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FATTY ACID DERIVATIVES OF DIETHANOLAMINE

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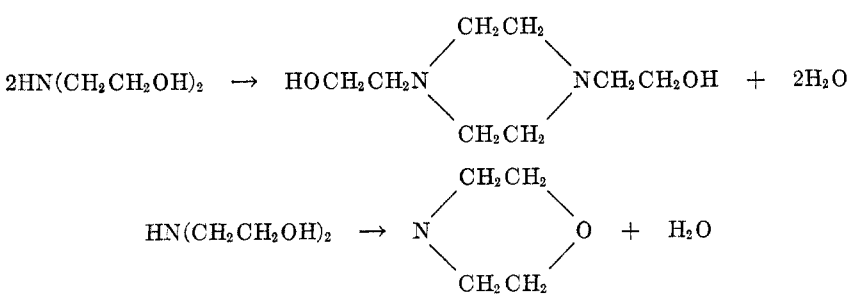
In recent years products prepared by the condensation of higher fatty acids with diethanolamine have become important in surface active systems (1). In the process of preparing these products by heating the two components at 150–200° water is distilled from the reaction mixture and the reaction has usually been described by the following equation:

$$RCOOH + HN(CH_2CH_2OH)_2 \rightarrow RCON(CH_2CH_2OH)_2 + H_2O$$

I

Although the synthesis and properties of the alkanolamides have been previously reported, our present work has shown that because of the complexity of the reaction the products have been impure. There has been much speculation concerning the course of the reaction but little experimental evidence has been presented (2, 3).

Previous examination of such products in our laboratories and elsewhere (4) has indicated that, in addition to the expected amide, they contain esters and tertiary amines. The formation of the latter is known to occur under certain conditions when diethanolamine undergoes self-condensation upon heating to form N,N′-bis-(2-hydroxyethyl)piperazine (5) or morpholine (6).



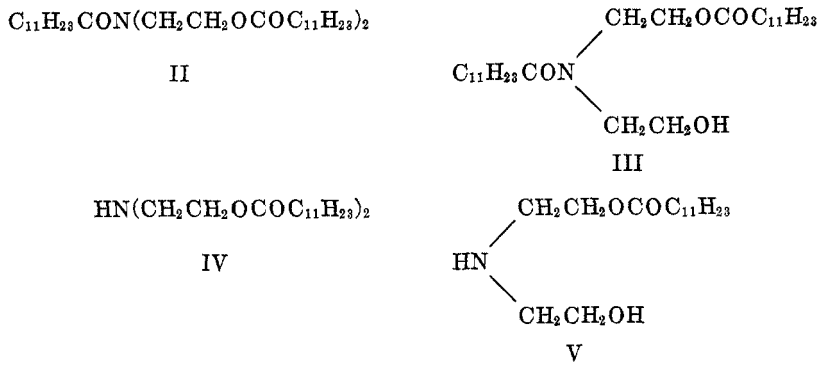
In order to evaluate the effect of ester impurities on the surface active properties of the product, the preparation of the individual acylated derivatives, amides and esters, of diethanolamine was undertaken.

In addition to lauric diethanolamide,[1] I ($R{=}C_{11}H_{23}$), we have prepared the mono- and di-lauric esters of lauric diethanolamide and of diethanolamine.

The preparation of the lauric esters, II and IV, was readily accomplished by acylation of lauric diethanolamide (I), and diethanolamine hydrochloride with two moles of lauroyl chloride in chloroform. The monolauric ester (III) was prepared similarly from I using one mole of lauroyl chloride and was purified by

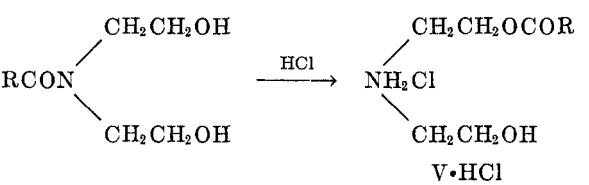
[1] The trivial name lauric diethanolamide is commonly used in the literature rather than the systematic name N,N-bis-(2-hydroxyethyl) lauramide.

recrystallization and preferential extraction of unchanged lauric diethanolamide and any of the diester, II, which may also have been formed.



Attempts to prepare the monolaurate (V) of the amine hydrochloride by direct acylation of diethanolamine hydrochloride with lauroyl chloride were unsuccessful; the only product isolated was the hydrochloride of the diester (IV). This was true even when a tenfold excess of diethanolamine hydrochloride over lauroyl chloride was used. The failure of this approach can be attributed to the fact that no suitable mutual solvent for lauroyl chloride and diethanolamine hydrochloride was found. Similarly, we were unable to find a mutual solvent for the diester amine hydrochloride, IV•HCl, and diethanolamine hydrochloride, so that an attempt to prepare the hydrochloride of V by ester displacement was unsuccessful.

A more fruitful approach to V was suggested by the numerous examples of the migration of acyl groups from nitrogen to oxygen in which hydroxy amides are transformed to amino esters by the action of strong mineral acids.



Desnuelle, *et al.* (7) have reported a closely analogous reaction of stearic monoethanolamide to yield the hydrochloride of 2-aminoethyl stearate. Transformations of this type have generally been carried out with excess acid and often at moderately high temperatures in solvents such as refluxing dioxane, alcohol, chloroform, or hydrochloric acid (7–9). When similar conditions were initially used for the transformation of lauric diethanolamide the products appeared to be complex mixtures of amino esters and we were unable to isolate the hydrochloride of V, but obtained small yields of the hydrochloride of the diester, IV.

Recently much evidence has been presented that these migrations proceed through an intramolecular displacement and this concept has proved useful in establishing the stereochemistry of amino alcohols (10). The study of the ben-

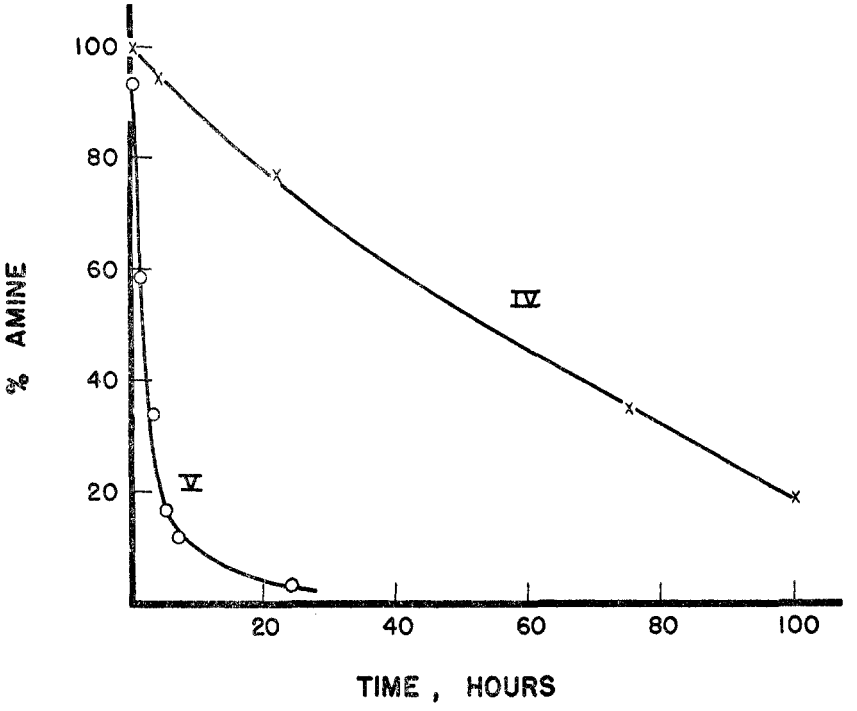


FIG. 1. RATES OF DISAPPEARANCE OF THE AMINES IV AND V FROM MELTS AT 56°

zoates of *cis* and *trans* 2-aminocyclopentanols by van Tamelen (8) and Fodor and Kiss (9) provides a classical example. This work suggested that the primary product in our case, V•HCl, was lost through further side reactions and that milder conditions would prove more successful. The desired reaction was accomplished and V•HCl was isolated in 54% yield when lauric diethanolamide was dissolved in dioxane containing an equivalent amount of hydrogen chloride and allowed to stand at room temperature. The ester amine hydrochloride crystallized slowly from this solution.

The free bases, IV and V, prepared by carefully neutralizing the hydrochlorides, were unstable solids at room temperature. We were able to obtain IV

TABLE I

DIETHANOLAMIDES FROM FATTY ACIDS

Diethanolamide	Melting Point, °C.[a]	Analysis Nitrogen	
		Calc'd	Found
Lauric	48.0–48.5 (38.7)	4.87	4.81
Myristic	57 –58 (47.9)	4.43	4.31
Palmitic	63 –64 (65.1)	4.08	3.91
Stearic	72 –73 (69.7)	3.78	3.76

[a] Values in parentheses are those previously reported (11).

in reasonable purity although a complete disappearance of amine function was noted on a two year old sample. We obtained V in about 93 % purity and noted a complete disappearance of amine function over a period of several months. Recrystallization of a year old sample of V yielded a product, m.p. 48°, which was identified as lauric diethanolamide. A comparison of the rates of disappearance of IV and V when molten at 56° is presented in Figure 1.

The myristic, palmitic, and stearic diethanolamides were also prepared. The melting points that we observed for this series, Table I, are substantially different from those previously reported by D'Alelio and Reid (11).

EXPERIMENTAL

Preparation of the diethanolamides. The preparation of the fractionated acid chlorides from the fatty acids and phosphorus trichloride has been described previously (12). The acid chloride, 0.1 mole, was dissolved in 25 ml. of chloroform and placed in a dropping-funnel attached to a three-necked flask, equipped with a stirrer and thermometer, which contained 0.3 mole of diethanolamine in 25–50 ml. of chloroform. (The larger amount of chloroform is preferred for the stearic derivative.) The acid chloride was added slowly with stirring while maintaining the contents of the flask at 15–20° with external cooling. When the addition of the acid chloride was complete, the product was washed with three to five 50-ml. portions of 5% sodium sulfate solution, until the washings were nearly neutral. The chloroform was removed under reduced pressure on the steam-bath. The product obtained then was purified by repeated recrystallization from acetone or ligroin. Approximately 1 part of amide to 7 parts of solvent was used. The product was allowed to crystallize at room temperature and then cooled to 0° before filtration. The product was presumed to be pure when amine and acid were absent and no ester carbonyl absorption at 5.7–5.8 μ was present in the infrared spectrum. Absorption maxima at 6.18 μ, amide carbonyl, and 2.95 μ, hydroxyl, were present. The yield of recrystallized product was 80–90% based on acid chloride. Analyses for nitrogen are presented in Table I. The hydroxyl value for lauric diethanolamide, determined by the method of Ogg, Willets, and Porter (13), was 11.72%, calc'd 11.85%.

Lauric bis-(2-lauroxyethyl)amide (II). Lauric diethanolamide, 28.7 g. (0.1 mole), and fractionated lauroyl chloride, 44 g. (0.2 mole), were dissolved in 100 ml. of chloroform and refluxed for three hours. At the end of this time the evolution of hydrogen chloride appeared to be substantially complete. Upon cooling to room temperature, a small precipitate (5–10 g.) separated and was removed by filtration. This precipitate, after recrystallization from chloroform, melted at 117–119°.

The main chloroform filtrate then was concentrated under a vacuum until most of the chloroform was removed. The residue, which solidified upon cooling, then was taken up in 700 ml. of boiling ligroin, cooled to 25°, and filtered from insoluble matter. The filtrate was finally chilled to −15° to yield 48 g. of product, m.p. 48–49°, which was found to contain about 0.5% free lauric acid by titration with standard alkali. It again was recrystallized from 250 ml. of ligroin to yield 42 g. of lauric bis-(2-lauroxyethyl)amide, m.p. 49–50°, which contained 0.2% free lauric acid by titration. Infrared absorption maxima at 6.04 and 5.76 μ were assigned to amide and ester carbonyl. The saponification equivalent of II, using 100% excess 0.1 *N* alcoholic potassium hydroxide and a two hour reflux period, was 221; 217 calculated for both amide and ester cleavage.

Anal. Calc'd for $C_{40}H_{77}NO_5$: N, 2.15. Found: N, 2.06.

Bis-(2-lauroxyethyl)amine (IV). A solution of 26.5 g. of diethanolamine (0.25 mole) in 100 ml. of chloroform was saturated with hydrogen chloride gas. Then 109 g. of fractionated lauroyl chloride (0.5 mole) was added and the mixture was refluxed with stirring until evolution of hydrogen chloride ceased (3–4 hours). The reaction mixture then was decanted

while hot from 1–2 ml. of an immiscible oil (presumably unreacted diethanolamine hydrochloride). The solid which crystallized upon cooling in the refrigerator was collected and recrystallized from 200 ml. of chloroform to yield 77 g. of IV •HCl, m.p. 119–120°; a maximum at 5.73 μ was assigned to ester carbonyl. A neutralization equivalent, found by titration of a sample in alcohol with 0.1 *N* sodium hydroxide to a phenolphthalein end point, was 502, calc'd 505.

Anal. Calc'd for $C_{28}H_{56}ClNO_4$: N, 2.77; Cl, 7.00.

Found: N, 3.03; Cl, 7.13.

A mixture melting point of IV•HCl with the by-product, m.p. 117–119°, isolated in the preparation of II was not depressed. To isolate the free base 5 g. of IV•HCl was suspended in a mixture of 50 ml. of chloroform and 50 ml. of water. The mixture was stirred vigorously while 0.1 *N* sodium hydroxide was added slowly over a period of 20 minutes until the mixture had a constant *p*H of 9. The chloroform phase was separated and concentrated under reduced pressure. The free base, IV, which separated on cooling was recrystallized from chloroform, m.p. 36–38°. The neutralization equivalent was found to be 468 (theory 469) by potentiometric titration of a sample dissolved in alcohol with 0.1 *N* methanolic hydrogen chloride.

Lauric (2-lauroxyethyl)-(2-hydroxyethyl)amide (III). Lauric diethanolamide, 28.7 g. (0.1 mole), and 8 g. (0.1 mole) of pyridine were dissolved in 75 ml. of chloroform. Lauroyl chloride, 21.8 g. (0.1 mole) was added with stirring over a period of 20 minutes. The reaction mixture then was washed with three 100-ml. portions of water and the chloroform was removed under reduced pressure. The oily residue, which solidified upon cooling, was dissolved in 200 ml. of petroleum hexane, b.p. 60–71°. This solution was washed with three 100-ml. portions of 80% aqueous methanol by volume (to remove lauric diethanolamide) and was placed in the refrigerator to crystallize. The solid was collected and recrystallized from hexane to yield 38 g. of III, m.p. 47.0–47.5°, absorption maxima at 6.22 μ, amide, 5.76 μ, ester, and 2.96 μ, hydroxyl. A mixture melting point of III and I was 40–44°, and similarly III and II melted at 44–46°. The saponification equivalent of III was 238, 235 calc'd for both ester and amide cleavage. The hydroxyl value found was 3.66%, calc'd 3.63%.

Anal. Calc'd for $C_{28}H_{55}NO_4$: N, 2.99. Found: N, 2.90.

(2-Lauroxyethyl)-(2-hydroxyethyl)amine (V). Dry hydrogen chloride was added to 620 ml. of purified dioxane until the solution contained 0.365 mole of acid. Lauric diethanolamide, 104.8 g. (0.365 mole) was added. The clear solution then was stoppered and allowed to stand 2 days at room temperature. The precipitate which formed was removed by filtration. After several additional days at room temperature a further crop of crystals was obtained. The combined crops were recrystallized from a mixture of chloroform and ligroin to yield 64 g. of shiny plates, m.p. 93–98°.

A small portion of the above product was recrystallized several times from chloroform-ligroin and from acetone to a constant melting point, 99.8–100.3°, determined with the Kofler hot stage. Absorption maxima were observed at 5.75 μ, ester, and 3.05 μ, hydroxyl.

Anal. Calc'd for $C_{16}H_{34}ClNO_3$: N, 10.99; Cl, 4.35.

Found: N, 10.84; Cl, 4.37.

To isolate the *free base* 20 g. of V•HCl was dissolved in 600 ml. of water. The solution was cooled to 8° and dilute sodium hydroxide was added slowly with stirring until the solution reached *p*H 10.5. The cold cloudy mixture then was extracted rapidly with several portions of cold ether. The ether extract was dried over magnesium sulfate in the refrigerator, filtered, and evaporated to dryness under reduced pressure. The residue was recrystallized from cold ligroin to yield the free base melting at 42–44° with a neutralization equivalent of 305 (theory for V is 287). The product, originally estimated to be 93% pure on the basis of its neutralization equivalent, decomposed on standing several months at room temperature with an almost complete disappearance of titratable amine. Lauric diethanolamide (I) was obtained in good yield and purity when an old sample of V was recrystallized from acetone.

The data plotted in Figure 1 were obtained from fresh samples of IV and V held at 56 ±

1°. Approximately 0.5-g. portions of the melts were withdrawn, dissolved in cold alcohol, and titrated with 0.1 *N* methanolic hydrogen chloride to a phenolthalein end point.

SUMMARY

Lauric, myristic, palmitic, and stearic diethanolamides have been prepared from fatty acid chlorides and excess diethanolamine.

The preparation of other acylated derivatives of diethanolamine is described. These include bis-(2-lauroxyethyl)amine hydrochloride, (2-lauroxyethyl)-(2-hydroxyethyl)amine hydrochloride, lauric bis- (2-lauroxyethyl)amide, and lauric (2-lauroxyethyl)-(2-hydroxyethyl)amide.

The ester amine hydrochlorides have been converted to the free bases which are unstable solids at room temperature, the monoester derivative being less stable than the diester derivative.

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