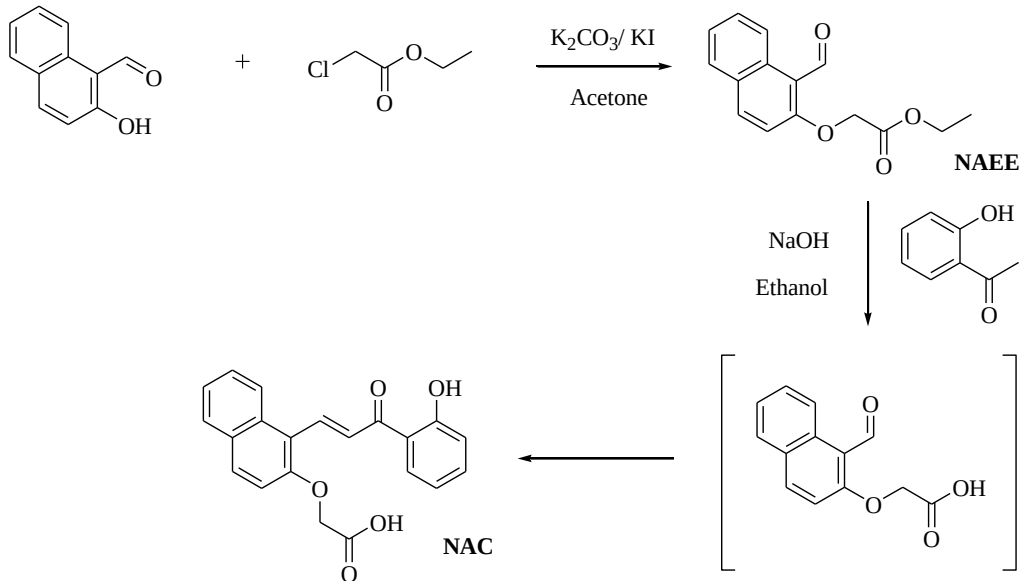


Figure 2.1 Synthesis of **NAC**.

2.2.2 Synthetic scheme of receptor {1-[3-Oxo-3-(3-oxo-3H-benzo[f]chromen-2-yl)-propenyl]-naphthalen-2-yloxy}-acetic acid (CAC)

The general synthetic route towards the formation of chalcone-based chemosensor **CAC** is summarized in Figure 2.2. Firstly, 2-hydroxy-1-napthaldehyde was alkylated with ethyl chloroacetate in base medium to form the intermediate **1** with 61% yield. At the same time, 2-hydroxy-1-napthaldehyde underwent condensation with ethyl acetoacetate to form intermediate **2** (75% yield). Finally, both intermediates were reacted and underwent hydrolysis and aldol condensation in a single step to form the target receptor **CAC** with 89% yield.

2.2.2(a) Synthesis of (1-Formyl-naphthalen-2-yloxy)-acetic acid ethyl ester (NAEE)

To a solution of 2-hydroxy-1-napthaldehyde (1.0 equiv.) and ethyl chloroacetate (1.0 equiv.) in acetone, potassium carbonate anhydrous (4.0 equiv.) was

added followed by a pinch of potassium iodide. After 24 hours reflux, the reaction mixture was filtered off to remove K_2CO_3 and the solvent was left to evaporate. The reaction mixture was treated with water and extracted with diethyl ether and the organic layer was dried on anhydrous Na_2SO_4. The crude product was washed with ethanol to afford a beige solid. Percent yield is 53%.

2.2.2(b) Synthesis of 2-Acetyl-benzo[f]chromen-3-one (ABCM)

To a solution of 2-hydroxy-1-napthaldehyde (1.0 equiv.) and ethyl acetoacetate (1.0 equiv.) in ethanol, 4 drops of piperidine were added. After refluxed for 3 hours, the reaction mixture was filtered and washed with diethyl ether to get a yellow solid. Percent yield is 85%.

2.2.2(c) Synthesis of {1-[3-Oxo-3-(3-oxo-3H-benzo[f]chromen-2-yl)-propenyl]-naphthalen-2-yloxy}-acetic acid (CAC)

Compound **NAEE** (1.0 equiv.) was added to a mixture of compound **ABCM** (1.0 equiv.) in ethanol and stirred for 15 mins. A 10% sodium hydroxide solution was added and stirred for overnight. The precipitate thus formed was filtered and dried. The product was washed with acetonitrile to get a dark red solid, **CAC**. Percent yield is 81%.

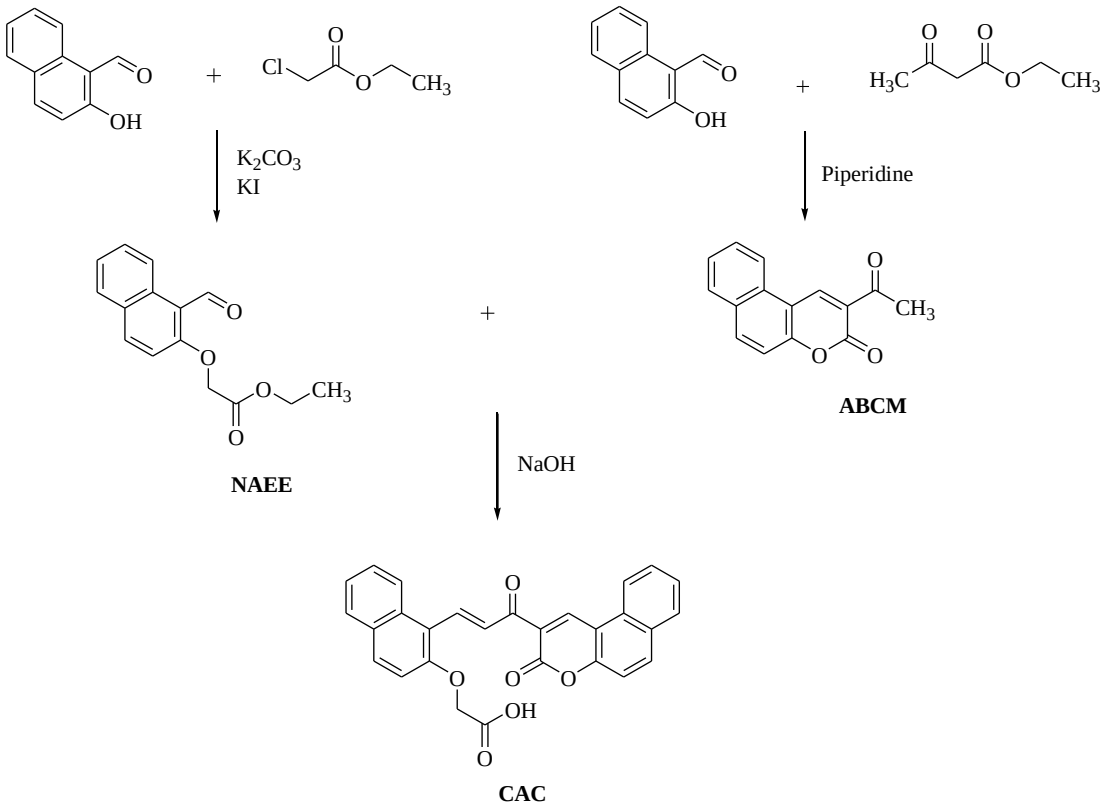


Figure 2.2 Synthesis of **CAC**.

2.2.3 Synthetic scheme of receptor 7-Diethylamino-3-[3-(2-hydroxy-naphthalen-1-yl)-acryloyl]-chromen-2-one (DNAC)

The general synthetic route towards the formation of chalcone-based chemosensor **DNAC** is summarized in Figure 2.3. Firstly, 4-(diethylamino)salicylaldehyde underwent condensation with ethyl acetoacetate to form intermediate **1** and finally reacted with 2-hydroxy-1-napthaldehyde through aldol condensation to lead to the formation of desirable receptor **DNAC** with 37% yield.

2.2.3(a) Synthesis of 3-acetyl-7-(diethylamino)-2H-chromen-2-one (ADCM)

In a two-neck round bottom flask, 4-(diethylamino)salicylaldehyde (1.0 equiv.) and ethylacetoacetate (1.2 equiv.) were dissolved in absolute methanol (15 mL). A