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MANUFACTURE OF MONO-ACYLATED ETHYLENE-DIAMINE AND ITS DERIVATIVES

Karl Wilhelm Rosenmund, Kiel, Germany

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A patent application has been filed in Germany on October 31, 1929.

This invention has reference to the manufacture of monoacyl-compounds of bivalent amines and of their derivatives, and it refers more particularly to monoacyl-compounds of ethylene-diamine and of derivatives thereof, and it is intended among other objects to devise means of obtaining a greater range of such compound than was obtainable heretofore and to improve and facilitate the process of manufacture generally.

The manufacture of monoacyl-compounds of ethylene-diamine with acyl-groups of higher fatty acids is well known. The usual process of their manufacture consists in the treatment of ethylene-diamine with esters, chlorides or anhydrides of higher fatty acids. Attempts to manufacture monoacyl-compounds of lower fatty acids in the same manner by means of chlorides or anhydrides however resulted merely in the production of diacyl-compounds. It has also become known from the prior art that ethylene-diamine fails to yield monoacyl-compounds for instance with aceto-substituted acetic acid ester and cyan-acetic acid ester, and it has been ascertained by investigations that benzoic-acid-esters, when heated with ethylene-diamine yield only diacyl-compounds, so that there was no possibility of obtaining monoacyl-compounds in accordance with the methods of the prior art.

It was obvious that higher fatty acids should react in a different manner than lower fatty acids, inasmuch as higher fatty acids and their derivatives are differentiated from the corresponding compounds of the lower fatty acids by their reduced chemical activity. Yet, from my investigations the unexpected result has been derived that the esters, but not the anhydrides and chlorides of the lower fatty acids produce a very good yield of the desired monoacyl-compounds. By this treatment mainly the monoacylated compounds are obtained, while only very small quantities of diacyl-derivatives are formed.

The lower homologues of the monoacyl-compounds are very similar to each other. They constitute basic substances, capable of distillation, and chemically reactive. On account of their chemical and physical properties they are very suitable to serve as materials for the production of various compounds and preparations of high importance in the arts and for therapeutic uses.

The reaction in my invention takes place according to the following formula:—

$$RCOOR_1 + NH_2CH_2CH_2NH_2 = RCONHCH_2CH_2NH_2 + R_1OH$$

In my invention ethylene diamines having the generic formula $NHK—CH_2—CH_2—NHK_1$ are mixed and heated with esters of aliphatic monobasic carboxylic acids containing not more than 10 carbon atoms to form monoacyl compounds of ethylene diamines, these compounds having the generic formula $NHK—CH_2—CH_2—NK_1—CO—R$; K and K_1 in the above formulæ representing hydrogen or alkyl groups and —CO—R representing the acyl group of an aliphatic monobasic carboxylic acid containing not more than ten carbon atoms.

Esters of non-substituted mono-carboxylic acids with not more than 10 carbon atoms react readily, no matter whether the carbon-chain is straight or branched out. The yields vary between 60% and 80%. Examples in which use is made of fatty acids with straight carbon-chain and with branched out chain, and with saturated and unsaturated chains, and of N-alkylated ethylene-diamine with secondary amino-groups are hereinafter enumerated, viz:—

(1) 1 molecule of ethyl acetate and 1.2 molecules ethylene-diamine-hydrate having the formula $C_2H_4(NH_2)2.H_2O$, are heated to 100 degrees Celsius for several hours under pressure, for instance, in an autoclave. The solution is freed by fractionation from the alcohol formed and from the excess of ethylene-diamine and is distilled under a high-vacuum. The resultant mono-acetyl-ethylene-diamine boils at 135–140 degrees Celsius under an absolute pressure of 2 millimeters. It constitutes a water-soluble oil of basic reaction.

(2) Butyryl-ethylene-diamine is obtained as follows:—10 grams ethylene-diamine are heated for 4 hours with a reflux-condenser with somewhat less than the calculated amount of ethyl-butyrate. The mono-butyryl-ethylene-diamine of which a yield of 70% is obtained is separated by distillation. The boiling point of this compound at 1.6 millimeters is 146–148 degrees Celsius.

By using instead of the butyric acid ester other aliphatic monobasic carboxylic-acid esters, for example esters of propionic acid, iso-butyric acid, iso-valerianic acid, crotonic acid and di-ethyl-acetic acid the corresponding monoacyl-compounds may be obtained. They all constitute viscous, basic liquids. Their respective boiling points are as follows:—

	Boiling point in degrees C.	Pressure in mm.	Yield
			Percent
Mono - butyryl - ethylene - diamine	138–145	1.8–2.2	70
Mono - iso - butyryl - ethylene-diamine	140–150	1.8–2.2	75
Mono-iso-valeryl-ethylene-diamine	136–142	1.8–2.2	70
Mono-diethyl-acetyl-ethylene-diamine	152–168	1.8–2.2	80
Mono - crotonyl - ethylene - diamine	160–170	20	60
Mono - propionyl - ethylene - diamine	138–143	2.0	80

(3) Cyclohexyl - monoacetyl-ethylene-diamine is obtained as follows:—5 grams cyclohexyl-ethylene-diamine are heated with somewhat less than the calculated amount of ethyl acetate at 110 degrees Celsius under pressure and the product obtained is distilled under high vacuum. It constitutes a thick, basic oil, having a boiling point of 168 degrees Celsius at 2.2 millimeters. Yield 75%. Its hydro-chloride salt melts at 186 degrees Celsius.

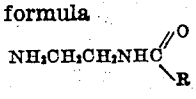
The cyclohexyl-ethylene-diamine used was obtained by the catalytic reduction of the constituents of a molecular mixture of ethylene-diamine and cyclohexanone according to the formula:—

$$C_6H_{10}O+NH_2CH_2CH_2NH_2+H_2=H_2O+C_6H_{11}NH\cdot CH_2CH_2NH_2$$

It should be understood that the scope of the invention is not to be limited to nor restricted by the examples herein described merely as illustrations of the embodiment of this invention, the invention being susceptible of modifications and changes of material and quantities thereof, except as otherwise appears from the appended claims.

I claim:—

1. Monoacyl-compounds of ethylene-diamine containing an acyl group of the lower fatty acids up to ten carbon-atoms in the molecule, constituting basic, readily reacting compounds, and having the generic formula



in which COR represents an aliphatic acyl radical.

2. Mono-butyryl-ethylene-diamine boiling at 150–160 degrees Celsius.

3. Mono-acetyl-ethylene-diamine constituting a basic, water soluble oil, and boiling at 135–140 degrees Celsius under 2 millimeters pressure.

4. In the manufacture of aliphatic monoacyl compounds of ethylene diamine, the process which comprises mixing and heating together ethylene diamine with an ester of an aliphatic monobasic carboxylic acid containing not more than ten carbon atoms, and recovering the resulting monoacyl compound from the reaction mixture.

5. In the manufacture of aliphatic monoacyl compounds of ethylene diamine, the process which comprises mixing and heating together an ethylene diamine having the generic formula $NHK—CH_2—CH_2—NHK_1$ with an ester of an aliphatic monobasic carboxylic acid containing not more than ten carbon atoms and recovering the resulting monoacyl compound from the reaction products: K and K_1 in the above formula representing hydrogen or alkyl groups.

6. The process of claim 5 wherein the reaction is conducted at superatmospheric pressures.

7. The process of claim 5 wherein the monoacyl compound is recovered from the reaction products by distillation.

8. The process of claim 5 wherein the reaction is conducted at superatmospheric pressures, at temperatures of about 100° to 110° C. and wherein the said ester is unsubstituted.

9. Monoacyl compounds of ethylene diamines having the generic formula $NHK—CH_2—CH_2—NK_1—CO—R$ wherein K and K_1 represent hydrogen or alkyl groups and —CO—R represents the acyl group of an aliphatic monobasic carboxylic acid containing not more than ten carbon atoms.

10. The monoacyl compounds of claim 9 wherein K and K_1 represent hydrogen atoms.

11. The monoacyl compounds of claim 9 wherein at least one of K and K_1 represents an alkyl group.

12. Cyclo-hexyl-monoacetyl-ethylene diamine, being a basic viscous oil boiling at about 168° C. at 2.2 mm. pressure.

13. The process of producing cyclohexyl-monoacetyl-ethylenediamine which comprises heating cyclohexyl-ethylenediamine under pressure with somewhat less than the theoretical quantity of ethyl acetate, and then distilling off the resulting product under a vacuum.

KARL WILHELM ROSENMUND.