EVALUATION OF MANUFACTURING PROCESSES FOR THE PRODUCTION OF ATRAZINE

by

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Promoter: Prof. B. Zeelie

Look thoroughly inside yourself; there is [redacted] rength that will always [redacted] should you seek it.

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- Mom, Dad and Selwyn, for endless love and motivation to strive for a dream.

SUMMARY

This report describes the results of investigations carried out with the view to find an alternative for MIBK as solvent for the production of atrazine as currently practised by Dow AgroSciences in South Africa. The main motivating factors for the said investigation was:

- to increase the yield of atrazine produced,
- to reduce the amount of organics, consisting essentially of reaction solvent containing dissolved product, in the aqueous process effluent, and
- to improve the properties of the solid (crystalline) product to enable easier product formulation.

Synthetic reactions carried out in the absence of organic solvent, *i.e.* in essentially a 10% NaCl solution containing a surfactant, proved rather disappointing. Low yields of atrazine were obtained together with relatively large amounts of by-products such as propazine and simazine, irrespective of the nature of the surfactant. The reason for the low yield of atrazine and high yields of by-products were established in competing substitution reactions. In these reactions, IPA was reacted with an equimolar mixture of cyanuric chloride and mono-i (first reaction intermediate) in both aqueous medium and in toluene as reaction solvent. The results of these experiments indicated that in aqueous medium IPA reacts faster with mono-i than cyanuric chloride to give propazine as by-product. In toluene, however, the preferred reaction is with cyanuric chloride to give more mono-i as product.

Toluene was investigated as an alternative organic solvent to MIBK in view of its desirable properties such as low solubility in water and ease of recovery and recycling. The synthesis of atrazine was optimised in terms of addition sequence and rates of amine reagents and base (HCl acceptor), both by means of bench-scale reactions and reaction calorimetry. Reaction energy profiles indicated that both the reaction of secondary amine/NaOH and primary amine/NaOH were virtually instantaneous. This implies that the reaction can be performed under feed control conditions. Of particular importance in ensuring high yields of high purity product was accurate temperature control (since both reaction steps are highly exothermic) and mixing. The latter was important in view of the rapid reaction of amine/NaOH with cyanuric chloride, as well as the possible reaction of mono-i, the first reaction intermediate, with IPA in cases of local excesses of reagent.

Under optimum conditions, a yield of atrazine > 97% could be achieved where the resultant product was well within stipulated product specifications. In view of the results obtained, the following recommendations regarding the synthesis of atrazine in toluene as reaction solvent can be made:

- Use a reagent addition sequence that staggers the addition of amine and NaOH in such a manner that amine is added first for a short while, followed by the simultaneous addition of amine and NaOH, and ending with NaOH.

- Use two reaction vessels in series, one for the IPA addition reaction and one for the MEA addition reaction. In this manner the reaction can be run on a continuous basis since no lag time between amine additions is required. Also, smaller reactors may be used whilst maintaining high production rates. Smaller reactors will improve both temperature control and mixing of reagents.

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CHAPTER 1

INTRODUCTION

1.1 Herbicides and their role in the agricultural industry

Herbicides, together with insecticides, fungicides and nematicides, form part of a collective group referred to as pesticides. Pesticides have faced some severe criticism for many years, mainly for having several undesirable side effects. However, this group of chemicals has been a major force in allowing the agricultural industry to "keep-pace" with the growing hunger problem we face today.

If it were not for pesticides, our present production rate of food crops would drop by 30% and livestock by 25%. Society would then be faced with a 50 to 75% increase in food prices. Pesticides have also allowed farmers to conserve wild land because now they only need approximately half of the area they used previously in order to have the same crop yield.

There are 4 distinguishing factors in the pesticide industry:

- The multiplicity of the chemicals used.
- A high price range.
- A rapid obsolescence for the chemicals employed.
- A high degree of government regulation.

In the United States, all pesticides used today must receive registrations from the EPA (Environmental Protection Agency). This would involve detailed toxicological and metabolic studies of both the active ingredient and any other impurities. The cost of the development of a new herbicide is estimated at close on $50 million (as opposed to $3 million in the 1950's). For every effective pesticide, over 22 000 compounds are screened.[1-3]

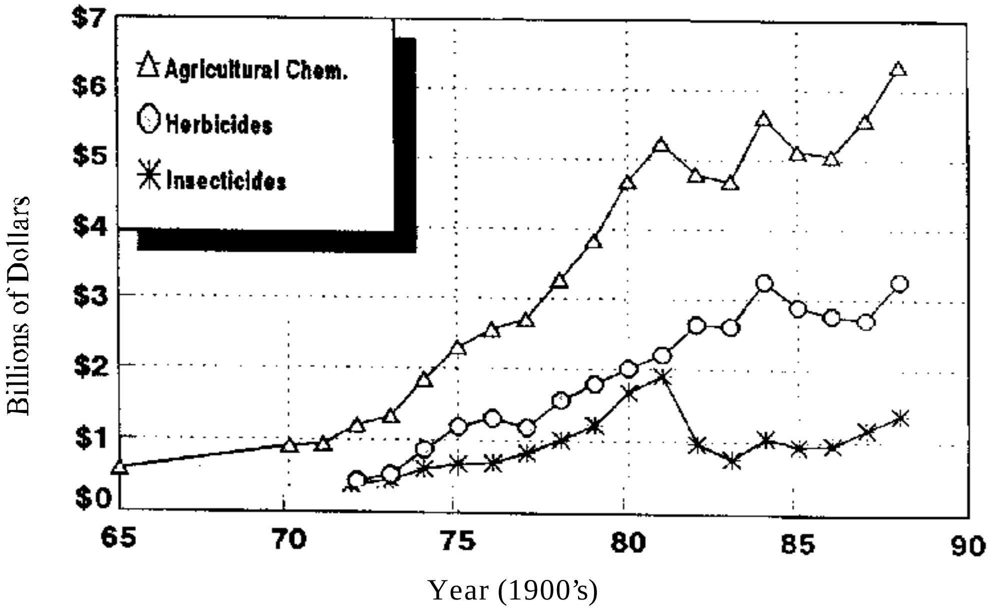


Figure 1.1 **U.S shipments of pesticides** [3]

Figure 1.1 represents the estimated size of the pesticide industry in terms of its monetary value (in billions of dollars) in the United States alone. The shipments for the two most important subsectors, herbicides and insecticides, are also shown. During the 1970's, the pesticide industry had a dramatic rise from $1 billion to $5 billion. The apparent dip in the growth rate in the 1980's can be attributed to the 1982 recession and the decreasing use of insecticides.

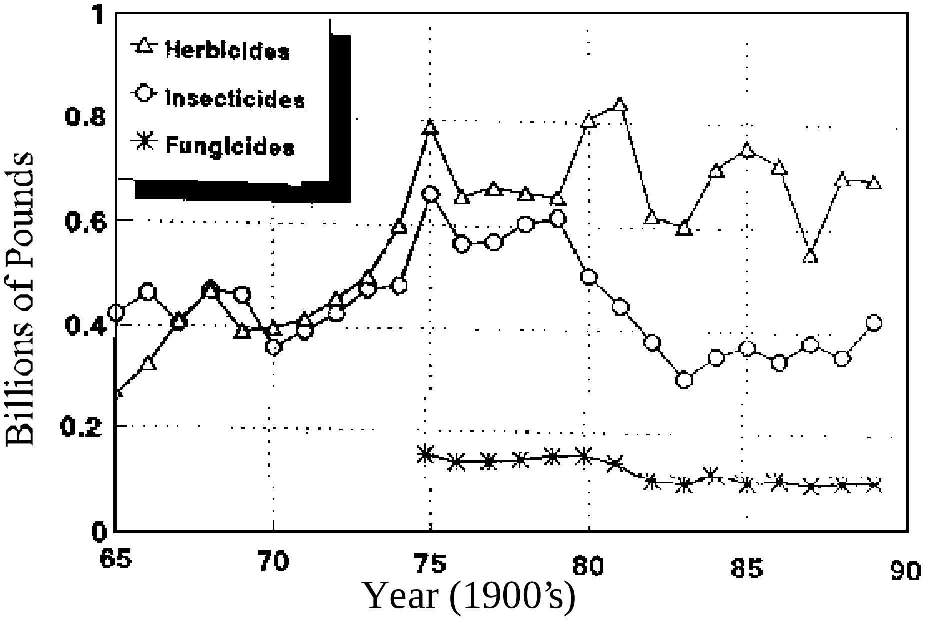


Figure 1.2 **Production of pesticides in the U.S.**[3]

Figure 1.2 shows the production of pesticides in billions of pounds. Over a billion pounds of total pesticides are made each year. Insecticides proved to be the largest branch during the 1950's, 1960's and 1970's; however, in the 1970's, herbicides surpassed them and have continued to show an increase since then. The total production of insecticides in 1989 was the same as in 1970, while herbicide use almost doubled in those two decades.

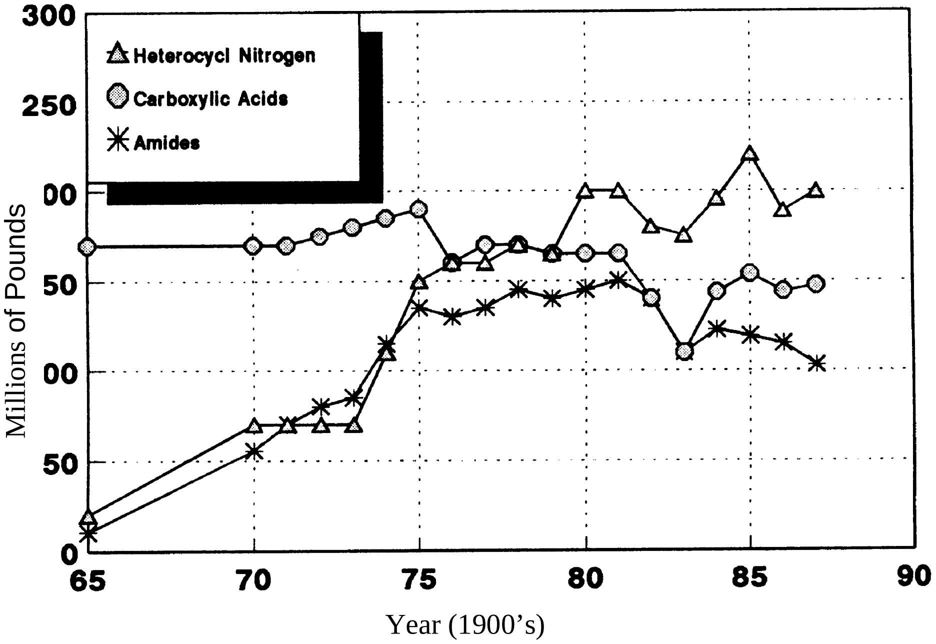


Figure 1.3 Production of herbicides in the U.S.[3]

Figure 1.3 shows an estimate of the present production percentages of different types of pesticides. These are categorized according to the types of pests they control.

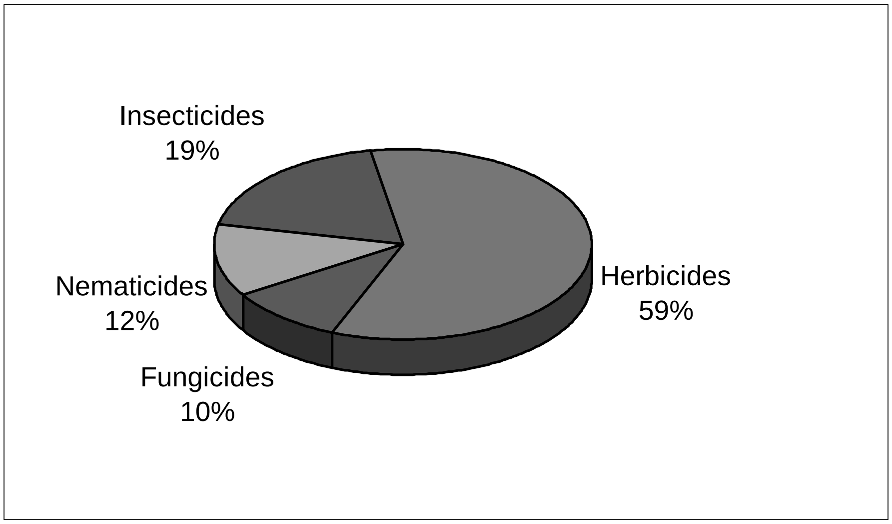


Figure 1.4 **Percentage use of various pesticides**[3]

Figure 1.4 illustrates the approximate percentage of pesticides used on various important agricultural crops.

The United States Department of Agriculture estimated that in the 1980's about 10% of the country's agricultural products would be lost because of weeds (close to $20 billion/yr). Almost 1500 species of weeds contribute to economic loss as mentioned earlier, the use of herbicides drastically increased in the 1970's and 1980's. The production of herbicides is currently leveling off at around 318 million kg/yr (worth over $3 billion/yr). In 1950 there were only 15 different herbicides, while today there are over 180.[3] The bulk of all herbicides produced today are mainly used on crops like corn, soyabeans, wheat and cotton.

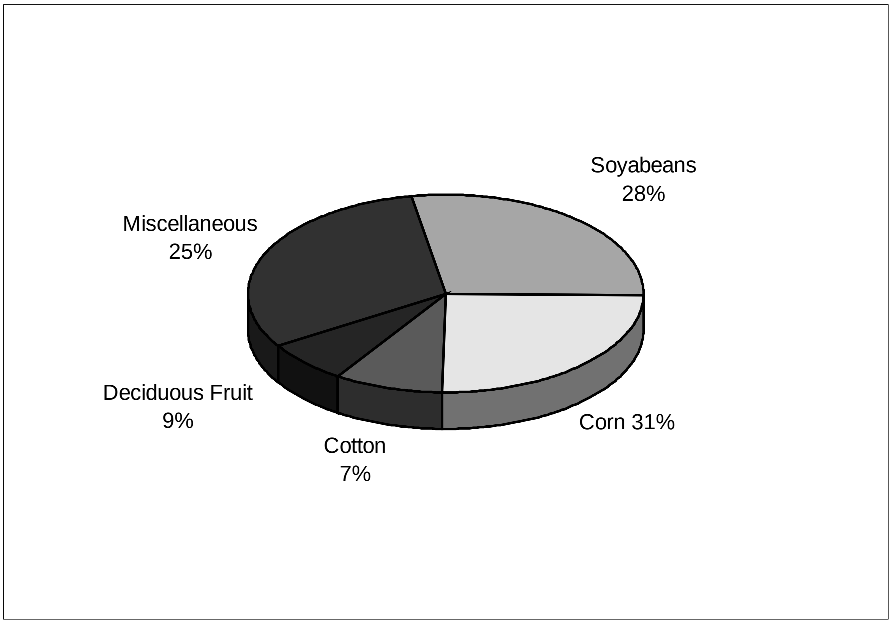


Figure 1.5 **Percentage use of pesticides on various crops**[3]

Figure 1.5 illustrates the production trend for the three most important types of herbicides. Heterocyclic nitrogen compounds replaced carboxylic acids, the first type of herbicide, in the 1970's. Amide herbicides fall in at a close third.

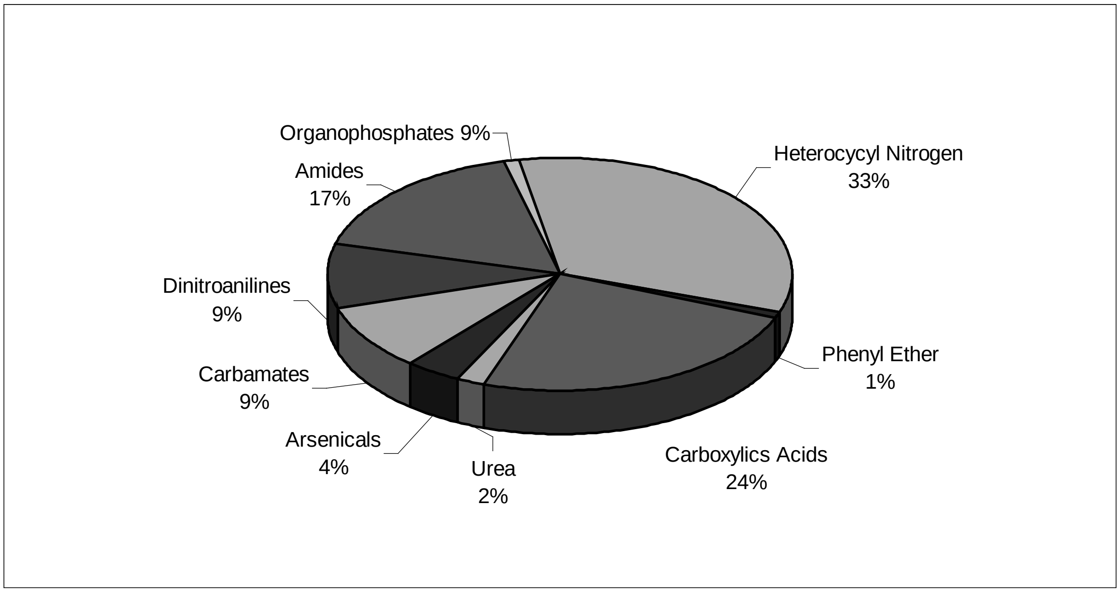


Figure 1.6 **Present production percentage of various herbicides**[3]

An estimate for the present percentage of production for herbicides is illustrated in Figure 1.6.

1.2 Heterocyclic nitrogen compounds (triazines)

Atrazine is a heterocyclic nitrogen herbicide, or an s-triazine compound. Triazine compounds, which consist of three nitrogens in the heterocyclic aromatic ring, are the most widely used herbicides today.

Atrazine is used especially on maize, pineapple and sugarcane crops, to name a few. It is synthesized by reacting cyanuric chloride successively with one equivalent of mono-isopropylamine and one equivalent of mono-ethylamine. Cyanuric chloride is made in one step from chlorine and hydrogen cyanide. This is illustrated in Figure 1.7, which also shows by means of a reaction scheme, how atrazine and simazine (a side product) are synthesized. Examples of other triazines are propazine, hydroxy-atrazine and hydroxy-simazine, these are discussed later.

Triazines will kill most types of plants except corn; this is thought to be due to the fact that the crop degrades the triazines before their toxic action can take effect.

Approximately 33.2 million kilograms of atrazine are consumed annually in the U.S. alone, this being from an estimated 142.6 million pounds of triazines in total.[3] In 1952, Ciba-Geigy started investigations with triazine derivatives, with the vision to use them as potential herbicides.[4,5] Atrazine was reported as a herbicide by H. Gysin and E. Knüsli.[6]

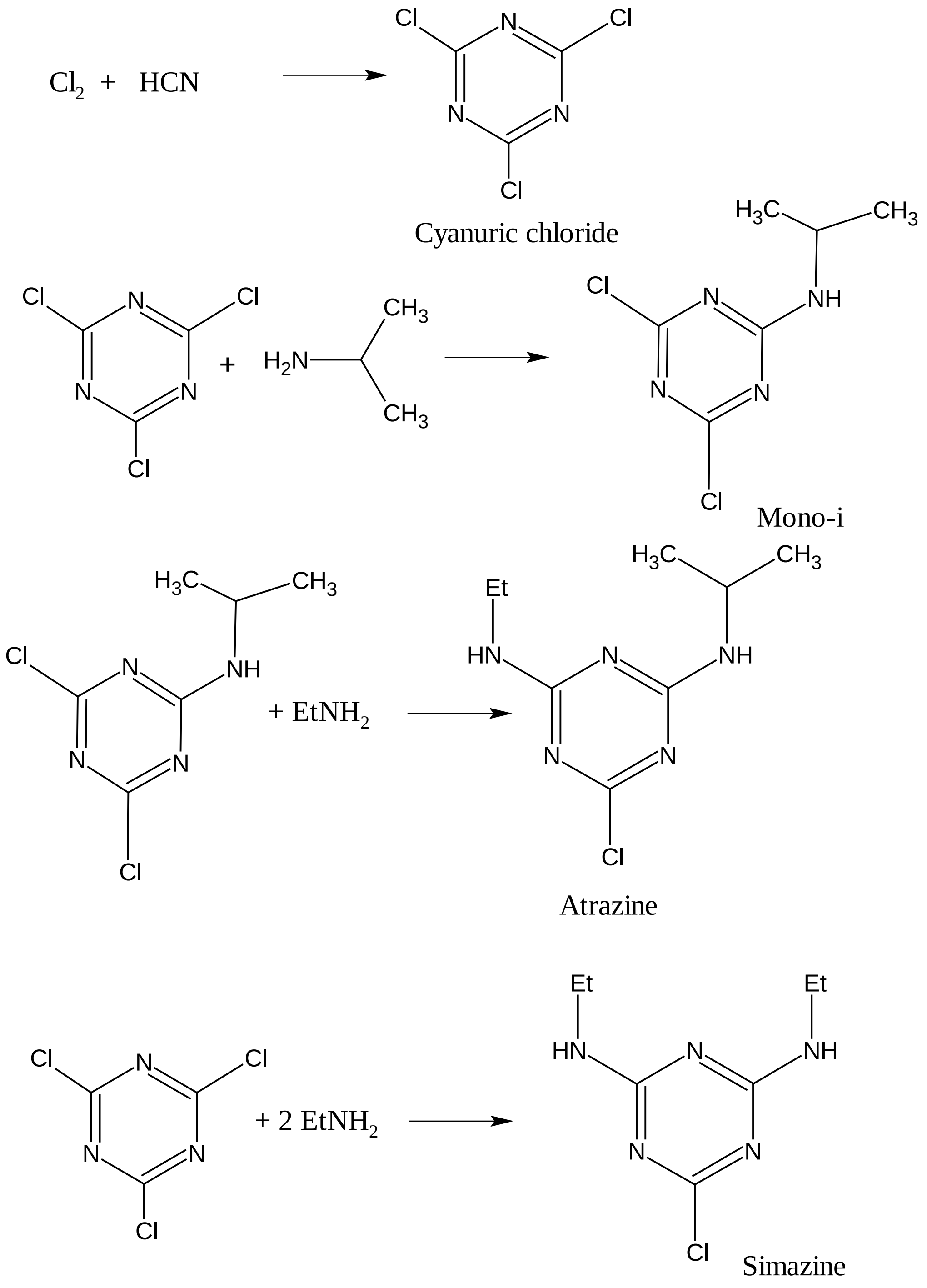


Figure 1.7 **Heterocyclic nitrogen herbicides. (triazines)** [3]

1.4.1 General information about s-triazines

Although triazine compounds control many different kinds of weeds, they have been found to be most effective on seedlings. Triazines are sold as granules or wettable powders, which are nonflammable and non-toxic to animals. Selectivity, or ability of the molecule to select which plant to attack or ignore, occurs when the molecule is transformed by resistant plants, most likely because of the removal of a chlorine atom from the ring. Another aspect in selective action is the fixation of the chemical in the upper levels of the soil, away from the absorbing regions of deeper-rooted plants.[7]

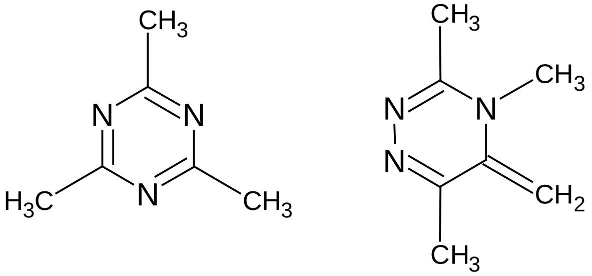
Triazines disappear from the soil by decomposition due to the action of microorganisms and the removal of crops or weeds. Photodecomposition may also occur. Atrazine and simazine, chlorinated s-triazines, are two of the most widely used triazines. The response of corn varies depending on the type of triazine used.[7]

Atrazine is slightly more soluble than simazine and will kill very small weeds by contact action; this is why it can be used post-emergence as well as pre-emergence if the application is made while the weeds are still very small. Atrazine is more effective than simazine under conditions of low rainfall because of its greater solubility.[8]

1.4.2 Chemical structure

s-Triazines are heterocyclic nitrogen derivatives, where the ring is composed of nitrogen and carbon atoms. Most triazine herbicides are symmetrical; by this it is meant that they have alternating carbon and nitrogen atoms in the ring. However, one exception is metribuzin, which is asymmetrical.

The water solubility of a series of triazines is markedly influenced by the nature of the substituent on the ring.[4]



Symmetrical triazine Asymmetrical triazine

Fig 1.8 **The symmetry of s-triazine rings** [4]

1.4.3 Metabolism of s-triazines in plants

The basic mode of s-triazine action centers on its ability to kill selected plants by destroying photosynthetic tissue. S-triazine herbicides act by inhibiting primary events in photosynthesis in the chloroplast by binding to the D-1 protein in photosynthetic electron transport. This binding stops photosynthesis. When these molecules bind to the D-1 proteins, they "steal" electrons from photosynthesis and form highly reactive free radicals; these unstable free radicals oxidize and destroy membranes, pigments etc., allowing chlorosis to follow. Chlorosis is the yellowing of leaf tips and then leaf margins; this is usually the first sign of atrazine injury on susceptible plants.[9]

In order for this inhibition to take place, light must be present and transpiration occurring, to move the chemical to foliage. Transpiration is the flow or movement of water through a plant, from the point of uptake from the soil by the roots, through the plant and out the leaves. Atrazine injury is increased with increasing amounts of sunlight and factors that increase transpiration rates in plants, such as increasing temperature, soil moisture, wind and decreased air humidity.[9]

Plants that are sensitive to atrazine do not metabolize or break down atrazine. Tolerant plants metabolize atrazine to hydroxy-atrazine and amino acid conjugates. Hydroxy-atrazine is then broken down further by dealkylation and hydrolysis.[10]

1.4.4 The process of photosynthesis

In order to appreciate how effective these herbicides are, it is important to understand a little of the chemistry involved when the process of photosynthesis takes place in a plant.

Photosynthesis can be defined as "the process whereby light energy is converted into chemical energy by green plants." In more detail, it may be described as the process in which "light energy is utilized to shift energy, in the form of electrons, from one chemical (chlorophyll) to certain other chemicals and, ultimately, the storage of this energy in glucose in a form that is readily available to, and utilizable by, the plant and other living organisms". This process is unique to green plants and certain microorganisms. The green pigment, chlorophyll is found in the chloroplasts. Photosynthesis occurs in two distinct phases, the light-dependent and the dark-dependent phases.[11]

The light-dependent phase

There are two distinct light systems that make up the light-dependent phase. These are commonly called System I and System II.

In light System I, the chlorophyll molecules are raised momentarily (10^{-9} sec) to an excited state by the absorption of a photon or quantum of infra red light, enabling the chlorophyll molecules to serve as electron donors. The organic electron acceptor ferredoxin, within the grana, accepts electrons form the energized chlorophyll molecules. (System I follows System II).

In System II, chlorophyll molecules are also raised to an excited state by the absorption of a photon or quantum of light, and electrons from the energized chlorophyll molecules pass to organic electron acceptors. The chlorophyll molecules immediately replace their lost electrons by hydrolyzing water (splitting water molecules to form hydrogen H^+ and hydroxyl OH^- ions and taking one electron from the hydroxyl group). Four hydroxyl ions then interact to form two molecules of water ($2H_2O$) and one molecule of gaseous oxygen (O_2). This gaseous oxygen escapes into the atmosphere as free oxygen.

The Hill reaction involves the photosynthetic release of oxygen by free illuminated chloroplasts in vitro, accompanied by the reduction of an ionizing substance. It has become common practice to refer to water hydrolysis during photosynthesis in vivo as the Hill reaction.

The hydrogen ion of the split water molecule indirectly reduces the coenzyme NADP (nicotinamide-adenine dinucleotide phosphate) to form energy rich $NADPH_2$, which in turn serves as an essential electron donor in the conversion of carbon dioxide to sugar in the “dark reaction” of photosynthesis. The energized chlorophyll molecule can also transfer energy to adenosine diphosphate (ADP) and phosphate to form energy-rich adenosine triphosphate (ATP). [11]

The dark- dependant phase

This phase of photosynthesis consists of the reduction (i.e. the addition of an electron) of carbon dioxide and the formation of energy-rich glucose. The energy derived from photosynthesis is used to reduce carbon dioxide during the synthesis of glucose, which completes the dark phase.[11]

To summarize, photosynthesis consists of the following steps:

- Light energy catalyzing the transfer of electrons form chlorophyll to organic electron acceptors.
- Hydrolysis of water and the release of oxygen to the atmosphere.
- Addition of the hydrogen ions from the hydrolyzed water to NADP to form $NADPH_2$.
- The formation of energy-rich ATP.
- The formation of glucose.[11]

1,3,5-Triazine herbicides are photosynthesis inhibitors. They interrupt the light-induced electron transfer of H_2O to NADP. [12]

1.4.5 Mode of action of s-triazine herbicides

The inhibition of plant growth caused by the presence of triazines in the soil is only a secondary effect induced by the absence of photosynthesis in the plant. Some visual signs of triazine herbicides include foliar chlorosis, followed by the death of the leaf. Chloroplast destruction and the loss of membrane integrity can also occur. Triazine herbicides can be absorbed by plant leaves, this foliar absorption varies for various compounds. For example, leaves poorly absorb propazine and simazine but ametryn and prometryn are readily absorbed. Other triazines are seen to be intermediate.[13]

The rate of degradation of triazine herbicides varies with different species. For example, in resistant species they are rapidly degraded. The rate of degradation appears to be the main basis of selectivity. Degradation occurs by hydroxylation, dechlorination, demethoxylation or demethylthiolation, depending of the form of the substituted group on the triazine ring. Some species initiate conjugation with glutathione or other peptides in order to achieve inactivation. Dealkylation of the alkyl side chains also occurs.[13]

The susceptibility of herbicides to deactivation by plant processes is greatly influenced by their chemical structure. Resistant plants like corn and sorghum readily deactivate the s-triazine herbicides by substituting chlorine for hydrogen at the 2-position of the ring structure of atrazine and propazine. These plants do not readily deactivate prometone and prometryne because they have a methoxy ($O\text{-}CH_3$) or methylthio ($S\text{-}CH_3$) group substituted at the 2-position.[11]

1.4.6 Mechanism of action

The mechanistic action of triazine herbicides prohibits the Hill reaction of photosynthesis from taking place.[14] The total herbicide effect is more complex than this because the plants don't just starve to death. This was seen when the triazine was applied by the pre-emergence method: seedlings of some weeds were killed so quickly that they failed to appear above ground. It has been suggested that the action involves the interaction of light, chlorophyll and triazine to produce a secondary phytotoxic substance.

The blocking of photosynthesis is thought to be a secondary response on the part of green plants in light to a more basic effect on the plant metabolism. Selectivity by chloro-substituted triazines results from replacement of the chlorine atom by a hydroxy group (hydrolysis), a substitution that forms a compound nontoxic to certain plants.[8]

Because of its effective solubility, atrazine will kill very small weeds by contact action. Its greater solubility also makes atrazine more effective than simazine under conditions of low rainfall. Consequently, atrazine can be used post-emergence and pre-emergence if the application is made when the weeds are very small.[8]

1.4.7 Triazines and soil pH

The soil pH affects triazines in the following ways:

- s-Triazine herbicides become more available for plant uptake in the soil water as the soil pH increases.
- As the soil pH increases, less herbicide is bound to the soil colloidal fraction (organic matter, clay mineral, etc.). The pH changes the ionic nature of the herbicide molecule.
- Liming increases the pH of soils and this agricultural practice can cause the release of atrazine from the colloid complex, making it more available for plant uptake.[7]

1.4.8 Characteristics of triazine herbicides

The following characteristics describe the behavior of triazines in the environment:

- Diamino-s-triazine herbicides are readily absorbed to soil colloids, and resist leaching. Some leaching can occur; this depends on the soil type, the herbicide involved and the volume of water moving through the soil.
- s-Triazine herbicides are most effective against broadleaved weeds, although they do control grass and broadleaved weed seedlings.
- Diamino-s-triazine herbicides do not control established annual or perennial weeds, or deep-rooted perennial weeds, when applied at dosages recommended for selective weed control in croplands.
- These herbicides are readily absorbed by the root systems of plants. Only certain members of this group are foliar absorbed. Adding a surfactant to the spray mixture can enhance foliar absorption for triazines.
- Diamino-s-triazines are readily translocated upward to the leaves of a plant after having been absorbed by the roots. However, translocation does not occur in the leaves, they only accumulate in the leaves.
- The mode of action of the diamino-s-triazine herbicides is inhibition of photosynthesis. This is achieved by interfering with CO_2 fixation, and the splitting of water into oxygen and hydrogen (the Hill reaction).
- Physiological tolerance (rapid detoxication of the absorbed chemical) of certain plants determines the selectivity of the herbicide.
- These herbicides can persist in the environment for 3 months or less to more than 12 months depending on the herbicide involved, the dosage applied, and environmental conditions like rainfall, organic matter and temperature. Generally, soil persistence is longer in arid than in humid regions.
- Chloro-diamino-s-triazine herbicides appear to be detoxified in soils, mainly by chemical hydrolysis. Methoxy- and methylthio-diamino-s-triazine herbicides are detoxified mainly by microbial action.

- Of the crop protection herbicides in use today, the diamino-s-triazine herbicides are amongst the least toxic to man and animals.[11]

1.4.9 Exceptional characteristics of s-triazine herbicides

The following characteristics set s-triazines apart from other herbicides:

- The chloro-diamino-s-triazine herbicides propazine and simazine are only used as pre-emergence herbicides because they do not have any foliar activity.
- Some herbicides that are foliar and root absorbed include atrazine, ametryn, cyanazine, cyprazine, prometon, prometryn and terbutryn. (Surfactants can enhance their foliar absorption, but this is not recommended for cyanazine.)
- Cyanazine, dipropetryn, prometryn and terbutryn persist in the soil for 1 to 3 months if the soil is warm, moist, and if it is applied at the recommended dosages.
- Detoxication occurs via a non-enzymatic reaction in tolerant plants, where a hydroxyl group replaces the chlorine atom at the 2-position of the azine ring. Eventually the molecule is degraded into simple compounds.
- Atrazine and simazine are recommended for nonselective vegetation control in noncrop areas at dosages of 5 to 40 pounds per acre, depending on the plants to be controlled.[11]

1.5 Atrazine

1.5.1 The importance of atrazine as a major s-triazine herbicide

Atrazine is a herbicide that selectively controls broadleaf (dicotyledonous) weeds, for example, pigweed, cocklebur, velvet-leaf and certain grass weeds in fields of corn and sorghum. Selective control means that the target weeds are controlled, with little or no injury to the crop. Atrazine is well tolerated by actively growing corn, which absorbs and metabolizes the herbicide, thereby detoxifying it.

In 1959, Atrazine was registered and approved as a herbicide in Nebraska, where approximately 15 million pounds is applied each year. It is still used today because it is economical and effectively reduces crop losses due to weed interferences.

When atrazine is applied, it begins to degrade through the action of soil microbes that use it as an energy source, and through chemical reactions with water. Under moist, warm conditions, the half-life of atrazine in topsoil is about 60 days. In subsurface soils or in water, atrazine's half-life is generally longer. The half-life in this context is defined as the length of time required for half of a herbicide to degrade. Because of its wide spread use and relative persistence in the environment, atrazine is frequently detected in surface and ground waters.[15]

1.5.2 The regulatory status of atrazine

Atrazine has been categorized as a RUP (Restricted Use Pesticide) due to its potential for ground water contamination. Atrazine is graded as a class III toxin – slightly toxic. Products containing atrazine must signal the word CAUTION. In 1994, the EPA initiated a review which could result in restrictions of atrazine if health data warrants such action.[16]

1.3.3 Toxicology

Atrazine is considered slightly to moderately toxic to humans and other animals. It can be absorbed orally, dermally and by inhalation. Symptoms of poisoning include abdominal pain, diarrhea and vomiting, eye irritation, irritation of mucous membranes, and skin reactions. When exposed to very high doses, rats show excitation followed by depression, slowed breathing, incoordination, muscle spasms and hypothermia. High oral doses cause muscular weakness, hyperactivity, breathing difficulty, convulsions and death. Atrazine is however a mild skin irritant causing rashes. The oral LD_{50} for atrazine is 3090 mg/kg in rats, 1750 mg/kg in mice, 750 mg/kg in rabbits, and 1000 mg/kg in hamsters. The data regarding atrazine's carcinogenic potential are thus far inconclusive.

Based on the results of animal studies, atrazine probably does not cause cancer, birth defects or genetic damage. There is not enough information available to determine whether atrazine has any effect on fertility or reproduction. Thus far there have been no reported cases of long term health effects in humans due to atrazine exposure.[11,16]

1.3.4 Ecological effects

Plants that appear to be resistant to atrazine metabolize or break it down into compounds that are less toxic. Despite the fact that atrazine is toxic to many plants, it is practically nontoxic to microorganisms and birds (940 to 2000 mg/kg), e.g. the LD_{50} is greater than 2000 mg/kg in mallard ducks. Atrazine is harmless to bees. However atrazine is slightly toxic to fish and other aquatic life. Bioaccumulation of atrazine occurs at a low level in fish, affecting the brain, liver, gut and gall bladder. Atrazine is slightly toxic to amphibian eggs and tadpoles, but is toxic to invertebrate animals. The toxicity to mammals is low (750 to 3080 mg/kg). Atrazine is considered a hazard to threatened and endangered species if it is used in an area where they live.[11,16]

1.3.5 Environmental fate

Atrazine is highly persistent in soil. Breakdown of atrazine occurs firstly with chemical hydrolysis, which is then followed by degradation by soil microorganisms. Hydrolysis is particularly rapid if the soil environment contains a large amount of organic material, or is either acidic or basic; consequently its decomposition is relatively slow at neutral pH's. Atrazine can persist for longer than 1 year under dry, cold conditions. If the clay or organic content of the resident soil is low, atrazine is found to be more mobile in the soil. This is because it does not adsorb as strongly to the soil particles, resulting in a lengthy half-life of 60 to 100 days. This means that atrazine has a high potential to become a ground water contaminant, despite the fact that it is only moderately soluble in water. Atrazine is now the second most common pesticide found in private wells and in community wells. Trace amounts have been found in drinking water samples and in ground water samples.

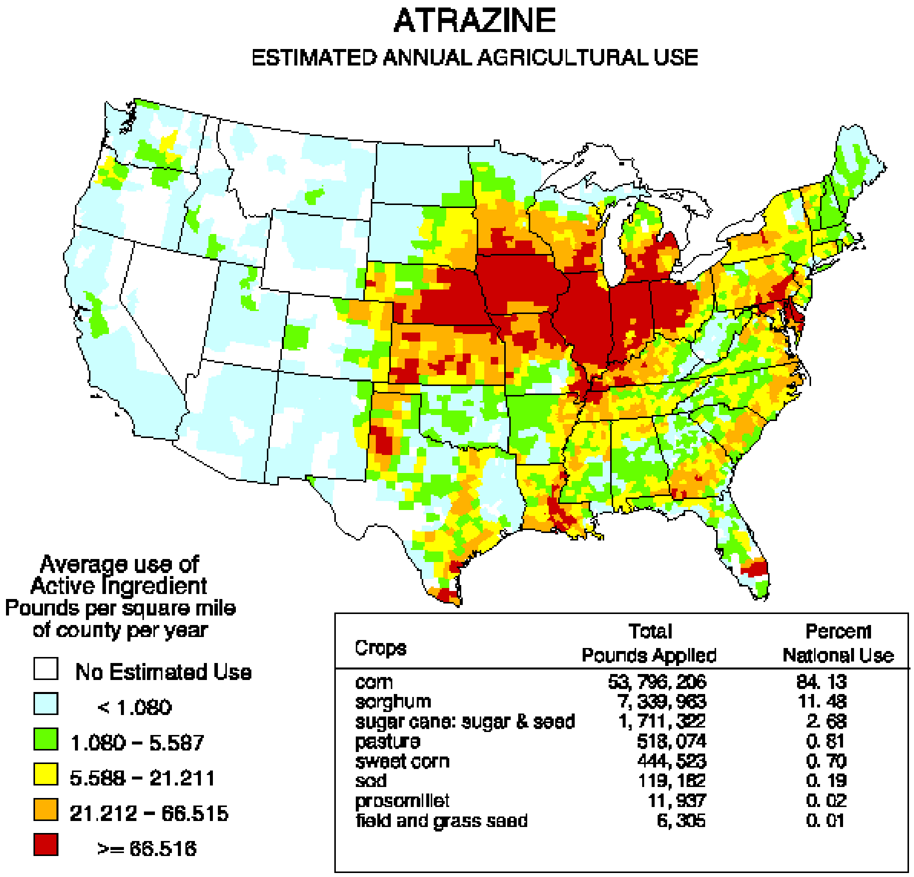
In aquatic environments, atrazine is biodegraded after hydrolysis has taken place. This may be the most important route of disappearance from water. The breakdown of atrazine in vegetation occurs when atrazine is absorbed by the plant through the roots and sometimes also the foliage. It is then translocated upwards, accumulating in the growing tips and new leaves of the plant. If a species is susceptible to the herbicide, photosynthesis is inhibited. Plants that tolerate atrazine metabolize it.[11, 16]

1.3.6 Mode of action of atrazine.

Atrazine kills plants by binding to the cell membrane on which photosynthesis occurs and thus inhibits photosynthesis. The plant dies of starvation due to the fact that photosynthesis is stopped, either by the bleaching of the plants chlorophyll or from the release of free radicals.

The root system of a plant absorbs the atrazine from the soil and translocation allows for the movement of atrazine to other parts of the plant above ground. Resistant plants, like corn, detoxify this poison due to the presence of an enzyme in its leaves. Corn roots contain a substance which helps break down atrazine molecules.[13]

1.3.7 The uses of atrazine



Crops	Total Pounds Applied	Percent National Use
corn	53, 796, 206	84. 13
sorghum	7, 339, 963	11. 48
sugar cane: sugar & seed	1, 711, 322	2. 68
pasture	518, 074	0. 81
sweet corn	444, 523	0. 70
sod	119, 182	0. 19
prosomillet	11, 937	0. 02
field and grass seed	6, 305	0. 01

Figure 1.9 The average distribution of atrazine in the United States given in terms of the total pounds applied and the percentage national use for various crop applications[17]

As mentioned previously, atrazine is used as a herbicide to control broad leaf dicotyledonous and grassy weeds such as pigweed, cocklebur, velvetleaf, quack grass and other perennial weeds. Although a wide variety of weeds are controlled by atrazine, it is most effective on seedlings.

Some crops that atrazine is applied to are corn, sugarcane, pineapple, christmas trees, conifer reforestation plantings, sorghum, macadamia nuts, certain tropical plantations, evergreen tree nurseries, lawns, turfs and citrus fruits. It is applied as pre-plant/soil-incorporated, at planting, either pre-emergence or post-emergence. Over 64 millions acres of cropland was treated with atrazine in the U.S. in 1990.[4,8-10,12] Atrazine has been used in the U.S since 1958. According to the EPA approximately 70 – 90 million pounds of active ingredient is used annually. More atrazine is used than any other U.S. pesticide.[13]

The triazines, especially the 2-chloro derivatives, have replaced the phenoxyalkanoic acid herbicides for weed control in corn.[14]

Atrazine is used as a nonselective herbicide on non-crop industrial lands and on fallow lands or rangelands, i.e. as a general weed control on industrial and non-agricultural land.

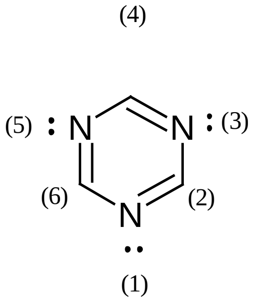
The accepted use rate is between 1-10 pounds of active ingredient per acre. The application which is most suitable is usually timed before or after plant growth begins. If it is necessary to apply once the weeds have started growing, it is best to use atrazine while the plants are still young and actively growing.[10] Atrazine can be applied immediately after plowing with little or no competitive effect from grasses.[8]

1.4 General chemistry of s-triazines

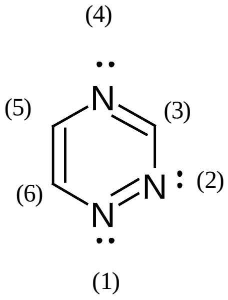
As mentioned before, triazines can be described as aromatic, six-membered rings containing three nitrogen atoms.

There are three possible derivatives of this ring system:

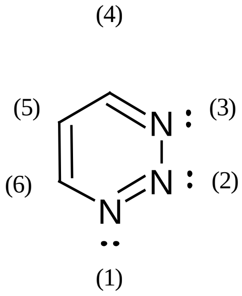
- 1,3,5-triazine (I)
- 1,2,4-triazine (II)
- 1,2,3-triazine (III)



(I)



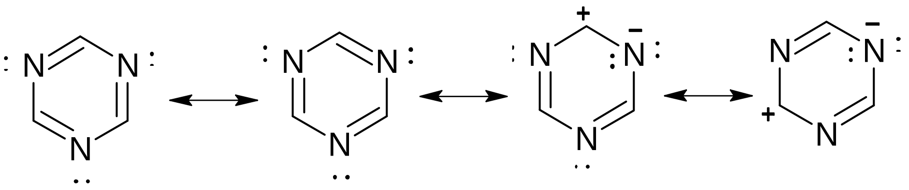
(II)



(III)

The high symmetry of 1,3,5-triazine has lead to the abbreviation sym- or s-triazine. Some of its derivatives are amongst the earliest known heterocyclic compounds, e.g. cyanuric acid, a tautomer of 2,4,6-trihydroxy-1,3,5-triazine, was known in 1776 to a scientist named Scheele. 1,3,5-Triazine was only prepared and correctly identified in 1954. 1,2,4-Triazine and 1,2,3-triazines have not yet been prepared, but derivatives of these systems are known.[18]

The triazine ring each contains six B - electrons that fill the three bonding molecular orbitals. There are also three pairs of non-bonding electrons in each molecule, which are responsible for the compounds having basic properties. Each of the triazines can be represented as resonance hybrids of hypothetical structures. In the case of 1,3,5-triazine, the most important canonical forms are:

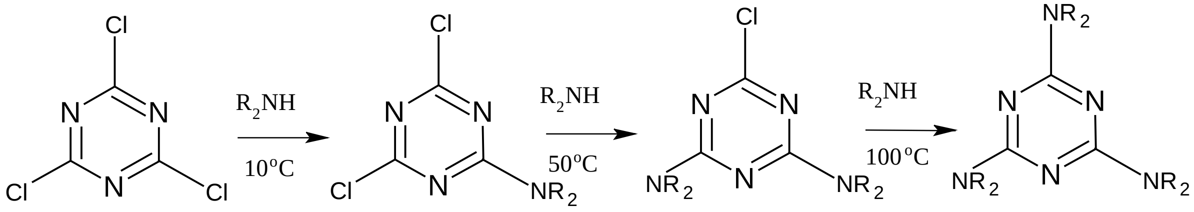


1,3,5-Triazines form colourless crystals; the molecular structure is highly symmetrical with all bonds equal in length, but with angles of alternating size.

Electrophilic substitution in 1,3,5-triazine occurs with difficulty and only in non-aqueous media, since aqueous acids readily hydrolyze the ring.

Nucleophiles attack the 1,3,5-triazine ring with great ease: for example, a 10% solution of the compound in water at 25°C contains no 1,3,5-triazine after 10 minutes.
The ring is also readily cleaved by primary amines.
The reaction of 1,3,5-triazine with amides under mild conditions was discovered in 1960. This led to the synthesis, in high yields, of mono, di- and trisubstituted triazines, depending on the quantity of amide used.

Nucleophilic substitution of the halogen atoms in cyanuric chloride occurs readily. The first halogen is readily removed at room temperature, the second at 50-70°C in the presence of sodium hydroxide and the third at even higher temperatures between 100 and 125°C. Hydrolysis of cyanuric chloride occurs easily in water.[18,19]



Cyanuric chloride

Figure 1.10 Nucleophilic substitution of halogen atoms in cyanuric chloride[20]

1.5.6 General features of the chemistry of 1,3,5-triazines

Properties that give general insight into the chemistry of 1,3,5-triazines are described as follows:

- As the number of ring nitrogens increases, the energies of the B molecular orbitals are lowered, particularly those orbitals with large coefficients on the nitrogen. As a result, electrophilic attack on the ring carbon atoms becomes increasingly difficult and nucleophilic attack becomes easier.
- All the ring carbon atoms in these heterocycles lie ortho or para to at least one ring nitrogen atom, (except C-5 of pyrimidine). The position of the nitrogen atom in the ring selectively activates specific positions in the ring system, concentrating the electron density in the ring to adjacent carbon atoms. Activation of the ring carbon atoms in 1,3,5-triazine is even greater because there are more ring nitrogen atoms and all three nitrogen atoms activate all the carbon atoms. Intermediates formed by nucleophilic attack or by deprotonation of alkyl substituents at these positions are therefore well stabilized.

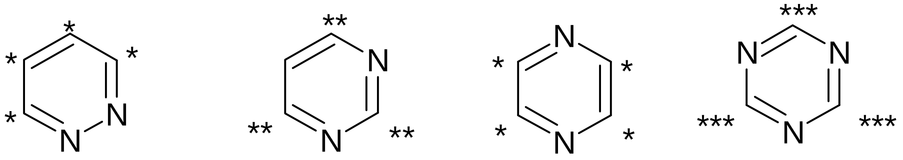


Figure 1.11 The selective activation of ring carbon atoms (asterisks indicate the number of ortho or para nitrogen atoms)[19]

- Electrophilic substitution in these heterocycles is very uncommon unless there are powerful electron-releasing substituents, e.g. hydroxy or amino groups, present to counteract the effect of the ring nitrogen atoms. The tendency towards attack by nucleophiles increases with increasing number of nitrogen atoms in the ring. This attack takes place preferentially at activated positions within a particular ring system.
- Due to the lower resonance energies of the ring systems, nucleophilic attack may lead to addition or ring cleavage, rather than to substitution. For example 1,3,5-triazine, which is thermally stable, rapidly hydrolyzes in water at 25°C.

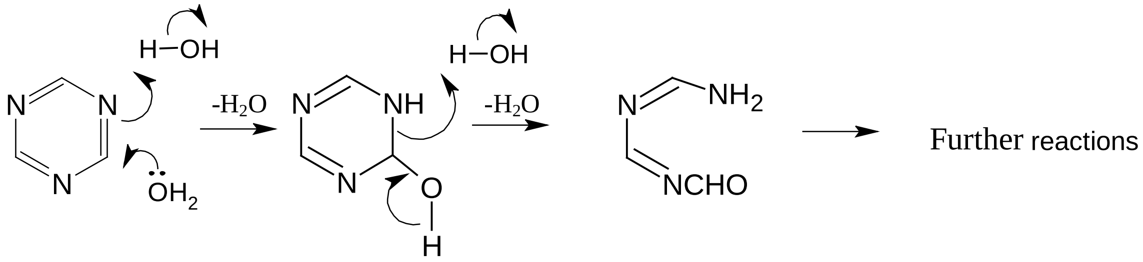


Figure 1.12 **Hydrolysis of 1,3,5-triazine**[19]

- This ring is also opened by reaction with other nucleophiles like ammonia and hydrazine.[17]

1.5.7 Chemical properties and synthesis of s-triazines

s-Triazines are synthesized from cyanuric chloride, which can be obtained by the trimerization of cyanogen chloride.

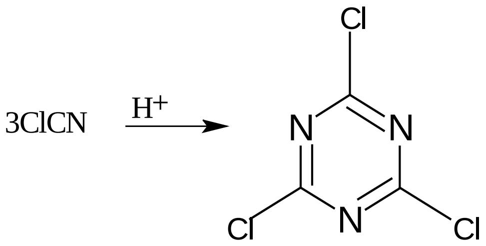


Figure 1.13 **The trimerization of nitriles**[20]

Commercially, cyanuric chloride is produced by gaseous trimerization of cyanogen chloride over charcoal catalysts.

The three chlorine atoms may be replaced by amines, phenols, alcohols, mercaptans, thiophenols and related compounds. 2,4,6-Trichloro-1,3,5-triazine (cyanuric chloride) behaves as a heterocyclic acid chloride analogue. The reactive chlorine atoms are easily substituted in S_NAr processes.

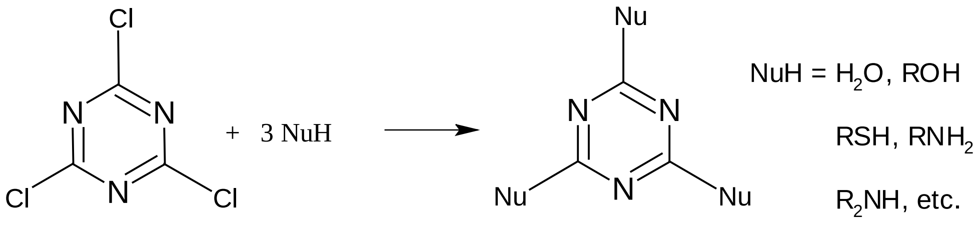


Figure 1.14 **S_NAr process**[12]

This explains why cyanuric chloride is used as a chlorinating and dehydrating agent: it transforms secondary alcohols into alkyl halides, carboxylic acids into acid halides, hydroxycarboxylic acids into lactones and alkoximes into nitriles.[12]

The three chlorine atoms are very reactive; this means that in order to replace a single chlorine atom, controlled reaction conditions are required. For example, temperatures between –15°C and 5°C are often employed. Sodium hydroxide or an amine is added to neutralize the liberated hydrogen chloride.

The alkylamino-s-triazines, or the tautomeric imino structure, form hydrogen bonds with water. This means that attack on a neighboring carbon-chlorine bond, as in the following structure, would be facilitated.[21]

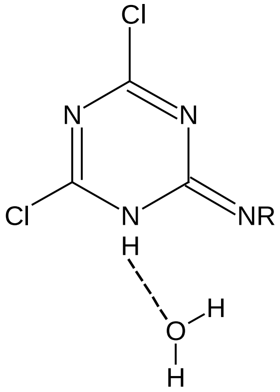


Figure 1.15 Hydrogen bonds formed with water by s-triazine[14]

The replacement of two chlorine atoms by amines, alcohols, or thiols requires somewhat higher reaction temperatures, generally 20-50°C. Base is then added to neutralize the liberated acid. A symmetrically alkylated 2-chloro-4,6-bis-(alkylamino)-s-triazine can be prepared in good yield by the reaction of two amines with cyanuric chloride. Hydrolysis of the 2-chloro compound by acid or base allows for the formation of 2-hydroxy-4,6-bis-(alkylamino)-s-triazines.

The heterocyclic ring of the s-triazine herbicides is very stable and is not cleaved except under drastic conditions. Triazines are decomposed by light and lose their herbicidal activity. In alcohols and water, halogen-substituted triazine herbicides are photolyzed to the corresponding alkoxy and hydroxy compounds. The rates of photolysis of atrazine, atraton and ametryn in water increase threefold to eleven fold when acetone is added as a photosensitizer. The products of the reaction are the mono- and di-N-dealkylated product and the corresponding hydroxy triazines.[14]

1.6 An s-triazine manufacturing process

1.6.1 General

As discussed before, atrazine is made by a two-step reaction of cyanuric chloride (CC) with mono-isopropylamine (IPA) and mono-ethylamine (MEA) using sodium hydroxide (NaOH) as an acid acceptor. This reaction takes place in a medium of water and methyl isobutyl ketone (MIBK), or some other suitable solvent (Figure 1.16).

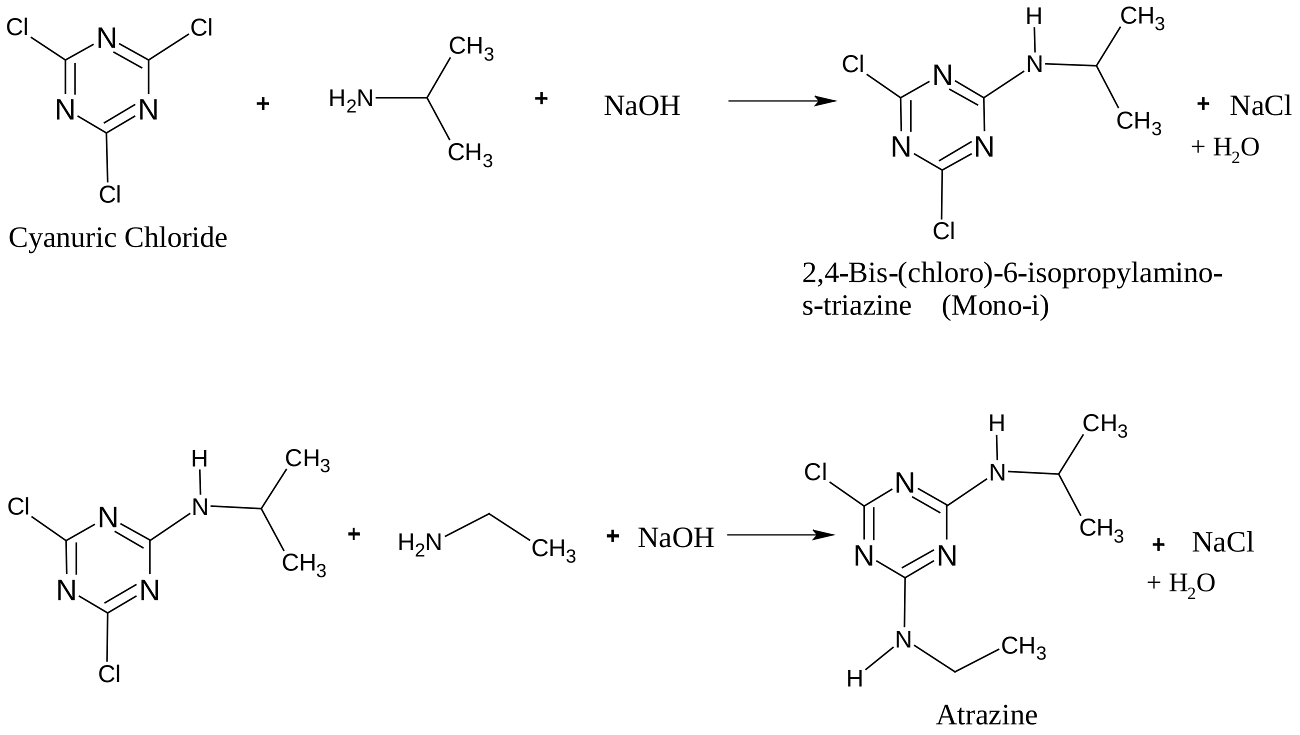


Figure 1.16 **Synthesis of atrazine in a medium of MIBK**

1.6.2 Chemistry and general synthesis

The synthesis of atrazine involves the nucleophilic addition / elimination reaction of alkyl amines (isopropylamine and ethylamine) with cyanuric chloride. Sodium hydroxide is used as HCl scavenger. The temperature of the first stage is maintained below 25°C in order to prevent disubstitutions.

Isopropylamine is reacted with cyanuric chloride first because it is less reactive than ethylamine and provides increased reaction selectivity with the cyanuric chloride, which is highly reactive. This is done in order to prevent a disubstitution taking place during the first stage. This results in the substitution of one chloride atom to form the mono-substituted intermediate product 2,4-dichloro-6-isopropylamine-s-triazine (mono-i) and sodium chloride (NaCl). The reaction proceeds halfway when the IPA is added first forming

IPA-chloride. The hydroxide is then added to complete the formation of the intermediate. The reaction of the second, less reactive chloro-group of this intermediate with ethylamine and NaOH results in the formation of atrazine and more salt. As in the first stage, the reaction of the amine proceeds halfway until the NaOH is added to complete the reaction. The temperature during the second stage is maintained below 60°C to prevent trisubstitution.

1.6.3 Process description

Atrazine is produced in a two-stage reaction of cyanuric chloride with mono-isopropylamine and mono-ethylamine in an alkaline medium. The reaction is highly exothermic and is carried out in a mixture of water and methyl isobutyl ketone (MIBK), or some other suitable solvent.

The water acts as a heat sink, a reactant carrier for the amines and the hydroxide, and as a solvent for the by-product sodium chloride. The MIBK acts as a dispersant for the organic product – the atrazine forms a colloidal suspension with the MIBK.

The first stage of the reaction is performed in R1 (Figure 1.17) where the heat of the reaction is removed by a refrigerated coolant which is passed through a jacket and cooling coil. The cyanuric chloride (solid) is added to the chilled reaction solvent mixture, MIBK and water, at 0°C. Isopropylamine is added to the reaction mixture over a 90 minute period, ensuring the reaction temperature does not exceed 5°C. NaOH (48%) is then added to the reaction mixture over a 90 to 120 minute period, still ensuring that the reaction temperature does not exceed 5°C, also ensuring that the pH does not exceed 8.5.

The second stage of the reaction is performed in R2 (Figure1.17). The heat of the reaction is removed by cooling water passed through the reactor jacket. It is not necessary to use a refrigerant in the second stage since the reaction can take place at a higher temperature. Mono-ethylamine is added to the reaction mixture during 90 minutes, ensuring that the reaction temperature does not exceed 20°C. NaOH (48%) is added to the reaction mixture during 90 to 120 minutes, ensuring that the reaction temperature does not exceed 35°C, nor the pH does not exceed 12.

The product from R2 is a slurry-like suspension in MIBK, while the sodium chloride is dissolved in the water. Because water and MIBK are almost immiscible, a two phase system results. This allows the slurry to be separated from the brine.

The reaction mixture is then transferred to a washing vessel where the water phase is drained off and pumped to a storage tank. The remaining slurry is washed three times with water during the wash cycle. This is done in order to remove residual sodium chloride from the organic phase. Chalk is added for pH control and the batch is transferred to a holding tank.

The MIBK / atrazine slurry is then dried azeotropically by the addition of water in a thin film drier. Technical atrazine is milled to a desired particle size distribution and then packed in a continuous operation. The dry powder is conveyed to a dust collector; from there it is fed into an Air Classifier Mill, and then conveyed to another dust collector where it is packaged.

In order to prevent / minimize the formation of side products, it is essential to maintain the reaction conditions which have been stipulated.[22]

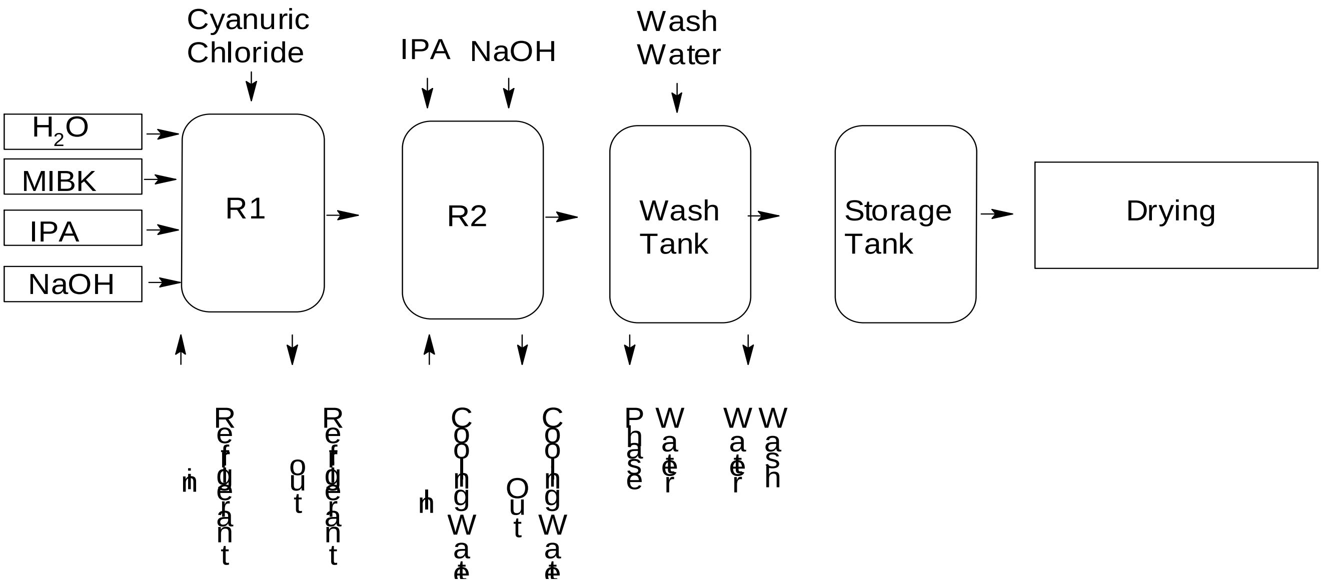


Figure 1.17 **A production scheme for atrazine**[22]

1.6.4 Formation of unwanted side products

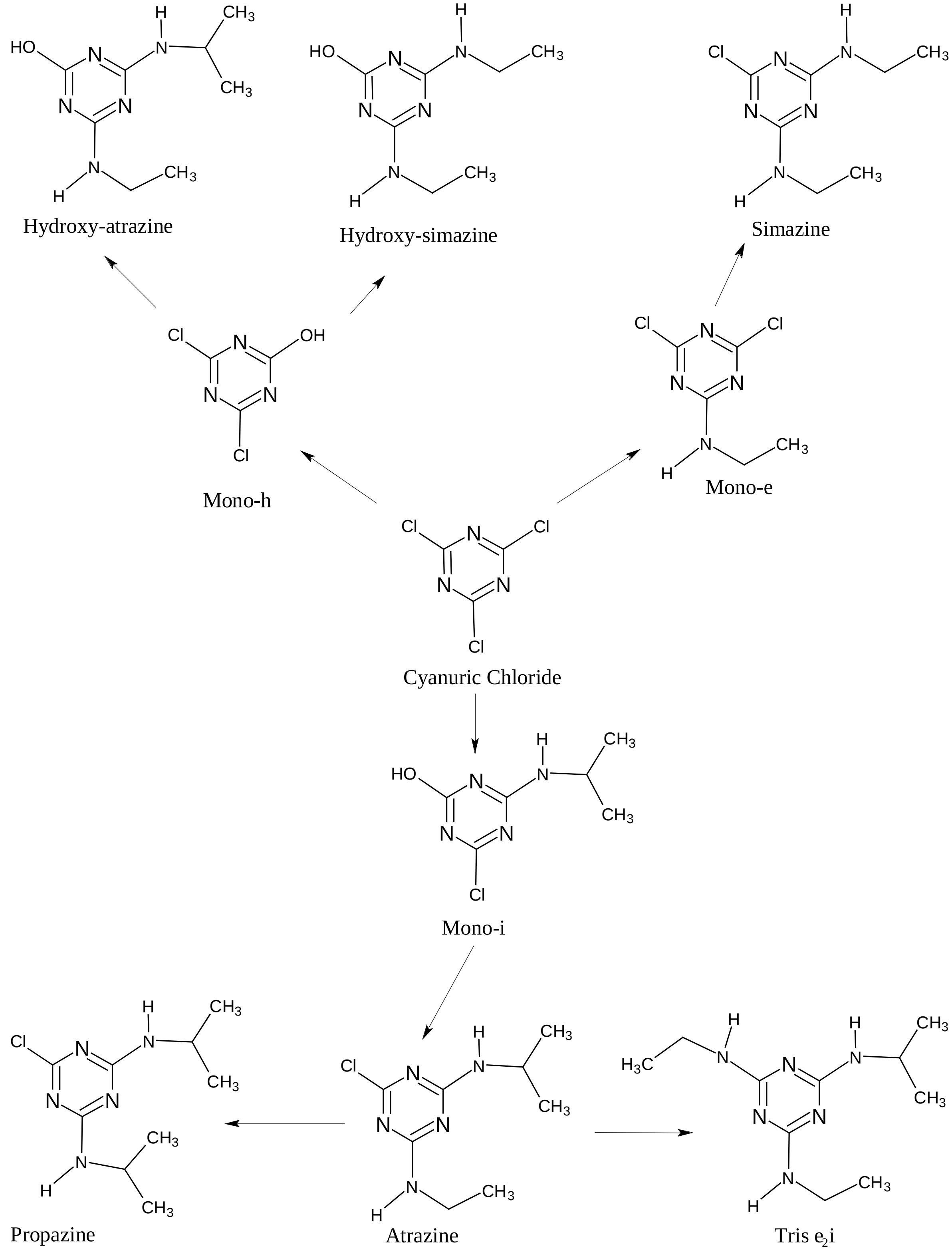
During the reaction, there are a number of by-products that can form. Reasons for the formation of side products from side reactions are:

- Incorrect amounts of reactants used.
- Incorrect addition rate of amines or sodium hydroxide.
- Incorrect temperature of reactions.
- An exchange of functional groups.

There are 4 major impurities that can form during this synthesis (Scheme 1.5.1):

a) Propazine: Forms due to poor agitation, and excess IPA loaded.
b) Simazine: Forms when residual cyanuric chloride is not converted to mono-i.
c) Hydroxy-triazines: Forms when cyanuric chloride hydrolyzes at temperatures above 5°C.

d) Tris-triazines: Forms when ethylamine is added at high temperatures (i.e. higher than 35°C).[23]



Scheme 1.5.1 Reaction side products[23]

1.6.5 Shortcomings of the process in MIBK

There are several shortcomings associated with the use of MIBK as reaction solvent that makes the elimination of MIBK from the process desirable. These are:

- MIBK is partially soluble in water.
  The washing procedure for the removal of sodium chloride from the atrazine / MIBK slurry requires large volumes of water. This results in a loss of MIBK and reaction product to the effluent due to its solubility in water.
- The presence of a solvent and atrazine in the effluent streams, enhanced due to the fact that the solvent is soluble in water, poses an environmental hazard.
- The atrazine / MIBK slurry must be dried at high temperatures to obtain technical-grade atrazine. This drying process results in the dimerisation of atrazine and crystallographic changes to the product, both of which are highly undesirable.
- The nature of the atrazine crystals formed depends on the nature of the reaction solvent. A consistent crystal structure, which is applicable in all formulations, is an important aspect in the production of this herbicide.
- Due to the losses of solvent and product, solvent consumption is unacceptably high while overall reaction yields are low.

1.5.6 Motivation for this study

Due to the shortcomings discussed above, it was necessary to investigate alternative technologies that will benefit the manufacturer, its customers and the environment.

The main objectives of this investigation included the maintenance, or even improvement, of the high quality of the s-triazine produced, the reduction of the environmental impact of the process, and the improvement of the financial performances of the operation. A major requirement was that the existing facilities had to be used for the proposed alternative process.

1.5.8 Specific objectives for this investigation

The specific objectives of this investigation were to:

- Investigate alternative solvent mediums for the production of atrazine.
- Attempt to optimize a reaction sequence in order to improve product yield.
- Assist in improving the present environmental impact due to “loss” of solvent and product during production.
- Consider the possibility of a solvent free process.
- Minimize the formation of side products.

CHAPTER 2

EXPERIMENTAL

2.1 General

In this section, details of the chemicals, equipment, standard methods of synthesis and analytical techniques used during this investigation, are given. Basic synthetic procedures are described before modifications for the optimization of various syntheses are discussed in future chapters. Specific properties and characteristics of prominent herbicides/side products are also included.

2.1.1 Trade names of atrazine

Atrazine is the common name for 6-chloro-N-ethyl-N'-(1-methylethyl)-1,3,5-triazine-2,4-diamine.[13] The IUPAC name is 6-chloro-N^2-ethyl-N^4-isopropyl-1,3,5-triazine-2,4-diamine, and its CAS RN is [1912-24-9]. There are several trade names for atrazine. Some of them are as follows: AAtrex®, Atrol®, Atranex, Atrantol, Atrataf, Azinotox, Atikon, Alazine, Atred, Crisazia, Farmco Atrazin, G-30027, Gesparim, Giffex 4L, Malermais, Primatol, Simazat and Zeaphos.[16] Atrazine is also a component of other herbicides such as Bicep, Bullet Extrazine, Prozine, Rastra, Stuazine and Tomahawk.[6,13,16] The major manufactures of Atrazine today are Ciba-Geigy Corp., E.I. du Pont de Nemours and Co. Inc., Drexel Chemical Co., Oxon Italia, Industria Prodotti Chemici, Agro Evo, Chemol, Compania Quimica, Du Pont, Griffin, Makhteshim-Agan, Rallis India and Dow AgroSciences.[6,13]

2.1.2 Physical properties

The physical properties of atrazine are listed below:

- Appearance: Atrazine is a white, crystalline solid or white powder.
- Molecular weight: 215.7 g/mol.
- Molecular Formula: $C_8H_{14}ClN_5$
- Water Solubility: 28 mg/L at 20°C.
- Solubility in organic solvents: Very soluble in chloroform, diethyl ether and dimethyl sulfoxide; partially soluble in methanol, ethyl acetate, acetone, dichloromethane, toluene, n-hexane and n-octanol.
- Melting point: 176°C.
- Vapor Pressure: 0.04 mPa at 20°C.
- Composition: Technical grade is ∃ 96% pure.
- Stability: Relatively stable in neutral, weakly acidic and weakly alkaline media. Rapidly hydrolyzed to the hydroxy derivative in strong acids and

alkalis, and at 70^{o}C in neutral media.[4,14]

- Atrazine is formulated as either a wettable powder, a flowable liquid suspension/concentrate or in granular form.
- The LD_{50} is 3090 mg /kg in rats.[4,24]

2.1.3 s-Triazine impurities generally found in atrazine

The following s-triazine compounds are formed in varying quantities during the synthesis of atrazine. Whilst these compounds are themselves active herbicides, they are, for the purposes of this study, seen as impurities and unwanted side products. It is however necessary to be aware of some of the properties and characteristics that each one has.

2.1.4 Propazine

Propazine is the common name for 2-chloro-4,6-bis-(isopropylamino)-s-triazine. Some common trade names for propazine are Milogard®, Maax and Propazine. The IUPAC name is 6-chloro-N,N'-bis(1-methylethyl)-1,3,5-triazine-2,4-diamine. Propazine exists as a white crystalline solid that has a water solubility of 8.6 ppm at 20^{o}C. It is formulated as a wettable powder, liquid and water dispersible granules. The LD_{50} is greater than 5 g/kg. Propazine provides good weed control under dry or minimum soil moisture conditions. The molecular formula of propazine is $C_9H_{16}ClN_5$ and the molecular mass is 229.7 g/mol.[4,24]

2.1.5 Simazine

Simazine is the common name for 2-chloro-4,6-bis-(ethylamino)-s-triazine. Some industrial trade names for simazine are Princep®, Caliber®90, Simazine, SimTrol® and Aquazine®. The IUPAC name is 6-chloro-N,N'-diethyl-1,3,5-triazine-2,4-diamine. Simazine exists as a white crystalline solid that has a water solubility of 3.5 ppm at 20^{o}C. It is formulated as a wettable powder, an emulsifiable concentrate or water dispersible granules. The LD_{50} is greater than 5g/kg. Simazine is effective for pre-emergence or pre-plant soil incorporation treatments to control annual grass and broad leaf weeds. Atrazine has now replaced simazine for this purpose. Previously, simazine was the first widely used triazine herbicide used on corn crops. The molecular formula of simazine is $C_7H_{12}ClN_5$ and the molecular mass is 201.7g/mol.[4,24]

2.1.6 Hydroxy-simazine

Also referred to as simazine-2-hydroxy, or 2-hydroxy-4,6-bis-(ethylamino)-1,3,5-triazine, with the chemical formula $C_7H_{13}N_5O$ and a molecular mass of 183.21 g/mol. Hydroxy- simazine is formulated as a white crystalline solid. This triazine forms as a result of hydrolysis of residual simazine.[4,24]

2.1.7 Hydroxy-atrazine

Also referred to as atrazine-2-hydroxy, or Pestanal®. Its chemical formula is $C_8H_{15}N_5O$ and has a molecular mass of 173.60 g/mol. This triazine forms as a result of hydrolysis the of residual atrazine.[4,24]

2.1.8 Cyanuric chloride, the starting material in the synthesis of atrazine

In the sequence of reactions that are discussed throughout this dissertation, cyanuric chloride is the key building block from which atrazine is synthesized. This starting material is added to a liquid (water or other solvent) in order to allow it to exist as a partially soluble suspension before reactants are added.

Cyanuric chloride or 2,4,6-trichloro-1,3,5-triazine,[25] with the molecular formula $C_3N_3Cl_3$ and a molecular mass 184.4 g/mole, forms white monoclinic crystals with a pungent odour. This compound is soluble in acetonitrile, ether, ketones and chlorinated hydrocarbons but is insoluble in water. It has an LD_{50} of 485 mg/kg. The vapor pressure of the solid is 0.00492 atm.[26]

2.1.9 Characteristics of mono-isopropylamine (IPA)

Isopropylamine has the chemical formula $(CH_3)_2CHNH_2$ and has a molecular mass of 59.1 g/mol. It exists as a colourless liquid, completely soluble in water, with a strong ammoniacal odour. It is a severe skin and eye irritant, and is considered a corrosive, flammable liquid. The oral LD_{50} is 0.82 g/kg in rats.[27]

2.1.10 Characteristics of mono-ethylamine (MEA)

Ethylamine has the chemical formula $C_2H_5NH_2$ and has a molecular mass of 45.0 g/mol. It is highly flammable, causes burns and is harmful by inhalation or skin contact. It is a colourless-yellow liquid with an amine-like odour and is miscible in water. The oral LD_{50} is 0.40 g/kg in rats.[28]

2.1.11 Specifications and limits for impurities for technical-grade atrazine

Recommended manufacturing specifications are as follows:

- Total triazine content: minimum of 98%
- Atrazine: >97 %
- Propazine: <1.5 %
- Simazine: <1.5%,

The total of propazine and simazine must not exceed a maximum of 3%

- Total hydroxy triazines: maximum of 0.6%
- Hydroxy-triazines: <0.1%
- Tris-triazines: <0.1 %
- Mono-substituted triazines: maximum of 0.1%. [21]

2.2 Materials

2.2.1 Reagents for synthesis

The following Tables (2.1–2.3) list all materials, together with their sources and corresponding grades used during the synthesis of atrazine (AR = analytical reagent and CP = chemically pure).

Table 2.1 Organic reagents for syntheses

Chemical	Formula	Supplier	Grade / Purity
Cyanuric chloride	$C_3H_3N_3$	Degussa	99%
Dichloromethane	CH_2Cl_2	Saarchem	AR
Isopropylamine	C_3H_9N	Air Products	100%
Monoethylamine	C_2H_7N	BASF	70%
Methyl isobutyl ketone (MIBK)	$(CH_3)_2CHCH_2COCH_3$	Sasol	99.5%
Toluene	C_7H_8	Saarchem	AR

Table 2.2 Inorganic reagents for syntheses

Chemical	Formula	Supplier	Grade / Purity
Sodium chloride	NaCl	ACE	AR
Sodium hydroxide	NaOH	ACE	CP

Table 2.3 Surfactants for synthesis

Chemical	Formula/ Description	Supplier	Grade / Purity
Arkopon T Pulver Hochkonz	Fatty acid methyl tauride sodium salt	Clariant	CP
Aliquat 336	Fatty quarternary ammonium chloride	Unilab	CP
Tetra butyl ammonium hydrogen sulphate	$[CH_3(CH_2)_3]_4NHSO_4$	Aldrich	97%
Rhodafac PS/17	Polyoxyethylene alkylphenyl ether phosphate	Rhone-Poulenc	CP
Triton X 100	Isooctylphenoxypolyethoxy ethanol	BDH	CP

2.5.4 Reagents for analysis

The reagents listed in Tables 2.4 and 2.5 were used as standard materials for high performance liquid chromatography (HPLC), where acetonitrile formed the basis for the mobile phase. All standards where used as received.

Table 2.4 Organic reagents for analysis

Chemical	Formula	Supplier	Grade / Purity
Acetonitrile	CH_3CN	BDH	AR

Table 2.5 Organic standards for analysis

Chemical	Formula	Supplier	Grade / Purity
Atrazine	$C_8H_{14}ClN_5$	Institute of organic industrial chemistry	98.7%
Atrazine 2-hydroxy	$C_8H_{15}N_5O$	Riedel-de Haën	94.7%
Simazine 2-hydroxy	$C_7H_{13}N_5O$	Industrial analytical	98.5%
Propazine	$C_9H_{16}ClN_5$	IOIC	99.7%
Simazine	$C_7H_{12}ClN_5$	IOIC	99.0%

2.6 Equipment for synthesis

2.6.1 Reactor apparatus

Figure 2.1 depicts the general reactor apparatus used in the synthesis of atrazine:

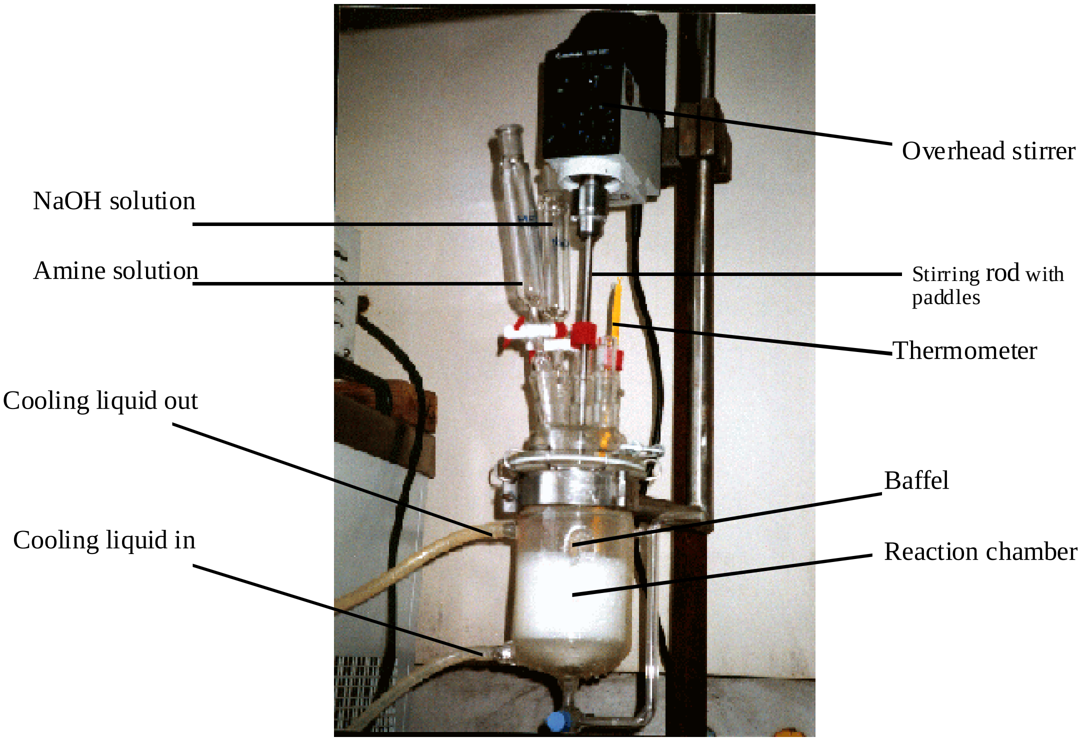


Figure 2.1 Reactor setup arrangement

2.6.2 General reactor setup for the synthesis of atrazine

The reactions performed in order to synthesize atrazine were carried out in a 500 mL double-walled glass reactor. A 20% ethylene glycol solution, contained in a cooling bath, was circulated through the reactor jacket in order to maintain the low temperatures needed to carry out these reactions (between –5°C and 20°C). An overhead stirrer, set in order to allow for high stirring rates and equipped with a stirring rod, was needed to provide adequate agitation in the reaction vessel, this agitation being aided by 4 baffles situated on the inside of the glass reactor. The reactor was tightly sealed with a Teflon seal and a reactor clamp in order to prevent any leaks occurring between the reactor body and lid. Sockets on the lid of the reactor held a thermometer, and two dropping funnels through which the amines and hydroxide were fed into the reaction mixture.

The entire apparatus was supported by a sturdy clamp stand, which was housed in a fume cupboard. Due to the fact that harmful and potentially dangerous chemicals were being used to carry out these reactions, and bearing in mind that these reactions are highly exothermic, it was necessary to take precautionary measures to ensure that the reactions were carried out in a safe and controlled environment.

2.6.3 General reaction procedure for the synthesis of atrazine

A 500 mL glass reactor fitted with overhead stirrer, agitator and thermometer, and connected to an external chiller, was charged with water (85 g) and methyl isobutyl ketone (MIBK) (90 g). The solvent mixture was cooled to 0°C and cyanuric chloride (60 g, 0.33 mol) was added. Isopropylamine (IPA, 99.7%) (19.2 g, 0.324 mol) was then added drop-wise from a dropping funnel over a period of 1 hour, ensuring that the reaction temperature did not exceed 5°C. Upon completion of the IPA addition, sodium hydroxide (NaOH, 45.0%) (28.9 g, 0.325mol) was added from a dropping funnel, also ensuring that the reaction temperature did not exceed 5°C. The reaction temperature was then allowed to increase to 15°C and mono-ethylamine (MEA, 70.4%) (21.4 g, 0.335 mol) was added drop-wise from a dropping funnel over a period of 1 hour, this time ensuring that the reaction temperature did not exceed 20°C. Sodium hydroxide (NaOH, 45.0 %) (29.8 g, 0.335mol) was then added and the reaction temperature was not allowed to exceed 35°C in this step. The reaction mixture was then agitated for a further 15 minutes and cooled to below 30°C.[21]

2.3.3.1 General sample preparation and recovery

The resulting reaction mixture was transferred to a separating funnel and the bottom aqueous phase removed. The atrazine/MIBK slurry was washed with water (4 x 45 g portions) and the effluent collected. The washed atrazine/MIBK slurry was then transferred to a rotary evaporator and the solvent recovered at 80°C under vacuum. The wet atrazine was dried in a vacuum oven at 60°C before analysis by HPLC.[23]

2.3.4 Results obtained for the synthesis of atrazine using MIBK as solvent

Table 2.6 summarizes the results obtained when MIBK was used as solvent in the preparation of atrazine.

Table 2.6 Results obtained for the synthesis of atrazine using MIBK

Compound	Compostion (%)[a]	Technical specification
Atrazine	98.81	Minimum of 96%
Propazine	1.20	Maximum of 3% in total
Simazine	0	
Hydroxy-atrazine	0	Maximum of 1% in total
Hydroxy-simazine	0	

[a] Refers to the % of compound observed according to HPLC analysis , where 100% represents the total amount of sample injected.

$$\text{Crude yield (\%)} = \frac{\text{Mass (g) of total s-triazines synthesized}}{\text{Calculated amount (g) of atrazine according to mass of cyanuric chloride used}} \times \frac{100}{1}$$

The crude percentage yield % = 90.41% which was calculated from the mass of triazines recovered after synthesis in terms of the mass of cyanuric chloride used for the reaction:

2.4 Synthesis of mono-i, the intermediate

It was necessary to synthesize mono-i separately in order to provide positive identification of this intermediate during sample analyses.

2.4.1 Experimental procedure

The following procedure was used to synthesize the intermediate.

1. The reactor was charged with toluene (175 g). The solvent mixture was cooled to 5°C and cyanuric chloride (60 g) added. The stirring rate was kept at 700 rpm.
2. Isopropylamine (IPA 99%) (19.2 g) and sodium hydroxide (NaOH, 45%) (28.9 g) were added drop-wise and simultaneously from separate dropping funnels during 50 minutes.
3. The reaction mixture was agitated for a further 15 minutes.
4. The mixture was filtered to recover the solid.
5. The wet mono-i was dried in a vacuum oven at 80°C before analysis by HPLC.

Table 2.7 summarizes the obtained results.

Table 2.7: Results obtained for the preparation of mono-i.

Crude yield	**78.66 %**
Product Compostion	
Compound	**Amount (%)**
Mono-i	61.01
Propazine	0

It was found that mono-i hydrolyzes very rapidly in water. Hence the product was not washed with water and during analysis, the sample was prepared in 100% acetonitrile. (to prevent any hydrolysis). This intermediate was successfully isolated and analysed. The product recovered existed as a fine suspension which was difficult to filter. It was also possible to recrystallize it from dichloromethane. The intermediate was used to study the formation profiles of each side product and atrazine in further work. Figure 2.2 shows the GC-MS trace obtained for mono-i.

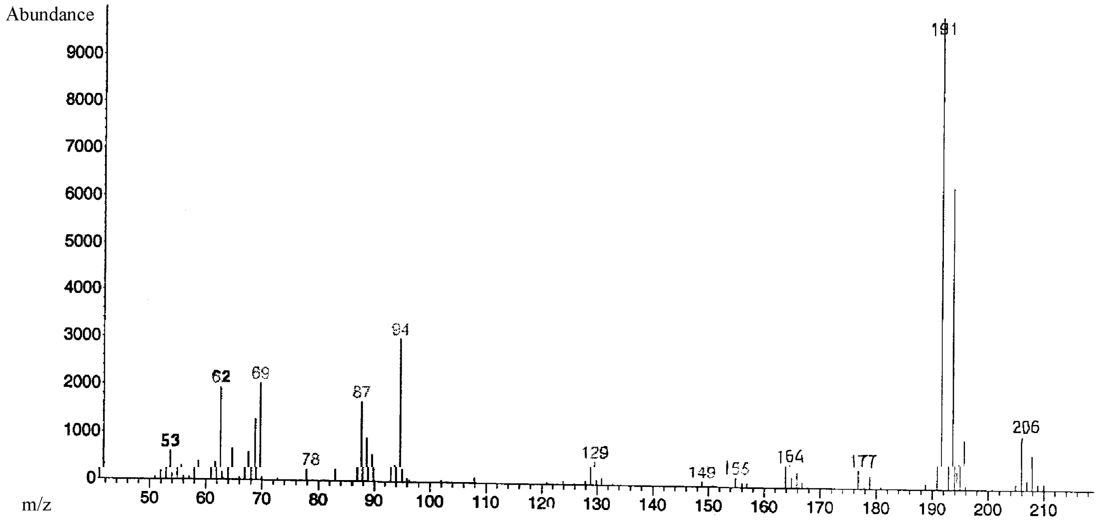


Figure 2.2 GC-MS of mono-i

2.5 Analytical techniques

The analytical technique of choice should allow complete separation of all the s-triazines of interest. In addition, the analytical responses for the individual components should be sufficient to allow accurate quantification of all components. This is especially important for the quantification of s-triazine impurities, which were present in small quantities in the product sample. The most suitable technique for these purposes was found to be high performance liquid chromatography (HPLC).

2.5.1 High performance liquid chromatography

HPLC analysis was performed on a Hewlett Packard Series 1100 equipped with a dual pump system, variable UV-visible wavelength detector and an auto sampler unit. HP Chemstation powers the LC software that allows for the accumulation of analytical data. HPLC grade solvent was used and was degassed prior to analysis with a Millipore vacuum-degassing unit. DI water and acetonitrile were used as the mobile phase, and isocratic elution formed the basis for the profile of the analysis. A 4.6 x 250 mm Waters Symmetry Shield RP_8 (serial no. T71701N04) was used for the analysis of the reaction samples.

The following conditions were used for the quantification of all five components normally found in atrazine samples:

- Injector volume: 10 microlitres
- Column: Waters Symmetry Shield RP_8 4.6 x 250 mm column
- Mobile phase: 50:50 acetonitrile/water mixtures
- Flow rate: 0.5 mL/min
- Total run time: 30 minutes
- UV detector wavelength: 240 nm

2.5.1.1 Preparation of sample solution

- 0.02 g of sample was weighed into a 100 mL volumetric flask and made to volume with a 50:50 acetonitrile/water mixture. The volumetric flask was then placed in an ultrasonic bath in order to aid dissolution of the sample.
- UV-visible spectra of all five components were recorded to allow the optimum wavelength for each component to be used during HPLC analyses.

2.5.2. Problems encountered during HPLC method development

2.5.2.1 Analyte stability

Initially, methanol was used instead of acetonitrile in the mobile phase for preliminary tests. GC-MS runs of the analyte solution showed that the components of the sample were reacting with the solvent medium (methanol and water) causing methoxylation of side products and starting material, which resulted in the formation of an ether group on the triazine ring. In order to eliminate this problem, acetonitrile was used and was found to be a more suitable solvent. Figure 2.3 is a GC-MS trace of the methoxylated triazine complex formed when atrazine is analysed on HPLC using methanol.

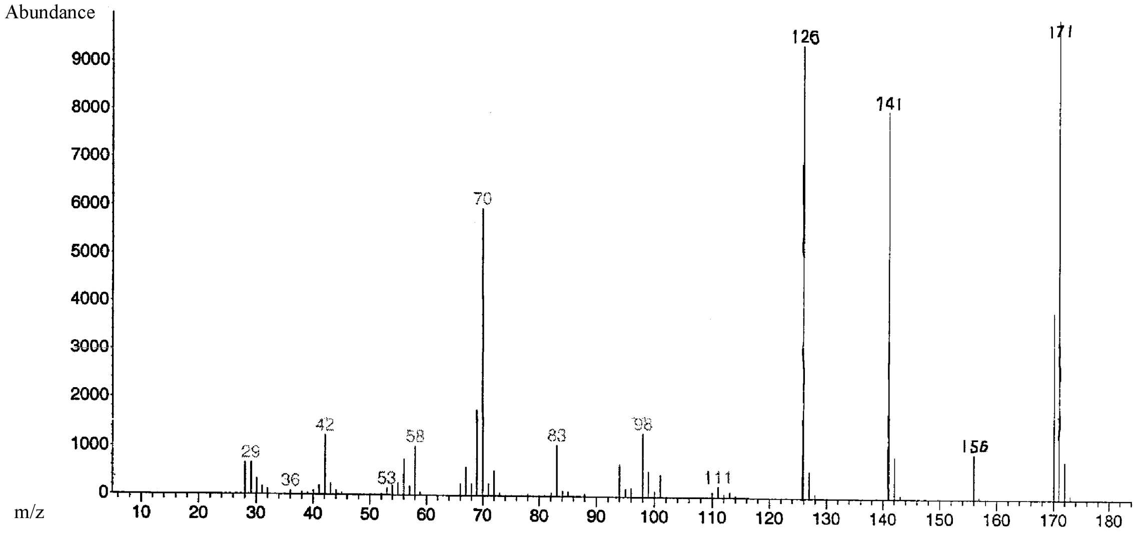


Figure 2.3 GC-MS showing a methoxylated triazine complex

2.5.2.2 Hydrolysis of cyanuric chloride and intermediate/s occurred

It was noted that rapid hydrolysis of the starting material and the intermediate occurred, both in the mobile phase during sample preparation and during the analysis. It was possible to quantify all of the components of the reaction except the starting material since cyanuric chloride was subject to hydrolysis, forming cyanuric acids.

2.5.3 Gas chromatography-mass spectrometry

GLC-MS Spectrometry was used to identify and confirm the composition of test samples. This analysis was performed on a Hewlett Packard 5890 series II Gas Chromatograph coupled to an HP 5972 series mass selective detector. The GC was equipped with an HP-5MS capillary column (30 m x 0.32 mm i.d.). Data were acquired from the detector by means of a Hewlett Packard personal computer equipped with HP G1034C software. Identification of cyanuric chloride, mono-i, atrazine and propazine was confirmed in this manner.

CHAPTER 3

SYNTHESIS OF ATRAZINE IN AQUEOUS MEDIA

3.1 General introduction

The ideal medium, in which a chemical reaction could take place, from an environmentally friendly point of view, is in water. This is provided that the product is completely recovered and none of the components of the reaction sequence escapes to form trace pollutants in the water, assuming water is the only "effluent".

Unfortunately this idea is not always practical, and invariably the next best option needs to be explored. To this end, a 10% sodium chloride solution, together with a particular choice of surfactant, was used to investigate the possibilities of this medium for the successful synthesis of atrazine. The surfactant was added in order to counteract hydrophobic properties of cyanuric chloride, which affected the availability of cyanuric chloride for the reactions.

The main objective for this section of work was to consider the possibility of synthesizing atrazine without the use of an organic solvent as part of the reaction matrix. Instead, a sodium chloride solution was used in order to prevent the hydrolysis of cyanuric chloride from occurring in water, before the amines and sodium hydroxide were added. As mentioned before, the MIBK that was used in the original process was soluble in water resulting in an undesired environmental hazard. Hence it was deemed necessary to investigate the reaction in a medium, which did not contain MIBK.

The basic advantages of using a surfactant in this system are:

- The process is organic solvent-free, and no solubility problems are introduced.
- The need for high temperature drying is eliminated.
- It is possible to choose a surfactant that is very selective or specific.

However some disadvantages do exist. Surfactants introduce problems of their own, such as for example, excess foaming, phosphate buildup, scum formation, and possible toxicity to the environment.

In order to investigate the effectiveness of surfactants, it was important to explore the properties of each of the various categories of surfactants. Surfactants are classified according to their electrochemical properties, namely:

- Anionic,
- Cationic,

- Non-ionic, and
- Amphoteric

An understanding of the properties of the surfactants would lead to an understanding of their interaction with the reaction matrix and how this would affect the yield of atrazine or influence the formation of other side products.

3.1.1 Surfactants in general[29-31]

Surfactants or surface-active agents are molecules with the following characteristics:

- An amphipathic structure: each molecule consists of groups of opposing solubility tendencies; a common example is an oil-soluble hydrocarbon chain and a water-soluble ionic group present in the same molecule.
- Solubility: a surfactant is soluble in at least one phase of a liquid system.
- Interface adsorption: the concentration of a surfactant at an interface is greater than its concentration in the bulk of the solution when at equilibrium.
- Interface orientations: these molecules and ions form monolayers at phase interfaces.
- Micelle formation: surfactants form aggregates of molecules or ions called micelles when the concentration of the surfactant in the bulk of the solution exceeds a limiting value - the critical micelle concentration.
- Functional properties: these include cleaning (detergency) ability, wetting, foaming, emulsifying, solubilizing and dispersing properties.

The most important characteristic of surfactants is that a single molecule contains two structurally dissimilar groups. A hydrophobic group, usually an aliphatic hydrocarbon residue with 10-18 carbon atoms or an alkylbenzene residue, is responsible for the surface activity. A hydrophilic group controls the solubility in water; this could be one of several groups, e.g. –COOH (soaps), $-OSO_3H$ (alkyl sulphates), $-SO_3H$ (alkane sulphonates) and ether-type oxygen bridges (non-ionic).

The surface activity of surfactants is determined by the makeup of the individual groups, solubility properties, relative size and location within the surfactant molecule. Surfactants that are effective wetting or emulsifying agents lower the surface tension in order to facilitate wetting.[29,31]

3.1.1.1 Anionic surfactants

This group of surfactants carries a negative charge on the active portion of the molecule, and these molecules are anion-active. The hydrophobic residues carry the anionic groups together with their small counter ions such as sodium, potassium or ammonium ions, which only influence the surface-active properties of the substance slightly. Examples of these surfactants are soaps, alkylbenzenesulphonates, alkyl sulphates and alkyl phosphates (Figure 3.1). Most anionic surfactants contain polar, solubilizing groups such as carboxylate, sulphonate, sulphate and phosphate groups.

Anionic surfactants are generally non-toxic to bacteria because they form neutral salts in surface waters. This group of surfactants is the most common in laundry detergents, dishwashing and general cleaning detergents. They have been categorized as having aquatic toxicity levels.[29-31]

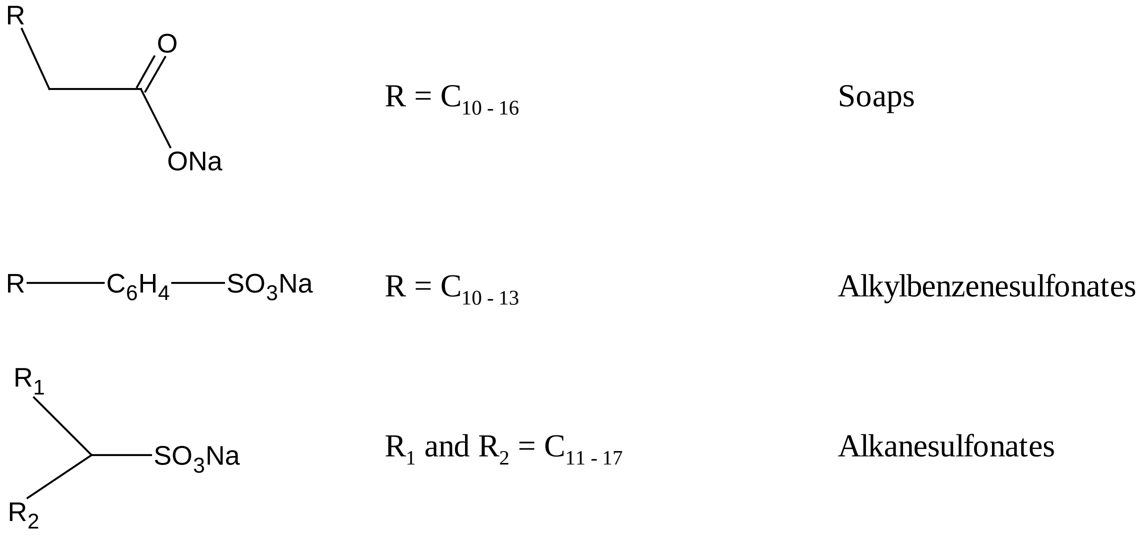
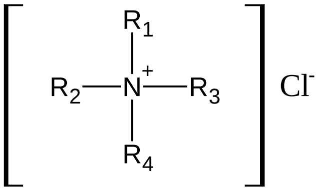


Figure 3.1 **Three examples of typical anionic surfactants**[28]

3.1.1.2 Cationic surfactants

This group of surfactants carries a positive charge on the active portion of the molecule, and these molecules are said to be cation-active, and exist as salts. The hydrophobic residues exist as cations with counter ions, e.g. chloride, sulphate, ammonium or acetate groups that also only influence active properties slightly. Examples of these surfactants are tetraalkyl ammonium chloride, N-alkylpyridinium chloride and quaternary nitrogen compounds (Figure 3.2).

These surfactants are used as microbicides, herbicides, corrosion inhibitors, oxidation inhibitors, adhesives, finishing and sizing agents, water repellants and fabric softeners, flotation aids, dispersants and leveling agents. Because of the positive charge, these allow for application in areas where ionic and non-ionic surfactants are less suitable. Their use is restricted to after treatment aids because these agents are incompatible with anionic surfactants. Cationic surfactants have a very high sorption power. They have been categorized as having aquatic toxicity levels.[29-31]


$$\left[R_2-\overset{R_1}{\underset{R_4}{N^+}}-R_3\right]Cl^-$$

$R_1, R_2 = C_{16-18}$

$R_3, R_4 = C_1$

Quaternary ammonium compounds such as tetraalkylammonium chloride

Figure 3.2 A typical example of a cationic surfactant[30]

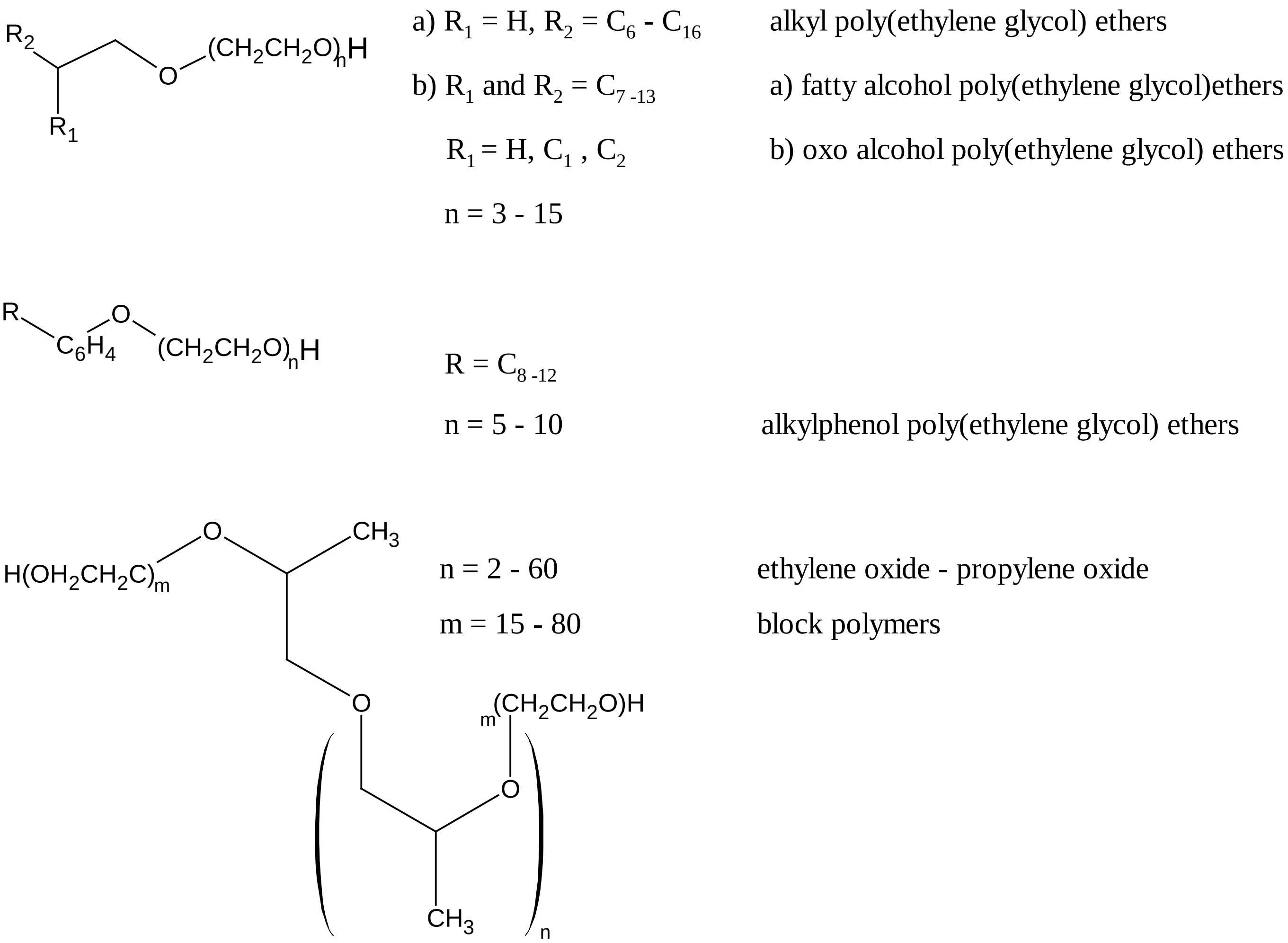
3.1.1.3 Non-ionic surfactants

These molecules are surfactants that carry no electrical charge, their water solubility being derived from the presence of polar functionalities capable of significant hydrogen bonding interaction with water. In other words, hydrophilicity in non-ionic surfactants is provided by hydrogen bonding with water molecules. Oxygen atoms and hydroxyl groups readily form strong hydrogen bonds, whereas ester and amide groups form hydrogen bonds less readily. These amphiphilic compounds are unable to dissociate into ions in aqueous solution. This is largely due to the special properties that non-ionic surfactants have, e.g.:

- The absence of electrostatic interactions,
- Behavior with respect to electrolytes,
- The possibility of favorable adjustment of hydrophilic-hydrophobic parameters, and
- Anomalous solubility.

For example alkyl polyglycol ethers do not dissociate in aqueous solution.

Some examples of these surfactants are alkyl and alkylphenyl polyethylene glycol ethers, fatty acid alkylolamides, sucrose fatty acid esters, alkyl polyglucosides and trialkylamine oxides (Figure 3.3).



a) $R_1 = H, R_2 = C_6 - C_{16}$ alkyl poly(ethylene glycol) ethers

b) R_1 and $R_2 = C_{7-13}$ a) fatty alcohol poly(ethylene glycol)ethers

$R_1 = H, C_1, C_2$ b) oxo alcohol poly(ethylene glycol) ethers

$n = 3 - 15$

$R = C_{8-12}$

$n = 5 - 10$ alkylphenol poly(ethylene glycol) ethers

$n = 2 - 60$ ethylene oxide - propylene oxide

$m = 15 - 80$ block polymers

Figure 3.3 Some examples of typical non-ionic surfactants[30]

Generally, non-ionic surfactants are less sensitive to water hardness than anionic surfactants. Aqueous solutions of non-ionic surfactants usually foam less than anionic surfactants.

The choice of non-ionic surfactant is usually governed by effectiveness, efficiency, toxicity, dermatological compatibility and biodegradability. These surfactants are generally non-toxic to bacteria and have a degree of biodegradability. Non-ionic surfactants are usually used in general cleaning detergents.

The reasons why non-ionic surfactants are usually favored have to do with their detergency properties with respect to synthesis, these being:

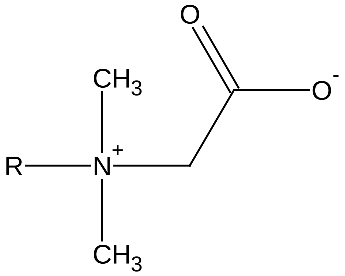
- Low critical micelle concentration,
- Very good detergency performance,
- Soil anti-redeposition characteristics with synthetic fibers,
- Tolerance to the presence of ionic and amphoteric surfactants,
- Existance as liquids and are not affected by hard water, and

- Can be used in either acidic or alkali media.[29-31]

3.1.1.4 Amphoteric surfactants

This category of surfactants has zwitterionic hydrophilic groups in its structure.

Examples are aminocarboxylic acids, betaines and sulfobetaines (Figure 3.4). They contain both an acidic and basic hydrophilic group. The electrical charge state depends on the pH of the solution.



$R = C_{12-18}$ alkylbetaines

Figure 3.4 An example of an amphoteric surfactant[30]

At low pH, these surfactants behave as cationic species, and at high pH as anionic species. The presence of an ether or hydroxyl group enhances the hydrophilicity of the molecule. The predominant functional groups are a basic nitrogen and an acidic carboxylate group. Amphoteric surfactants are sensitive to water hardness and are slightly toxic. They are however compatible with other surfactants, but are not as widely used as the other three types of surfactants already discussed. Instead, amphoteric surfactants are used in mixtures of surfactants to enhance desired effects. Amphoteric surfactants are generally considered specialty surfactants.[29-31] Table 3.1 lists the different surfactants investigated for a series of experiments, which were carried out to determine which of these allows the most promising conversion of cyanuric chloride to atrazine. A brief description and their ionic characteristics are also listed.

Table 3.1 The different surfactants investigated, and their characteristics [32,33]

Name of surfactant	Formula/Description	Category
Arkopon T Pulver hochkonz	Fatty acid methyl tauride sodium salt	Anionic
Aliquat 336	Fatty quaternary ammonium chloride: methyl tricaprylyl ammonium chloride or methyl trioctyl ammonium chloride	Cationic
Tetra Butyl Ammonium Hydrogen Sulphate (TBAHS)	$[CH_3(CH_2)_3]_4NHSO_4$	Cationic
Triton X100	Isooctylphenoxypolyethoxyethanol or [polyoxyethylene(10) isooctylphenyl ether] $4\text{-}(C_8H_{17})C_6H_4(OCH_2CH_2)_nOH$ $n = 10$	Non-ionic
Rhodafac PS/17	Polyoxyethylene alkylphenyl ether phosphate potassium salt	Non-ionic

3.2 The method used for the synthesis of atrazine using different surfactants[34]

In this section, the method used in order to observe trends in the yield of atrazine and other side products, when different surfactants were used are highlighted. Further reactions were done with modified versions of this method in order to emphasize how changes to the reaction conditions effect the performance of the surfactants, and consequently the yield of atrazine.

3.2.1 Chemicals for the synthesis

The quantities of chemicals used for the experiments are best described using Table 3.2:

Table 3.2 Chemicals quantities used in the reactions

Chemical	Quantity (g or mL)
10% Sodium Chloride (NaCl)	250 mL
Cyanuric Chloride	30 g
Surfactant added 1) Powder 2) Liquid	0.5 g 1.0 mL
20.2% Mono-isopropyl amine (IPA)	50 mL
10.0% Sodium Hydroxide (NaOH)	55 mL
39% Mono-ethylamine (MEA)	21.5 mL
10.1% Sodium Hydroxide (NaOH)	50 mL

3.2.2 General experimental procedure

The method described below describes the general experimental procedure for the results given in Table 3.3

- A 500 mL reactor was charged with 250 mL of a 10.0% NaCl solution and 30 g (0.163 mol) of cyanuric chloride was added to the reactor. The solution was cooled to 5°C and the overhead stirrer set to 700 rpm..
- 1 mL of the surfactant was added (if it is in a liquid form), or 0.5 g (if in powder form).
- IPA (0.170 mol) 50 mL of a 20.2% solution was added drop-wise over a period of 50 minutes.
- NaOH (0.138 mol) 55 mL of a 10.0% solution was added drop-wise over 50 minutes.
- MEA (0.130 mol) 21.5 mL of a 39% solution was added over a period of 50 minutes.
- NaOH (0.126 mol) 50 mL of a 10.1% solution was added for a time span of 40 minutes.
- The white sludge/slurry so-formed was filtered off using a Buchner funnel and 300 mL of water was used to wash the sludge and remove the foam.
- The resulting "cake" was dried in a vacuum oven overnight at 80°C and a sample of this product was then analyzed on the HPLC.

3.3.3 Various surfactants and the relative percentage atrazine obtained

The percentages shown below correspond to the composition of solid obtained from HPLC analyses (Table 3.3).

Table 3.3 Results obtained for the synthesis of atrazine using various surfactants

Surfactant	Category	**Atrazine %**	**Mono-I %**	**Propazine %**	**Simazine %**	**TOTAL**[a]
Arkopon T	Anionic	65.68	6.50	15.34	3.84	91.3
Aliquat 336	Cationic	47.02	5.13	29.15	8.63	89.9
TBAHS	Cationic	55.63	3.59	13.56	2.92	75.7
Triton X100	Non-ionic	42.23	2.93	34.01	17.85	97.0
Rhodafac	Non-ionic	67.50	3.95	18.52	3.55	93.6

[a] The total % selectivity is given in terms of the sum of four triazines; however this does not include unreacted cyanuric chloride and any hydroxy compounds formed.

Non-ionic Rhodafac yielded the most promising results; it was for this reason that Rhodafac was used in experiments dealing with other aspects discussed in the following sections. Cationic surfactants were not suitable for this reaction medium as seen by the poor yields obtained. Triton X100 seemed to favor the formation of molecules with two identical groups substituting chlorine groups on the triazine ring.

There were no significant improvements in the yield of atrazine despite the selection of surfactants used. Propazine is encouraged to form easily in significant quantities by each surface-active agent used. It is suspected that other factors like high agitation and lower cyanuric chloride loading could improve the yields of atrazine and help suppress the formation of propazine.

The anionic surfactant gave reasonable yields, though the reaction medium favored the formation of propazine. An explanation for this would be that if there was a large amount of propazine in the mixture, there would be a significant amount of unreacted cyanuric chloride in the reactor, and consequently, any MEA that is added would quickly react to form simazine. This is in agreement with the results obtained, i.e., 15.34% propazine and 3.84% simazine was obtained.

If the cyanuric chloride loading was decreased to 15 g, the quantities of the surfactant maintained and the concentrations of the amines and hydroxide adjusted accordingly, where the total volume of solution added was kept constant, the yield of atrazine was found to be 55.54%. This modification allowed one to observe more pronounced trends in the reaction matrix. In this case the yield of propazine was 13.80%, mono-i 11.41% and simazine 6.28%. This suggested that the intermediate was favorably converted by easily reacting to form propazine.

The yields obtained for a reaction using Arkopon T as the surfactant and 15 g cyanuric chloride were as follows: atrazine - 54.56%, propazine - 12.63%, simazine - 6.28% and mono-i -11.07%.

3.3 The effect of selected parameters

3.3.1 The effect of the volume of the surfactant

The effect of surfactant volume may best be described using the following Table of results (Table 3.4):

Table 3.4 Results obtained when varying the amount of Rhodafac

Volume of Rhodafac	% Atrazine	% Propazine	% Simazine	% Mono-i	TOTAL[a]
0.1 mL	62.63	21.90	8.4	3.2	96.1
1.0 mL	67.38	18.52	3.55	3.95	93.5
No surfactant	21.54	27.38	23.15	2.12	74.2
1.0 mL and 15 g cyanuric chloride	55.54	13.8	6.28	11.41	87.0

[a] The total % is given in terms of the sum of four triazines; however this does not include unreacted cyanuric chloride and any hydroxy compounds formed.

- From these results, it can be seen that the presence of a surfactant drastically improves the yield of atrazine formed.
- Increasing the volume of surfactant from 0.1 to 1.0 mL, where 30 g of cyanuric chloride was used, also resulted in an increased the yield of atrazine.

3.3.2 Solution additions

It was deemed necessary to investigate whether the addition of the amine solutions either consecutively or simultaneously with sodium hydroxide, would improve the reaction and afford desirable yields of atrazine (Table 3.5).

Table 3.5 Results for simultaneous and consecutive addition techniques

Addition Technique	% Atrazine	% Propazine	% Simazine	% Mono-i	TOTAL[a]
Simultaneous	**32.11**	**9.03**	**3.74**	**48.28**	**93.1**
Consecutive	**55.54**	**13.08**	**6.28**	**11.41**	**86.3**

[a] The total % is given in terms of the sum of four triazines; however this does not include unreacted cyanuric chloride and any hydroxy compounds formed.

It was found that the simultaneous addition did not favour the formation of atrazine, and consecutive addition was significantly better. These reactions where carried out using 15 g of cyanuric chloride and 1.0 ml of surfactant. Unfortunately not much improvement is seen by this, however if more time is allowed after addition for extra agitation, this could allow for the formation of the intermediate. The simultaneous addition is more promising from the viewpoint that in comparing that technique to consecutive addition, where the total time allowed is 4 hours, simultaneous addition is quicker (2 hours). As can be shown in the next paragraph, an extra 20 minutes stirring time makes a marked improvement on the yield of atrazine.

3.3.3 Stirring times

An extra stirring time of 20 minutes, when simultaneous addition was used, resulted in a marked improvement in the yield of atrazine. However, there was still a significant quantity of propazine in the reaction mixture (Table 3.6).

Table 3.6 Results obtained when a longer stirring time was used

% Atrazine	% Propazine	% Simazine	%Mono-i	TOTAL[a]
68.98	24.72	4.85	2.96	101.6

[a] The total % is given in terms of the sum of four triazines; however this does not include unreacted cyanuric chloride and any hydroxy compounds formed.

3.3.4 Reactions using a modified stirring rod

As mentioned previously, agitation plays a significant role when it comes to the synthesis of atrazine. In these reactions, the agitation was improved using a stirring rod that had two propellers on the shaft, in order to offer more mixing power than the one used up until this stage. One propeller was situated at the base of the rod and the other 5 cm higher. Table 3.7 summarizes the results obtained with this rod at two different stirring rates.

Table 3.7 Varying rates of stirring using a new stirring rod

Stirring rate (Rpm)	% Atrazine	% Propazine	% Simazine	% Mono-i	TOTAL[a]
700	68.05	2.98	4.9	2.98	79.0
1500	75.97	16.65	2.35	4.39	99.5

[a] The total % is given in terms of the sum of four triazines; however this does not include unreacted cyanuric chloride and any hydroxy compounds formed.

Increasing the stirring rate from 700 rpm to 1500 rpm showed a marked improvement in the yield of atrazine.

3.3.5 The effect of the NaCl concentration on the reaction matrix

Drastic changes in the salt concentration during the reaction or before reaction have little or no effect on the yield of atrazine. The results of these experiments are shown in Table 5.8:

Table 3.8 Results obtained when varying the NaCl concentration in the reaction medium

NaCl concentration	Atrazine %	Propazine %	Simazine %	Mono-i %	TOTAL*
0 %	69.52	19.05	3.78	4.5	96.9
10 %	66.98	24.72	4.85	2.96	99.6
20 %	69.25	22.14	4.6	3.3	99.3

3.4 Reaction profile diagrams

3.4.1 Construction of reaction profile diagrams for NaCl and toluene media.

In order to observe and explain the sequence of events that occur in the reaction vessel when IPA was added to the 10% NaCl and cyanuric chloride (with a surfactant) medium, several samples were taken during the first step of this reaction in order to construct a reaction profile diagram which could help explain the trends observed so far.

In all the reactions performed up to this point, the formation of propazine was highly favored, suggesting that the mono-i intermediate became more reactive than cyanuric chloride at some stage during the reaction. Two reaction profiles were constructed to test this theory, one in a 10% NaCl solution using Rhodafac as surfactant and the other in the presence of an organic solvent, toluene. During these experiments, the disappearance of mono-i and the formation of propazine was monitored during the simultaneous addition of IPA and NaOH to a mixture containing equimolar amounts of cyanuric chloride and mono-i. In this way, it was possible to compare the relative reactivities of cyanuric chloride and mono-i in two different reaction mediums.

The procedure used for the aqueous medium is summarized below:

- 250 mL of a 10% NaCl solution was prepared.
- 7.5 g each of mono-i and cyanuric chloride (0.045 and 0.042 moles respectively) were weighed and ground into a fine powder, and then added to the reactor.
- 1 mL of Rhodafac was added.
- IPA (0.085 moles in 50 mL water) and NaOH (0.07 moles in 55 mL water) solutions were prepared and these added simultaneously.

The procedure used when toluene was the solvent:

- A 50:50 (m/m) mixture of cyanuric chloride (0.042 moles) and mono-i (0.045 moles) were added to 175 g toluene.
- IPA (0.085 moles in 50 mL water) and NaOH (0.076 moles in 55 mL water) were added simultaneously.
- Samples were analyzed on the HPLC.

Note: 1.0 mL samples were taken as the addition was started, these taken at 5 minute intervals. Each 1.0 mL sample was made up to 50 mL using a 50:50 acetonitrile/water mixture. Addition of the reactants took 50 minutes to complete, followed by an additional 20 minutes stirring (700rpm).

The following product distribution diagrams show the results obtained (Figure 3.5 and 3.6):

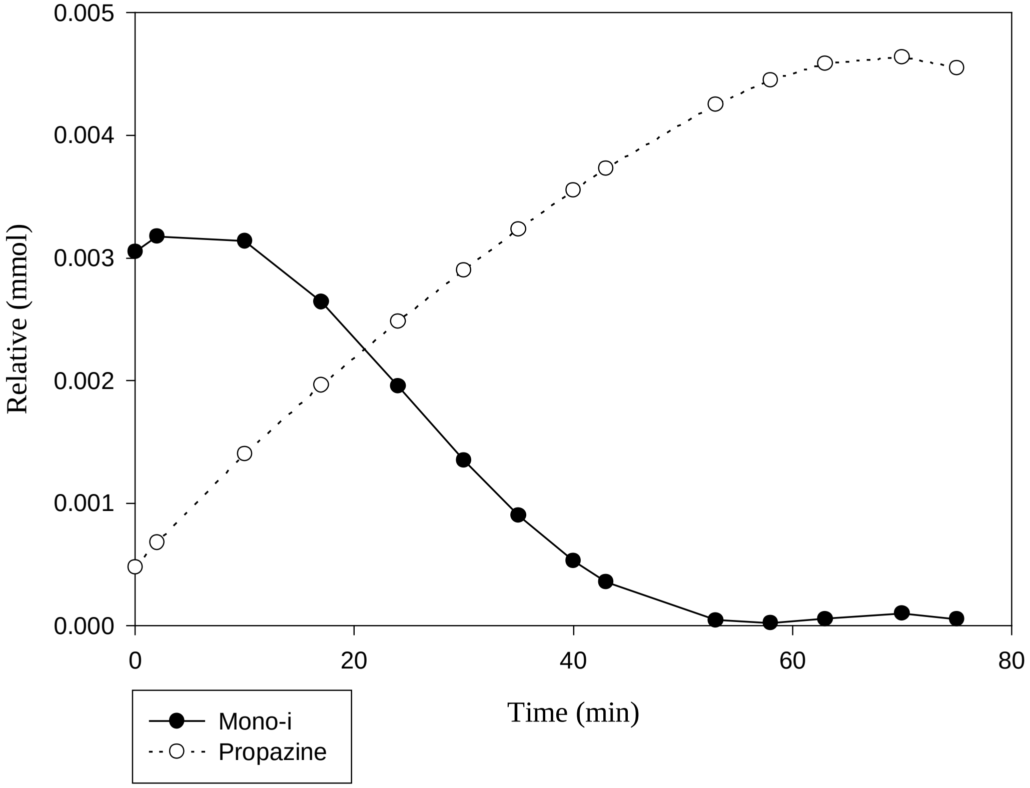


Figure 3.5 Reaction profile diagram for the reaction of IPA with an equimolar ratio of cyanuric chloride and Mono-i in a 10% NaCl medium

Figure 3.6 Reaction profile diagram for the reaction of IPA with an equimolar ratio of cyanuric chloride and mono-i in a medium of toluene

In these reactions it may be expected that the preferential reaction of IPA with cyanuric chloride will result in an initial increase in mono-i before propazine build-up is observed. Conversely, preferential reaction of IPA with mono-i will result in a continuous build-up in propazine from the moment of IPA addition onwards. From Figure 3.5 it is clear that IPA preferentially reacts with mono-i, no increase in the initial mono-i amounts and a continuous, rapid build-up in propazine. For the reaction in toluene, however there is a clear and sharp increase in mono-i as IPA is added, in stark contrast with the results obtained for the aqueous medium. These results, therefore, strongly indicate that the displacement of one chloride on cyanuric chloride by IPA makes the resulting mono-i intermediate more “wettable” by the surfactant leading to its preferential reaction with IPA to form propazine.

3.4.2 Summary

In view of the results described in the preceding sections, the successful production of atrazine from cyanuric chloride in aqueous media and in the presence of a surfactant appears to be extremely unlikely. The main reason for this is that the first reaction intermediate, mono-i, is made more reactive than the starting material due to its wettability, hence availability for reaction, in the presence of a surfactant. The use of different types, and varying amounts of surfactant does not appear to affect these observations. These observations also explain the relatively large amounts of propazine and simazine formed during these reactions. In view of these findings, further work will concentrate on the use of an organic solvent for the said synthesis.

CHAPTER 4

SYNTHESIS OF ATRAZINE IN NON-AQUEOUS MEDIA – TOLUENE

4.3 General

In this part of the investigation, the use of alternative organic solvents for the production of atrazine was considered. The main motivation for using a solvent was that current production facilities could easily be adapted to a new solvent. Given the main disadvantages of MIBK as reaction solvent, an alternative solvent should preferably be less soluble in water and should be easily recovered before the final product is washed and dried. Toluene was considered as the solvent of choice because it is currently being used by other atrazine producers, and because the resultant atrazine product is said to have desirable properties, required for product formulation.

4.1.1 Methodology

Initially MIBK was used in a test reaction in order to replicate the method used by Dow AgroSciences to produce atrazine. The results of the experiment have been given elsewhere (Section 2.3.3).

Due to the differences in properties between toluene and MIBK (Table 4.1), it was initially necessary to use different reaction conditions for the two solvents (Table 4.2). The main difference was the loading of the cyanuric chloride used in toluene, approximately 40% of the loading in MIBK. This was done in order to get as close to a homogeneous solution as possible, which was necessary for the calorimetric work described later in this chapter. The effect of higher substrate loading, effectively slurries of cyanuric chloride in toluene, will be considered separately.

Table 4.1 Physical properties of solvents MIBK and toluene[35]

Solvent Properties	**MIBK**	**Toluene**
Molecular formula	$C_6H_{12}O$	C_7H_8
Molecular weight	100.16	92.14
Boiling Point (^oC)	117	111
Density ($20^oC – 4^oC$)	0.801	0.867
Flash point ^oC	16	6
Solubility	H_2O (slightly soluble); ethanol (miscible); ether (miscible); acetone (miscible)	H_2O (insoluble); ethanol (miscible); ether (miscible) acetone (soluble)
Solubility in water	19 g/L (at 20^oC)	0.05 g/L (at 20^oC)

Table 4.2 Comparison of methods: MIBK and toluene methods

MIBK Method	Chemical Compound	Toluene Method
----	Toluene	175 g
90 g	MIBK	----
85 g	Water	----
60 g	Cyanuric Chloride	24.5 g
19.2 g (in 30 mL water)	IPA	8.0g (in 4.1mL H_2O)
21.4 g (in 25 mL water)	MEA	8.6g (in 4 mL H_2O)
28.9 g	NaOH (1)	5.4 g
29.8 g	NaOH (2)	5.4 g
250 mL reactor		500 mL reactor
Stirrer at 600 rpm		Stirrer at 750 to 800 rpm
Temperature Range 0°C to 35°C		Temperature Range 5°C to 30°C
Wash with water in a separating funnel		Rotovap to remove Toluene
Rotovap to dryness		Filter off and wash with water at 60°C
Vacuum oven at 60°C		Vacuum oven at 60°C

4.1.2 Characteristics of cyanuric chloride

The following points regarding cyanuric chloride and its utilization were useful in order to develop an understanding of how this starting material behaves chemically in different chemical environments.

- Cyanuric chloride usually reacts in a similar fashion to an acid chloride with the formation of hydrogen chloride.
- A suspension of cyanuric chloride in ice water remains fairly stable for 12 hours. It is this temporary stability at low temperatures that makes several processes involving this chloride, e.g. reaction with primary and secondary amines, possible.
- At 30°C, more than 40% of the compound is hydrolyzed within 1 hour to cyanuric acid.

- With water, cyanuric chloride is hydrolyzed to cyanuric acid. The hydrolysis takes place in stages, with all three chlorine atoms of the molecule being substituted at different rates. Figure 2.1 below illustrates this.

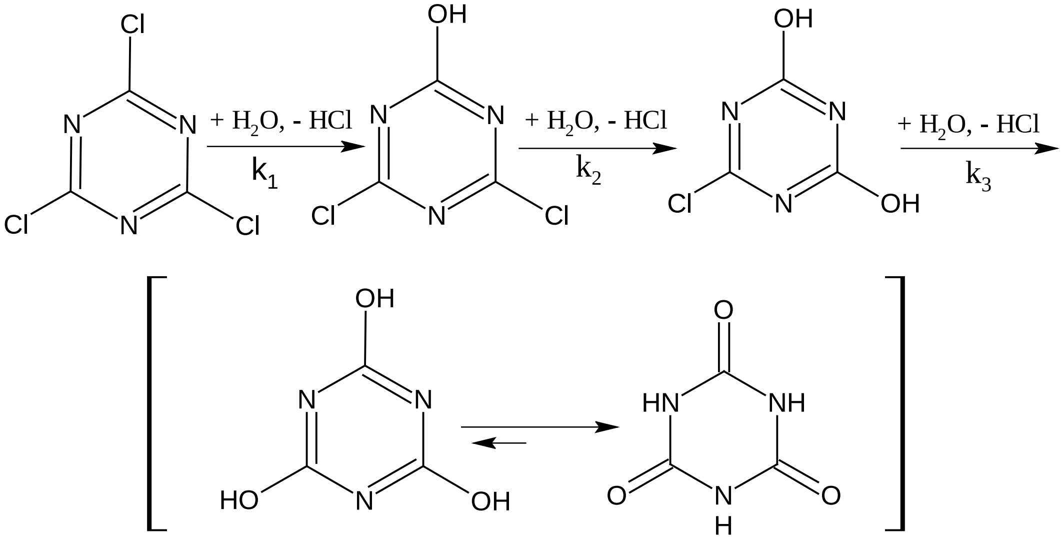


Figure 4.1 **Successive hydrolysis of cyanuric chloride**

- NaOH, sodium hydrogen carbonate, disodium hydrogen phosphate and tertiary amines can be used as HCl scavengers during reactions with amines to facilitate the substitution with amines.
- Solvents such as acetone, methyl ethyl ketone or toluene are often used for reactions of cyanuric chloride with amines.
- Cyanuric chloride is usually dissolved/suspended in the solvent with the nucleophile and treated with aqueous NaOH.
- Care must be taken to neutralize the liberated hydrochloric acid and to dissipate the heat of reaction; otherwise the exothermal substitution of cyanuric chloride ($\Delta H =$ -2164 kJ/kg) may become uncontrollable.
- Hydrolysis is accelerated by water-miscible solvents and occurs more rapidly at low pH values.
- Hydrolysis caused by improper handling may result in contamination with cyanuric acid, which is found as insoluble matter in dried solvents such as toluene. Cyanuric chloride should be stored in strictly dry conditions, and in a cool place to avoid clumps of powder forming.[26,36]

4.1.3 Toxicology

Cyanuric chloride strongly irritates the skin, mucous membranes, including those of the eyes, and the respiratory and gastrointestinal tracts. The 1-minute threshold irritation effect on mucous membranes is produced by 0.3mg/m^3. Allergic reactions are possible, and so direct contact with cyanuric chloride should be avoided, and ventilation is necessary.[26]

4.2 Parameters investigated

Several possible modifications to the synthetic method in toluene were investigated to determine the effect on the atrazine yield and purity. These were:

- Order of amine and hydroxide addition,
- Method of product isolation,
- Cyanuric chloride loading,
- Reaction temperature, and
- Other amine addition sequences

4.7.12 Order of amine and hydroxide addition

4.2.1.1 NaOH before IPA and again before MEA

NaOH was added to the reaction mixture in two batches, one before each amine. Mixing was difficult because, on addition of NaOH, during the first batch, globules of cyanuric chloride formed inside the reaction mixture, hampering the efficiency of the IPA reaction.

4.2.1.1.1 Experimental procedure

The method used for this experiment is described in the following stepwise sequence:

1 A 500 mL glass reactor connected to an external chiller unit and fitted with an overhead stirrer, agitator (700 rpm) and thermometer, was charged with toluene (175 g). The solvent mixture was cooled to 5^{o}C and cyanuric chloride (24.5 g; 0.133 mol) was added.

2 Sodium hydroxide (NaOH, 45%) (5.4 g; 0.14 mol) was added from a dropping funnel during 5 minutes at a reaction temperature of 5^{o}C.

3 Isopropylamine (IPA, 99%) (8.0 g; 0.13 mol) was added drop-wise from a dropping funnel during 8 minutes.

4 Sodium hydroxide (NaOH, 45%) (5.4 g; 0.14 mol) was added from a dropping funnel during 7 minutes at a reaction temperature of 25^{o}C.

5 Monoethylamine (MEA, 70.4%) (6.0 g; 0.11 mol) was added drop-wise from a dropping funnel during 7 minutes.

6 The reaction mixture was agitated for a further 15 minutes.

7. The mixture was filtered to recover the slurry.

8. The wet atrazine was dried in a vacuum oven at 80^{o}C and analyzed by HPLC (Table 4.3).

Table 4.3 Results obtained for the experiment: NaOH before IPA and MEA

Crude Yield*	**72.57 %**
Product Composition	
Compound	**Amount (%)**
Atrazine	40.34
Propazine	1.16
Simazine	18.7
Observed Reaction Temperatures	
Step one: addition of NaOH and IPA	**Temperatures (°C)**
Temperature before NaOH	5
Temperature after addition of NaOH	7
Temperature before addition of IPA	7
Temperature after addition of IPA	15
Step two: addition of NaOH and MEA	
Temperature before NaOH	25
Temperature after addition of NaOH	24
Temperature before addition of MEA	23
Temperature after addition of MEA	29

*Crude yield percentage is defined as:

$$\text{Crude yield (\%)} = \frac{\text{Mass (g) of total s-triazines synthesized}}{\text{Calculated amount (g) of atrazine according to mass of cyanuric chloride used}} \times \frac{100}{1}$$

The composition of the crude product in these results is expressed in terms of the area percentages from HPLC analysis.

A low yield was obtained when NaOH was introduced before each amine. Not only did little atrazine form, but these results suggest that there was a significant amount of unreacted cyanuric chloride in the reaction mixture. The formation of simazine was largely favored, suggesting that the initial presence of NaOH hampers the initial substitution of a chlorine by IPA. This is probably a direct consequence of the reduced mixing efficiency caused by the lumping of cyanuric chloride upon addition of NaOH.

4.2.1.2 NaOH after IPA and again after MEA

NaOH was added to the reaction mixture in two batches as before, but only after the addition of each amine was completed.

4.2.1.2.1 Experimental procedure

The method was similar to the one described for the previous experiment (Section 4.2.1.1.1), with some modifications which are shown in Table 4.4, and the results in Table 4.5:

Table 4.4 Modifications made to the experiment

Step No.	Description
2	IPA (99%) (8.0 g; 0.13 mol) was added over a duration of 8 minutes at a reaction temperature of 4°C
3	NaOH (45%) (5.4 g; 0.135 mol) was added over a duration of 5 minutes at a reaction temperature of 10°C
4	MEA (70.4%) (8.6 g; 0.135 mol) was added over a duration of 6 minutes and the reaction temperature was allowed to increase to 25°C
5	NaOH (45%) (5.4 g; 0.135 mol) was added over a duration of 4 minutes
6	The mixture was agitated for a further 15 minutes at 20°C and worked up as described previously (Section 4.2.1.1.1).

Table 4.5 Results obtained for the experiment: NaOH after IPA and again after MEA

Crude Yield	**85.50 %**
Product Composition	
Compound	**Amount (%)**
Atrazine	77.9
Propazine	3.44
Simazine	17.73
Observed Reaction Temperatures	
Step one: addition of IPA and NaOH	**Temperatures (°C)**
Temperature before IPA	4
Temperature after addition of IPA	13
Temperature before addition of NaOH	10
Temperature after addition of NaOH	16
Step two: addition of MEA and NaOH	
Temperature before MEA	26
Temperature after addition of MEA	29
Temperature before addition of NaOH	25
Temperature after addition of NaOH	29

A significant improvement in the amount of atrazine in the crude reaction product was observed using this method compared to the previous experiment; however, propazine and simazine were still formed in large quantities. The improved productivity, as measured by the increase in the amount of atrazine formed, is probably related to the observation that, at the rate of stirring employed, a colloidal suspension could be maintained for each addition without forming large masses in the reactor.

4.2.1.3 Effect of addition rates/ reagent concentrations

The order of addition of reagents described in the preceding run was repeated, but the rate of their addition was decreased significantly.

4.2.1.3.1 Experimental procedure

A similar experimental procedure as those described before (Section 4.2.1.1.1) was followed; changes made are shown in Table 4.6:

Table 4.6 A description of the modifications introduced to accommodate a slower addition rate for the reactants

Step No.	Description
2	IPA (99%) (8.0 g; 0.133 mol) was added over a duration of 25 minutes at a reaction temperature of 4°C
3	NaOH (45%) (5.4 g; 0.139 mol) was added over a duration of 12 minutes, the temperature of the reaction was allowed to increase to 15°C
4	MEA (70.4%) (8.6 g; 0.135 mol) was added over a duration of 15 minutes at a reaction temperature of 15°C
5	NaOH (45%) (5.4 g; 0.135 mol) was added over a duration of 10 minutes
6	The reaction mixture worked up as described previously (Section 4.2.1.1.1)

Results obtained for this experiment are summarized in Table 4.7:

Table 4.7Results obtained when using slower addition rates for the reactants

Crude Yield	**75.80 %**
Product Composition	
Compound	**Amount (%)**
Atrazine	97.46
Propazine	<0.1
Simazine	<0.1
Observed Reaction Temperatures	
Step one: addition of IPA and NaOH	**Temperatures (°C)**
Temperature before IPA	4
Temperature after addition of IPA	5
Temperature before addition of NaOH	3
Temperature after addition of NaOH	8
Step two: addition of MEA and NaOH	
Temperature before MEA	15
Temperature after addition of MEA	18
Temperature before addition of NaOH	17
Temperature after addition of NaOH	19

A significant improvement in the amount of atrazine present in the crude product (97%) was observed as the addition rates were decreased. Consequently, impurities were significantly reduced. As a result of the slow rates of addition, the reaction temperature during the addition of reactants varied little.

4.2.1.4 Simultaneous addition of amines and hydroxide

Although slower addition rates resulted in significantly improved performance, overall reaction times became very long. To decrease the overall reaction time, an addition sequence where amine was added over a short period, followed by the simultaneous addition of amine and base thereafter, was investigated.

4.2.1.4.1 Experimental procedure

The following modifications shown in Table 4.8 were made to the standard method (Section 4.2.1.1.1):

Table 4.8 Modifications introduced to the method when the reactants were added simultaneously

Step No.	Description
2	IPA (7.86 g; 0.133 mol) and NaOH (5.4 g; 0.135 mol) were added simultaneously over 35 minutes
3	The reaction temperature was allowed to increase to 15^{o}C
4	MEA (8.6 g; 0.13 mol) and NaOH (5.4 g; 0.135 mol) were added simultaneously over 32 minutes
5	The reaction mixture was worked up

Results obtained for this experiment are summarized in Table 4.9:

Table 4.9 Results obtained for the simultaneous addition of the reactants

Crude Yield	**80.84 %**
Product Composition	
Compound	**Amount (%)**
Atrazine	95.79
Propazine	0
Simazine	3.57
Observed Reaction Temperatures	
Addition Steps	**Temperatures (^{o}C)**
Temperature before IPA and NaOH addition	5
Temperature after addition of IPA and NaOH	5
Temperature before addition of MEA and NaOH	15
Temperature after addition of MEA and NaOH	15

Despite the high atrazine content in the crude reaction product for the consecutive addition experiment, the actual mass recovered was relatively low (Table 4.7, 76%) in comparison to that obtained for the simultaneous addition reaction (Table 4.9, 81%). For this reason, it was decided to concentrate on simultaneous additions. The loss of product was thought to occur during the washing process where deionized water, heated to 60°C, was used. Temperature fluctuations during this reaction were minimal for both sets of additions, allowing for a more temperature-stable medium, as this was essential to control the selective substitution sequence of chlorine.

4.2.2 Method of product isolation

The experiment described in Section 4.2.1.4.1 was repeated but the final product that was recovered after the reaction was washed with cold water (20°C) rather than warm water (60°C). The remaining supernatant liquid after filtration was re-extracted with 200 mL of toluene in order to recover any residual product; the toluene was then re-filtered. Results are shown in Table 4.10.

Table 4.10 Results obtained using a cold water wash

Crude Yield	**81.09 %**
Product Composition	
Compound	**Amount (%)**
Atrazine	98.61
Propazine	0
Simazine	0
Hydroxy-Atrazine	0.3
Hydroxy-Simazine	0

Bearing in mind that 24.5 g of starting material was used and 81% of the product was recovered despite a relatively large hold-up of crude product in the equipment used, it was thought that the use of a larger substrate loading should lead to improved recoveries. At this stage, the atrazine content of the crude product was 99% with only trace amounts of impurities present. Results obtained thus far were comparable to those obtained from the reaction carried out in MIBK, the only difference being the quantity of cyanuric chloride used.

4.2.3 Cyanuric chloride loading

This is a repeat of the experiment described in Section 4.2.2 (simultaneous addition with a cold water wash), but the volume of cyanuric chloride was increased from 24.5 g to 60 g (0.33 mol). The volumes of amines and hydroxide were adjusted accordingly. The supernatant was re-extracted with toluene in order to recover any lost product from the first filtration.

4.2.3.1 Experimental procedure

The following modifications were made to the standard method described previously (Table 4.11).

Table 4.11Modification made when using 60 g cyanuric chloride

Step No.	Description
2	IPA (99%) (19.2 g; 0.324 mol) and NaOH (45%) (28.9 g; 0.326 mol) were added simultaneously over 40 minutes
3	The reaction temperature was allowed to increase to 15^{o}C
4	MEA (70.4%) (21.4 g; 0.336 mol) and NaOH (45%) (29.8 g; 0.336 mol) were added simultaneously over 30 minutes
5	After agitating the reaction mixture for 15 minutes, the general isolation procedure was followed.

Results so obtained are summarized as follows (Table 4.12):

Table 4.12 Results obtained when a higher substrate loading is used

Crude Yield	**92.32 %**
Product Composition	
Compound	**Amount (%)**
Atrazine	82.77
Propazine	0
Simazine	0
Hydroxy-Atrazine	4.51
Hydroxy-Simazine	0.32
Observed Reaction Temperatures	
Step One: addition of IPA and NaOH	**Temperatures (^{o}C)**
Temperature before IPA and NaOH addition	6
Temperature after addition of IPA and NaOH	15
Step Two: addition of MEA and NaOH	
Temperature before addition of MEA and NaOH	10
Temperature after addition of MEA and NaOH	15

The handling of the larger mass of cyanuric chloride required more care during the addition of the amines and NaOH in order to keep the reaction temperature within specified limits. This experiment showed a good crude recovery of 92%, but the atrazine content was only 83%. As the results show, hydroxy products were encouraged to form during this reaction. This was found to occur when hydrolysis was promoted during stages in the reaction where the temperature fluctuated above 5°C.

4.2.4 Reaction temperature

Two reactions were carried out at –5°C for the first step and 10°C for the second step. The same general procedure was followed as in prior reactions where simultaneous additions were used.

The results obtained are shown in Table 4.13.

Table 4.13 Results obtained for low temperature reactions

Crude yield (%)	109.72	102.44
Product Composition		
Compound	**Amount (%)**	**Amount (%)**
Atrazine	81.96	86.04
Simazine	1.58	3.42
Propazine	15.1	6.44
Hydroxy-atrazine	0	0
Hydroxy-simazine	0.25	0
Mono-i	0.86	1.26

A significantly large amount of propazine was formed during these reactions. This would suggest that a slightly higher temperature would be the best operating temperature to work at. When comparing the results obtained for reactions carried out at 5°C to these reactions, it can be seen that no mono-i or hydroxy products formed and comparatively less propazine and simazine were produced.

4.2.5 Other amine addition sequences

A reaction was carried out in which a slight modification was made in the addition of the amines. IPA was added alone for a minute before the NaOH addition was started. The NaOH, however, was introduced into the reactor at a rate approximately twice as fast as the IPA addition in order to prevent a larger volume of NaOH having to be added after the addition of IPA was complete. It was thought that this sequence of addition would minimize the quantity of hydroxy product formed during the reaction.

4.2.5.1 Experimental procedure

The same experimental procedure used for a simultaneous addition (Section 4.2.1.4.1), and quantities of reactants for the reaction using 60 g of cynauric chloride (Section 4.2.3.1) were followed. Each set of additions took 20 and 18 minutes to complete, respectively. Table 4.14 shows the results.

Table 4.14 Results obtained for the one minute amine addition

Crude Yield	**96.59 %**
Product Composition	
Compound	**Amount (%)**
Atrazine	95.9
Propazine	2.42
Simazine	0.42
Hydroxy-Atrazine	0
Hydroxy-Simazine	0
Observed Reaction Temperatures	
Step One: addition of IPA and NaOH	**Temperatures (^oC)**
Temperature before IPA and NaOH addition	5
Temperature after addition of IPA and NaOH	17
Step Two: addition of MEA and NaOH	14
Temperature before addition of MEA and NaOH	30
Temperature after addition of MEA and NaOH	5

The crude yield increased to 97% with an atrazine content of 96%. No hydroxy products were observed in the HPLC traces of the crude product.

4.3 Confirmation of reaction parameters

A full experiment was carried out, taking into account all the modifications made to the reaction. It was performed several months after the initial trial experiments and allowed for confirmation of the versatility of the reaction. At this point, a modified method for the synthesis of atrazine in toluene can be described. The results were used in the mass balance shown in Section 4.4.

4.3.1 The modified method for the synthesis and isolation of atrazine

The method used for the modified experiment is described in the following stepwise sequence:

1. The cooling bath was set to a temperature of 0°C; this was done in order to ensure that a reaction temperature no greater than 5°C is maintained.
2. The reactor was charged with 175 g toluene and 60 g (0.33 mol) cyanuric chloride.
3. A solution of IPA, 19.2 g (0.325 mol) in 10 mL water, was prepared.
4. A solution of NaOH, 28.9 g (0.325 mol) in 64 mL water, was prepared.
5. The IPA and NaOH solutions were added drop-wise to the reactor, starting initially with the addition of IPA alone for an interval of 1 minute, and then commencing the simultaneous addition of the NaOH solution.
6. A solution of MEA, 21.4 g (0.333 mol) in 10 mL water, was prepared.
7. A solution of NaOH, 29.8 g (0.336 mol) in 66 mL water, was prepared.
8. The reactor temperature was set to 15°C.
9. The MEA and NaOH solutions were added drop-wise to the reactor, starting with the addition of MEA for an interval of 1 minute, followed by the simultaneous addition of the NaOH solution.
10. A mixing period of 15 minutes was allowed after the addition was complete.
11. The content of the reactor was transferred to a round bottomed flask; the reactor was rinsed with approximately 60 mL of toluene, and these washings were added to the flask.
12. The flask was placed on a rotovap and most of the toluene distilled off at 60°C (140 mbar).
13. Water (400 mL at 25°C) was poured into the flask in order to dissolve the NaCl formed.
14. The slurry was filtered to recover the product, and the supernatant re-filtered.
15. The semi-dry product was transferred to an evaporating dish and placed in a vacuum oven at 90 – 100 °C. The results of this experiment are summarized in Table 4.15.

Table 4.15 Results obtained for the modified method of synthesis of atrazine

Crude Yield	**109.67 %**
Product Composition	
Compound	**Amount (%)**
Atrazine	97.62
Propazine	1.27
Simazine	1.10
Hydroxy-Atrazine	0
Hydroxy-Simazine	0

The results obtained show this procedure to be viable and effective for the synthesis of atrazine in toluene with minimal side product formation. The fact that the crude yield exceeds 100% can possibly be attributed to residual NaCl that was not completely removed during the washing process. These results fall well within the specifications outlined by the chemical company concerned.

4.4 Mass Balance

4.4.1 General

The complete accounting of all mass in a chemical process referred to as a material or mass balance, is required to bring a chemical reaction from an idea to a larger scale commercial process. In a batch or semi-batch process, the chemicals are added to the reactor in one or more operations, and this type of process best describes the synthesis of atrazine carried out in our laboratories.[37]

The material balance for such cases is given by:

Accumulation of atomic species in the system = Total atomic species entering system - Total atomic species leaving the system

A complete experimental mass balance for the atrazine synthesis is shown in Figure 4.2.

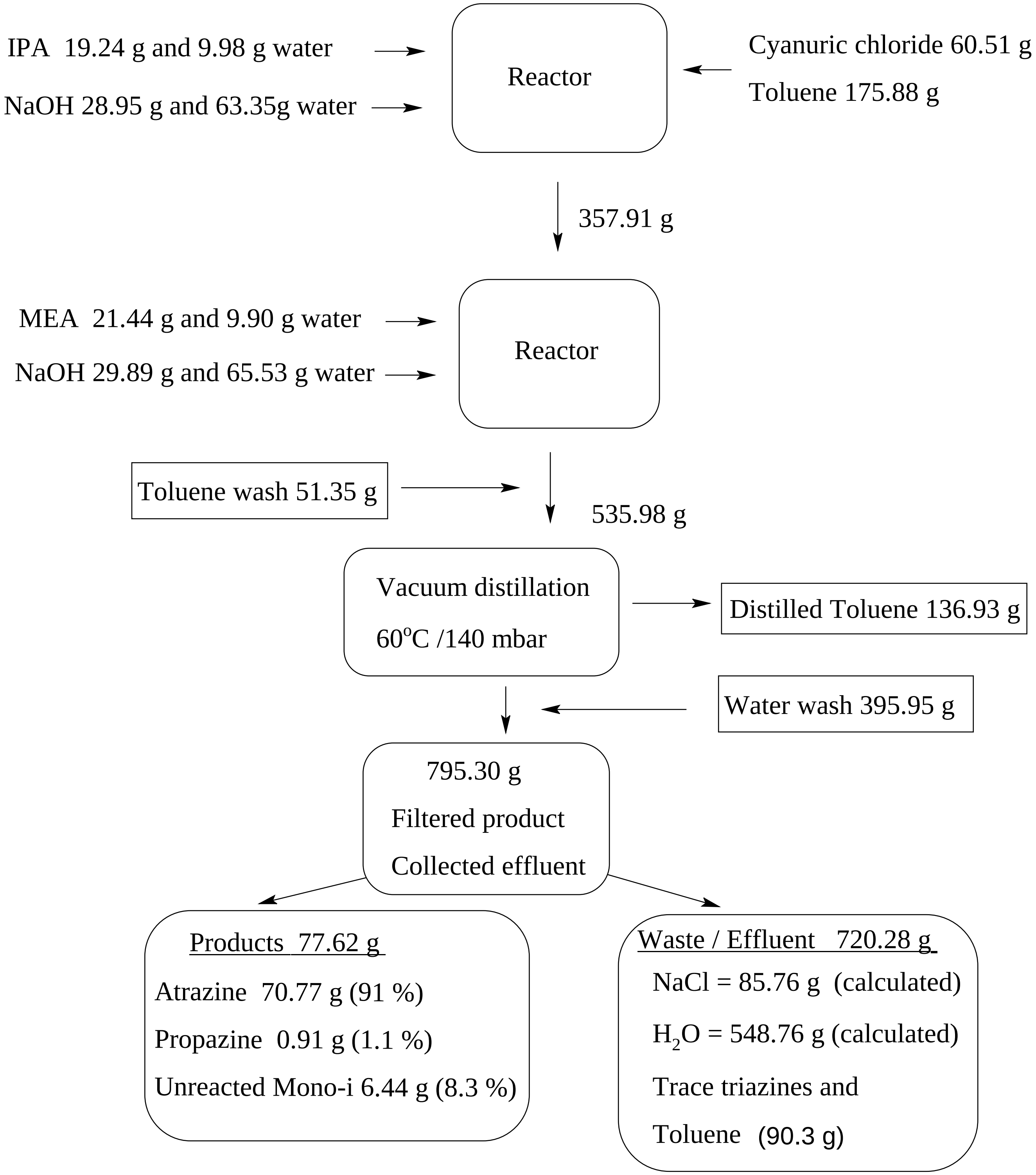


Figure 4.2 **Mass balance for the synthesis of atrazine**

Most of the toluene (136.9 g, 78.00 %) was recovered using a rotavap. The remaining toluene was removed from the filtered product during drying in a vacuum oven at a temperature range of 90 - 100°C. The filtered product was analyzed by HPLC to give atrazine (70.77 g, 328.0 mmoles, 91.20 %), propazine

(0.91 g, 4.0 mmoles, 1.2 %) and unreacted mono-i (6.44 g, 37.9 mmoles, 8.86 %). The effluent stream, which contained only trace amounts of toluene, was essentially a saline solution.

4.5 Reaction profile for the synthesis of atrazine in toluene

4.5.1 General

A product distribution diagram was constructed for the synthesis of atrazine with the objective to obtain a "picture" of the entire reaction as it occurs. A distribution diagram allows one to observe trends with regards to the formation of intermediates, side products and product as the reaction proceeds. The main objective was to follow the disappearance of cyanuric chloride and appearance of the intermediate, mono-i, atrazine, and any side products. Both IPA and MEA addition steps were investigated. This experiment was carried out using the modified method (Section 4.3.1).

4.5.2 Sampling procedure during experimental work-up

Samples (1 mL) were taken at three-minute intervals over the entire reaction period. These samples were made to volume with acetonitrile in 50 mL volumetric flasks. This was done in order to prevent any toluene in the samples from forming an emulsion with water, which would have been the case if a 50:50 solution of acetonitrile/water was used. A sample was taken before addition of IPA and NaOH at "time = 0", as well as before the MEA addition and after stirring for 10 minutes (in order to allow for the temperature to reach 15^{o}C for the second stage). The sampling sequence over the duration of the reaction is given in Table 4.16.

Table 4.16 A sampling profile showing the intervals and stages at which samples were taken in order to construct a distribution diagram

Sample No.	Time (min)	Comments
1	0	Starting material in toluene
2	0:57	IPA added for 1 minute
3	2:45	Add NaOH
4	4:01	Add IPA and NaOH
5	6:00	Intermediate samples
6	9:00	
7	12:00	
8	15:30	IPA/NaOH addition completed
9	22:49	Sample taken before adding MEA
10	23:49	MEA added for 1 minute
11	25:00	Add MEA and NaOH
12	28:00	Intermediate samples
13	31:00	
14	33:00	
15	36:00	MEA/NaOH addition completed
16	51:00	Sample taken after 15 minutes

4.5.3 Distribution diagrams

The results obtained from the analysis performed on these samples (Section 4.5.2) were used to compile the following two distribution diagrams (Figure 4.3 and 4.4):

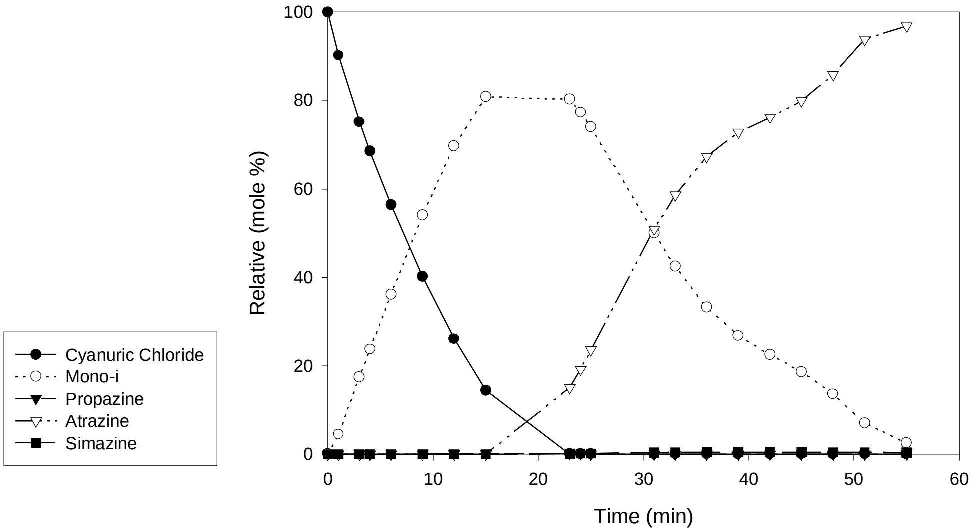


Figure 4.3 **Distribution diagram showing the profile of reactants and products in the preparation of atrazine**

The curves representing propazine and simazine are shown more clearly in Figure 4.4.

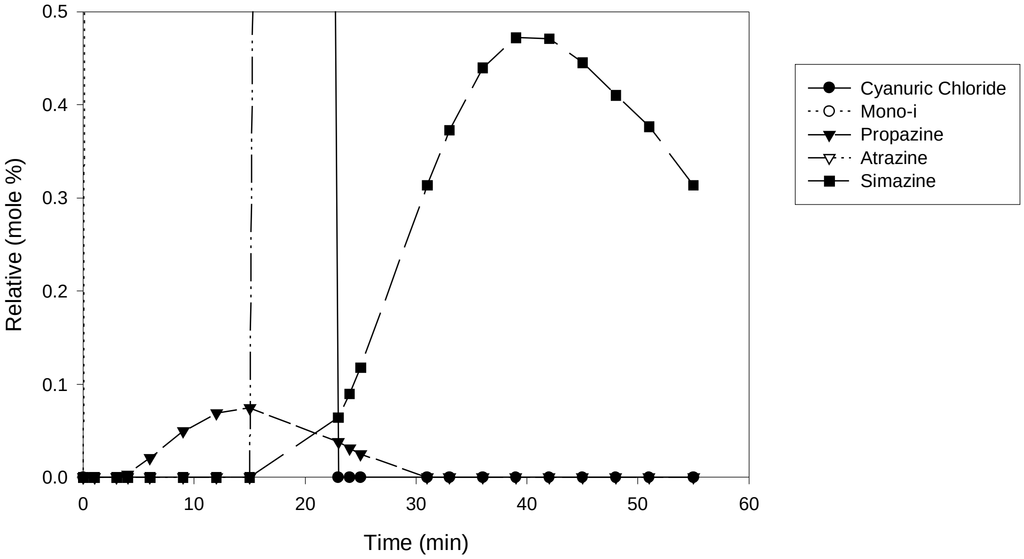


Figure 4.4 Distribution diagram showing the formation and decline of propazine and simazine during the preparation of atrazine

The only “unexpected” observation from the above distribution diagrams was the behavior of the two side products, propazine and simazine. Propazine seemed to increase to a maximum during the first step (IPA addition), but when the second amine (MEA) was added, its concentration decreased again. This behavior may be the result of either the hydrolysis of propazine at higher temperatures, or due to amine exchange during the MEA addition step.

4.6 Amine exchange between side products

The aim of this final experiment was to observe whether amine exchange occurred when MEA (3.56 g, 0.0553 mol) and NaOH (4.9 g, 0.056 mol) in 10 mL water was added to a mixture of propazine (10 g, 0.044 mol) and toluene (30 g) at 15°C over 20 minutes (Table 4.17). There was no cyanuric chloride present in this mixture.

Table 4.17 Results showing the degree to which amine exchange can occur

Compound	Composition (%)
Propazine	90.28
Mono-i	0.24
Atrazine	0.24
Simazine	0.04

In a solution where propazine is the starting material, mono-i, atrazine and simazine formed, but only to a small extent (<0.3%). These results suggest that amine exchange is not important and the observed decreases in the amounts of simazine and propazine are probably the result of hydrolysis.

4.7 Reaction calorimetry

4.7.1 General introduction

Reaction calorimetry is an efficient tool for the generation of very specific data for scale-up purposes, rapid process development and hazard identification. The most common application of a reaction calorimeter is the determination of the heat released/absorbed during a process. Apart from these applications, measuring the heat output/requirement for a reaction can provide valuable information regarding the reaction mechanism. Heat uptake or release is associated with specific events that could be followed precisely by means of reaction calorimetry.

Heat flow is the most widely used method in reaction calorimetry. Heat generated/required by the reaction is removed/supplied by the heating/cooling oil in the reactor jacket. By employing precise temperature measurements on the reaction mass and the jacket-inlets and jacket-outlets before, during and after the reaction, the energy evolved or consumed by the reaction can be determined. The calorimetric principle used in heat flow methods is based on the continuous measurement of the temperature difference between the reactor contents (T_R) and the heat transfer fluid in the reactor jacket (T_J). The measured values of T_R and T_J are used twice, first as input quantities (actual values) for the control of the reaction, then as basic quantities for the heat flow calculation. The total heat flow through the reactor wall is directly proportional to the temperature difference ($T_R – T_J$). It is the sensitivity of the measurement of these two quantities that constitutes the physical basis for the derivation of reaction data such as kinetics, mass transfer and thermal data.[38-44]

4.7.2 Power compensation calorimetry

The principles of this method are now described briefly. A constant temperature differential (ΔT) is set up between the reactor contents (reaction mixture) and the reactor jacket in such a way that the temperature of the reactor contents is always 10 – 40°C higher than the temperature of the cooling liquid in the jacket. This is achieved through the use of an internal heater to heat and keep the reaction mixture at the desired temperature. At the onset of a chemical reaction, heat is either released or taken up by the reaction mixture. If the reaction is exothermic, the internal heater will need to provide less heat in order to maintain the constant temperature differential (ΔT) between the reactor jacket and the reaction mixture. Conversely, if the reaction is endothermic, the internal heater would have to supply more heat. By accurately measuring the power to the internal heater, the total heat given out/taken up by a reaction can be calculated. Figure 4.5 demonstrates the principle of power compensation calorimetry.

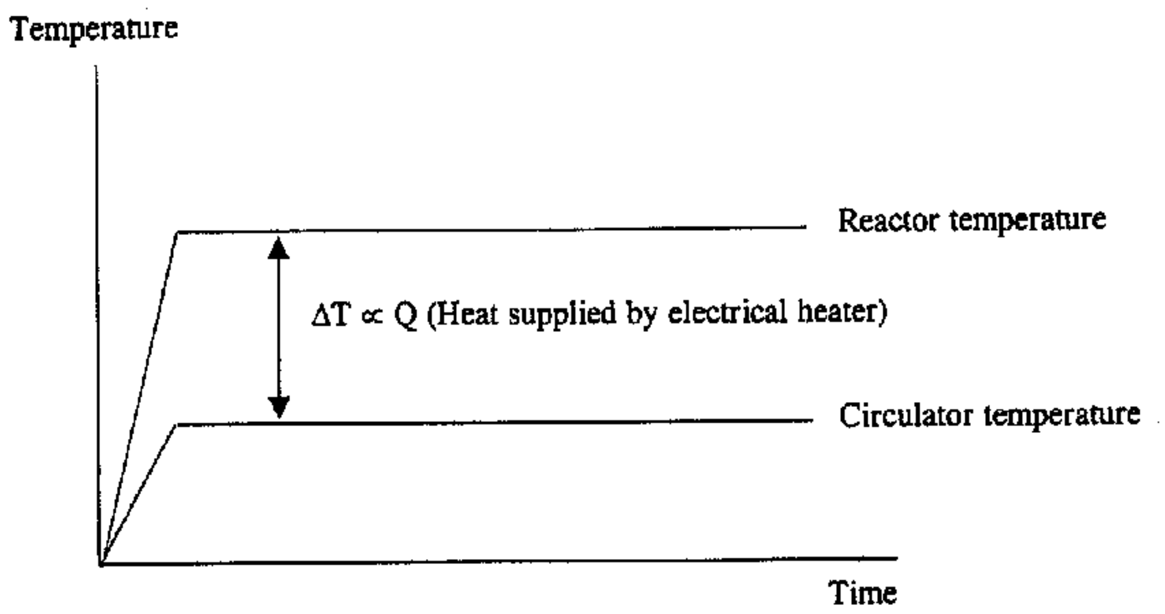


Figure 4.5 **Power compensation**[45]

4.7.3 Comparison between heat flow and power compensation

In the case of heat flow calorimetry, the variable under examination is the reactor-jacket temperature difference. Equation 4.1 describes the relationship between this quantity and heat flow from the reactor:

$$\mathbf{Q_{flow} = UA\,(T_{reactor} - T_{jacket})} \qquad \textbf{Equation 4.1}$$

Where UA is the coefficient of heat flow and ($T_{reactor} - T_{jacket}$) the reactor temperature difference. If UA changes, $T_{reactor}$ and Q_{flow} remain constant.

In the case of power compensation calorimetry, the variable under examination is the electrical power supply to the compensation control heater and, within baseline regions, this variable is synonymous with the heat loss from the system. ΔT is held constant by the controller.[39]

Power compensation was used in this investigation because:

- It is less time consuming,
- It improves temperature control, and
- It provides intuitive "live" results.

4.7.4 Experimental setup

The reaction calorimeter was set up for the atrazine synthesis, allowing for the controlled addition of each amine and NaOH respectively. (The calorimeter can be controlled to the extent that both the feed rate and total quantity to be added are correct.)

While the reaction was running, the heat output of the reaction was measured as a function of time. This allowed for the observation of changes inside the reactor as they occurred. It was furthermore possible to calculate the energy released/taken up during the reaction.

The reaction calorimeter setup, shown in Figure 4.6, has the following features:

- The reactor vessel, with a capacity of 500 cm^3, has low thermal expansion properties, and is made of chemically resistant material. The reactor is connected to the oil circulator and heat exchanger.
- The lid sockets are in turn used for the stirrer shaft, calibration (internal) heater (~), pH probe (pH), feed entry and temperature probes (T).
- Various outputs, such as the reactor temperature and cooling oil temperature are monitored and recorded by the software.
- The cooling/heating facility consists of a combined oil circulation and heating unit plus a shell-and-tube heat exchanger.[39]

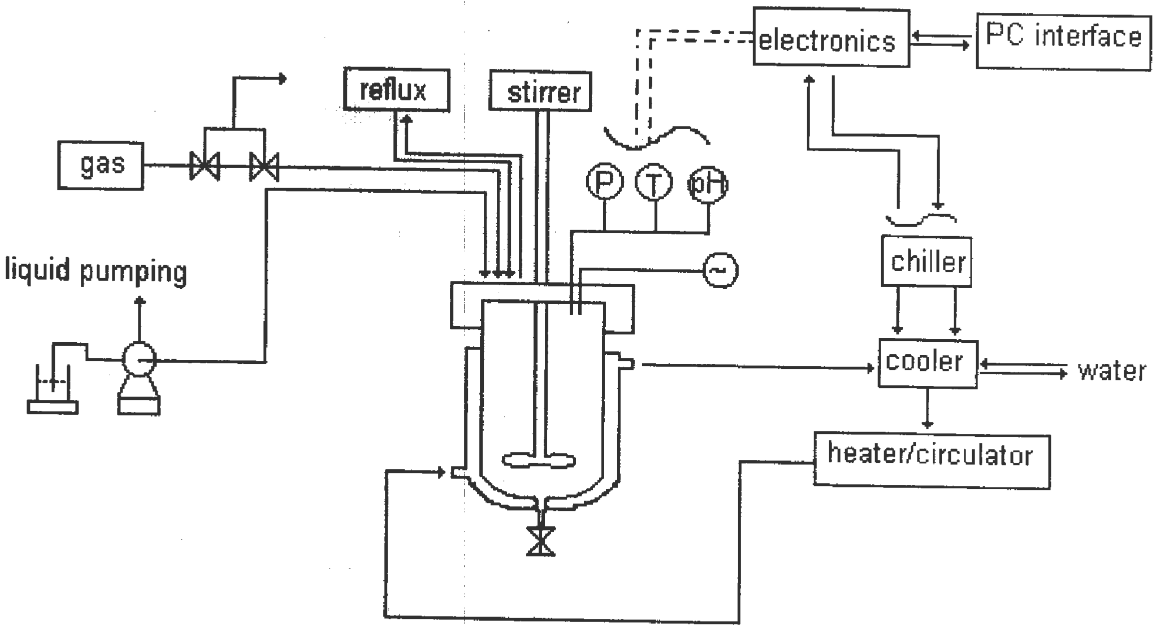


Figure 4.6 Schematic representation of reaction calorimeter[39,45]

4.7.5 Objectives of the reaction calorimetry study

The objectives of this part of the investigation may be summarized as follows:

- To measure the heat of reaction for each of the reaction steps,
- To obtain a qualitative measure of the rates of reaction in the various steps,
- To evaluate the effect of different reagent addition sequences on reaction rates, hence heat output, and
- To evaluate the potential build-up of energy in the reactor during reagent addition sequences.

4.7.6 Investigation of the IPA addition step

The first step of the synthesis, namely the addition of IPA, was investigated by varying the sequence of reagent addition to the substrate. For these reactions, the power compensation technique was used to reduce the overall time needed for these evaluations. In order to ensure that the heat measured reflects that of the chemical reaction and not of any mixing effects, a 14% loading of cyanuric chloride in toluene was used to ensure a homogeneous solution.

For each experiment, suitable quantities of the starting material and solvent (cyanuric chloride and toluene) were added to the reactor (Table 4.18). The system was cooled and allowed to equilibrate at 5^{o}C for 30 minutes. The reactants, IPA and NaOH, were fed into the reactor by dosing pumps from calibrated balances. The compensation drop was set to $\Delta T = 10^{o}C$.

The following addition sequences were investigated:

- **IPA followed by NaOH**

  The IPA solution was added to the reactor at a rate of 0.5 g/min. A total of 18.2 g (0.308 mol) was added over a time period of 37 minutes. The system was allowed to equilibrate again at 5^{o}C before the NaOH solution was added. A total of 33.9 g (0.381 mol) NaOH was added over a period of 35 minutes.

- NaOH followed by IPA

  A NaOH solution was added to the reactor at a constant rate of 1.0 g/min. The system was allowed to equilibrate at 5^{o}C until a stable power baseline was obtained, before the IPA solution was introduced at a rate of 0.5 g/min.

- IPA and NaOH simultaneously

  IPA was first added at a rate of 0.5 mL/min for 2 minutes, after which simultaneous addition commenced by starting with the addition of NaOH at a rate of 0.93 mL/min for 34.4 min.

Table 4.18 Quantities of chemicals used for each experiment

Compound	**Quantities**
Toluene	280 g
Cyanuric chloride	39.8 g (0.216 mol)
IPA	16.74 g (0.198 mol) of a 70% m/m solution in 6.5 cm^3 water weighing 18.204 g in total
NaOH (25% m/m)	8.64 g (0.054 mol) in 25.9 cm^3 water weighing 33.890 g in total

The results obtained for the different addition sequences are illustrated by the heat profiles obtained for these reactions in Figures 4.7 – 4.9. The energies and molar enthalpies obtained from these curves are summarized after each experiment.

4.7.7 Results for the step: IPA followed by NaOH

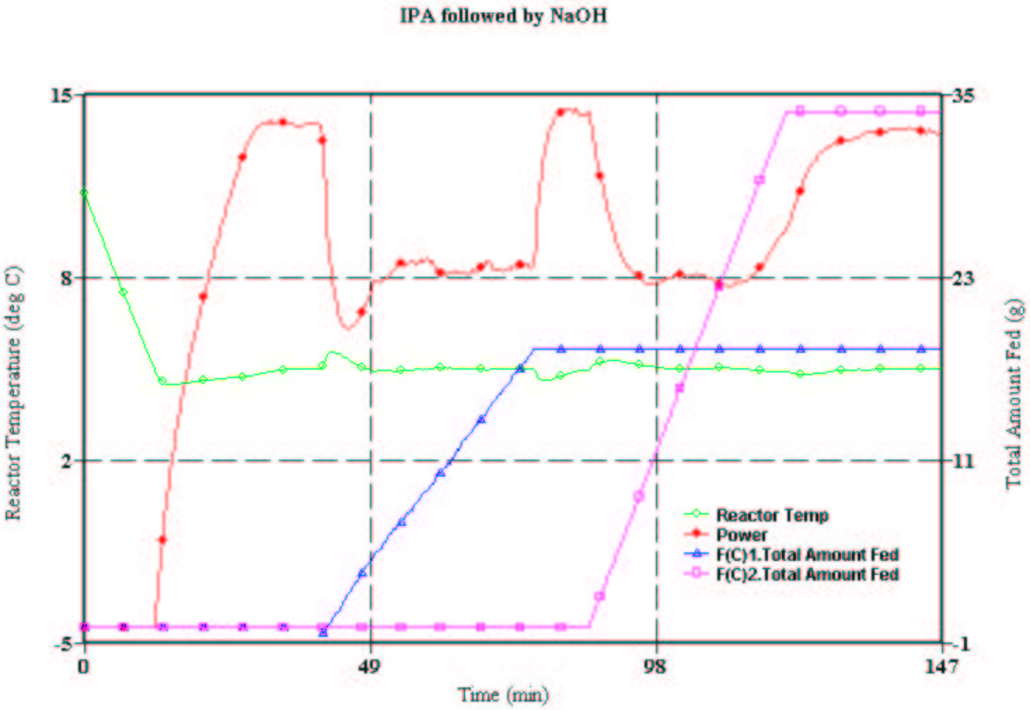


Figure 4.7 Illustration of the profile obtained when the addition of IPA was followed by the addition of NaOH (*F1 = IPA feed, *F2 = NaOH feed)

Even without detailed evaluation, this typical square-shaped energy profile is indicative of a classic dose-controlled reaction, as shown by the sharp rise and fall of heat output with initiation/termination of feed. The reaction rate is therefore equal to the feeding rate of reactants. In addition, there is no energy build-up during the addition of reagents showing that a homogeneous solution with sufficient mixing supports effective heat dispersion.

In order to demonstrate how the calorimeter makes use of energy lost and generated by the system, the following definitions and methods were used.[39,46]

- C_p = the heat capacity at constant pressure. The molar heat capacity is the energy in joules (or kJ) required to raise the temperature of one mole of a substance by one degree Kelvin ($J.mol^{-1}.K^{-1}$). It can also be expressed per kilogram or per gram ($J.g^{-1}.K^{-1}$, $J.kg^{-1}.K^{-1}$, $kJ.kg^{-1}.K^{-1}$).
- Since $C_p = \frac{dq_p}{dT}$, this can be written as $dq_p = C_p dT$, where dq_p is the infinitesimal amount of heat q at constant pressure and dT is equivalent to any small temperature increase. This results in the following integrated equation:

$$q_p = \int_{T_1}^{T_2} C_p dT$$ **Equation 4.2**

- The area under a curve is due to the heat q used to increase the temperature of 1 mole of substance from T_1 to T_2.
- In this case, the plot has power on the y-axis, given in $J.s^{-1}$. When this is multiplied by time in seconds, we are left with J or q, the heat of the reaction.
- As the power fluctuates during a reaction, the calorimeter integrates the area beneath or above these curves (with reference to a baseline temperature). In order to calculate the total amount of power applied by the heater or removed from the system by cooling, the accumulated effect is given by Q. The following heat balance can be formulated:

$$\mathbf{Q_r = Q_{rem} + Q_{loss} + Q_{accum} + Q_{dose}}$$ **Equation 4.3**

Q_r = the reaction power
Q_{rem} = power removed from the system
Q_{loss} = power loss from the system
Q_{accum} = power accumulated in the system
Q_{dose} = heat loss due to the cooling or heating effect of the feed

This principle is applied for all the experiments where the energy and molar heats are calculated.

The energy report generated with the aid of HEL Wincalc software gave results which are summarized in Table 4.19. (E = Total Flow / Balance Energy, and)H = Molar Heat.)

Table 4.19 **Results generated by the calorimeter for the experiment: IPA followed by NaOH**

Energy Results		
	IPA Addition Step	**NaOH Addition Step**
E (kJ)	21.68	18.30
)H (kJ.mol^{-1})	- 100	- 80
Analytical Results		
Conversion*	99.20 %	
Mono-i	96.24 %	

* Conversion is given in terms of HPLC results.

4.7.8 Results for the step: NaOH followed by IPA

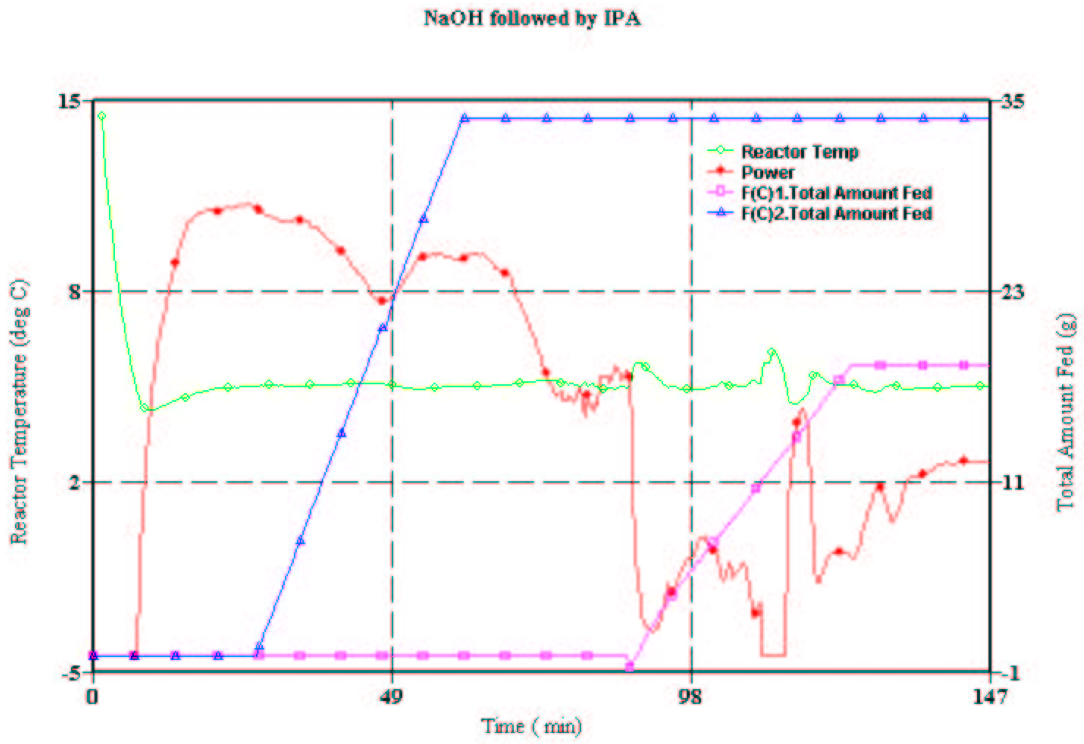


Figure 4.8 Illustration of the profile obtained when the addition of NaOH was followed by the addition of IPA

This curve is highly undesirable largely due to the high degree of fluctuation displayed by heater power output. The reason for this became apparent when the reactor was opened: large clumps of solid had formed. These large solid particles disrupted dispersion of the slurry causing poor mixing as had been observed previously when NaOH was added prior to the amines. This resulted in poor heat transfer. The inefficient mixing inside the reactor would in turn have contributed to the formation of propazine. This addition sequence was therefore not feasible. Table 4.20 summarizes the results obtained.

Table 4.20 Results generated by the calorimeter for the experiment: NaOH followed by IPA

Energy Results		
	IPA Addition Step	**NaOH Addition Step**
E (kJ)	4.89	19.54
)**H (kJ.mol^{-1})**	-22	-90
Analytical Results		
Conversion	96.25% Poor mixing caused by the initial presence of NaOH in the mixture resulted in a significant amount of propazine being formed	

4.7.9 *Results for the step: simultaneous addition of IPA and NaOH*

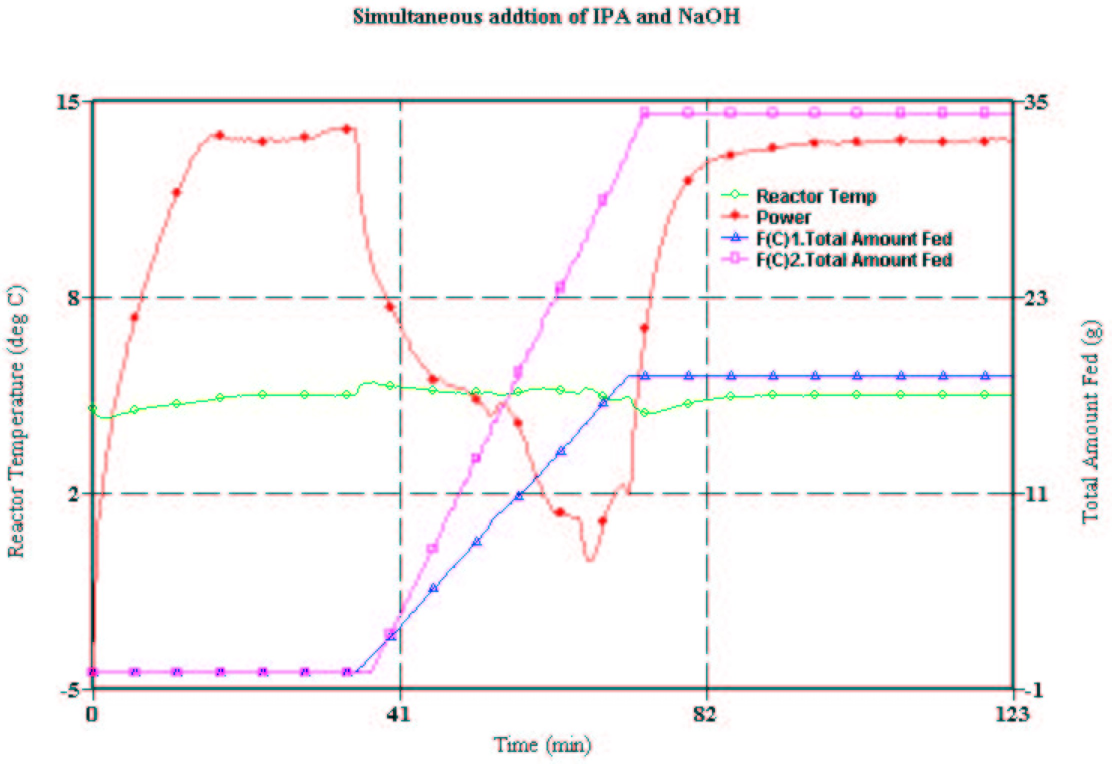


Figure 4.9 Illustration of the profile obtained when IPA and NaOH were added simultaneously

This curve, apart from a sharp drop near the end, is again typical of a dose-controlled reaction, indicated by a sharp rise and fall in power output with commencement or termination of reagent feed respectively. The drop in power output towards the end of the reaction may possibly be explained in terms of decreased mixing efficiency as the mono-i started to precipitate out from solution. Results are displayed on Table 4.21.

Table 4.21 Results generated by the calorimeter for the experiment: IPA and NaOH simultaneously

Energy Results	
	IPA and NaOH simultaneously
E (kJ)	37.18
)H (kJ.mol^{-1})	-172
Analytical Results	
Conversion	99.79%
Mono-i	96.60%

4.7.10 Calorimetric investigation of both IPA and MEA additions using simultaneous addition of amine and hydroxide

This experiment investigates of the thermal events taking place during the addition of both amines. The quantities used in this reaction were similar to those used in the previous calorimetric experiments, and performed using the power compensation mode.

4.7.10.1 Experimental procedure

The method used for the simultaneous addition of both the IPA and MEA steps are described below:

1. The temperature differential between the reactor contents and jacket was set to 5^{o}C; this allowed the reactor contents and jacket to cool.
2. Isopropylamine (12.74 g; 0.215 mol in 6.5 mL water) and sodium hydroxide (8.64 g; 0.216 mol in 25.9 mL water) solutions were prepared and placed on the respective calorimeter balances; the pumps were calibrated and pump lines loaded.
3. After a temperature of 5^{o}C was reached, toluene (280 g) and cyanuric chloride (39.8 g; 0.216 mol) were added to the reactor. The overhead stirrer was set to 600 rpm.
4. The first step of the reaction began with the addition of IPA for 1 minute (1.0 g at a rate of 0.5 g/min) followed by the commencement of the simultaneous addition of NaOH (0.93 g/min for 32.0 g NaOH and 0.5 g/min for 17.204 g IPA) over a period of 36 minutes. The remaining 1.890 g NaOH was added at a rate of 0.93 g/min as before. The reaction mixture was then monitored for 60 minutes.
5. The reaction was stopped and the feed lines reloaded and calibrated with MEA. Monoethylamine (14.2 g; 0.220 mol in 6.64 mL water) and NaOH (8.64 g; 0.216 mol in 25.9 mL water) solutions were prepared and placed on the respective calorimeter balances.
6. For the second step of the reaction, the temperature was set to 15^{o}C. The reaction continued with the addition of MEA for 1 minute (1.0 g at a rate of 0.5 g/min), followed by NaOH (0.93 g/min for 32.0 g

NaOH and 0.5 g/min for 20.031 g MEA) over a period of 41 minutes. The remaining 1.0 g NaOH was added at a rate of 0.8 g/min. A stirring time of 40 minutes was allowed in order for the system to stabilize.

Figures 4.10 and 4.11 illustrate the energy profiles obtained for the two steps

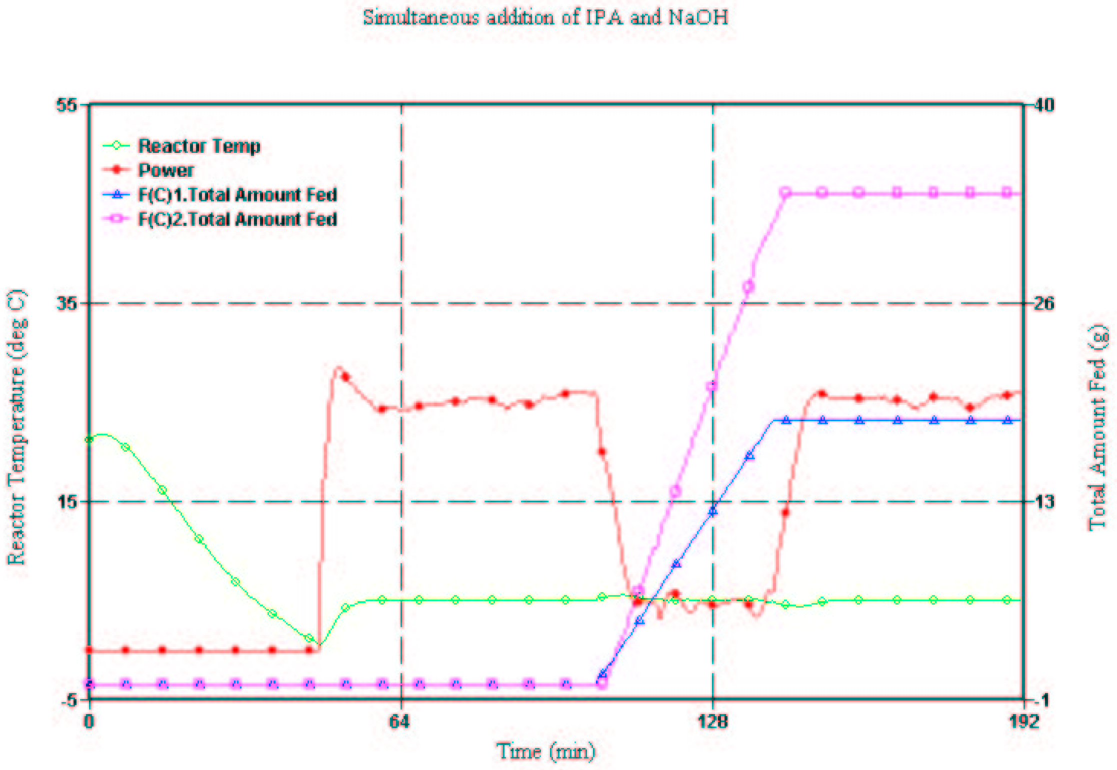


Figure 4.10 Illustration of the profile obtained when IPA and NaOH were added simultaneously

The energy plot for the addition step of IPA is similar to that obtained previously (Fig.4.9), except that no evidence of mono-i precipitation is present in the above case. The square-shaped energy profile again shows that the reaction is dose-controlled and no build-up of reagents occurred during the addition stage.

The total reaction energy, calculated by integration of the area under the energy curve using WinCalc, is 38.03 kJ.

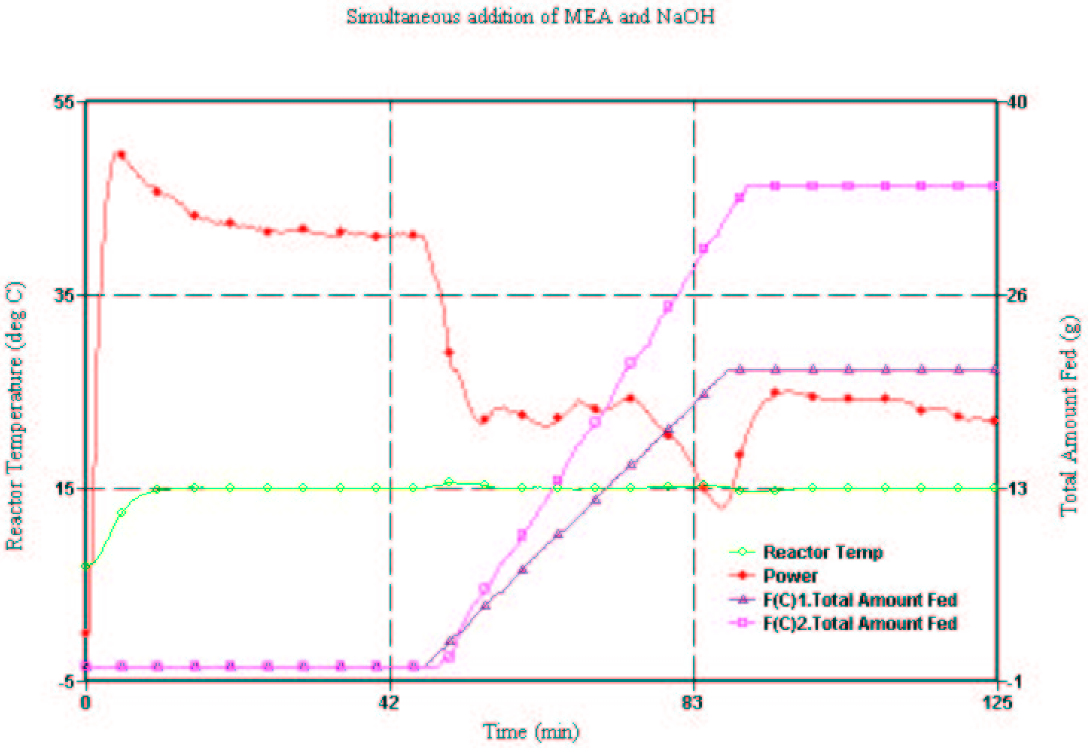


Figure 4.11 Illustration of the profile obtained when MEA and NaOH were added simultaneously

The energy curve obtained for the MEA addition step is less desirable for the calculation of reaction energies than those obtained for the addition of IPA. The first half of the curve is virtually identical compared to IPA, but about halfway through the addition of MEA, precipitation of atrazine commences as indicated by a further drop in energy. The result of the formation of solid atrazine is to completely change the thermal and mixing properties of the reaction mixture. This is clearly indicated by the fact that the final energy baseline is considerably lower than the baseline at the start, and as more atrazine precipitates, the baseline continues downwards. Despite the complications described above, it is still clear that the reaction of MEA with mono-i is identical to the reaction of IPA with cyanuric chloride. As MEA addition commences, the reaction proceeded at a rate equal to the rate of MEA/NaOH addition as no reagent build-up is observed (lagging temperature curve at the end of the reaction). Thus, both the reaction of IPA with cyanuric chloride, as well as the reaction of MEA with mono-i, can be considered to be instantaneous (when NaOH is added simultaneously with the amine).

In view of the changes in the nature of the reaction mixture from a virtually homogeneous solution to a slurry of atrazine in a mixture of toluene and water, the calculation of the energies for the addition of MEA was not straightforward. Two estimates of the reaction energy were made as shown in Figure 4.12 and the values obtained are given in Table 4.22

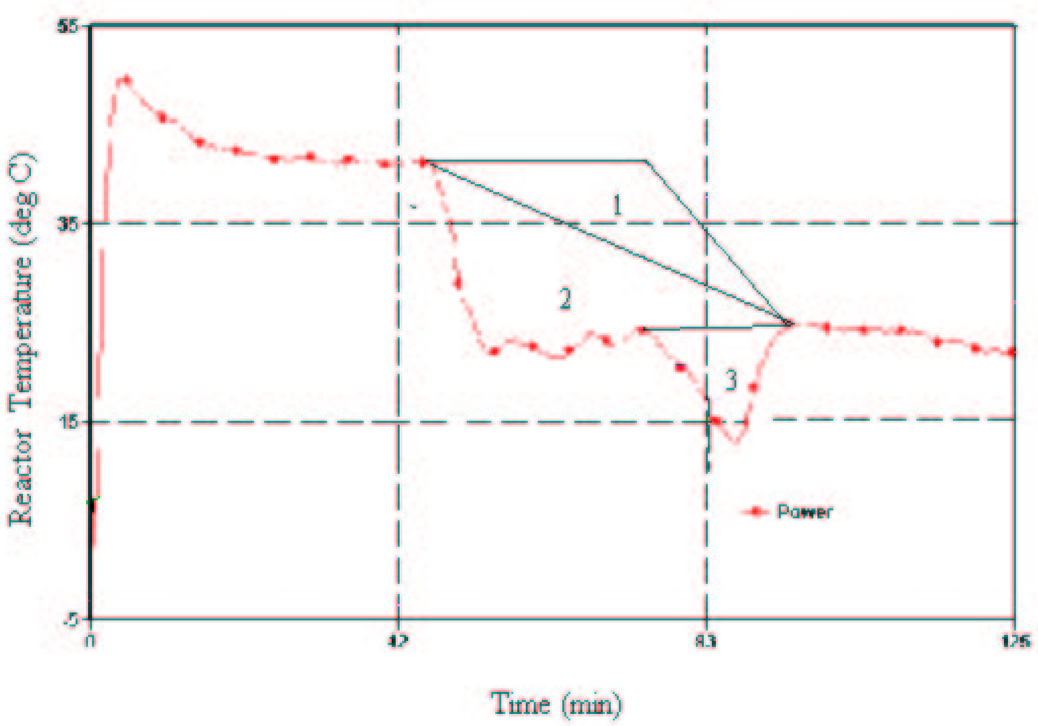


Figure 4.12 Schematic illustration of the integrated areas used to determine the energies for the overall reaction

In Figure 4.12 it should be noted that the area for no. 1 includes no. 2 and 3. Similarly, no. 2 incorporates no.3. The energy values corresponding to the numbers on Figure 4.12 are shown in Table 4.23.

Table 4.22 Energy results generated by the calorimeter for the experiment: IPA and NaOH / MEA and NaOH simultaneously

Energy Results		
	IPA and NaOH Addition Step	**MEA and NaOH Addition Step**
E (kJ)	38.03	(40.47)[1] (24.38)[2]
)H (kJ.mol^{-1})	- 175.73	(-187.52)[1] (- 112.96)[2]

[1] – Corrected values for the overall reaction. [2] – The experimental values for the overall reaction.

It should be noted that both estimates of the reaction energy includes the energy of crystallization of atrazine, estimated as –20.14 kJ.mol^{-1} as indicated in Figure 4.12

The)H value obtained for no.1 (-187.518 kJ.mol^{-1}) and energy (40.47 kJ) are the corrected values for the overall reaction.

These experimental and calculated values may be compared to those cited in literature. Table 4.23 lists the heats of formation for the reactants and products for this reaction scheme.

Table 4.23 Heats of formation of reactants and products found in literature

Compound	**Chemical Formula**	**Quantity**	**Value (kJ.mol^{-1})**
Cyanuric chloride[47]	$C_3N_3Cl_3$	)H_f^osolid	94.3∀2.5
Isopropyamine[48]	C_3H_9N	)H_f^oliquid	-112.3∀0.67
Sodium hydroxide[49]	NaOH	)H_f^osolid	425.93
Mono-i [a]	$C_6H_8N_4Cl_2$	)H_f^osolid	-79.13
Monoethylamine[51]	C_2H_7N	)H_f^oliquid	-84.5
Atrazine[52]	$C_8H_{14}N_5Cl$	)H_f^osolid	-125.4∀9.5
Sodium chloride[49]	NaCl	)H_f^osolid	-411.12
Water[49]	H_2O	)H_f^oliquid	-285.8

[a] This is a calculated value for the heat of formation of mono-i using Hess's Law.[50]

$$)H^o = 3()H_f^o(\text{Products})) - 3()H_f^o(\text{Reactants})) \qquad \textbf{Equation 4.4}$$

4.8 Summary

From the sequence of reactions presented in Section 4.7 certain aspects affecting the reaction conditions have been shown to play a vital role in ensuring that the conditions chosen for the reactions are optimal for this synthesis. For example, efficient mixing at high stirring speeds is necessary to promote good agitation during the reaction. In addition to this, it was proven that the best reactant addition technique to use is the simultaneous addition of an amine with NaOH. Efficient temperature control throughout the reaction is vital to promote the formation of mono-i during the first step and prohibit the formation of propazine and other side products. Lengthy stirring times, which usually followed each addition step, may be eliminated because the instantaneous nature of the reaction renders this pointless.

In order to use this information in a manner that could improve the production of atrazine, these aspects should be manipulated in such a way as to utilize the full potential offered. This can be done by recommending another avenue to explore; this would be to use two small reactors in series. The IPA and NaOH would be added to the first reactor, the intermediate produced could be pumped into the second reactor, while the first is recharged with cyanuric chloride and toluene. The reaction would then be completed by the addition of MEA and NaOH to the second reactor and work up of the product.

CHAPTER 5

SUMMARY AND CONCLUDING REMARKS

5.1 Synthesis of atrazine in an aqueous medium

Despite all attempts to improve on the yield of atrazine in aqueous media by using various surfactants, the results obtained were rather disappointing. Atrazine yields were never higher than *ca.* 70% and in all cases contained significant amounts of propazine, simazine and hydroxy byproducts. Of the various surfactants investigated, Rhodafac gave the most promising results, but these were poor in comparison with synthetic procedures employing a reaction solvent such as MIBK or toluene. In addition to the poor yields of product obtained, other problems were experienced during these procedures that make the possible success of such procedures unlikely. These were:

- Excessive foaming occurred during the filtering process, which would necessitate the use of anti-foaming agents on a large scale.
- A poor, powder-like solid product, that was difficult to filter and recover, was obtained.
- A large percentage of side products formed.

The formation of large quantities of propazine and simazine during these reactions were explained in terms of the preferential reaction of IPA with the initially formed intermediate, mono-i, to form propazine. Unreacted cynauric chloride may then react with MEA in the second step, forming simazine. These observations were explained in terms of the improved wettability properties of mono-i as compared to cynauric chloride as was shown by competitive reaction of IPA with cyanuric chloride and mono-i in aqueous media and toluene. The formation of hydroxy byproducts may be explained in terms of the increased hydrolysis of cynauric chloride in aqueous media, despite the use of relatively high NaCl loadings to suppress such hydrolysis reactions.

5.2 Synthesis of atrazine in toluene

Each parameter that was investigated, for example, cyanuric chloride loading, product isolation, low temperatures, addition sequence, and rates of amine reagents and base, provided a clear indication as to the effect these have on the crude yield and composition of the atrazine. The accumulated effects of these results have lead to the development of successful bench scale reactions.

Addition techniques of the amines and NaOH have great influence on the product, yield and quality, and this was demonstrated when a selection of addition combinations were attempted (simultaneous and consecutive). The most effective technique consisted of a one-minute addition of the amine before simultaneous addition with the NaOH was commenced.

Simultaneous addition of IPA and NaOH was clearly the most heat efficient combination. This was confirmed by the observation that after the addition of secondary amine/NaOH and primary amine/NaOH, the power compensation stopped, confirming the instantaneous nature of the reaction. This allows for these reactions to be performed under feed control conditions.

Despite this reaction being instantaneous, the temperature needed to be controlled very carefully in order to ensure high yields and a highly pure product. Temperature control was required in order to remove latent heat caused by the exotherm that accompanied the reaction. It is therefore possible to increase the rate of addition of amines and NaOH, provided there was adequate cooling and mixing.

Mixing played a major role, especially when it came to distributing the amines effectively as they were added. This was largely because of the rapid reaction occurring between amine/NaOH and cyanuric chloride, and the possibility of mono-i reacting with any local excess of IPA. Not only did the stirring rate have to be as high as possible; the design of the blades on the shaft, together with baffles inside the reactor, make for ideal agitation.

As long as a homogeneous slurry was maintained, an effective cooling method was in place and adequate agitation used, the cyanuric chloride dispersed well in a medium of toluene giving rise to high yields of atrazine.

The high quality of atrazine demanded for commercial purposes was maintained when using toluene as the reaction medium. Because this solvent can be recovered during the process, and because it has very low water solubility, the potential impact on the environment may hence be reduced.

The environmental concerns, these being the loss of organic solvent and the loss of product during production with regards to the old process, have been addressed. This was possible because a large amount of toluene could be recovered after the synthesis by distillation. The consistency of the slurry due to the presence of toluene made it easy to filter and recover, unlike the powdery fine suspension obtained in the case of the aqueous reactions.

The recovery and composition of atrazine (> 97%) under optimum conditions was within range of the specifications listed by Dow AgroSciences. In order to take full advantage of the aspects discussed above contributing to optimal conditions for the reaction, it can be recommended that two reaction vessels be used in series, the first for the IPA/NaOH addition reaction and the second for the MEA/NaOH addition reaction. It would then be possible to carry out the reaction on a continuous basis whilst eliminating any time delays between amine additions. Small reactors would have the added advantage of allowing for effective temperature control and more efficient mixing.

5.3 The advantages and disadvantages of replacing MIBK with toluene

The advantages of replacing MIBK with another solvent like toluene can be summarized as follows:

- This solvent can be implemented at a lower cost, bearing in mind that at the moment, a solvent is still being used for the synthesis.
- Toluene affects the crystal shape of the atrazine solid, giving a more rounded crystal, unlike the needle-like crystals formed when using MIBK.
- The final product is “bright-white” and does not have the characteristic yellow tinge thought to be due to MIBK.
- The need for high temperature drying is eliminated.
- The total volume of effluent can be greatly reduced.
- The solvent can be recovered and recycled on an industrial scale.
- The hazard posed by the partial solubility of solvent in waste streams is reduced/eliminated.

Some disadvantages of this process to consider are that:

- The use of a solvent has not been eliminated in the process.
- The effluent discharge would still contain traces of solvent.

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