Bachelor's thesis

NTNU
Norwegian University of Science and Technology
Faculty of Natural Sciences
Department of Materials Science and Engineering

Brage Bang

Synthesis of reference standards for Quaternary ammonium compounds (QUATS)

Bachelor's thesis in Chemical Engineering
Supervisor: Eirik Sundby
Co-supervisor: Huiling Liu
May 2022

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Kunnskap for en bedre verden

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Preface

My biggest motivation in this project has been to improve as a chemist, but also an engineer. These are things you don't necessarily learn much of while studying. Although I have completed three years in the chemical engineering bachelor course on NTNU, and had many hours of practice in the university laboratory, it was simply an introduction to the working life. There are several lessons I've been taught during the last months working on this thesis, and I am very happy to have experienced it. First of all: Working alone can be difficult! The main benefit of working alone is that you can control everything. The biggest impede is also that only you control where the project is headed. Simply put, I found it was very important to discuss the problems and ideas that surfaced. Second: The problem is as hard as you want it to be. As a student, over complicating things is a normal occurrence because theory is what we know. Learning how to not beat yourself up is a very helpful lesson. Third: Don't underestimate workload. Even if you simplify the problem, describing the problem is often way more simple than solving them. There are probably some more lessons I forgot that my informal lab supervisor, Alexey Gorovoi, told me. Thank you for answering my "interesting questions", aiding with your practical finesse and doing the washing machine when I could not! You made this project much easier for me. Now I am one step closer to becoming a true organic chemist!

Having somebody to give you a direction during a project can be very boosting. My two supervisors, Huiling Liu and Eirik Sundby helped me greatly by defining and simplifying the project for me - making my life easier. They are always available, and I am very thankful for that! Thank you! Also, I really want to thank everyone in Chiron for helping me with their practical knowledge, stopping by for a talk or even go bouldering! Human relations, I have learned, is a big part of professional work. Working at Chiron has been one of the most earning periods in my life, giving me a true introduction to what working in a professional company feels like. Thank you, Jon Eigill Johansen, for giving me this opportunity!

I want to thank my friends and family for sometimes taking my mind off work. My mental health is owed to you! Thank you, mom, for reading through the thesis and giving feedback. Your constructive comments provided me some additional motivation. Thank you to my girlfriend for keeping up with the late working nights, lending me her books and showing support to my endeavour. Your patience has been astounding!

Brage Bang

May, 2022

Contents

Sammendrag

I dette prosjektet ble elleve kvartære ammonium stoffer (QUATS) syntetisert for bruk som referansestandarder. Åtte av disse stoffene tilhører gruppen dialkyldimetylammonium klorider (DDACs) og tre tilhører gruppen benzylalkyldimetylammonium klorider (BACs). Reaksjonen fulgte en vanlig S_N2 reaksjon der et tertiært amin alkyleres med alkyl klorider (Menshutkin reaksjon). Forberedelsen av stoffene fulgte tre hovedsteg: syntese, rengjøring og analyse. I syntesen ble utgangsstoffene blandet i et godt egnet løsemiddel. Høye temperaturer og konsentrasjoner av utgangsstoff ble vist til å gi et godt reaksjonsutbytte. I rengjøringsfasen ble produktet vasket i løsemidler som selektivt løser opp utgangsstoffene. Kald heksan egnet seg godt for vask av de mer upolare saltene. Omkrystallisering ble utført på nesten hvert produkt. For BACs ble aceton eller etyl acetat brukt for å omkrystallisere, for DDACs - dietyleter og heksan. Utbyttet på BACs var generelt bedre enn for DDACs. Hvert produkt ble analysert ved hjelp av HPLC eller diverse NMR metoder. Renheten på mange av produktene overgikk 98% renhet (NMR).

Abstract

In this project, eleven quaternary ammonium compounds (QUATS) were synthesized for the purpose as reference standards. Of these eleven, eight were dialkyldimethylammonium chlorides (DDACs) and three benzylalkyldimeththylammonium chlorides (BACs). The reaction followed an S_N2 reaction mechanism with alkylation of a tertiary amine (Menshutkin reaction). The preparation of the QUATS followed three major steps: synthesis, workup/purification and analysis. In the synthesis, the starting materials was dissolved in a suitable solvent. It was found that a high temperature and long reaction time yielded a good conversion rate from starting material to product. In the workup and purification stage, the crude products were concentrated and washed with a solvents that selectively dissolves starting materials, but not product. For the most non-polar products, washing in cold hexane gave the best result. Crystallization was done on every product, but generally, BACs crystallized well in acetone and ethyl acetate while DDACs crystallized in diethylether and hexane. The end yield for BACs was generally higher than for DDACs. Each product was analysed using HPLC and various methods of NMR to determine purity. Many of the purities achieved were over 98% (NMR).

Introduction

This bachelor thesis was written in direction by NTNU for Chiron AS. In this work, several quaternary ammonium compounds were synthesized for use as reference standards for use in environmental and food analysis.

Structure of the report

In chapter 1 - Theoretical section, the scope of the project is described as well as review of previous literature for synthesis. Chapter 1.1 defines the QUATS that will be synthesized. Chapter 1.2 describes and discusses favourable reaction conditions for the synthesis. Chapter 1.3 covers some basic methods of purification and briefly how previous studies have performed them. Chapter 1.4 briefly describes the principles behind some analytical methods for analysis of said compounds.

In chapter 2 - Method, the most successful syntheses among many are described in detail, and how analysis was performed for each.

Results and discussion in chapter 3 and 4 display and explain the results from the analyses, and possible improvements for the methods used.

About the project

Quaternary ammonium compounds (QUATS) designate an important class of chemicals widely distributed among households and industries. They function as strong cationic surfactants, and are commonly used in disinfectants, biocides and detergents [1]. QUATS, specificaly alkyldimethylbenzylammonium chlorides (BACs) and dialkyldimethylammonium chlorides (DDACs), are also proven to cause birth defects and decrease fertility rate in mice. Defects according to [2] were caused by a mixture of the latter two QUATS. Since the spiking of disinfectant use since the start of covid-19, questions of the safety of QUAT use have surfaced. Effects on humans have still not been documented well enough, but indications by experiments with mice suggest it can be detrimental to human health [3].

Chiron is a company that produces reference materials for numerous industries. Up to date, Chiron has a portifolio of over 15000 unique products including Novel Psychoactive Substances, biomarkers, PAH metabolites, pollutants in food and environment, patented products and the new carbon-13 labeled drug standards [4]. This project will be about a small scale synthesis and purification of various quaternary ammonium compounds (QUATS). Specifically, the product has to be 98% pure to qualify as a reference standard. It will be investigated how pure QUATS can be synthesized in an efficient manner with some basic process optimalization. Preparation of some QUATS have been described previously [1, 5–7]. These studies will be used as a reference point for this project. The goal of this project is to establish a good working method for synthesizing QUATS in lab scale.

1 Theoretical section

1.1 QUATS and definitions

The QUAT structure is generalized by a central nitrogen bonded to four alkyl groups. The two groups og QUATS in this projects are: Benzylalkyldimethylammonium chlorides (BACs) and Dialkyldimethylammonium chlorides (DDACs). They have general structure shown in figure 1.

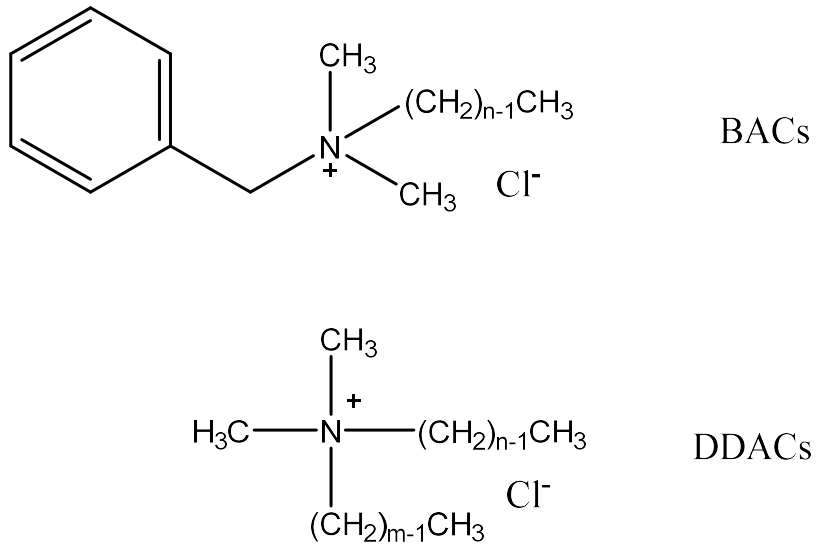

Figure 1: General structures of benzylalkyldimethylammonium chlorides (BACs) and dialkyldimethylammonium chlorides (DDACs). Side chains may vary in length.

Table 1 displays the list of QUATS that will be attempted to be synthesized during this project. Classifications (a,b) denote the compound group (BAC, DDAC) and numbers - variations in chain lengths. n and m describes carbon chain lengths in figure 1.

Table 1: List of all compounds synthesized in project. n and m describe carbon chain lenghts from figure 1.

Code	Name	Abbreviation	n	m
a1	Benzylhexyldimethylammonium chloride	BAC-6	6	-
a2	Benzyldimethyloctylammonium chloride	BAC-8	8	-
a3	Benzyldecyldimethylammonium chloride	BAC-10	10	-
b1	Dihexyldimethylammonium chloride	DDAC-C6	6	6
b2	Dimethyldioctylammonium chloride	DDAC-C8	8	8
b3	Didecyldimethylammonium chloride	DDAC-C10	10	10
b4	Didodecyldimethylammonium chloride	DDAC-C12	12	12
b5	Dimethylditetradecylammonium chloride	DDAC-C14	14	14
b6	Hexadecyldimethyldiammonium chloride	DDAC-C16	16	16
b7	Dimethyldioctadecylammonium chloride	DDAC-C18	18	18
b8	Dimethyldecyloctylammonium chloride	BTC-818	8	10

In a previous study by Kamil Kuca et al., the melting points of some benzalkonium bromides (BACs) were determined [1]. Results for 3 relevant BACs are shown in table 2. Data for DDACs are missing

Table 2: Melting points of some BACs (bromides).

Compound	Melting point (°C)
a1	122.0-123-5
a2	53.0-56.0
a3	34.0-37.5

1.2 Kinetics

Quaternization rate is dependent on numerous factors. Some of these factors are: type of halide on substituent group, chain length on substituent, solvent, concentration temperature and pressure [5, 8]. Of these factors, temperature, solvent and concentration are easy parameters to control for any reaction. Several studies have been conducted to find ideal reaction conditions for some QUATS, which will be discussed briefly in this section.

Synthesis of QUATS follow an S_N2 reaction mechanism, where a tertiary amine reacts with an alkyl halide in a nucleophilic substitution. This specific case of reaction is commonly referred to as the Menshutkin reaction (MR). MR is defined as the trialkyl-ammonio-dehalogenation of an alkyl halide [1, 5, 8].

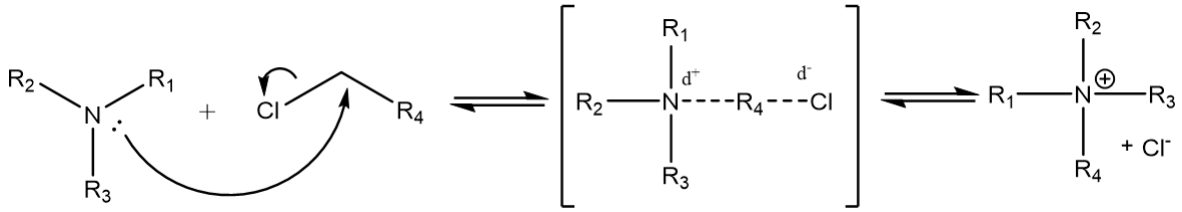

Figure 2: A general reaction mechanism for Menshutkin reaction. The free electron pair of nitrogen attacks the alkyl halide and knocks electrons to the halide. As the halide is a better leaving group than the amine, product is formed.

Since MR is an S_N2 reaction, the reaction rate is dependent of the reactant concentrations $[A]$ and $[B]$ as well as its' reaction coefficient k as shown in differential equation 1.

$$\frac{d[A]}{dt} = -k[A][B] \tag{1}$$

k is the reaction coefficient and varies with temperature described by Arrhenius' equation 3. Assuming the concentration of the reactants A and B are equal, a solution to the differential equation can be written as equation 2.

$$[A]_t = [B]_t = \frac{[A]_0}{1 + [A]_0 kt} \tag{2}$$

In combination with the Arrhenius parameters in equation 3, the reaction kinetics can be estimated for the quaternization rate of amines.

$$ln(k) = ln(A) - \frac{E_a}{RT} \tag{3}$$

Where A is the frequency factor, E_a is the activation energy, R is the gas constant and T is the temperature (in Kelvin) [9, p.268-80].

Solvents in MR (S_N2) are preferrably aprotic and polar. Polar solvents have the ability to stabilize the transition state of the molecule (figure 1), which in turn facilitates the reaction [10]. The aprotic nature of the solvent prevents competetive reactions with either the amine (H^+ attacks amine) or alkyl halide (OH^- attacks alkyl halide). Lewis acids and bases can thus be used to quench the reactions. This principle has been adopted in the kinetic study by Roel J.T Kleijwegt et.al where 12 M HCl was used to quench the reaction [5]. A similar approach was adopted by Ten-Tsai Wang and Ting-Chia Huang [11]. By dissolving the QUAT reaction mixture in benzene followed by shaking the mixture with water, further reaction in the analysis stage was neglected.

In [5], the benzylation rate of benzyldecyldimethylammonium chloride was investigated with regards to different solvents and temperatures. The solvents investigated were acetone, methanol and acetonitrile and temperatures ranged from 0-50°C. The raw data [5, Appendix A] for quaternization rate between decyldimethylamine and benzyl chloride was collected and analysed in Microsoft Excel to give the Arrhenius plot shown in figure 3. The plot is derived from equation 3 by using $1/T$ as the x-variable and $ln(k)$ as the y-variable.

According to the results, acetonitrile had the highest reaction rate in the temperature ranges that were studied. Despite this, it was also concluded that the reaction rate constant for methanol would surpass that of acetonitrile for higher temperatures. This can be explained because of the higher activation energy E_A for methanol (67.76 kJ/mol) compared to acetonitrile (39.51 kJ/mol) as shown in table 3.

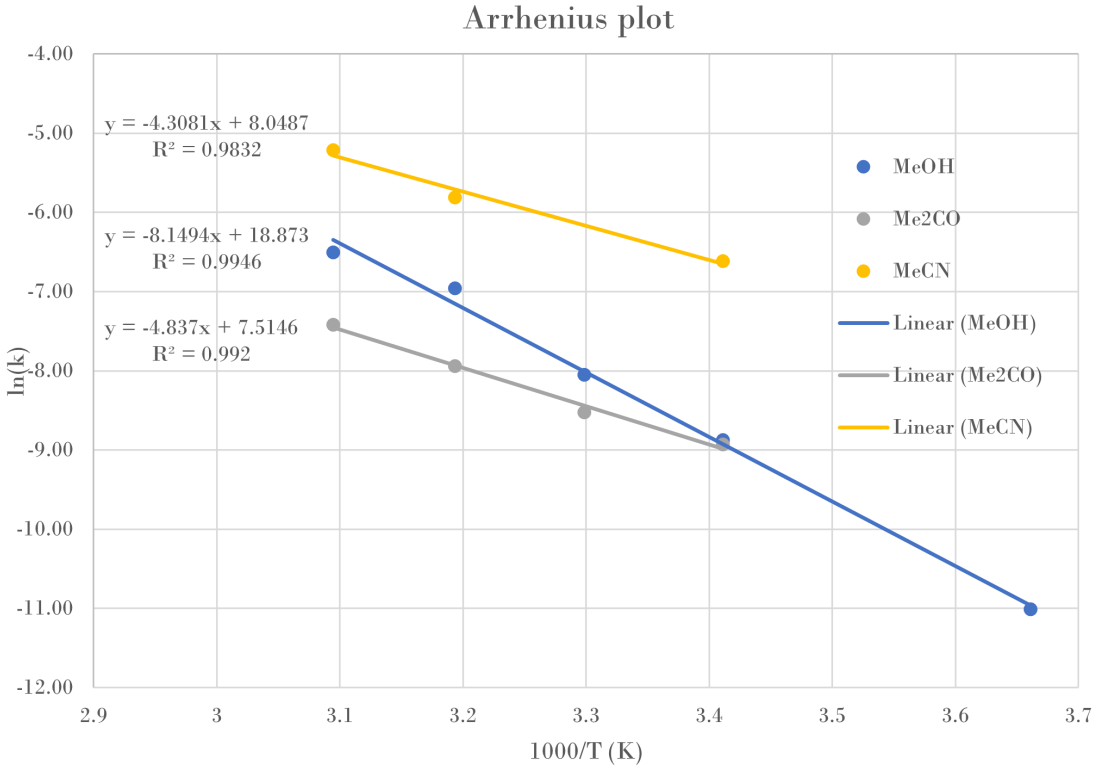

Figure 3: Arrhenius plot for quaternization between decyldimethylamine and benzyl chloride in methanol (blue), acetone (grey) and acetonitrile (yellow). Concentrations varied between 0.2-0.7 M and temperatures between 0-50°C. Next to each plotline is the respective regression curve for each solvent [5, Appendix A].

Solvent	Boiling Point (°C) [12]	ϵ [12]	E_a (kJ/mol) [5]
Acetonitrile	81.65	36.64 (20°C)	39.51
Acetone	56.05	21.01 (20°C)	40.22
Methanol	64.6	32.6 (25°C)	67.76

Table 3: Boiling points, dielectric constants and activation energies for acetonitrile, acetone and methanol. The activation energies are related to the synthesis of benzyldecyldimethylammonium chloride [5].

Assuming the linearity of the graph due to $-E_a/R$ being a constant gradient, a value for $ln(k)$ can be estimated for different temperatures. k should strictly increase with temperature, which in turn will cause $[A]_t$ in equation 2 to converge faster - producing product more rapidly [11].

Concentration is another variable that greatly affects the reaction rate. By plotting the theoretical reaction time (for 95% conversion of starting material) against temperature (x) and concentration (y), figure 4 is obtained. It is clear from the plot that the reaction time decreases with increasing temperature and reactant concentration. This plot only applies to **a3**. In this plot, the assumption was made that reactant concentrations are equal, chemical activity remains constant, it is atmospheric pressure and that equilibrium is negligible. The values for 100°C was found by extrapolating the data in figure 3 to produce a new reaction constant k. The calculations are shown in appendix C.

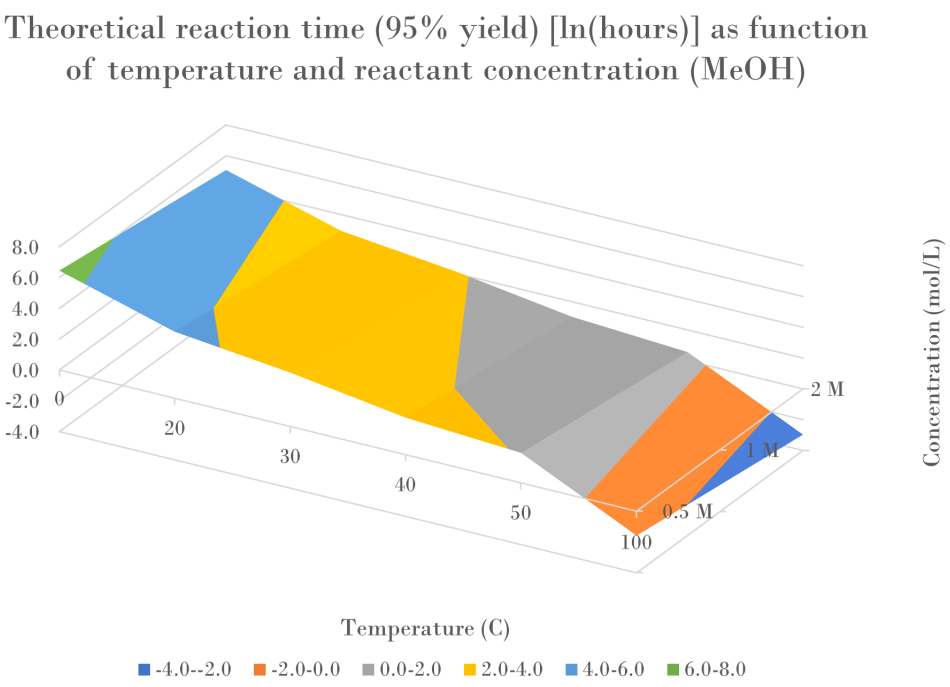

Figure 4: 3D graph shows the natural logarithm of the reaction time (hours) for 95% conversion. The two variables are concentration in moles per liter and temperature in °C. Assumptions 1: the reactant concentrations are equal. Assumption 2: reactivity remains constant. Assumption 3: equilibrium is neglible. Assumption 4: The pressure is 1 atm. Calculated results for 100°C are found by extrapolating the data from [5].

1.3 Workup and Purification

After the reaction is finished, workup and purificaion are the next steps in order to produce a pure product, preferably with good yield. The workup phase mainly consists of removing carrier solvents from the crude product so that purification becomes a less cumbersome process. Removal of carrier solvent can be performed by simply reducing pressure and increasing temperature of the mixture. However, solvent can be bound to the compounds. For this, fractional evaporation can be adopted to remove residue carrier solvent. By adding a extraction solvent with lower boiling point than the carrier solvent to the system, the overall boiling point is lowered, and both solvents are evaporated. A better description can be found in literature [9, p.158-65][13, p.117-23].

1.3.1 Crystallization

Purification of a product can be conducted in several ways. One of the most common techniques for purification is crystallization. The process involves dissolving the compound in small volumes of hot solvent, and slowly cooling down the solution. Crystallization by evaporation/volume reduction is also another method, but can yield lesser purity than the prior method. Failure of crystallization usually means that either too much solvent has been added or that the solution is supersaturated. The crystallization of a supersaturated solution can be accelerated by adding a seeding crystal from the same compound [14, p.99].

The choice of solvent is a critical step in crystallization. At lower temperatures, the compound should be insoluble or partly soluble, while completely soluble at higher temperatures. Impurities should be either soluble or partially insoluble for all temperatures. The boiling point of the solvents should also be lower than the melting point of the compound [14, p.95].

When a suitable single solvent system can not be found, a mixed solvent system can be adopted. In this method, the compound is dissolved in a small amount of good solvent (in which the product is miscible) under continuous heating and added poor solvent (in which the product has poor solubility) drop-wise until the solution becomes turbid. The good solvent should generally have the lower boiling point [15].

In previous studies, BACs were recrystallized using acetone [1]. Some DDACs were recrystallized using methanol:ethyl acetate or methanol:diethylether with cooling [6].

1.4 Analytical methods

After successful synthesis and (presumably) purification, the compounds have to be tested using qualitative and quantitative analytical methods. In this part, three such methods are described. HPLC can give a column separation between products and impurities while also giving an indication on purity. MS can thereafter identify the ionized molecule masses. The coupled HPLC-MS system can be a powerful qualitative and quantitative tool. NMR is another method can be used to identify molecule structures, which makes it a powerful qualitative tool. It can also be used to determine impurities.

1.4.1 HPLC - High Performance Liquid Chromatography

High Performance Liquid Chromatography (HPLC) is a method for distinguishing molecules from each other based om various mechanisms. Partition chromatography, particularly *reverse phase liquid chromatography* (RP-LC) is a method of separating molecules based on polarity. The stationary phase in RP-LC is non-polar while the mobile phase is a polar solvent. In RP-LC Compounds with high polarity will have low affinity for the stationary column, thus having the shortest retention time t_R [16, p.921-23].

In HPLC, UV detectors are often used to detect chromophores[1]. Conjugated double bonds have this property of absorbing absorbing light. Generally, the more conjugated bonds, the higher the wavelenght. Fewer than eight conjugated bonds result in UV light being detected. Therefore, arenes and specifically benzyl groups can absorb UV light in wavelenghts between 200-260 nm [17, p.149][18, p.82]. This principle can be used to detect the BACs in table 1.

1.4.2 MS - Mass Spectrometry

The LC system will often be coupled with a mass spectrometer (MS) to identify the peaks from HPLC. MS is a method of distinguishing molecules based on mass. Molecules are converted into gaseous ions by an ionizing source and separated based on their mass-to-charge ratio m/z. Ions of different m/z values are directed to a transducer, and are displayed on a mass spectrum. There are several methods for producing ions in MS. Some methods like *electron impact (EI)* fragments the molecule into smaller parts while others

[1] A part of a compound that can absorb and emit electromagnetic radiation[17, p. 149]

like *electrospray ionization (ESI)* outputs charged molecular ions $M+$. These ions are then detected using detectors like the quadropole [16, p.802-17][18, p.85-94].

1.4.3 NMR - Nuclear Magnetic Resonance

Nuclear magnetic resonance (NMR) allows for detection of atomic nuclei and their surroundings based on molecule properties. Nuclei with spin quantum number $1/2$, such as ^{1}H or ^{13}C, align along or against a strong magnetic field. There is a certain energy difference between the two alignments depending on the magnetic field strength. The sample is irradiated by a short pulse of radiation to promote some of the nuclei to the higher energy level. Only. The energy is thus given out as radiation and detected [17, p.269-97][19, p.392-401]. There are three main factors coming into play when analyzing an NMR spectrum.

1. *Chemical shift* (δ) chemical shift is often denoted in parts per million (ppm), which is directly derived from dividing the frequency of the resonating atom by the frequency of the magnetic field (not considering the reference standard). In NMR spectra, the chemical shift indicates how "shielded" an atom is. Nuclei close to very electronegative atoms such as oxygen, nitrogen or fluorine experience very little shielding due to "losing electrons". This effect of "deshielding" is what causes the effective magnetic field to decrease and thus chemical shifts to increase. On the contrary, saturated carbon chains with no functional groups experience no deshielding, thus having a lower chemical shift. Benzyl groups is a special case where a local induced magnetic field causes deshielding of hydrogens while carbons experience no effect [17].

2. *Quantitative analysis*: The area under the peaks in NMR correlate with the amount of atoms in a similar/identical environment on a molecule. Integration mainly applies to abundant isotopes, as this statistically gives a stronger quantitative basis. For instance, deuturated compounds do not show peaks in NMR on contrary to the more abundant isotope ^{1}H (99.985% natural abundance) due to ^{2}H not having spin quantum number $1/2$ [17]. On contrary, the NMR active ^{13}C isotope is much less abundant than the non-active ^{12}C. Using this principle, purity of the compound can be estimated by integrating peaks with impurities [20, p.34].

$$P_m = P_n \cdot \frac{M_x}{\sum_1^i M_i} = \frac{I_x \cdot M_x}{N_x} \cdot \sum_1^i \frac{N_i}{I_i \cdot M_i} \tag{4}$$

Where P_m, P_n, I, N and M are are purities in terms of mass and moles, integration, number of protons and molar masses, respectively [21]. Here, x represents the sample of interest, and i represents all the signals, including impurities and x.

3. *Coupling* is a phenomenon where a proton group H^x interacts with with another nearby proton group H^A through C-C bonds by splitting its' signal. This occurs because the quantum spin(s) of each hydrogen in H^X either applies or subtracts a field to H^A. From this, the N+1 rule is derived, where N is the amount of neighbouring hydrogen atoms, and N+1 is the amount of local signals. For example, two neighbouring hydrogens give rise to a triplet. The difference in local chemical shifts for H^A is called the *coupling constant* J_{AX}, and is measured in Hz. The interaction also goes the other way around (J_{XA}). An important factor affecting the coupling is the through-bond distance. A normal coupling through three bonds (H-C-C-H) are designated $^{3}J_{HH}$. These are usually visible in the ^{1}H-NMR specrum. Four-bond coupling $^{4}J_{HH}$ is usually

not visible, but can also occur in special cases like aromatic rings (meta-coupling). Coupling is mostly used to describe H-H relations, but C-H coupling can also occur in some instances. Due to the scarcity of the ^{13}C isotope, these coupling peaks are substantially smaller by integration, but can sometimes be visible in ^{1}H-NMR [17, p.285-300]. There are many other factors affecting coupling, but these are not as relevant in this project [20, p.85-108].

Some methods in NMR include ^{1}H, ^{13}C and COSY (Correlated Spectroscopy), the latter one being what's called a 2-dimensional (2D) NMR method while the prior ones are 1-dimensional (1D). COSY is a common method to determine what hydrogens are coupled, and can be a useful tool to determine what the peaks in the 1D proton spectra represent. Tables for typical solvent NMR shifts can be used to find impurities in the 1D spectra [22].

2 Method

2.1 Experimental Section

Although many experiments were conducted in this project, only 12 of these will be included in this report. The summarized list of experiments and corresponding compound is shown in table 6. The experiments described in this procedure are: 1-11.

The *BACs* were prepared by reacting N,N-dimethylalkylamines with benzyl chloride. For **a1-a3** dimethylhexylamine, dimethyloctylamine and dimethyldecylamine were the nucleophiles, respectively. **a3** was also synthesized using deuturated benzyl chloride.

The *DDACs* were prepared by reacting N,N-dimethylalkylamines with their corresponding alkyl chlorides. The exception was **b8**, where dimethyldecylamine reacted with octyl chloride. For **b1-b7**, the alkyl chains used were hexyl, octyl, decyl, dodecyl, tetradecyl, hexadecyl and octadecyl, respectively. So two identical alkyl chains per ammonium salt.

The list of starting materials and their signal words can be found in appendix D.

2.1.1 General procedure

Amine and corresponding alkyl chloride was dissolved in a suitable solvent. Methanol worked for all experiments. Reaction could either run in reflux or in a closed system (pressure tube) at 70-140 °C. After 1-22 days, the reactions were quenched by removing from heat. The reactions were not monitored in the reaction process. For workup, the crude products were added diethylether/n-hexane and concentrated on rotavapor. This step could be repeated numerous times. It was also important to keep watch over the rotavapor so that product would not be lost due to burst bubbling. Thereafter, diethylether or n-hexane was used to remove starting materials and residue solvent. The white emulsions that could emerge from the washing was let to settle before decanting to avoid excessive product loss. This step could be repeated until the crude product became gradually more viscous, or if white crystals precipitated

In purification, adequate solvent systems were adopted to preferably recrystallize the products. The solvent systems used were quite individual, and will be described further in the next section. The solvent systems

often consisted of two solvents. One solvent which the product easily dissolves in (minimal amounts), and another that does not dissolve the product as easily. After crystal/solid formation, filtration with filter paper was performed. Additionally, washing with solvent that does not dissolve the product was done to remove residue solvents and/or starting materials.

In some cases, products with large crystals were crushed, added the poor solvent and set on ultrasonic bath to dissolve residue solvents/starting materials. The last steps was drying using vacuum for several hours/days followed by analysis.

For products that "oiled out" in an attempt to precipitate/crystallize, additional washing steps with hexane/EtOEt were performed to remove reaction solvent and starting material. Thereafter, a suitable solvent system was used to precipitate/recrystallize in a cold environment (either 4 or -20 °C). If this method did not work, the product (oil) was dried in high vacuum to remove the volatile washing solvent.

Additionally, solubilities for all amines and products were estimated in various solvents such as methanol, ethyl acetate, hexane and diethylether.

2.1.2 Experimental procedure

Experiment 1 **a1** was prepared in two seperate reactions, but mixed together in the workup phase. In one reaction, amine (0.67 g, 5.2 mmol) and benzyl chloride (0.66 g, 1 eq) were weighted off and added to a round bottom flask. The flask was added 20 mL acetonitrile and set on reflux with stirring at 95 °C for 12 days. In the other, amine (0.65 g, 5.0 mmol) and benzyl chloride (0.64 g, 1 eq) were weighted off and added to a closed system pressure tube with 10 mL ethanol. Reaction was set with stir at 95 °C for 11 days. Crude products were mixed together and concentrated on rotavapor. The remaining oil was washed with diethylether (4x10 mL) until a white slurry formed. Thereafter the compound was recrystallized from hot acetone. The crystals were filtered to a filter paper and let to dry in room temperature for one day.

Experiment 2 **a2**. Dimethyloctylamine (2.84 g, 18.0 mmol) and benzyl chloride (2.30 g, 1 eq) in a pressure tube with 3.0 mL methanol. Reaction was run at 100°C for 15 days without supervision before workup. The crude product was concentrated in the rotavapor and washed once with 5 mL hexane. The product was added 5 mL diethylether and concentrated on rotavapor to remove methanol. This was repeated 4 times. The crude viscous oil was dissolved in minimal amounts of hot acetone and added ethyl acetate until saturation. The solution was set to crystallize at -24°C. Crystals were filtered and transferred to a beaker. The beaker was added diethylether while and set on ultrasonic bath while crushing the crystals with a glass rod. The diethylether was decanted. Remaining powder was transferred to a vial and dried on high vacuum (7 mbar, 60°C) for 16 hours.

Experiment 3 **a3**. Dimethyldecylamine (5.13 g, 32.6 mmol) was mixed with benzyl chloride (4.43 g, 1.1 eq) in a pressure tube and added 3 mL methanol. Reaction was run at 80°C for 190 hours. Crude product was washed 4 times with 5-10 mL diethylether and 4 times with 5-10 mL hexane. Emulsion was let to settle after each wash followed by decanting. Supernatant was decanted after each cycle. Product was dissolved and recrystallized from ethyl acetate by volume reduction in a dish at room temperature. A higher surface

area produced crystals more rapidly than a lower surface area. Crystals were washed on ultrasound bath with diethylether and put on high vacuum (7 mbar, 25°C) for 18 hours.

Experiment 4 **a3(d7)**. A deuterated version of **a3** was synthesized and purified using the same method as described in experiment 3. Dimethyldecylamine (1.384 g, 8.800 mmol) and benzyl chloride-d7 (0.991 g, 0.8 eq) were mixed in a pressure tube with 2.0 mL methanol. Reaction was run at 100°C for 45 hours. The drying was done for 2 days.

Experiment 5 **b2**. Dimethyloctylamine (2.63 g, 16.7 mmol) and 1-chlorooctane (3.12 g, 1.25 eq) was mixed with 3 mL methanol in a pressure tube. Reaction was run at 70°C for 140 hours. The crude product was concentrated in excess diethylether in rotavapour 4 times to remove methanol. Product was crystallized by dissolving in minimal amounts of diethylether and adding hot hexane until saturation. Crystals were filtered and washed with hexane. Then product was dried for 18 hours at high vacuum (7 mbar, 50 °C).

Experiment 6 **b3**. Dimethyldecylamine (2.61 g, 14.1 mmol) and 1-chlorodecane (3.11 g, 1.25 eq) was mixed with 20 mL methanol in a pressure tube. Reaction was run at 70 °C for 144 hours. Crude product concentrated on rotavapor and recrystallized from diethylether:hexane (2:7) and ethyl acetate. Crystals formed in room temperature, were filtered and transferred to a vial. Product was dried on high vacuum (7 mbar, 50 °C).

Experiment 7 **b4**. Dimethyldodecylamine (2.61 g, 12.2 mmol) and 1-chlorododecane (3.12 g, 1.2 eq) was mixed in 20 mL acetone in a pressure tube. Reaction was run at 70 °C for 168 hours. Crude product was concentrated until crude (yellow) crystals formed. Crystals were dissolved and recrystallized in minimal volume of hot diethylether. The recrystallization process took approximately one week (but could be less). Crystals were filtered and transferred to a vial followed by drying on high vacuum (7 mbar, 50°C).

Experiment 8 **b5**. Dimethyltetradecylamine (2.50 g, 10.7 mmol) and 1-chlorotetradecane (2.61 g, 1 eq) were mixed with 3 mL in a pressure tube. Reaction was run at 100°C for 1 month. Crude product was concentrated in rotavapor until white solid formed. This solid was washed with ice cold hexane (-20°C). The solid was recrystallized from EtOAc and dried in a vacuum dessicator (7 mbar, 25°C) for 2 hours.

Experiment 9 **b6**. Dimethylhexadecylamine (2.59 g, 9.61 mmol) and 1-chlorohexadecane (3.18 g, 1.27 eq) were mixed with 10 mL acetone in a pressure tube. Reaction was run for 78 hours at 70°C. When it cooled down, it precipitated immediately. The crude product was cooled down, filtered and washed with diethylether 3 times and hexane one time. Product was dried in high vacuum (7 mbar, 50°C) for a few hours.

Experiment 10 **b7**. Dimethyloctadecylamine (3.94 g, 13.2 mmol) and 1-chloroodcadecane (3.80 g, 1 eq) were mixed with 10 mL methanol in a pressure tube. Reaction was run for 7 days at 95°C. Crude product was concentrated on rotavapor and recrystallized in ethanol. The solid was filtered and transfered to a vial after drying for 1 hour in room temperature.

Experiment 11 **b8**. Decyldimethylamine (5.47 g, 29.5 mmol) and 1-chlorooctane (5.73 g, 1.30 eq) were mixed in 50 mL methanol in a pressure tube. The reaction was run at 70°C for 8 days before quenching. The crude product was concentrated on rotavapor and washed with hexane and pentane to remove methanol. Diethylether dissolved the product, and could not be used for this step. The product was dried on high vacuum (7 mbar, 50°C) for a day.

2.2 Analysis

Analysis were performed using HPLC-MS and NMR. The LC-MS system was used for determination of purities, retention times and ion masses of the compounds. NMR for characterization of molecule structure and purity determination.

2.2.1 HPLC-MS

AgilentTechnologies 1290 infinity HPLC system and AgilentTechnologies 6130 Quadropole LC/MS was used for the RP-LC analysis. The column used for analysis was Restek Raptor Biphenyl Column (90Å, 2.7 μm, 2.1x100 mm) while the mobile phase consisted of:

(A) 2 mM ammonium formate in H_2O, 0.1 v/v% formic acid.

(B) 2 mM ammonium formate in MeOH, 0.1 v/v% formic acid

The gradient HPLC analysis followed the specifications in table 4. In the MS, electron spray ionization (ESI, 150 V) was used as a fragmentor and quadropole as a mass analyser.

Table 4: Method used in HPLC analysis

Time [min]	A [%]	B [%]	Flow [mL/min]	Max. Pressure Limit [bar]
0.00	95.00	5.00	0.55	600.00
0.10	95.00	5.00	-	-
9.00	0.00	100.00	-	-
10.00	0.00	100.00	-	-
10.01	95.00	5.00	-	-

Approximately 1 mg of each product was added to their own respective vial, and dissolved in 0.7 mL of mobile phase B.

2.2.2 NMR

A Bruker 400 MHz Avance III HD was used for NMR analysis. Products were dissolved in various solvents: MeOD, DMSO-d6 and $CDCl_3$. Data processing was performed in TopSpin version 4.1.4. The NMR methods used were ^{1}H-NMR, ^{13}C-NMR and COSY. All final products were tested in this manner. Microsoft Excel was used to calculate the product purities from the ^{1}H-NMR spectra in terms of mass and moles using equation 4.

3 Results

Table 5 displays the appendices for each experiment (experiment 1-11). HPLC was not conducted for experiment 4: **a3(d7)**. In the HPLC appendices (B), data for column retention, MS intensity and MS fractions are included for each experiment. For the NMR appendices (A), spectrums of ^{1}H-NMR, ^{13}C-NMR and COSY are included for each experiment except experiment 11 where only ^{1}H-NMR is shown.

Table 5: List of experiments with appendices for HPLC and NMR.

Experiment	Code	Appendix (HPLC)	Appendix (NMR)
1	a1	B-1	A-1
2	a2	B-2	A-2
3	a3	B-3	A-3
4	a3(d7)	-	A-4
5	b2	B-4	A-5
6	b3	B-5	A-6
7	b4	B-6	A-7
8	b5	B-7	A-8
9	b6	B-8	A-9
10	b7	B-9	A-10
11	b8	B-10	A-11

3.1 Yields and Purities

Final products were tested on HPLC and NMR. Table 6 displays the summarized results for yields and purities. In this report, error margins were not considered. Of many experiments performed, experiment 4 obtained the highest yield of 95.5% after weighting. This was also the last product to be synthesized due to the cost of deuterated benzyl chloride. Data for NMR was gathered from appendix A. Experiment

Table 6: List of compounds made in this project with corresponding codes and experiments. Code a1 corresponds to experiment 1 etc. Yields and purities in terms of NMR (mass and moles) and HPLC (LC and MS) are also listed.

Exp.	Compound	Code	Yield%	P% (NMR: mass)	P% (NMR: moles)	P (LC)	P (MS)
1	BAC-6	a1	56.5	99.80%	99.00%	99.9%	97.9%
2	BAC-8	a2	82	99.45%	97.56%	99.9%	70-80%
3	BAC-10	a3	81.4	99.99%	99.96%		
4	BAC-10-(d7)	a3(d7)	95.5	99.79%	99.26%		
5	DDAC-C8	b2	11.1	99.96%	99.86%		
6	DDAC-C10	b3	15.5	99.99%	99.96%	71.3%	94.6%
7	DDAC-C12	b4	11	99.99%	99.96%	75.2%	87.5%
8	DDAC-C14	b5	5.9	99.88%	98.87%		
8.1			75.3	99.88%	98.90%	56.6%	86.2%
9	DDAC-C16	b6	10.1	95.63%	91.74%	53.5%	88.5%
10	DDAC-C18	b7	35.5	56.82%	26.55%	26.5%	52.1%
11	BTC-818	b8	-	97.20%	83.85%	62.0%	81.8%

3.2 HPLC results

Table 7 shows the retention times (in minutes) and ion mass of the cation [m/z] for all compounds synthesized and purified. Results show that polarity decreases with increasing chain length. The MS spectrum measured the mass of the ions minus the chloride.

Table 7: The table shows an overview of retention times and ion masses measured using HPLC-MS. The data is gathered from appendix B.

Code	Compound	t_R [min]	M+ [m/z]
a1	BAC-6	4.87	220.2
a2	BAC-8	5.56	248.3
a3	BAC-10	6.36	276.3
a3(d7)	BAC-10-d7	-	-
b2	DDAC-8	6.57	270.3
b8	BTC-818	7.15	298.4
b3	DDAC-10	7.48	326.7
b4	DDAC-12	8.04	382.4
b5	DDAC-14	8.50	438.5
b6	DDAC-16	8.80	495.5
b7	DDAC-18	9.03	551.6

3.3 NMR spectral data

Products (**b4-b7**) were partially soluble/insoluble in DMSO, but soluble in MeOD and $CDCl_3$. All products were soluble in MeOD, but the residual peak for MeOD (δ 3.31) overlapped with some of the product. Appendix A shows all the NMR diagrams (^{1}H, ^{13}C and COSY) for experiments shown in table 5 with explanations. Impurities were identified using an NMR table [22] and quantified using equation 4. The results from the NMR purity analysis were summarized in table 6.

Decyldimethylamine (**a3,** S_m amine). ^1H-NMR (DMSO-d6): δ 0.86 (t, J=6.60 Hz. 3H, CH_3CH_2) 1.24 (bs, 14H, $(CH_2)_7$) 1.37 (p, J=6.97, 2H, (CH_2CH_3N) 2.09 (s, 6H, $(CH_3)_2N$) 2.15 (t, J=7.37 Hz, CH_3N).

Benzylhexyldimethylammonium chloride (**a1**). ^1H-NMR (MeOD): δ 0.94 (t, J=6.88 Hz, 3H, CH_3CH_2 1.40 (bs, 6H, $(CH_2)_3$); 1.89 (p, J=3.90, 2H, $CH_2CH_2N^+$); 3.03 (s, 6H, $(CH_3)_2N^+$); 3.30 (m, 2H, $(CH_2CH_3N^+$); 4.53 (s, 2H, $PhCH_2N^+$); 7.56 (m, 5H, Ph).

Benzyldimethyloctylammonium chloride (**a2**). ^1H-NMR (DMSO-d6): δ 0.87 (t, 3H, CH_3CH_2); 1.27 (bs, 10H, $(CH_2)_5$); 1.79 (p, 2H, $CH_2CH_2N^+$); 3.00 (s, 6H, $(CH_3)_2N^+$); 3.31 (p, J=4.25 Hz, 2H, $(CH_2CH_3N^+$); 4.65 (s, 2H, $PhCH_2N^+$); 7.53 (m, 5H, Ph).

Benzyldecyldimethylammonium chloride (**a3**). ^1H-NMR (MeOD): δ 0.84 (t, 3H, CH_3CH_2); 1.24 (bs, 14H, $(CH_2)_7$); 1.78 (p, 2H, $CH_2CH_2N^+$); 3.03 (s, 6H, $(CH_3)_2N^+$); 3.36 (p, J=4.25 Hz, 2H, $(CH_2N^+$); 4.72 (s, 2H, $PhCH_2N^+$); 7.56 (m, 5H, Ph).

Benzyl(d7)decyldimethylammonium chloride (**a3-(d7)**). ^1H-NMR (DMSO-d6): δ 0.87 (t, 3H, CH_3CH_2); 1.27 (bs, 14H, $(CH_2)_7$); 1.78 (p, 2H, $CH_2CH_2N^+$); 2.96 (s, 6H, $(CH_3)_2N^+$); 3.26 (p, J=4.25 Hz, 2H, $(CH_2N^+$).

Dioctyldimethylammonium chloride (**b2**). ^1H-NMR (DMSO-d6): δ 0.87 (t, 6H, CH_3CH_2); 1.27 (m, 20H, $(CH_2)_5$; 1.63 (p, 4H, $CH_2CH_2N^+$); 3.02 (s, 6H, $(CH_3)_2N^+$); 3.26 (m, 4H, CH_2N^+).

Didecyldimethylammonium chloride (**b3**). ^1H-NMR (DMSO-d6): δ 0.86 (t, 6H, CH_3); 1.26 (bs, 28H, $(CH_2)_7$; 1.63 (p, 4H, $CH_2CH_2N^+$); 2.98 (s, 6H, $(CH_3)_2N^+$); 3.22 (m, 4H, CH_2N^+).

Didodecyldimethylammonium chloride (**b4**). ^1H-NMR ($CDCl_3$): δ 0.88 (t, J=6.73 Hz, 6H, CH_2CH_3); 1.26 (bs, 36H, $(CH_2)_9$; 1.69 (p, 4H, $CH_2CH_2N^+$); 2.98 (s,6H, $(CH_3)_2N^+$); 3.22 (m, 4H, CH_2N^+).

Dimethylditetradecylammonium chloride (**b5**). ^1H-NMR (DMSO-d6): δ 0.86 (t, 6H, CH_3); 1.26 (bs, 44H, $(CH_2)_{11}$; 1.63 (p, 4H, $CH_2CH_2N^+$); 3.00 (s,6H, $(CH_3)_2N^+$); 3.24 (m, 4H, CH_2N^+).

Dimethyldihexadecylammonium chloride (**b6**). ^1H-NMR (MeOD): δ 0.92 (t, 6H, CH_3); 1.31 (bs, 52H, $(CH_2)_{13}$); 1.77 (p, 4H, $CH_2CH_2N^+$); 3.08 (s,6H, $(CH_3)_2N^+$); 3.30 (m, 4H, CH_2N^+).

Dimethyldioctadecylammonium chloride (**b7**). ^1H-NMR ($CDCl_3$): δ 0.88 (t, 6H, CH_3); 1.26 (bs, 60H, $(CH_2)_{15}$); 1.68 (p, 4H, $CH_2CH_2N^+$); 3.42 (s,6H, $(CH_3)_2N^+$); 3.49 (m, 4H, CH_2N^+).

Decyldimethyloctylammonium chloride (**b8**). ^1H-NMR (MeOD): δ 0.91 (t, 6H, CH_3CH_2); 1.32 (m, 24H, $(CH_2)_7$); 1.74 (p, 4H, $CH_2CH_2N^+$); 3.06 (s, 6H, $(CH_3)_2N^+$); 3.29 (p, Hz, 4H, $(CH_2N^+$);

4 Discussion

4.1 Reaction conditions, workup and purification

a1, Experiment 1. This experiment was successful despite two different reaction conditions being blended together. Both ethanol and acetonitrile are solvents that can work well for this synthesis. The reaction ran unsupervised for 11 days, making it difficult to discern whether the conditions were efficient or not. The initial reactant concentrations were 0.24 and 0.39 mol/L, which means good yield can be obtained with lower concentrations. It is possible that it still did not react fully. The yield was only 56.5%, probably due to the fact that the recrystallization in acetone was only conducted once with a large volume of acetone (approx 300 mL). With repeated recrystallization in hot acetone, the yield could be improved considerably, but this would require a lot of solvent. Acetone also yielded crystals at over 98% (NMR) purity, meaning it works well as a recrystallization agent. If this experiment is to be conducted again, methanol would be used at 100°C for at most 3 days. Acetone would be used as a crystallization agent, and crystallization would be repeated 3 times.

a2, Experiment 2. This experiment was quite successful both in terms of yield and purity. The yield of 81.95% was probably so high partially because the reaction ran unsupervised for 15 days so that most of the starting material could react. Also, very little of the product was lost in the form of an emulsion because the washing was only conducted once with 5 mL hexane. The product had a low estimated solubility in hexane, while the amine had a high estimated solubility. Some product was however lost in the rotavapor, meaning a potentially higher yield could be achieved. The recrystallization step in minimal amounts of hot acetone/ethyl acetate gave purity at over 98% (NMR). By putting the saturated solution in the freezer at -24°C, the crystallization rate increased, but a risk of this method was crystallizing the impurities as well.

This, however did not prove to be an issue, due to the product already being quite pure from the workup and washing phase.

a3, Experiment 3. This experiment was quite successful in terms of both yield and purity. The yield of 87.45% could be because the reaction ran unsupervised for 6 days, meaning a theoretically high conversion rate from starting material to product. Despite being washed considerably more than **a2** in experiment 2, the yield was superior. This indicated that the emulsions that BACs produce with ether and/or hexane are so diluted that product loss from washing/decanting could be neglected. Since both **a1** and **a2** were both more polar than **a3** according to table 7, their solubilities in hexane and diethylether would be considerably lower than for **a3**. Also, the estimated solubilities in room temperature of both starting materials (amine and alkyl chloride) in diethylether and hexane were high. This means that diethylether and hexane are both great washing solvents for removal of carrier solvent (methanol) and starting materials from **a3**. This would also apply to **a1** and **a2**.
The purity above 98% was probably due to the successful workup and washing phase. It was attempted several ways to crystallize this product from various solvent systems, but the product "oiled out" instead. This could be explained by the low melting point 34-37.5°C compared to **a1** (122.0-123.5°C) and **a2** (53.0-56.0°C). These melting points were for the bromide salt of **a3**, possibly deviating from the melting point of the chloride. The only working method of crystallization found was to dissolve the product in hot ethyl acetate and let it rest in open air (with cover) until the solvent evaporated. This method of crystallization was prone to trapping impurities in the crystals. Such impurities were not observed on NMR. Crushing and washing impure crystals with diethylether most likely increased the purity further.

a3(d7), Experiment 4. This experiment was very successful both in terms of yield and purity. The yield of 95.5% is significantly higher than in experiment 3, **a3** despite the reaction only running for 45 hours in 100°C. The start concentration of staring materials was 1.6 mol/L. This means that the reactions for **a1-a3** could theoretically be run for less than 2 days under these conditions. This project does not provide the kinetic data to say exactly how long this process should take ideally, but since very little product was lost and the temperature does not seem to decompose the product, it is therefore recommended to use 100°C for the synthesis. This compound, similarly to **a3**, melted into an oil at 7 mbar in room temperature. After taking off vacuum, it crystallized from the oil. This suggested that oils could be pure.

b2, Experiment 5. This experiment was quite successful in terms of purity, but the yield was poor at 11.14%. The poor yield was due to several factors. For one, some product was lost in the rotavapor. This could be avoided by concentrating down more gradually instead of using high vacuum. The reaction ran for 6 with an amine start concentration of 0.5 mol/L. After the reaction finished, there were two phases, bottom phase being crude product and top being methanol (with some dissolved product). Since there was no existing kinetic data on the DDACs, it was difficult to estimate the conversion rate from starting material to product. The biggest loss was probably when the crude product was washed repeatedly with hexane. This produced an emulsion that was decanted prematurely. Since the product was quite soluble in EtOEt, its' solubility in hexane could not be neglected. However, a crystallization using a small volume diethyl ether with hexane produced products with over 98% purity. It is possible that some product was left in the mother liquor after the first crystallization.

b3, Experiment 6 was successful in terms of purity, but the yield was only 15.5%. This reaction was run with the same conditions as experiment 5. Likewise, two phases formed. This may be because the product has limited solubility in methanol. In this experiment, the major source of product loss was due to the washing in hexane and diethylether (which dissolved the product). This was a mistake. Instead, the solution should have been concentrated and crystallized directly using diethylether:hexane or ethyl acetate. If done properly, this could both increase yield and purity.

b4, Experiment 7. This experiment was quite successful in terms of purity (over 98% NMR), but the yield was poor at 11.0%. In contrary to the experiments 5 and 6, this reaction was conducted with acetone for 1 week. The start concentration of the amine was 0.45 mol/L. It was crystallized only once in diethylether, possibly leaving much of the product in the mother liquor. This crystallization step took several days, but yielded a very pure product. Excessive washing with diethylether and hexane caused product loss.

b5, Experiment 8. This experiment yielded over 75% and had a good purity above 98% (NMR). This was this high despite losing a lot of product in filtration by accident. Since ice cold hexane was used for washing, it was thought that the product did not dissolve/suspend much compared to previous experiments 6 and 7. The product most likely had lower solubility in ice cold hexane compared to room temperature. Experiment 8 ran at 100°C in methanol for 20 days (1.2 mol/L start concentration). The reaction time could be the reason that the conversion rate was so high. The possibility of DDACs' synthesis being a slow process is therefore not neglible. A high activation energy (not measured) might have also been a cause of this observation. For comparison, experiment 8.1 ran at 70°C in acetone for a week. The start concentration was also 0.4 mol/L. The yield in experiment 8.1 was only 5.8%. The purification of experiment 8.1 was conducted in the same manner as in experiment 7. This mean that the product loss lies in the reaction time, reactant concentration, temperature or purification stage. By increasing all of these parameters, high yield would be obtained. Increasing the temperature could decrease the reaction time, but too much temperature increase could also break down the starting materials. If the reactions could be run again, the kinetics would be studied in order to find how long (ideally) the reaction should be run for at least a 90% conversion from starting material to product.

b6, Experiment 9. This experiment was unsuccessful in both yield (10.1%) and purity 91-95% NMR). There was most likely some residue starting material in the product due to poor washing. Crushing the crystals might have been a necessary step in order to extract the starting material and other impurities from the product. The reaction ran only for only 3 days at 70°C in acetone. These conditions are perhaps not the most favourable, given the yield. However, direct recrystallization in acetone seemed like a good solution for this product since it dissolved at high temperatures, but precipitated in low temperatures. A big mistake was not performing the recrystallization step more than once. Additionally, since the washing was performed with diethylether, some product might have been dissolved, leaving a bad yield. If this experiment was to be rerun, the reaction would be run at a higher temperature with either acetone and methanol for approximately one week. Then the product would be recrystallized from acetone and washed in ice cold hexane like in experiment 8.

b7, Experiment 10. This experiment was unsuccessful in terms of both yield and purity. The low yield at 35.5% (impure mass) was due to several factors such as losing product in rotavapor and poor reaction and recrystallization condititions. The most prominent impurities were the starting material itself and ethanol.

By letting the mother liquor rest in room temperature instead of in the fridge, this crystallization step could have been more selective. Additionally, it was thought that the volume of ethanol used for recrystallization was too small, as the solid was bulk instead of crystalline. This was attempted, and it resulted in spherical crystals. However, these were still containing impurity (appendix A-10). After 1 week in MeOH at 80°C, conversion from starting material to product was not ideal. The purity on NMR was only 26.6% in terms of moles and 56.8% in terms of mass. Most of the impurity belonged to the starting material at 33-36% (NMR).

b8, Experiment 11. This experiment was not successful in terms of purity. Although some crystals could form from crystallization in acetone and hexane, they melted in room temperature as semisolids. The semisolid behavious could be because the mixture was impure. This product was quite similar to **b2** or **b3** by the looks of the molecular structure, suggesting a similar workup and crystallization could work. Attempting crystallization in diethylether and hexane, however, caused the product to oil out instead of producing crystals. Several steps of washing with hexane was attempted in order to remove starting material and impurities. This did seem to remove starting material according to NMR, but instead there were traces of unknown impurities that made the exact purity hard to determine. It is possible that high heat on the hot plate during the crystallization process decomposed some of the product. If this experiment was to be repeated, the same reaction conditions would be followed, except by attempting to recrystallize from ethyl acetate by volume reduction.

5 Conclusion

Eleven Quaternary Ammonium Compounds (QUATS) were synthesized. More specifically, three benzylalkyldimethhthylammonium chlorides (BACs) and eight dialkyldimethylammonium chlorides (DDACs). Methanol and acetone worked for most reactions due to universal solubility. Running the reactions at 100°C proved to make most reactions run well without product decomposing. However, the DDACs had poor yields for reasons undetermined. The reactions were run in a closed pressure tube with suitable solvents on medium to high heat (70-140°C).

It was found that BACs produced the highest yield and best purities due to the short reaction times and simple workup and purification. Removal of reaction solvent and starting materials was done by repeated fractional evaporation with diethylether or hexane. This step made crystallization simpler. Crystallization was performed by using acetone, ethyl acetate or a mixture of both. The purities obtained this way exceeded 98% by a good margin and the yields were over 50%, up to 95%.

DDACs generally resulted in poorer yields than the BACs, ranging between 5% and 75%. The cause of this could have been a combination of unfavourable reaction conditions and product loss in the washing/purification process. It was also observed that leaving a reaction running for over 20 days produced a very high yield (experiment 8), suggesting that DDACs react slower than the BACs. Purification through washing was slightly more cumbersome, due to products **b2-b8** being slightly soluble in diethylether and hexane. Therefore, a higher yield could be acieved by direct recrystallization with a suitable solvent system. The solvent system used was usually a mixture between diethylether and hexane. An exception was **b7**, which dissolved in hexane, but crystallized well in ethanol. The purities of the compounds, however, were more

than adequate. Most of the compounds had a purity above 98% (NMR).

Suggestion for further studies: DDAC kinetic studies using NMR with internal standards.

Appendices

1. Appendix A - NMR spectra
2. Appendix B - HPLC-MS data
3. Appendix C - Kinetic calculations
4. Appendix D - Starting materials and signal words

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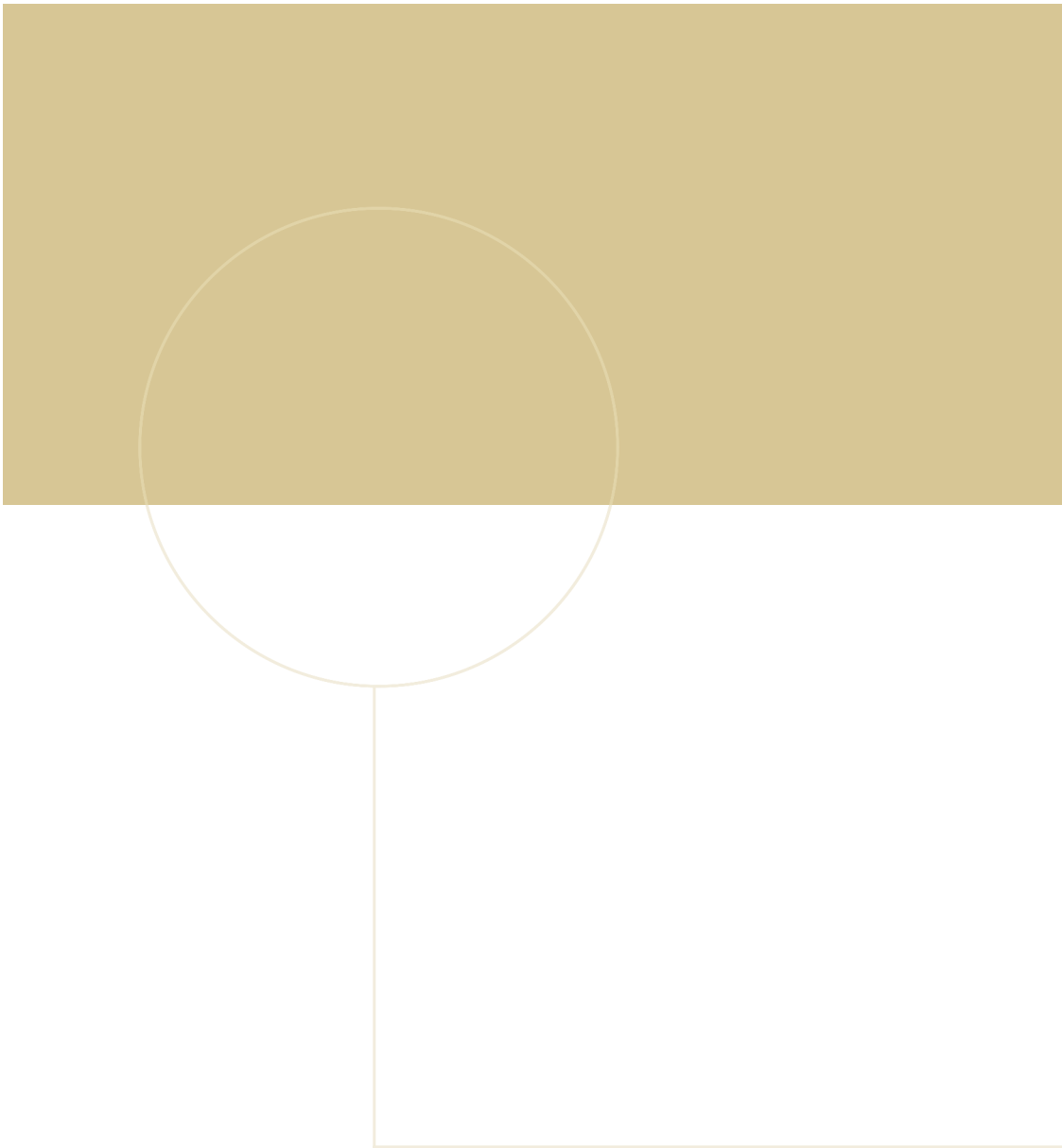

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