### Question #61079 - Chemistry - Organic Chemistry

Write all the steps involved in the preparation of the following:

### i) A synthetic detergent

#### Answer:

The liquid detergent manufacturing consists of a wide range processing and packaging operations and the size and complexities of these operations may vary depending on factors, such as the size of plant and the manufacturing process undertaken. products may range from an all-purpose laundry cleaner to specialty cleaner such as glass cleaner.

The first step in the manufacturing of liquid detergents is the selection of raw materials. Raw materials are selected on the basis of several factors, such as human and environmental safety, cost, compatibility with other ingredients and the form and he specific properties desired in the final product. While the actual production processes may vary from manufacturer to manufacturer, some processes and techniques are common for all.

Chemical Processes

For manufacturing liquid detergent, both the batch as well as continuous blending processes is used. Both batch and continuous blending processes are used to manufacture liquid and gel cleaning products. Stabilizers may be added during manufacturing to ensure the uniformity and stability of the finished product.

In a typical continuous process, dry and liquid ingredients are added and blended to a uniform mixture using in-line or static mixers.

Recently, more concentrated liquid products have been introduced and a technique for developing these products is through the use of new high-energy mixing processes in combination with stabilizing agents.

To make liquid detergent, the dry powder is simply mixed back in with a solution consisting of chemicals and water, called as "solubilizers." These chemicals help the water and detergent to blend together more evenly. The amount of light reflected, in comparison to the amount reflected by a sample of the original fabric, is a measure of the degree of cleanliness. A reflection rate of 98 % is considered as quite good and shows that the detergent has cleaned properly.

LIQUID DRY INGREDIENTS
INGREDIENTS

**BLENDING PROCESS** 

Manufacture Process - Stages Involved
The different stages involved in soap manufacturing include -

- Soap premix manufacture Liquid detergents contain a combination of soap and synthetic surfactants. These are made first as a premix, after which other ingredients are blended into it. This stage simply consists of neutralizing fatty acids with either caustic soda (NaOH) or potassium hydroxide.
- Ingredient mixing All ingredients except the enzymes are added and mixed at a high temperature. The ingredients used in the manufacturing of liquid detergents are usually sodium tripolyphosphate, caustic soda, sulphonic acid, perfume and water.
- Enzyme addition In this stage, the mixture is cooled and milled, and the enzymes are added in powder form.

Also see attached file.

#### ii) An azo dye

### Answer:

Azo compounds are compounds bearing the functional group R-N=N-R', in which R and R' can be either aryl or alkyl.

See attached file.

### iii)An Analgesic

#### Answer:

Aspirin (acetyl salicylic acid or ASA) is one of the most commonly taken medications yet the mode of action is not yet completely understood. Aspirin is an analgesic (relieves pain), an antipyretic salicylic acid acetyl salicylic acid (reduces fever) and an anti-inflammatory (reduces swelling). Studies also suggest that aspirin can also reduce the risk of heart attack. Aspirin was developed in order to avoid the irritation problems associated with salicylic acid, the active ingredient in willow bark whose curative effects have been known since 1763. N-acylated aromatic amines (those having an acyl group, R C O , substituted on nitrogen) are important in over-the-counter headache remedies. Over-the-counter drugs are those you may buy without a prescription. Acetanilide, phenacetin, and acetaminophen (see over for structures) are mild analgesics and antipyretics and are important, along with aspirin, in many nonprescription drugs.

The discovery that acetanilide was an effective antipyretic came about by accident in 1886. Two doctors, Cahn and Hepp, had been testing naphthalene as a possible vermifuge (an agent that expels worms). By accident, they mixed up a bottle of acetanilide and the bottle of naphthalene. The patient's worms didn't disappear but his fever did - dramatically. In another instance of serendipity, the publication of Cahn and Hepp describing their experiments with acetanilide, caught the attention of Carl Duisberg, director of research at the Bayer Company in Germany. Duisberg was confronted with the problem of profitably getting rid of nearly 50 tons of p-aminophenol, a by-product from the synthesis of one of Bayer's other commercial products. He immediately saw the possibility of converting p-aminophenol to a compound similar in structure to acetanilide, by putting an acyl group on the nitrogen. It was then believed, however, that all compounds having a hydroxyl group on a benzene ring (that is, phenols) were toxic. Duisberg devised a scheme of structural modification of p-aminophenol to get the compound phenacetin. The reaction scheme is shown here.

Deactivation of the supposedly toxic phenol acylation p-Aminophenol Phenacetin Phenacetin turned out to be a highly effective analgesic and antipyretic. A common form of combination pain reliever, called an APC tablet, was once available. An APC tablet contained Aspirin, Phenacetin, and Caffeine (hence, APC). Phenacetin is no longer used in commercial pain-relief preparations. It was later found that not all

aromatic hydroxyl groups lead to toxic compounds, and today the compound acetaminophen is very widely used as an analgesic in place of phenacetin. 'Acetaminophen' (4-acetamidophenol) is sold as the over-the-counter analgesic "Tylenol". ANAL 1.3 This synthesis will involve the reaction of two functional groups, an alcohol and an acid anhydride (a carboxylic acid derivative), to form a product, an ester. The ester product will be isolated, and purified by recrystallisation. The efficiency of the recrystallisation will be monitored using a simple functional group test. Salicylic acid (o-hydroxy benzoic acid) reacts with acetic anhydride to form acetyl salicylic acid and acetic acid according to the following equation:

The most likely impurities in the crude acetyl salicylic acid are unreacted salicylic acid and a polymeric ester by-product. The polymeric by-product is not soluble in sodium bicarbonate an can be removed by dissolving the crude product in sodium bicarbonate, filtering to remove the insoluble polymer then acidifying to recover the acetyl salicylic acid. The phenol functional group reacts with ferric chloride to give a complex with a definite colour ranging from red to violet, depending on the particular phenol present. Unlike salicylic acid, pure acetyl salicylic acid has no phenolic -OH and therefore does not give a colour change. Therefore, the presence of contaminating salicylic acid in the crude product can be detected using ferric chloride and removed by recrystallization.

This synthesis will involve the reaction of two compounds, an amine and a carboxylic acid derivative, to form a product, an amide. The amide product will be isolated, and purified by recrystallisation.

### iv) An antibiotic

#### Answer:

Antibiotics are chemical substances that can inhibit the growth of, and even destroy, harmful microorganisms. They are derived from special microorganisms or other living systems, and are produced on an industrial scale using a fermentation process. Although the principles of antibiotic action were not discovered until the twentieth century, the first known use of antibiotics was by the Chinese over 2,500 years ago. Today, over 10,000 antibiotic substances have been reported. Currently, antibiotics represent a multibillion dollar industry that continues to grow each year.

## Background

Antibiotics are used in many forms—each of which imposes somewhat different manufacturing requirements. For bacterial infections on the skin surface, eye, or ear, an antibiotic may be applied as an ointment or cream. If the infection is internal, the antibiotic can be swallowed or injected directly into the body. In these cases, the antibiotic is delivered throughout the body by absorption into the bloodstream.

Antibiotics differ chemically so it is under-standable that they also differ in the types of infections they cure and the ways in which they cure them. Certain antibiotics destroy bacteria by affecting the structure of their cells. This can occur in one of two ways. First, the antibiotic can weaken the cell walls of the infectious bacteria, which causes them to burst. Second, antibiotics can cause the contents of the bacterial cells to leak out by damaging the cell membranes. Another way in which antibiotics function is by interfering metabolism. with the bacteria's Some antibiotics such as and erythromycin interfere with protein synthesis. Antibiotics like rifampin inhibit nucleic acid biosynthesis. Still other antibiotics, such as sulfonamide or trimethoprim have a general blocking effect on cell metabolism.

The commercial development of an antibiotic is a long and costly proposal. It begins with basic research designed to identify organisms, which produce antibiotic compounds. During this phase, thousands of species are screened for any sign of antibacterial action. When one is found, the species is tested against a variety of known infectious bacteria. If the results are promising, the organism is grown on a large scale so the compound responsible for the antibiotic effect can be isolated. This is a complex procedure because thousands of antibiotic materials have already been discovered. Often, scientists find that their new antibiotics are not unique. If the material passes this phase, further testing can be done. This typically involves clinical testing to prove that the antibiotic works in animals and humans and is not harmful. If these tests are passed, the Food and Drug Administration (FDA) must then approve the antibiotic as a new drug. This whole process can take many years.

The large-scale production of an antibiotic depends on a fermentation process. During fermentation, large amounts of the antibiotic-producing organism are grown. During fermentation, the organisms produce the antibiotic material, which can then be isolated for use as a drug. For a new antibiotic to be economically feasible, manufacturers must be able to get a high yield of drug from the fermentation process, and be able to easily isolate it. Extensive research is usually required before a new antibiotic can be commercially scaled up.

# History

While our scientific knowledge of antibiotics has only recently been developed, the practical application of antibiotics has existed for centuries. The first known use was by the Chinese about 2,500 years ago. During this time, they discovered that applying the moldy curd of soybeans to infections had certain therapeutic benefits. It was so effective

that it became a standard treatment. Evidence suggests that other cultures used antibiotic-type substances as therapeutic agents. The Sudanese-Nubian civilization used a type of <u>tetracycline antibiotic</u> as early as 350 A.D. In Europe during the Middle Ages, crude plant extracts and cheese curds were also used to fight infection. Although these cultures used antibiotics, the general principles of antibiotic action were not understood until the twentieth century.

The development of modern antibiotics depended on a few key individuals who demonstrated to the world that materials derived from microorganisms could be used to cure infectious diseases. One of the first pioneers in this field was Louis Pasteur. In 1877, he and an associate discovered that the growth of disease-causing <a href="mailto:anthrax">anthrax</a> bacteria could be inhibited by a saprophytic bacteria. They showed that large amounts of anthrax bacilli could be given to animals with no adverse affects as long as the saprophytic bacilli were also given. Over the next few years, other observations supported the fact that some bacterially derived materials could prevent the growth of disease-causing bacteria.

In 1928, Alexander Fleming made one of the most important contributions to the field of antibiotics. In an experiment, he found that a strain of green *Penicillium* mold inhibited the growth of bacteria on an agar plate. This led to the development of the first modern era antibiotic, penicillin. A few years later in 1932, a paper was published which suggested a method for treating infected wounds using a penicillin preparation. Although these early samples of penicillin were functional, they were not reliable and further refinements were needed. These improvements came in the early 1940s when Howard Florey and associates discovered a new strain of *Penicillium*, which produced high yields of penicillin. This allowed large-scale production of penicillin, which helped launch the modern antibiotics industry.

After the discovery of penicillin, other antibiotics were sought. In 1939, work began on the isolation of potential antibiotic products from the soil bacteria streptomyces. It was around this time that the term antibiotic was introduced. Selman Waxman and associates discovered streptomycin in 1944. Subsequent studies resulted in the discovery of a host of new, different antibiotics including actinomycin, streptothricin, and neomycin all produced by *Streptomyces*. Other antibiotics that have been discovered since include bacitracin, polymyxin, viomycin, <u>chloramphenicol</u> and tetracyclines. Since the 1970s, most new antibiotics have been synthetic modifications of naturally occurring antibiotics.

### Raw Materials

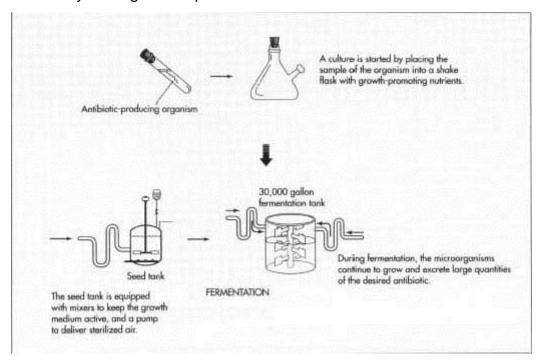
The compounds that make the fermentation broth are the primary raw materials required for antibiotic production. This broth is an aqueous solution made up of all of the ingredients necessary for the proliferation of the microorganisms. Typically, it contains a carbon source like molasses, or soy meal, both of which are made up of lactose and glucose sugars. These materials are needed as a food source for the organisms. Nitrogen is another necessary compound in the metabolic cycles of the

organisms. For this reason, an <u>ammonia</u> salt is typically used. Additionally, trace elements needed for the proper growth of the antibiotic-producing organisms are included. These are components such as phosphorus, sulfur, magnesium, zinc, iron, and copper introduced through water soluble salts. To prevent foaming during fermentation, anti-foaming agents such as lard oil, octadecanol, and silicones are used.

# The Process

# Manufacturing

Although most antibiotics occur in nature, they are not normally available in the quantities necessary for large-scale production.



For this reason, a fermentation process was developed. It involves isolating a desired microorganism, fueling growth of the culture and refining and isolating the final antibiotic product. It is important that sterile conditions be maintained throughout the manufacturing process, because contamination by foreign microbes will ruin the fermentation.

### Starting the culture

- 1 Before fermentation can begin, the desired antibiotic-producing organism must be isolated and its numbers must be increased by many times. To do this, a starter culture from a sample of previously isolated, cold-stored organisms is created in the lab. In order to grow the initial culture, a sample of the organism is transferred to an agar-containing plate. The initial culture is then put into shake flasks along with food and other nutrients necessary for growth. This creates a suspension, which can be transferred to seed tanks for further growth.
- 2 The seed tanks are steel tanks designed to provide an ideal environment for growing microorganisms. They are filled with the all the things the specific

microorganism would need to survive and thrive, including warm water and <u>carbohydrate</u> foods like lactose or glucose sugars. Additionally, they contain other necessary carbon sources, such as acetic acid, alcohols, or hydrocarbons, and nitrogen sources like ammonia salts. Growth factors like vitamins, amino acids, and minor nutrients round out the composition of the seed tank contents. The seed tanks are equipped with mixers, which keep the growth medium moving, and a pump to deliver sterilized, filtered air. After about 24-28 hours, the material in the seed tanks is transferred to the primary fermentation tanks.

### **Fermentation**

• 3 The fermentation tank is essentially a larger version of the steel, seed tank, which is able to hold about 30,000 gallons. It is filled with the same growth media



found in the seed tank and also provides an environment inducive to growth. Here the microorganisms are allowed to grow and multiply. During this process, they excrete large quantities of the desired antibiotic. The tanks are cooled to keep the temperature between 73-81° F (23-27.2 ° C). It is constantly agitated, and a continuous stream of sterilized air is pumped into it. For this reason, anti-foaming agents are periodically added. Since pH control is vital for optimal growth, acids or bases are added to the tank as necessary.

### Isolation and purification

 4 After three to five days, the maximum amount of antibiotic will have been produced and the isolation process can begin. Depending on the specific antibiotic produced, the fermentation broth is processed by various purification methods. For example, for antibiotic compounds that are water soluble, an ion-exchange method may be used for purification. In this method, the compound is first separated from the waste organic materials in the broth and then sent through equipment, which separates the other water-soluble compounds from the desired one. To isolate an oil-soluble antibiotic such as penicillin, a solvent extraction method is used. In this method, the broth is treated with organic solvents such as butyl acetate or methyl isobutyl ketone, which can specifically dissolve the antibiotic. The dissolved antibiotic is then recovered using various organic chemical means. At the end of this step, the manufacturer is typically left with a purified powdered form of the antibiotic, which can be further refined into different product types.

### Refining

- 5 Antibiotic products can take on many different forms. They can be sold in solutions for intravenous bags or syringes, in pill or gel capsule form, or they may be sold as powders, which are incorporated into topical ointments. Depending on the final form of the antibiotic, various refining steps may be taken after the initial isolation. For intravenous bags, the crystalline antibiotic can be dissolved in a solution, put in the bag, which is then hermetically sealed. For gel capsules, the powdered antibiotic is physically filled into the bottom half of a capsule then the top half is mechanically put in place. When used in topical ointments, the antibiotic is mixed into the ointment.
- 6 From this point, the antibiotic product is transported to the final packaging stations. Here, the products are stacked and put in boxes. They are loaded up on trucks and transported to various distributors, hospitals, and pharmacies. The entire process of fermentation, recovery, and processing can take anywhere from five to eight days.

# **Quality Control**

Quality control is of utmost importance in the production of antibiotics. Since it involves a fermentation process, steps must be taken to ensure that absolutely no contamination is introduced at any point during production. To this end, the medium and all of the processing equipment are thoroughly steam sterilized. During manufacturing, the quality of all the compounds is checked on a regular basis. Of particular importance are frequent checks of the condition of the microorganism culture during fermentation. These are accomplished using various chromatography techniques. Also, various physical and chemical properties of the finished product are checked such as pH, melting point, and moisture content.

In the United States, antibiotic production is highly regulated by the Food and Drug Administration (FDA). Depending on the application and type of antibiotic, more or less

testing must be completed. For example, the FDA requires that for certain antibiotics each batch must be checked by them for effectiveness and purity. Only after they have certified the batch can it be sold for general consumption.

# The Future

Since the development of a new drug is a costly proposition, pharmaceutical companies have done very little research in the last decade. However, an alarming development has spurred a revived interest in the development of new antibiotics. It turns out that some of the disease-causing bacteria have <u>mutated</u> and developed a resistance to many of the standard antibiotics. This could have grave consequences on the world's public health unless new antibiotics are discovered or improvements are made on the ones that are available. This challenging problem will be the focus of research for many years to come.