



UNIVERSITI PUTRA MALAYSIA

**THE SYNTHESIS OF QUATERNARY AMMONIUM SALTS WITH
CARBONYL FUNCTIONALITY AND STUDIES OF THEIR PHYSICAL
PROPERTIES**

WONG CHAN HOONG

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By

WONG CHAN HOONG

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

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

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This study is mainly focused on the synthesis of compounds of quaternary ammonium compounds. Iodoacetone has been produced through a simple method by reacting crystalline iodine and acetone in aqueous medium without adding any acid or base catalyst. Iodoacetone has been shown to react with various types of amines to produce tertiary and quaternary ammonium salts. For example, the reaction between pyridine and iodoacetone produced *N*-acetyl pyridinium iodide. Iodoacetone reacts with triethylamine to produce *N*-acetyl triethylammonium iodide and it reacts with triethanolamine to produce *N*-acetyl triethanolammonium iodide. The reaction has been shown to be a general one. In many cases, single crystal x-ray analysis was used to solve the structure of the salts. We have found that the crystal system for *N*-acetyltrimethylammonium iodide, *N*-acetyltriethylammonium iodide, *N*-acetylpyridinium iodide, 1-(1-ethyl-2-oxo-propyl)-pyridinium iodide and 2-hydroxy-



4,4-bis-(2-hydroxy-ethyl)-2-methyl-morpholin-4-ium iodide were monoclinic. Whereas *N*-acetyltributylammonium iodide was tetragonal and *N*-acetyltripropylammonium iodide was orthorhombic. The benefit in choosing crystalline iodine instead of other halogens as the reactant is mainly related to its low toxicity compared to chlorine and bromine. Surface tension measurements showed that for most of the salts synthesized performance as surface lowering agents were not very good. Nevertheless, *N*-acetyltridodecylammonium iodide and *N*-acetyltriethylammonium iodide showed very low critical micelle concentration. Antibacterial and antifungal activity tests were also carried out on the quaternary ammonium compounds. We found that *N*-acetyltriethylammonium iodide was active against four types of bacteria namely *Bacillus subtilis* mutant, *Bacillus subtilis* wild type, Methicillin resistant *Staphylococcus*, and *Pseudomonas aeruginosa*. The antifungal assay tested on three types of fungi; *Saccharomyces cerevisiae* (20341), *Candida albicans* (CA), and *Aspergillus ochraceus* (398). Only *N*-acetyl tributylammonium iodide and *N*-acetyltriethylammonium iodide were active against the fungi.



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

**SINTESIS GARAM KUATERNARI AMONIUM YANG MENGANDUNGI
KUMPULAN BERFUNGSI KARBONIL DAN KAJIAN KE ATAS CIRI-CIRI
FIZIKAL SEBATIAN**

Oleh

WONG CHAN HOONG

Julai 2002

Pengerusi : Profesor Madya Karen Badri, Ph.D.

Fakulti : Sains dan Pengajian Alam Sekitar

Kajian ini adalah terutamanya memberi tumpuan ke atas penghasilan sebatian kuaternari ammonium. Iodoaseton telah dihasilkan melalui kaedah yang senang dengan menindakbalaskan hablur iodine dengan aseton dalam larutan akuas tanpa penambahan sebarang asid atau bes sabagai mangkin. Iodoaseton telah ditunjukkan dapat bertindakbalas dengan pelbagai jenis amina untuk menghasilkan garam kuaternari amonium. Sebagai contoh, tindak balas di antara piridin dan iodoaseton dapat menghasilkan *N*-asetonil piridinium iodida. Iodoaseton dapat bertindakbalas dengan trietilamina untuk menghasilkan *N*-asetonil trietilamonium iodida. Tindakbalas ini boleh dikatakan berlaku secara umum. Dalam banyak kes, analisis sinaran-X hablur telah digunakan untuk menyelesaikan struktur molekul untuk sebatian-sebatian itu. Kami telah mendapati bahawa sistem hablur untuk *N*-asetoniltrimetilamonium iodida, *N*-asetoniltriethylamonium iodida, *N*-asetonilpiridinium iodida, 1-(1-etil-2-okso-propil)-



pidinium iodida dan 2-hidroksi-4,4-bis-(2-hidroksi-etil)-2-metil-morfolin-4-ium iodida adalah monoklinik. Namun begitu, *N*-asetonitributilamonium iodida adalah tetragonal dan *N*-asetonitripropilamonium iodida adalah ortorombik. Kebaikan dalam pemilihan hablur iodin dan bukannya halogen yang lain sebagai reaktan berkaitan terutamanya dengan ketoksikan yang rendah berbanding dengan klorin dan bromin. Pevukatan tegangan permukaan menunjukkan bahawa kebanyakan garam yang dihasilkan menunjukkan peranan sebagai agen merendahkan tegangan permukaan yang sederhana. Walau bagaimanapun, *N*-asetonitridodesilamonium iodida dan *N*-asetonitriheksilamonium iodida telah menunjukkan nilai kepekatan kritikal misel (CMC) yang sangat rendah. Ujian aktiviti antibakteria dan antifungi juga dijalankan ke atas garam kuaternari amonium. Kami mendapati bahawa *N*-asetonitriheksilamonium iodida adalah aktif dalam perencatan terhadap pelbagai jenis bacteria contohnya *Bacillus Subtilis* mutant *Bacillus Subtilis* jenis liar, Methicillin resistant *staphylococcus* dan *Pseudomonas Aeruginosa*. Ujian antifungi telah dijalankan ke atas tiga jenis fungi *Saccharomyces cerevisiae* (20341), *Candida albicans* (CA) dan *Aspergillus ochraceous* (398). Hanya *N*-asetonitributilamonium iodida dan *N*-asetonitriheksilamonium iodida adalah aktif dalam merencat pertumbuhan fungi.

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TABLE OF CONTENTS

	Page
ABSTRACT	ii
ABSTRAK	iv
ACKNOWLEDGEMENTS	vi
APPROVAL SHEETS	vii
DECLARATION FORM	ix
LIST OF TABLES	xiii
LIST OF FIGURES	xvii
LIST OF ABBREVIATIONS	xix
CHAPTER	
1	INTRODUCTION 1
	Halogenated Organic Compounds 1
	α -Iodoketones 7
	Iodination of Acetone 7
	Halogenation of Ketones 10
	The Physical Properties of Iodine 11
	Quaternary Ammonium Compounds 12
	Properties of Quaternary Ammonium Compounds 14
	Biological Properties 15
	Phase Transfer Catalyst 16
	Preparation of Quaternary Ammonium Compound 17
	Cationic Surfactants 18
	Surfactant Solubility 20
	Micelles and Critical Micelle Concentration (CMC) 21
	Carbonyl Functionality 22
	Objectives 23
2	MATERIALS AND METHODS 24
	Chemicals 24
	Physical Measurements and Elemental Analyses 26
	CHN Elemental Analysis 26
	Infrared Spectra (IR) 26
	Nuclear Magnetic Resonance (^1H NMR) 26
	Gas Chromatography and Mass Spectra (GCMS) 26
	X-ray Structure Analysis 27
	Surface Tension Measurement 27
	Thin Layer Chromatography (TLC) 27



	Iodination of Acetone	28
	Iodination of 2-pentanone and 3-pentanone	28
	General Method in Producing Quaternary Ammonium Compounds	29
	Preparation of Other Quaternary Ammonium Compounds	30
	<i>N</i> -Acetylpyridinium Iodide	30
	<i>N</i> -Acetyltributylammonium Iodide	30
	2-Hydroxy-4,4-bis-(2-hydroxy-ethyl)-2-methyl- morpholin-4-ium Iodide	30
	General Procedure in Surface Tension Measurement	31
	Surface Tension Measurement	31
	<i>N</i> -Acetyltriethylammonium Iodide	31
	<i>N</i> -Acetyltridodecylammonium Iodide	32
	Antimicrobial Activity	32
	Preparation of Nutrient Broth Culture	33
	Procedures of Growing Microbes	33
	Quantitative Antimicrobial Assay	34
3	RESULTS	
	Iodoacetone	35
	3-Iodo,pentan-2-one and 2-iodo,pentan-3-one	36
	Characterization of Quaternary Ammonium Compounds	39
	<i>N</i> -Acetyltrimethylammonium Iodide	39
	<i>N</i> -Acetyltriethylammonium Iodide	42
	<i>N</i> -Acetyltripropylammonium Iodide	45
	<i>N</i> -Acetyltributylammonium Iodide	48
	<i>N</i> -Acetyltriethylammonium Iodide	51
	<i>N</i> -Acetyltridodecylammonium Iodide	54
	2-Hydroxy-4,4-bis-(2-hydroxy-ethyl)-2-methyl- morpholin-4-ium Iodide	57
	1-(1-Ethyl-2-oxo-propyl)-pyridinium Iodide	59
	<i>N</i> -Acetylpyridinium Iodide	60
	Surface Tension Measurements	63
	<i>N</i> -Acetyltrimethylammonium Iodide	64
	<i>N</i> -Acetyltriethylammonium Iodide	66
	<i>N</i> -Acetyltripropylammonium Iodide	68
	<i>N</i> -Acetyltributylammonium Iodide	70
	<i>N</i> -Acetyltriethylammonium Iodide	72
	<i>N</i> -Acetyltridodecylammonium Iodide	74
	2-Hydroxy-4,4-bis-(2-hydroxy-ethyl)-2- methyl-morpholin-4-ium Iodide	76
	<i>N</i> -Acetylpyridinium Iodide	78
	1-(1-Ethyl-2-oxo-propyl)-pyridinium Iodide	80
	Qualitative and Quantitative Antimicrobial Assays	82
4	DISCUSSION	84
	Hemiacetal	90



	Intramolecular Hemiacetal	90
	X-ray Structure Analyses	93
	<i>N</i> -Acetyltrimethylammonium Iodide	93
	<i>N</i> -Acetyltriethylammonium Iodide	96
	<i>N</i> -Acetylpropylammonium Iodide	100
	<i>N</i> -Acetyltributylammonium Iodide	104
	2-Hydroxy-4,4-bis-(2-hydroxy-ethyl)-2-methyl- morpholin-4-ium Iodide	108
	<i>N</i> -Acetylpyridinium Iodide	112
	1-(1-Ethyl-2-oxo-propyl)-pyridinium Iodide	116
	Antimicrobial Activity	125
5	CONCLUSION	127
	REFERENCES	129
	APPENDICES	133
	VITA	148



LIST OF TABLES

Table		Page
1.1	Summary of Substitution and Elimination Reactions of Alkyl Halides	2
1.2	Dissociation Energies of Halogenation Molecules	11
1.3	Ionization Potential and Electron Affinity of Halogens	13
1.4	Properties of Quaternaries and Chain Length	15
3.1	^1H NMR (400, CDCl_3) Assignments for ATMAI	40
3.2	^1H NMR (400, CDCl_3) Assignments for ATEAI	43
3.3	^1H NMR (400, CDCl_3) Assignments for ATPAI	46
3.4	^1H NMR (400, CDCl_3) Assignments for ATBAI	49
3.5	^1H NMR (400, CDCl_3) Assignments for ATHAI	52
3.6	^1H NMR (400, CDCl_3) Assignments for ATDAI	55
3.7	Elemental Analysis of Quaternary Ammonium Salts	62
3.8	Surface Tension of ATMAI	64
3.9	Surface Tension of ATEAI	66
3.10	Surface Tension of ATPAI	68
3.11	Surface Tension of ATBAI	70
3.12	Surface Tension of ATHAI	72
3.13	Surface Tension of ATDAI	74
3.14	Surface Tension of HEMI	76
3.15	Surface Tension of API	78
3.16	Surface Tension of EOPPI	80



3.17	Diameter Inhibition Zone (mm) of the QAC	82
3.18	Minimum Inhibitory Concentration (MIC)	83
4.1	Crystal data and structure refinement of ATMAI	94
4.2	Bond lengths and angles for ATMAI	95
4.3	Crystal data and structure refinement of ATEAI	97
4.4	Bond lengths and angles for ATEAI	98
4.5	Crystal data and structure refinement of ATPAI	101
4.6	Bond lengths and angles for ATPAI	102
4.7	Crystal data and structure refinement of ATBAI	105
4.8	Bond lengths and angles for ATBAI	106
4.9	Crystal data and structure refinement of HEMI	109
4.10	Bond lengths and angles for HEMI	110
4.11	Crystal data and structure refinement of API	113
4.12	Bond lengths and angles for API	114
4.13	Crystal data and structure refinement EOPPI	117
4.14	Bond lengths and angles for EOPPI	118
A1	EIMS data of iodoacetone	133
A2	EIMS data of 3-iodopentan-2-one	133
A3	EIMS data of 2-iodopenta-3-one	133
A4	Atomic coordinates and equivalent isotropic displacement parameters of ATMAI	134
A5	Hydrogen coordinates and isotropic displacement Parameters of ATMAI	134
A6	Anisotropic displacement parameters of ATMAI	135



\7	Atomic coordinates and equivalent isotropic displacement Parameters of ATEAI	135
\8	Hydrogen coordinates and isotropic displacement Parameters of ATEAI	136
\9	Anisotropic displacement parameters of ATEAI	137
\10	Atomic coordinates and equivalent isotropic displacement Parameters of ATPAI	137
\11	Hydrogen coordinates and isotropic displacement Parameters of ATPAI	138
\12	Anisotropic displacement parameters of ATPAI	139
\13	Atomic coordinates and equivalent isotropic displacement Parameters of ATBAI	139
\14	Hydrogen coordinates and isotropic displacement Parameters of ATBAI	140
\15	Anisotropic displacement parameters of ATBAI	140
\16	Torsion angles of ATBAI	141
\17	Atomic coordinates and equivalent isotropic displacement Parameters of HEMI	141
\18	Hydrogen coordinates and isotropic displacement Parameters of HEMI	142
\19	Anisotropic displacement parameters of HEMI	142
\20	Torsion angles of HEMI	143
\21	Atomic coordinates and equivalent isotropic displacement Parameters of API	143
\22	Hydrogen coordinates and isotropic displacement Parameters of API	144
\23	Anisotropic displacement parameters of API	144
\24	Torsion angles of API	145
		xx

$\lambda 25$	Atomic coordinates and equivalent isotropic displacement Parameters of EOPPI	145
$\lambda 26$	Hydrogen coordinates and isotropic displacement Parameters of EOPPI	146
$\lambda 27$	Anisotropic displacement parameters of EOPPI	146
$\lambda 28$	Torsion angles of EOPPI	147



LIST OF FIGURES

Figure		Page
1.1	Mechanism of the Acid-Catalyzed Halogenation of Ketones	10
1.2	Synthesis of Cationic Cleavable Surfactant	19
3.1	EIMS Spectrum of Iodoacetone	35
3.2	IR Spectrum of 3-iodopentan-2-one	37
3.3	IR Spectrum of 2-iodopentan-3-one	37
3.4	EIMS Spectrum of 3-iodo,pentan-2-one	38
3.5	EIMS Spectrum of 2-iodo,pentan-3-one	38
3.6	IR Spectrum of ATMAI	40
3.7	^1H NMR spectrum of ATMAI (400 MHz, CDCl_3)	41
3.8	IR Spectrum of ATEAI	43
3.9	^1H NMR spectrum of ATEAI (400 MHz, CDCl_3)	44
3.10	IR Spectrum of ATPAT	46
3.11	^1H NMR spectrum of ATPAI (400 MHz, CDCl_3)	47
3.12	IR Spectrum of ATBAI	49
3.13	^1H NMR spectrum of ATBAI (400 MHz, CDCl_3)	50
3.14	IR Spectrum of ATHAI	52
3.15	^1H NMR spectrum of ATHAI (400 MHz, CDCl_3)	53
3.16	IR Spectrum of ATDAI	55
3.17	^1H NMR spectrum of ATDAI (400 MHz, CDCl_3)	56
3.18	IR Spectrum of HEMI	58



3.19	IR Spectrum of EOPPI	60
3.20	IR Spectrum of API	61
3.21	The Surface Tension Versus Logarithm Molarity of ATMAI	65
3.22	The Surface Tension Versus Logarithm Molarity of ATEAI	67
3.23	The Surface Tension Versus Logarithm Molarity of ATPAI	69
3.24	The Surface Tension Versus Logarithm Molarity of ATBAI	71
3.25	The Surface Tension Versus Logarithm Molarity of ATHAI	73
3.26	The Surface Tension Versus Logarithm Molarity of ATDAI	75
3.27	The Surface Tension Versus Logarithm Molarity of HEMI	79
3.28	The Surface Tension Versus Logarithm Molarity of API	77
3.29	The Surface Tension Versus Logarithm Molarity of EOPPI	81
4.1	¹ H NMR spectrum of HEMI (400 MHz, CDCl ₃)	89
4.2	¹ H NMR spectrum of API (400 MHz, CDCl ₃)	92
4.3	ORTEP diagram of ATMAI	95
4.4	ORTEP diagram of ATEAI	99
4.5	ORTEP diagram of ATPAI	103
4.6	ORTEP diagram of ATBAI	107
4.7	ORTEP diagram of HEMI	111
4.8	ORTEP diagram of API	115
4.9	ORTEP diagram of EOPPI	119



LIST OF ABBREVIATIONS

ATMAI	- N-Acetyltrimethylammonium Iodide
ATEAI	- N-Acetyltriethylammonium Iodide
ATPAI	- N-Acetyltripropylammonium Iodide
ATBAI	- N-Acetyltributylammonium Iodide
ATHAI	- N-Acetyltriethylammonium Iodide
ATDAI	- N-Acetyltridodecylammonium Iodide
API	- N-Acetylpyridinium Iodide
°C	- degree in Celsius
CHN	- Carbon, Hydrogen, Nitrogen Analyses
CMC	- Critical Micelles Concentration
δ	- chemical shift in ppm
d	- doublet
EIMS	- Electron Impact-Mass Spectroscopy
EOPPI	- 1-(1-Ethyl-2-oxo-propyl)-pyridinium Iodide
FTIR	- Fourier Transfer Infra-Red
HEMI	- 2-Hydroxy-4,4-bis-(2-hydroxy-ethyl)-2-methyl-morpholin-4-ium Iodide
Hz	- Hertz
<i>J</i>	- Coupling constant in Hz
ml	- mililitre
m.p.	- melting point
MIC	- Minimum Inhibition Concentration
MPOB	- Malaysian Palm Oil Board



ORTEP	- Oak Ridge Thermal Ellipsoid Plot (from the program for Crystal Structure Illustration)
QAS	- Quaternary Ammonium Salt
NMR	- Nuclear Magnetic Resonance
s	- singlet
TLC	- thin layer chromatography
μg	- microgram
QAC	- Quaternary Ammonium Compounds
m	- multiplet



CHAPTER 1

INTRODUCTION

Halogenated Organic Compounds

Halogenated organic chemicals are important not only in themselves as finished products such as organochlorofluorocarbons, or precursors to finished products, such as polyvinylchloride, but also as intermediates for downstream products. In the latter case this is so because a halogenated organic compound can undergo various reactions such as

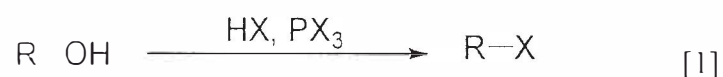
Nucleophilic substitution

Dehydrohalogenation

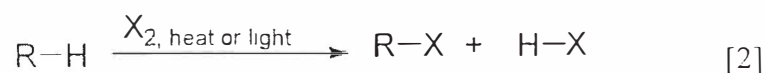
Preparation of Grignard Reagents

Reduction

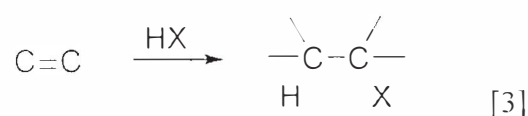
There are many methods available for synthesizing alkyl halides in the laboratory. Most of these methods produce good yields of single products. For example, halogenated hydrocarbons are generally produced from the conversion of alcohols. This reaction is generally satisfactory for the preparation of bromides and iodides (Fiestel *et al.* 1961)



Halogenated hydrocarbons can also be produced from alkanes using free-radical halogenation



Addition of hydrogen halides to alkenes will also produce halogenated hydrocarbons



(Wade, 1987)

Alkyl halides are versatile organic compounds, easily converted to most of the other functional groups. The most important property of alkyl halides is the ability of the halogen atom to leave with its bonding pair of electrons to form a stable halide ion. Many of the reactions of alkyl halides can be classified as eliminations or as nucleophilic substitutions. Some of these reactions are summarized in Table 1.1

Table 1.1 Summary of Substitution and Elimination Reactions of Alkyl Halides

<i>Nucleophile</i>		<i>Product</i>	<i>Class of product</i>
R-X + -OH	→	R-OH	alcohol
R-X + -OR'	→	R-OR'	ether
R-X + -NH ₃	→	R-NH ₃ ⁺ X ⁻	amine
R-X + ⁻ :C≡C-R'	→	R-C≡C-R'	alkyne
R-X + ⁻ :C≡N	→	R-C≡N	nitrile
R-X + R'-COO ⁻	→	R'-COO-R	ester

Iodination of palmitic acid, PA, has been carried out in several solvent systems. The two phase system composed of dichloroethane/ acetone/ water was found to be the preferred solvent (Muhammad *et al.*, 2000). Acetone was used to facilitate the reaction between iodine and palmitic acid. Iodoacetone was obtained as a side product or perhaps was an essential intermediate. This compound was also found to be highly reactive with tertiary amines forming quaternary ammonium salts.

Therefore it was wise to focus on the reaction between acetone and iodine in an attempt to improve upon its synthesis. Several reaction conditions have been modified to obtain a better yield. Once an easy route to iodinated acetone was found, the technique was applied to other ketones. Compared to conventional quaternary ammonium compounds, the newly synthesized products with carbonyl functionality were considered as unique and perhaps possess several special properties.

In an investigation of the reaction of compounds containing a reactive hydrogen atom with iodine in the presence of a base, King *et al.* (1944 and 1946) attempted to make some aryl methyl ketones react with iodine and pyridine. They were able to prepare the substituted β -ketoalkylpyridinium iodides such as 1-phenacylpyridinium iodide (I), 1-(1-naphthoymethyl)-pyridinium iodide (II), 1-(1-anthroylmethyl)-pyridinium iodide (III), and 1-(α -methylphenacyl)-pyridinium iodide (IV). These products were accompanied by some hydroiodide of the base as shown in reaction [4]. In each of the reactions studied, approximately half of the iodine used appeared as pyridine

hydroiodide. Each of the substituted β -ketoalkylpyridinium iodides produced by the above reaction gave characteristic hydroxy acids when cleaved by means of aqueous alkali [5] (King *et al.*, 1945).

