UNIVERSITI PUTRA MALAYSIA

SYNTHESIS AND CHARACTERIZATION OF QUATERNARY AMMONIUM SALTS CONTAINING CARBONYL FUNCTIONALITY

NORAZLINALIZA BINTI SALIM

SYNTHESIS AND CHARACTERIZATION OF QUATERNARY AMMONIUM SALTS CONTAINING CARBONYL FUNCTIONALITY

By

NORAZLINALIZA BINTI SALIM

Thesis Submitted to the School of Graduate Studies, Universiti Putra Malaysia, in Fulfilment of the Requirements for the Degree of Master of Science

June 2007

This thesis is dedicated to my family, whose name:

Salim b Abd. Rahman
Lailawati bt M. Roseli
Tengku Muhamad Azlin b Tuan Siri
Nor Azreen bt Salim
Nor Arianti bt Salim
Nor Amira bt Salim

for their support and understanding.
"THANKS FOR YOUR LOVE AND PRAYERS"

Abstract of thesis presented to the Senate of Universiti Putra Malaysia in fulfilment of the requirement for the degree of Master of Science

SYNTHESIS AND CHARACTERIZATION OF QUATERNARY AMMONIUM SALTS CONTAINING CARBONYL FUNCTIONALITY

By

NORAZLINALIZA BINTI SALIM

June 2007

Chairman : Professor Badri Muhammad, PhD

Faculty : Science

This study is mainly focused on the synthesis of quaternary ammonium salts (QASs) derived from long-chain ketones as starting materials. The procedure used in this study is an extension of a new procedure for the preparation of iodinated acetone successfully developed in our lab and shown to be a generalized procedure for the preparation of iodinated ketones (Wong (2002), Badri (2000)), used to produce a class of quaternary amines containing a carbonyl functionality. Eight new QASs were produced; *N*-acetonyl-3-methylpyridinium iodide (**17**), *N*-acetonyl-4-methylpyridinium iodide (**18**), *N*-(2-oxoheptan-3-yl)pyridinium iodide (**19**), 2-methyl-*N*-(2-oxoheptan-3-yl)pyridinium iodide (**20**), *N*-2-oxoundecanylpyridinium iodide (**21**), 3-methyl-*N*-(2-oxoundeca-3-yl)pyridinium iodide (**22**), *N*-(2-oxododecyl)pyridinium iodide (**23**) and *N*-acetonyltrioctylammonium iodide (**24**). These compounds were characterized by FT-IR, ^{1}H and ^{13}C NMR and CHN elemental analysis. Single crystal x-ray analysis was used to solve the structures of **17** and **18**. The crystal systems for both compounds were

monoclinic. In the surface tension study, it was found that all of the QASs prepared lower the surface tension of water. The critical micelles concentration (CMC) value for the compound **24** (0.0339 mM) is the lowest of all the quaternary ammonium compounds prepared. Qualitative and quantitative antimicrobial assays showed that not all of the QASs prepared were active against bacteria and fungi tested. Only some of them were found to be active against the microorganisms. The compound **23** was strongly active (diameter>15 mm) against *Salmonella choleraessuis* and *Bacillus subtilis* wild type with 20 mm and 25 mm diameter inhibition zones, respectively. There are higher than the control, Streptomycin (17 mm and 15 mm respectively). The presence of long-chain ketones moderately increases the inhibiting effect against the selected microorganisms. The MIC value for the compound **23** against *Salmonella choleraessuis* is 12500 μg ml^{-1}. The MIC value for the compound **23** (1560 μg ml^{-1}) against *Bacillus subtilis* is higher than the control, Streptomycin (48.8 μg ml^{-1}).

Abstrak tesis yang dikemukakan kepada Senat Universiti Putra Malaysia sebagai memenuhi keperluan untuk ijazah Master Sains

SINTESIS DAN PENCIRIAN GARAM KUATERNARI AMINA YANG MENGANDUNGI KUMPULAN BERFUNGSI KARBONIL

Oleh

NORAZLINALIZA BINTI SALIM

Jun 2007

Pengerusi : Profesor Badri Muhammad, PhD

Fakulti : Sains

Penyelidikan ini khususnya mengkaji sintesis sebatian garam kuaternari amina (QASs) yang dihasilkan daripada keton berantai panjang sebagai bahan pemula. Prosedur yang digunakan dalam kajian ini adalah sambungan daripada kaedah baru dan telah berjaya dimajukan untuk menghasilkan aseton teriodin ((Wong (2002), Badri (2000)) dan ini telah digunakan untuk menghasilkan satu kelas kuaternari amina yang mengandungi kumpulan berfungsi karbonil. Terdapat lapan QAS baru yang telah dihasilkan iaitu; *N*-asetonil-3-metilpiridinium iodida (**17**), *N*-asetonil-4-metilpiridinium iodida (**18**), *N*-(2-oksoheptan-3-il)piridinium iodida (**19**), 2-metil-*N*-(2-oksoheptan-3-il)piridinium iodida (**20**), *N*-2-oksoundekanilpiridinium iodida (**21**), 3-metil-*N*-(2-oksoundeka-3-il)piridinium iodida (**22**), *N*-(2-oksododesil)piridinium iodida (**23**) dan *N*-asetoniltrioktilammonium iodida (**24**). Kesemua sebatian yang telah dihasilkan dicirikan melalui FT-IR, ^{1}H-, ^{13}C-NMR dan juga analisis unsur CHN. Analisis kristal X-ray telah digunakan untuk membuktikan struktur-struktur sebatian **17** dan **18**. Didapati bahawa sistem kristal bagi

kedua-dua sebatian ini adalah monoklinik. Bagi kajian tegangan permukaan, didapati bahawa kesemua sebatian kuaternari amina yang dihasilkan telah merendahkan tegangan permukaan air. Nilai CMC bagi sebatian **24** (0.0339 mM) adalah yang paling kecil jika dibandingkan nilai CMC bagi sebatian-sebatian yang lain. Secara analisis kualitatif dan kuantitatif antimikrob menunjukkan tidak kesemua sebatian yang dihasilkan adalah aktif terhadap bakteria dan fungi. Sebatian **23** adalah yang paling aktif (Diameter>15 mm) terhadap *Salmonella choleraessuis* and *Bacillus subtilis* jenis liar dengan diameter zon perencatan masing-masing 20 mm dan 25 mm. Nilai ini lebih tinggi daripada Streptomycin (17 mm dan 15 mm masing-masing). Dengan kehadiran keton berantai panjang, ia akan meningkatkan kesan perencatan terhadap mikroorganisma terpilih. Nilai MIC bagi sebatian **23** terhadap *Salmonella choleraessuis* adalah 12500 μg ml^{-1}. Manakala nilai MIC bagi sebatian **23** (1560 μg ml^{-1}) terhadap *Bacillus subtilis* jenis liar adalah melebihi nilai MIC bagi Streptomycin (48.8 μg ml^{-1}).

ACKNOWLEDGEMENTS

Alhamdulillah….thank you to Allah S.W.T for bestowing me with many blessings. Here I would like to take this opportunity to express my sincere and deepest appreciation to my supervisor Prof. Dr. Badri Muhammad for his guidance, his constructive criticism and valuable advice deserve special thanks. I'm also indebted to my co-supervisor Assoc. Prof. Dr. Md. Aspollah Hj. Sukari for his invaluable guidance, his keen interest, encouragement and criticism, which kept me in a right track. Financial support from IRPA program (09-02-04-0752-E001) and my Pasca Scheme scholarship are also greatly appreciated.

Great thanks to my lecturers, Prof. Dr. Karen Anne Crouse and Dr. M. Ibrahim M. Tahir for their kindness and advice throughout the course of my research. I am also indebted to the staff of the Chemistry Department of UPM for helping me with the various analyses of my samples.

Special thanks to Khoo Teng Jin for solving my crystals at Oxford University, UK. A ton of thanks and love to all my labmates, Thahira, Fiona, Mat, Eddy, Teng Jin, Fatah and Tan for their continuous encouragement, inspirations and support whenever I need. Thanks for being so sweet and for making me smile☺. At last to my husband and my family for giving me everything especially their love and prayers throughout my study in Universiti Putra Malaysia and for encouraging me to be the best I can be. Thank You So Much.

I certify that an Examination Committee met on 13th June 2007 to conduct the final examination of Norazlinaliza Binti Salim on her Master of Science thesis entitled "Synthesis and Characterization of Quaternary Ammonium Salts Containing Carbonyl Functionality" in accordance with Universiti Pertanian Malaysia (Higher Degree) Act 1980 and Universiti Pertanian Malaysia (Higher Degree) regulations 1981. The Committee recommends that the candidate be awarded the relevant degree. Members of the Examination Committee are as follows:

M. Ibrahim M. Tahir, PhD
Lecturer,
Faculty of Science
Universiti Putra Malaysia
(Chairman)

Mawardi Rahmani, PhD
Professor
Faculty of Science
Universiti Putra Malaysia
(Internal Examiner)

Gwendoline Ee Cheng Lian, PhD
Associate Professor
Faculty of Science
Universiti Putra Malaysia
(Internal Examiner)

Datin Zuriati Zakaria, PhD
Professor
Faculty of Science and Technology
Universiti Kebangsaan Malaysia
(External Examiner)

HASANAH MOHD. GHAZALI, PhD
Professor/ Deputy Dean
School of Graduate Studies
Universiti Putra Malaysia

Date: 16 August 2007

This thesis submitted to the Senate of Universiti Putra Malaysia and has been accepted as fulfilment of the requirement for the degree of Master of Science. The members of the Supervisory Committee are as follows:

Badri Muhammad, PhD
Professor
Faculty of Science
Universiti Putra Malaysia
(Chairman)

Md. Aspollah Hj. Sukari, PhD
Professor
Faculty of Science
Universiti Putra Malaysia
(Member)

AINI IDERIS, PhD
Professor/Dean
School of Graduate Studies
Universiti Putra Malaysia

Date: 13 September 2007

DECLARATION

I hereby declare that the thesis is based on my original work except for quotations and citations which have been duly acknowledged. I also declare that it has not been previously or concurrently submitted for any other degree at UPM or other institution.

_____

NORAZLINALIZA BINTI SALIM

Date: 24 July 2007

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

δ	Chemical shift in ppm
μg	Microgram
17	*N*-acetonyl-3-methylpyridinium iodide
18	*N*-acetonyl-4-methylpyridinium iodide
19	*N*-(2-oxoheptan-3-yl)pyridinium iodide
20	2-methyl-*N*-(2-oxoheptan-3-yl)pyridinium iodide
21	*N*-2-oxoundecanylpyridinium iodide
22	3-methyl-*N*-(2-oxoundeca-3-yl)pyridinium iodide
23	*N*-(2-oxododecyl)pyridinium iodide
24	*N*-acetonyltrioctylammonium iodide
CHN	Carbon, Hydrogen, Nitrogen Analyses
CMC	Critical Micelles Concentration
d	Doublet
dd	Doublet of doublet
DI-MS	Direct Injection-Mass Spectroscopy
DMSO	Dimethylsulphoxide
EI-MS	Electron Impact-Mass Spectroscopy
FT-IR	Fourier Transform-Infrared
Hz	Hertz
J	Coupling constant in Hz
m	Multiplet

m.p.	Melting point
MIC	Minimum Inhibitory Concentration
ml	Milliliter
NMR	Nuclear Magnetic Resonance
^{o}C	Degree in Celsius
ORTEP	Oak Ridge Thermal Ellipsoid Plot (from the program for Crystal Structure Illustration)
s	Singlet
t	Triplet

CHAPTER I

INTRODUCTION

Quaternary Ammonium Salts (QASs), their application and uses

Amine compounds in which the nitrogen is bound to four carbon atoms through covalent bonds are known as quaternary ammonium salts (QASs). Originally, it was considered that the R groups were only hydrocarbon radicals attached to the nitrogen by a C-N bond. The alkyl radicals may be substituted or unsubstituted, saturated or unsaturated, aliphatic or aromatic, or branched or normal chains. QASs are stable compounds that are not converted to amines by treatment with base and generally show good water solubility because of their ionic structure.

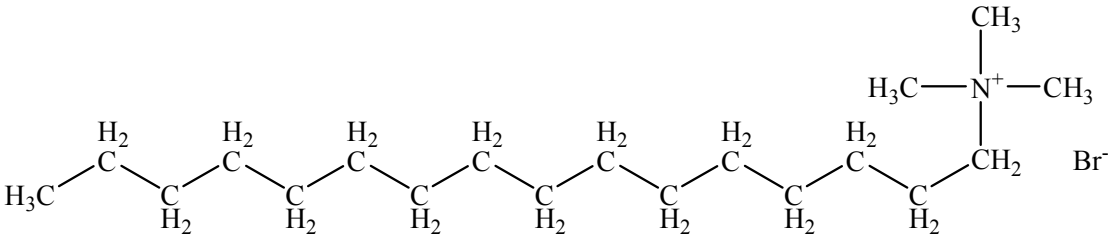
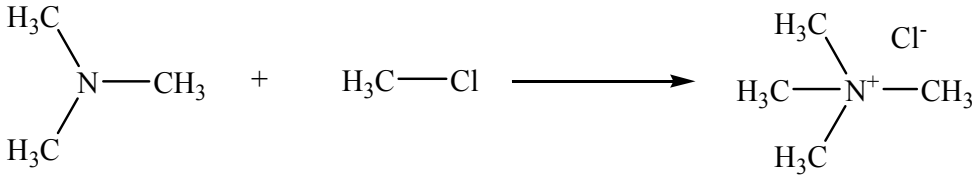


Figure 1: Example of Quaternary Ammonium Salt (Cetyltrimethylammonium bromide)

QASs are made by reacting tertiary amines with halogenated compounds; for example, trimethylamine with chloromethane gives tetramethylammonium chloride **(1.1).** QASs of this type do not liberate the free amine when alkali is added, and

quaternary hydroxides (such as $(CH_3)_4N^+OH^-$) can be isolated. Such compounds are strong alkalis, comparable to sodium hydroxide (Daintith, 2000).



(1.1)

QASs constitute a huge group of organic compounds. N-substituted salts of pyridine and related compounds are one of the most important and versatile being investigated in chemical synthesis (Sliwa, 1996). They are widely used as cationic surfactants, drugs, and herbicides. Because of the formal positive charge on the nitrogen atom, these compounds possess many unique properties, which have been utilized in numerous applications (Bluhm and Li, 1998). For example, a number of molecular recognition systems for nucleotide triphosphates are based on quaternary ammonium compound (Li and Disderich, 1992).

The fabric softening agents for example, widely used now are nitrogen-containing cationic compounds. The existence of positively charged nitrogen atoms leads to a marked difference in the nature of the surface active properties compared to the anionic and nonionic compounds. The positively charged nitrogen atom enables the molecule to be absorbed onto negatively charged surfaces. Also, positively charged fabric softening agents posses antistatic properties. The various types of softening agents in the market mostly are high molecular weight i.e. dialkyl dimethyl quaternary ammonium compounds (**1)** and diamidoamine quaternaries (**2)** (Idris, 1998).