During the early 1960s attempts were made to market a pharmaceutical product consisting of fractionated fish oil triglycerides and fatty acids for treatment of heart patients for reduction of serum cholesterol. This attempt was premature because most of the evidence that such fatty acids were effective was based upon rat-feeding tests and with only a very few extremely short term human feeding tests at that time having been made. Since then, at least one very long term dietary test has been carried out by a heart specialist who advised his patients who had suffered a heart attack to go on a diet with high fat seafood consumed several times per week. This physican succeeded in getting a portion of his patients to follow the diet for up to nineteen years and with very dramatic results (7). Of the 80 patients who adhered to the diet, 51 (57%) were alive after the 16 to 19 years of the test. In contrast, only 10 of the 116 (9%) undieted patients survived. Also, the average months of remaining life of those dying from subsequent heart attacks was 109 months for the dieted patients as compared to only 58 months for those not dieted. These impressive results would indicate there could be a demand for fish oil polyunsaturated fatty acids as a pharmaceutical which could replace the more troublesome dietary regime and extend the life of patients unwilling to follow the rigid diet.

Other possible pharmaceutical applications for polyunsaturated fish oil fatty acids include use for multiple sclerosis (8) and for gall stone treatment (9). There also might be considerable use made of highly polyunsaturated, omega-3 fatty acids in the industrial field as a starting point for chemical synthesis of a variety of substances.

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Nitrogen Derivatives (Amides, Diamides, Nitriles, Primary Amines and Oxides)

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ABSTRACT

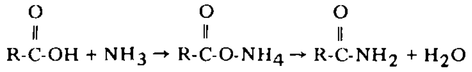
Without a doubt the nitrogen derivatives are the most broadly diversified family of fatty acid derivatives. Today they account collectively for perhaps 400 million pounds of products per year in the USA alone. Although fatty amides may be produced by a large number of synthetic routes, industrially only two are of any commercial importance. Diamides are the difunctional analogs of simple amides, and a typical one that is in medium scale production volume is ethylene bis(stearamide). Industrially, the production of fatty nitriles in the fatty acid derivative industry is exclusively by ammonolysis of fatty acids at temperatures somewhat above those required to produce amides, or roughly, 300-320 C. Both vapor phase catalytic and liquid phase ammonolysis processes may be employed. Nitriles have limited uses as such, but find their utility as fatty derivative intermediates only. The primary amines, RNH_2, are produced industrially by the catalytic hydrogenation of nitriles. The general conditions for the conversion of nitriles to primary amines with a minimum content of secondary or tertiary amines is with nickel catalyst using an excess of ammonia at relatively low temperatures (130-140 C). Amine oxides are derived from tertiary amines by a controlled reaction with hydrogen peroxide. In addition to tertiary amines, the monoalkyl diethoxylated amines can be considered as in the same class. These are made by the addition of ethylene oxide to primary amine. Two moles of ethylene oxide can be added without catalyst. Additional ethoxylation does require a basic catalyst. These amines, besides having end uses of their own, can be converted to amine oxides or can be converted to ethoxylated quaternary ammonium salts.

AMIDES

Primary amides of fatty acids can be regarded as simple substitutes of the hydroxyl of the carboxyl group with an amino function. Simple amides have strong association because of hydrogen bonding, which leads to relatively high melting points for fatty acid derivatives and low solubilities in most solvents. All fatty amides are essentially insoluble in water. In polar solvents solubility decreases with increasing chain lengths, and above dodecanamide it is low in all solvents. Fatty amides have good stability towards air oxidation, heat and dilute acids or bases. The stability is, of course, affected by the degree of unsaturation in the alkyl chain.

Manufacture

Most simple amides of fatty acids are prepared by the reaction of the appropriate fatty acid with anhydrous ammonia in a batch process:



$$R\text{-}\overset{\overset{O}{\|}}{C}\text{-}OH + NH_3 \rightarrow R\text{-}\overset{\overset{O}{\|}}{C}\text{-}O\text{-}NH_4 \rightarrow R\text{-}\overset{\overset{O}{\|}}{C}\text{-}NH_2 + H_2O$$

The reaction is conducted at 180-200 C under slight pressure (50-100 psi) for 10-20 hr. Pressure is maintained by the rate of addition of ammonia and the water of reaction is removed continuously. The effluent stream is collected and the ammonia portion is recovered and can be recycled. While most simple amides are made by this procedure, the starting material can be an ester. Various catalysts have been employed in the manufacture of amides. Among them are boric acid (1), Al_2O_3 (2), and zinc alkoxides (3).

If the use of ammonia is not convenient, it is possible to prepare simple amides by reacting urea with a fatty acid in a sealed vessel at 170-240 C for 2 hr at elevated temperatures (4). Other methods reported in the literature for the

TABLE I

Solubilities of Normal Amides @ 30 C (g/100 g)

Solvent	Caprylamide	Capramide	Lauramide	Myristamide	Palmitamide	Stearamide
Acetonitrile	5.4	1.4	0.9	0.6	0.3	0.2
Methanol	53.0	15.2	12.4	2.7	1.2	0.7
Ethanol 95%	32.8	12.0	11.4	3.8	1.5	0.8
Isopropanol	26.3	10.9	11.4	3.2	1.8	1.0
n-Butanol	25.8	9.1	10.1	3.8	1.9	1.1
Acetone	7.8	3.8	3.4	1.0	0.8	0.5
2-Butanol	8.3	3.8	3.8	1.2	1.0	0.7
Ethyl Acetate	5.7	2.2	2.5	1.0	0.6	0.3
Butyl Acetate	6.0	2.9	3.0	1.2	0.8	0.5
Carbon Tetrachloride	0.4	0.2	0.4	0.1	0.1	0.1
Nitroethane	2.1	1.1	1.1	0.5	0.3	0.2
Hexane	0.02	0.01	Nil	Nil	Nil	Nil
Benzene	0.6	0.8	1.0	0.4	0.4	0.4
Cyclohexane	0.1	0.4	0.5	0.2	0.3	0.3

preparation of fatty amides include hydrogenolysis of hydroxamic acids (5) and hydrazides (6).

The solubility of simple amides in a variety of solvents is compiled in Table I. In general, the lower alkyl amides are quite insoluble in nonpolar solvents and more soluble in polar solvents. At higher temperatures the higher alkyl amides will dissolve in polar solvents.

Uses

The solubility characteristics of the simple amides lead to their main use, the most important of which is as an antislip and antiblock additive for polyethylene film. For this use, octadecenamide and docosenamide are the most important. This is the same property of wax-coated and resin-coated papers which permits one film to slide horizontally on another. Only 0.1-0.5% of amide is used in plastic films, but even at these concentrations the color stability of the amide is important. The use of these additives is permitted in food packaging materials by FDA regulations.

Another use of long chain saturated amides is as an intermediate in the production of water repellents for textiles of the Zelan or Velan type. The products of reaction of the amide with formaldehyde, pyridine, and hydrochloric acid are water soluble quaternary salts which are applied to the fabric and heated to form a water repellent film, probably diamide in structure.

Films of fatty acid amides are deposited from a variety of formulations as mold-release agents. A solution of the amide is usually sprayed onto the mold. With molded rubber goods, the saturated amide is added to the rubber mix before curing and assists in curing and improvement of the mechanical properties.

Fatty acid amides improve the properties of printing ink by assisting slip, reducing gloss, reducing block and tack, and improving resistance to scuffing, scratching, and rub-off. Better spreading properties at the ink-paper interface are obtained along with improved adhesion of the ink to the paper.

The ability of fatty acid amides in hydrocarbon solvents to adhere to metal surfaces makes them valuable additives in lubricants. They increase the wear characteristics of the lubricant and leave no carbon deposits on the metal surface. Both saturated and unsaturated amides may be used for this purpose.

Diamides

Fatty bisamides, or diamides of two types, are produced. One is methylene bisstearamide, which is manufactured by reacting two moles of stearamide with one mole of formaldehyde:

$$2R\text{-}CO\text{-}NH_2 + H_2CO \rightarrow R\text{-}CO\text{-}NHCH_2\text{-}NH\text{-}CO\ R + H_2O$$

The reaction is conducted at 180-200 C and produces a hard waxy product which is useful in powder metallurgy or plastic extrusion lubricants.

Ethylene bisamides are another class of diamides that have industrial significance. These compounds are produced by the condensation of 1 mole of ethylenediamine and 2 moles of stearic acid:

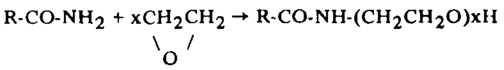
$$2R\text{-}CO\text{-}OH + H_2NCH_2CH_2NH_2 \rightarrow R\text{-}CONHCH_2CH_2NHCOR + 2H_2O$$

In some cases, catalysts can be used, but are not necessary. The reaction is run at 180-185 C.

Ethylene bisstearamide is used as a lubricant in plastic extrusions, mold release agents, and as a defoamer in paper manufacture.

Ethoxylated Amides

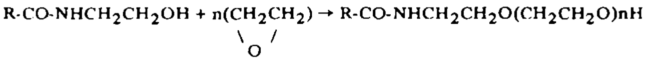
A large variety of ethoxylated amide derivatives can be and are produced. The initial discussion will involve the ethylene oxide condensates of primary amides. The reaction is:



$$R\text{-}CO\text{-}NH_2 + x\underset{\diagdown O \diagup}{CH_2CH_2} \rightarrow R\text{-}CO\text{-}NH\text{-}(CH_2CH_2O)xH$$

It is conducted at 150-200 C using a basic catalyst. A large variety of ethoxylated amides are prepared in this manner and as is expected, the degree of ethoxylation controls HLB value and/or water solubility.

Similar compounds can be prepared by first synthesizing a substituted amide followed by ethoxylation.



$$R\text{-}CO\text{-}NHCH_2CH_2OH + n(\underset{\diagdown O \diagup}{CH_2CH_2}) \rightarrow R\text{-}CO\text{-}NHCH_2CH_2O(CH_2CH_2O)nH$$

There is ample evidence that the ethylene oxide reacts with the hydroxyl function rather than the secondary amido hydrogen (7).

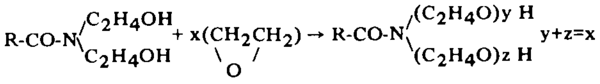
Esters of fatty acids when reacted with diethanolamide produce a high activity or "superamide" containing over 90% n-alkyldiethanolamide (8-10). This type of amide is by far the most important, from a commercial point of view, of the fatty amides. The reaction is run at 115-160 C, using methyl esters of fatty acids, 1.3 moles of diethanolamide and a catalytic amount of sodium methoxide. The methanol is distilled off as it is produced. The alkanolamides are nonionic surface-active agents and have many applications in liquid detergents; such as dishwashing compounds, shampoos, cosmetics, latex stabilizers, and dye leveling agents. They function as foam stabilizers, emulsifiers, viscosity controllers and corrosion inhibitors. Most superamides are produced from either whole coconut

TABLE II

Melting Points of Saturated Primary Amines

	(R—NH$_2$)		
R=	M.p.C.°	R=	M.p.C.°
CH_3	92.5	$C_{11}H23$	16.5
C_2H_5	-80.6	$C_{12}H_{26}$	28.0
C_3H_7	-83.0	$C_{13}H_{27}$	279
C_4H_9	-50.5	$C_{14}H_{29}$	37.9
C_5H_{11}	-55.0	$C_{15}H_{31}$	
C_6H_{12}	-19.0	$C_{16}H_{33}$	46.2
C_7H_{15}	-23.0	$C_{17}H_{35}$	49
C_8H_{17}	0.04	$C_{18}H_{37}$	51.8
C_9H_{19}		$C_{20}H_{41}$	57.8
$C_{10}H_{21}$	15.0	$C_{22}H_{45}$	62.7

fractions or the so-called middle cut which contain essentially 70% C_{12} and 30% C_{14} homologs.



$$R\text{-}CO\text{-}N\begin{matrix}/C_2H_4OH \\ \backslash C_2H_4OH\end{matrix} + x(\underset{\backslash\ O\ /}{CH_2CH_2}) \rightarrow R\text{-}CO\text{-}N\begin{matrix}/(C_2H_4O)y\ H \\ \backslash(C_2H_4O)z\ H\end{matrix}\quad y+z=x$$

In this case, there will be two ethylene oxide chains instead of one, as produced by ethoxylation of primary amides.

Another class of substituted fatty amides, N,N-dimethylalkylamides were introduced in 1961 (11). These products are different in physical and chemical properties and are different in physical and chemical properties and are especially useful as high boiling polar solvents. The amides can be prepared at 140 - 170 C under moderate pressures by reacting either the fatty acid or ester with dimethylamine, continuously venting excess dimethylamine and water or alcohol, separating the DMA and recycling. It has been reported that a 96%+ conversion of the methyl ester to amide can be obtained at 30 C using sodium methoxide as catalyst.

The production of many other substituted amides or diamides is also possible by substituting various other primary or secondary amines in the matrix. In général, the reaction conditions are the same, and the end product obtained is strictly dependent on the structure of the starting components.

FATTY NITRILES

Fatty nitriles are produced by the reaction of fatty acids with ammonia at temperatures of 280-360 C. The reaction can be considered as one of simple dehydration of ammonia soaps and amides, but side reactions and equilibrium reactions involving water have to be considered (12-18). The overall result is:

$$R\text{-}CO\text{-}OH + NH_3 \rightarrow R\text{-}C \equiv N + 2H_2O$$

but the equilibrium reactions are:

$$RCONH_2 \rightleftharpoons RCN + H_2O \text{ and } RCONH_2 + H_2O \rightleftharpoons RCO_2H + NH_3$$

Unless the water of reaction is continuously removed, the end product can contain undesirable contaminants.

Commercial practice today is to produce the nitriles by either a batch or continuous process. The batch or liquid phase procedure can take as long as 24 hours to run, and the end product is usually distilled before further use. Unsaturated feedstocks have a tendency to polymerize at higher temperatures, so they are usually run at lower temperatures, but require a longer reaction time. Catalysts such as ZnO or $Mn(CH_3CO_2)_2$ at 0.1-0.25% by weight can be used. The ammonia rate is adjusted to the rate of reaction and usually about two moles per mole of acid are required.

The continuous process is really used by one company, and is the invention of Potts (18). In this method fatty acids are fed continuously to a liquid reactor, vaporized and passed through a catalytic reactor column countercurrently with ammonia. Excess ammonia and water are removed at the top of the column, and the stream is sent to an ammonia absorber for recovery and recycling. The product nitrile is removed from the reactor column as a vapor and is condensed and used as is. Usually no additional distillation is needed.

Fatty Nitriles

Nitriles, as such, have found limited commercial use, but have been suggested as plasticizers, petroleum lubricant additives, penetrating oils and extreme pressure lubricant additives. The only large use is as an intermediate in production of fatty amines.

PRIMARY AMINES

A large number of methods are known for the preparation of amines, but commercial production is usually based on hydrogenation of a nitrile in either a batch or continuous process. Several nickel and cobalt catalysts are used for this purpose. Caustic and/or ammonia metal soaps have been used to suppress the formation of secondary amine in the Raney nickel- or cobalt-catalyzed hydrogenation of fatty nitriles to primary amines (19,20). These alkalies, however, are reported to yield an undesirable residue during hydrogenation. This can be avoided (21) by using ammonia and a small amount of water instead of alkali. Waddleton (22) has obtained over 96% yield of primary amine by hydrogenating a nitrile at 130-140 C with a partial pressure of ammonia of 2.07 MPa (300 psi) and a total pressure of 3.45 MPa (500 psi) with hydrogen in the presence of Raney nickel catalyst. Other catalysts evaluated include mixtures of Ni, Al, Co oxides (22), $Zn\text{-}Al_2O$ or Zn-Cr oxides (23) and Cu-Cr-alkali and tertiary amines. In continuous processes for making primary amines, both Raney cobalt and nickel catalysts are useful. Ammonia, lower alkylamines, or substances yielding hydroxyl ions are used as suppressants of secondary amine formation. Other procedures include recycling partially converted primary amines, nitrile, ammonia, and hydrogen over a cobalt catalyst bed (25) and introducing hydrogen in small fractions at regular intervals along the reaction zone using Raney nickel catalyst (26). The unsaturation can be preserved during cobalt- or nickel-catalyzed hydrogenations of unsaturated nitriles under certain conditions (27-29).

Fatty acids can be converted directly to primary amines by catalytic hydroammonolysis at high temperatures (300 C) and pressures (30.4 MPa or 440 psi) in the presence of nickel and/or cobalt (30,31) or zinc and/or chromium (32) can be directly converted to amines. In a continuous manufacturing process for diamines, dicarboxylic acids react with excess ammonia in the presence of hydrogen and powdered cobalt oxide at high temperature and pressure (33).

The physical properties of the primary amines were extensively studied by Ralston, et al. (34) in the 1938-1950 era. The boiling point data will be found in Figure 1.

Since the initial uses for primary amines were because of their solubilities, cationic nature and characteristics of their salts, much physical data on these matters was collected. The melting points are shown in Table II.

Primary amines of the saturated higher members are used as hard rubber mold release agents, and dodecylamine is used in reclaiming both natural and synthetic rubber. The amines and their salts are effective flotation agents for

TABLE III

Surface Tension and Wetting Time of Solutions of ETHOMEENS in H_2O

	Surface tension of solution (25 C) Dynes/cm		Canvas-disc method (63)		Official (Draves) method (64)
Derivative	0.1%	1.0%	0.1%	1.0%	0.5%
ETHOMEEN C/15		33	90	3	3.5
ETHOMEEN C/20	39	38	115	11	14
ETHOMEEN C/25	41	41	173	49	
ETHOMEEN T/15	34	33	226	12	23
ETHOMEEN T/25	41	40	157	27	53
ETHOMEEN S/15	33	33	269	23	28
ETHOMEEN S/20	40	39	179	25	29
ETHOMEEN S/25	43	43	198	67	
ETHOMEEN 18/25	34	Gel	360	Gel	

concentrating lower grades of phosphate rock (35), and effective collectors for mica, feldspar, and silica. Amines are the basis for formulations used in protecting hygroscopic materials against atmospheric moisture. They can be used in anticaking granular and blended fertilizers and the single salts of ammonium nitrate, sylvite, sodium nitrate, ammonium sulfate, and urea. The fatty amines are of considerable value in the petroleum industry at all stages from the well head through the finished product. The inherent oil solubility, affinity for metal surfaces, oiliness properties, and acid neutralizing and bactericidal activity are of value for lubricating additives, corrosion inhibitors, and fuel and gasoline additives. The amines are extensively used as intermediates in the manufacture of salts, quaternaries, ethoxylated derivatives, and isocyanates.

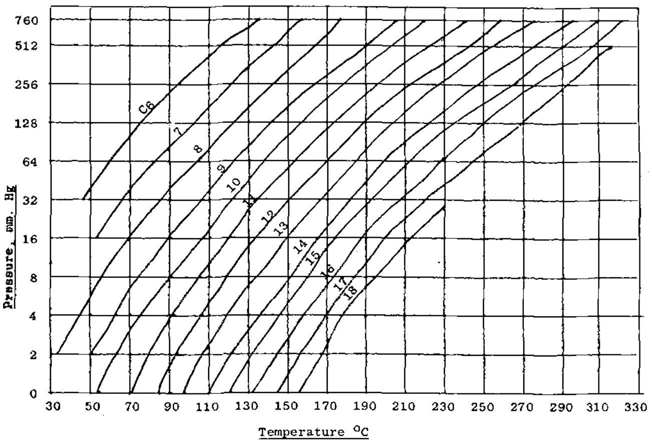
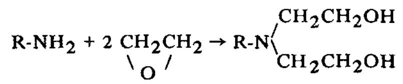


FIG. 1. Vapor pressure of primary N-alkyl amines.

POLYOXYETHYLENE ALKYLAMINES

Preparation of ethoxylated amines was first published in 1934 (36). Since that time, literally hundreds of variations have been described starting with a large variety of amine compounds or derivatives with reactive hydrogens. (37). Included in the great variety of commercially available ethoxylation products are also poly-functioned amines. While the polyoxyethylene alkylamine surfactants are cationic in nature, the cationic activity decreases as the ethylene oxide chain increases.

The reaction of ethylene oxide with primary amines first occurs at 100 C by addition of 2 moles of ethylene oxide to the two active hydrogens without any added catalyst (38):

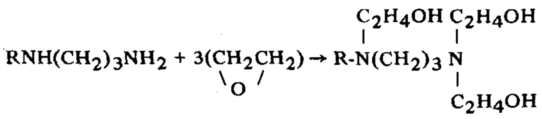


$$\mathrm{R{-}NH_2} + 2\,\underset{\backslash\,\mathrm{O}\,/}{\mathrm{CH_2CH_2}} \rightarrow \mathrm{R{-}N}\begin{matrix}\diagup\mathrm{CH_2CH_2OH}\\ \diagdown\mathrm{CH_2CH_2OH}\end{matrix}$$

Additional ethoxylation requires a basic catalyst and temperatures above 150 C.

The use of secondary amines to produce ethoxylated derivatives is also possible. In this case, only a single ethylene oxide chain is produced.

The most significant ethoxylated diamines produced are manufactured from n-alkyl-1,3 propanediamines:



$$\mathrm{RNH(CH_2)_3NH_2} + 3(\underset{\backslash\,\mathrm{O}\,/}{\mathrm{CH_2CH_2}}) \rightarrow \mathrm{R{-}}\overset{\mathrm{C_2H_4OH}}{\overset{|}{\mathrm{N}}}\mathrm{(CH_2)_3}\underset{\underset{\mathrm{C_2H_4OH}}{|}}{\overset{\overset{\mathrm{C_2H_4OH}}{|}}{\mathrm{N}}}$$

Again, with the use of basic catalysts additional moles of ethylene oxide can be added.

Physical Properties

These cationic surfactants are characterized by a hydrophobic cation when the surfactant is dissolved in water. This makes the surfactant properties somewhat dependent on pH. The lower ethylene oxide adducts are predominantly cationic in character, being insoluble in water at neutral or basic conditions, and will become better surfactants at lower pHs, owing to the formation of water soluble ammonium ions. This improvement in surfactant properties is not true for oxyethylated amines of predominantly nonionic character that are already soluble at neutral or basic conditions. Also, as is generally known for nonionic surfactants, the surface tension lowering is inversely proportional to the length of the ethylene oxide chain.

Table III gives the surface tension of 0.1 and 1.0 % solutions of ETHOMEENS in distilled water at 25 C. The nature of the fatty acids from which compounds in Table V are derived has a direct bearing on surface tension and wetting. Starting with coco-derived compounds, we see that an increase in EO chain length results in increased surface tension and wetting time: unsaturated compounds have lower surface tension and faster wetting times than similarly saturated derivatives.

Applications

Polyoxyethylene alkylamines have a great variety of end uses as emulsifiers in neutral and acid solution, as foaming or frothing agents, as corrosion inhibitors, emulsion breakers, wetting agents, mud-drilling additives, leveling agents for dyes, and as textile-finishing agents (37). They can also be neutralized with organic or inorganic acids to form a new series of surfactants with different general properties. Neutralization with inorganic acids will result in greater water solubility, whereas neutralization with organic acids increases oil solubility.

TABLE IV

Emollient Dishwashing Detergent

	Wt. %
Alkyl ether sulfate	25
Alkyl sulfate	15
Cetyl alcohol	3
Dimethylcocoamine oxide	2.5
Acetic acid	3.2
Sodium acetate	8
Ethanol	8
Water and miscellaneous	35.3

TABLE V

Shampoo Formulation

	Wt. %
Dimethyldodecylamine oxide'	7
Sodium salt of sulfated condensation product of 1 mole of coconut (dodecyl) alcohol with 3 moles of EO	7
Dodecanoyldiethanolamide	5
Perfume, color, citric acid to pH 7.9, water	Balance

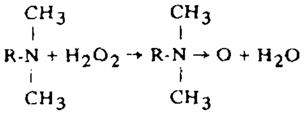
Other formulations using amine oxides in shampoos, detergents, bubble baths, and shaving creams have been published (46).

AMINE OXIDES

Fatty derived aliphatic oxides are a class of nitrogen derivatives that can be classified as weak cationic surfactants. Almost all production is done from tertiary amines that have a long chain aliphatic group and two methyl groups or two hydroxyethyl groups. Amine oxides are hygroscopic compounds that have large dipole moments and are soluble in polar solvent, but relatively insoluble in nonpolar solvents.

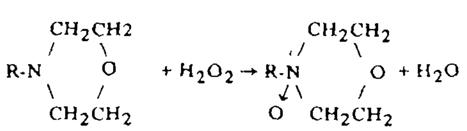
Manufacture

The largest volume industrial amine oxides are derived from alkyldimethylamines, alkylbis(2-hydroxyethyl-) amines, and amidoamines. All cases contain the alkyl group which may have 8-20 carbon atoms and may or may not be unsaturated. The general reaction is:



$$R\text{-}\overset{\overset{CH_3}{|}}{\underset{\underset{CH_3}{|}}{N}} + H_2O_2 \rightarrow R\text{-}\overset{\overset{CH_3}{|}}{\underset{\underset{CH_3}{|}}{N}} \rightarrow O + H_2O$$

In addition, there has been some interest in n-alkylmorpholine oxides which are prepared as follows:



Most frequently the commercially available amines are homologous mixtures. The procedure employed for oxidation consists essentially in adding aqueous hydrogen peroxide to a well sitrred solution or dispersion of the amine at 60-80 C. Since the reaction is exothermic, cooling may be necessary during addition of the hydrogen peroxide. However, when addition is complete, it is usually necessary to supply heat in order to maintain the desired temperature during a digestion period.

The amine oxide reactor and its auxiliary equipment (amine and solvent feed lines, product lines, agitator, heat exchange coils, and product storage tanks) are constructed of 316 stainless steel or may be glass-lined. For safe operation, the reactor should be open to the atmosphere. When a lower alcohol or acetone is used as the solvent, an efficient condenser is required. A vacuum capability for the reactor is desirable, although not necessary, since the same reactor may then be used for stripping the solvent to concentrate the product, as long as excess H_2O_2 is first destroyed. Because of the foaming tendencies of amine oxides, there should be at least 20% headspace in the reactor.

With isopropyl alcohol or aqueous isopropyl alcohol as the solvent, concentrations of amine oxide up to 65-70% can be attained. When a strictly aqueous system is employed, final concentrations of amine oxide should be limited to 35% since higher concentrations tend to gel and prevent good mixing. Because hydrogen peroxide is sensitive to heavy metals and amine oxides are readily decomposed by iron salts, sequestering agents are generally added to the reaction mixture, particularly when water is the solvent.

Uses

Aromatic amine oxides have been found useful in the pharmaceutical field as analgesics, antihistaminics, antitussives, diuretics, tranquilizers, and drug potentiators. In many cases, the N-oxides of pharmacologically active tertiary amines have proven to possess added benefits ranging from lower toxicity and better solubility to enhanced therapeutic behavior. The biological activity of these materials has led to patented uses as bactericides, fungicides, insecticides, nematocides, filaricides, amoebicides, anthelmintics, antiparasitics, and disinfectants. The pharmacology and biochemistry of amine oxides has been reviewed (40). Earlier references covering these and other applications were reported in a survey on amine oxides by the DuPont Company (41).

Applications of fatty amine oxides in detergents and cosmetics depend primarily upon their surfactant properties. Such properties were first disclosed in 1939 when these materials were described as wetting, cleaning, and dispersing agents (42). However, it was not until the 1960s that these materials were employed in detergent formulations (43) and shampoos (44). The first product that used significant quantities of amine oxides was a liquid household detergent formulation for dishwashing. In this application, the amine oxides replaced fatty alkanolamides as foam boosters.

A recent patent (45) gives the following general formulation for an emollient dishwashing detergent shown in Table IV.

The detergent, foaming, antistatic, and antiseptic properties of amine oxides are of interest for shampoo formulations. Owing to these properties, shampoos containing amine oxides not only clean the hair but give it body and luster, as well as make it more manageable. Shown in Table V is a shampoo formulation incorporating amine oxide (44).

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