

UNITED STATES PATENT OFFICE

2,548,156

PREPARATION OF N-DIALKYL
HYDRACRYLAMIDES

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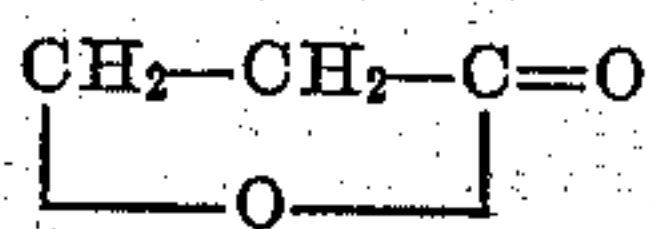
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This invention relates to the preparation of nitrogen and oxygen containing organic compounds, particularly N,N-dialkyl amides of beta-hydroxy saturated aliphatic monocarboxylic acids, such as hydracrylic acid, and beta-N,N-dialkyl-amino saturated aliphatic monocarboxylic acids, such as propionic acid, and pertains particularly to the preparation of such compounds by the reaction of dialkyl amines with beta-lactones.

It is disclosed in U. S. Patent 2,356,459 to Frederick E. Küng that beta-lactones, that is, lactones or inner esters of beta-hydroxy carboxylic acids, may be obtained in good yields by the reaction of a ketene with an aldehyde or ketone. In this manner, beta-propiolactone (also called hydracrylic acid lactone) which has the structure

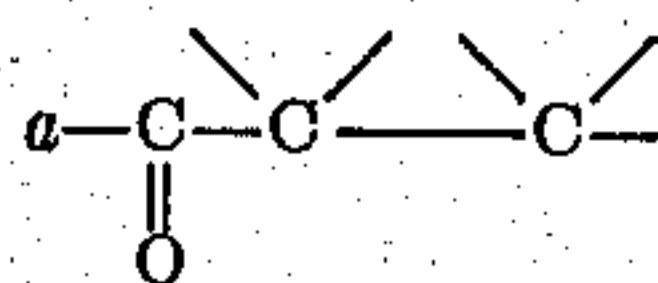


is economically obtained from ketene and formaldehyde.

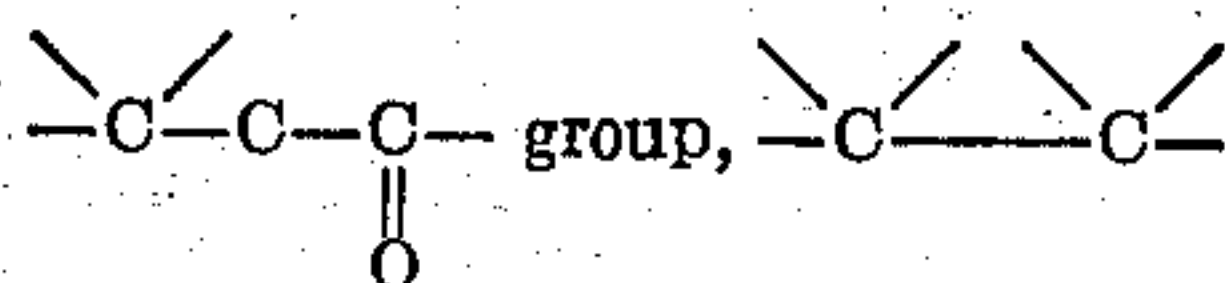
We have discovered that beta-propiolactone, and also the liquid homologs thereof (that is, liquid saturated aliphatic beta-lactones) will react with dialkyl amines in a completely organic liquid medium (that is a medium formed by admixing the two reactants either alone or in the presence of a substantially inert organic solvent or diluent) to form in very high yields nitrogen and oxygen containing compounds of the general structure



wherein each R is alkyl and R₁ is a bivalent aliphatic structure composed of a carbonyl group attached to one of the two valences of an alkylene radical having its two valences on adjacent carbon atoms (that is,



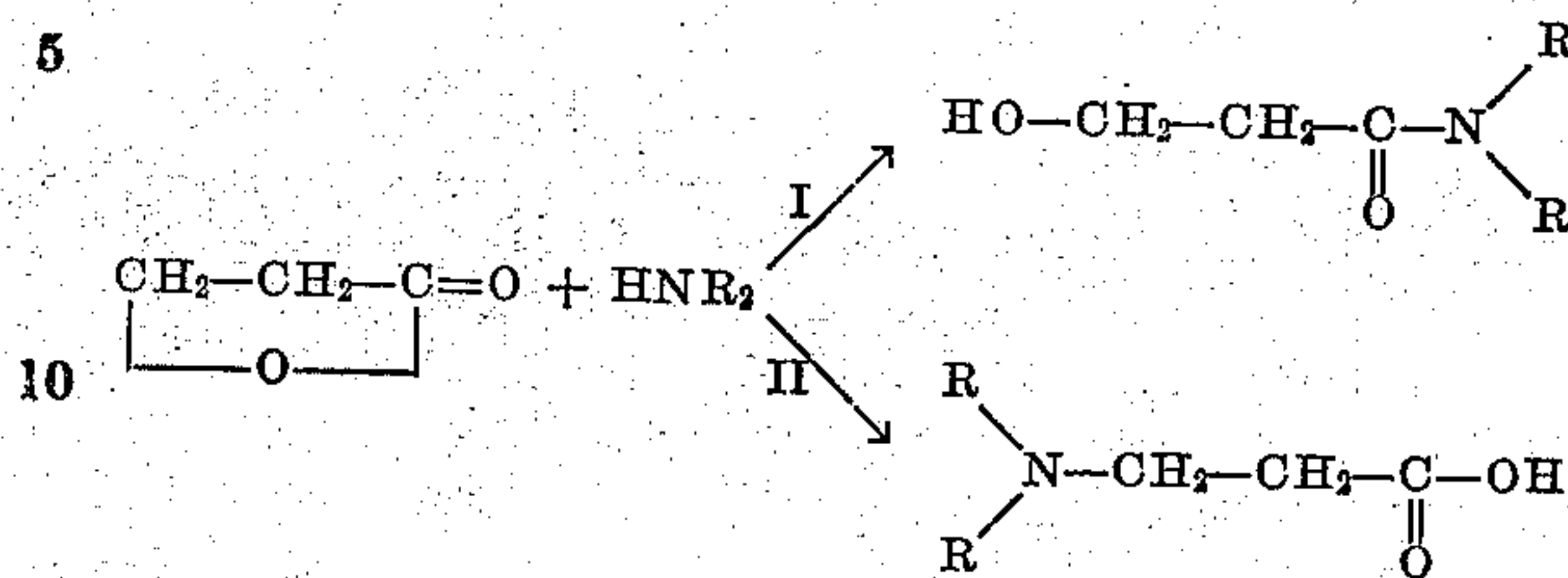
or



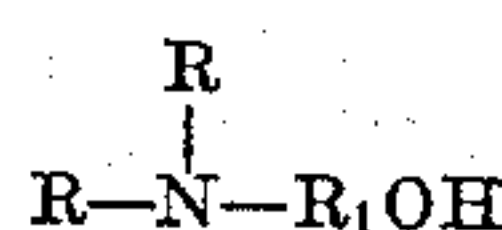
representing the alkylene radical), and that this reaction provides a convenient and economical method of obtaining numerous organic compounds useful as organic intermediates and for other purposes, many of which have not heretofore been prepared or have been obtained only with difficulty and/or from relatively costly raw materials.

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The reaction between beta-propiolactone and a dialkyl amine in a completely organic medium proceeds as shown by the following equation:



It will be noted that the reaction follows two courses involving opening of the beta-lactone ring on different sides of the ring oxygen atom, and that the product of course I is an N,N-dialkyl amide of hydracrylic acid whereas the product of course II is a beta-N,N-dialkyl-amino propionic acid. Each of the products, however (as well as the products from other liquid saturated aliphatic beta-lactones, which react in the same manner as beta-propiolactone), is a compound of the general formula



as set forth hereinabove.

While both products are ordinarily formed at least to some extent when any dialkyl amine is reacted with beta-propiolactone either in the absence of any added ingredients or in the presence of an inert organic solvent, the predominant product of the reaction will depend upon the particular dialkyl amine being used, and the method of bringing the reactants together. In any event, however, the recovered yield of the two products combined is very high, generally above 90% and is limited only by ability to recover all of the products from the reaction mixture.

When the dialkyl amine used is dimethyl amine and the reaction is effected by adding this amine to beta-propiolactone alone or to a solution thereof in an inert organic solvent, the product of the reaction consists substantially entirely of beta-N,N-dimethyl-amino propionic acid, which precipitates from the reaction mixture and is recovered in very high yield simply by filtration. The process of preparing beta-N,N-dimethyl-amino propionic acid in this manner, while an embodiment of the invention herein disclosed, is more particularly disclosed and claimed in our copending application Serial No. 61,125, filed November 19, 1948 now U. S. Patent 2,526,556.

On the other hand, when beta-propiolactone is added to liquid dimethyl amine or to a solution

thereof in an inert organic solvent, the reaction follows course I in preference to course II with the result that the recovered product consists of above 90% of N,N-dimethyl hydracrylamide and only a few percent of beta-N,N-dimethyl-amino propionic acid. When both the amine and the beta-propiolactone are simultaneously added to a solvent, the reaction proceeds in both ways simultaneously with the result that both the amide and the amino acid are recovered in 40-50% yield.

It is thus seen that predominant yields of either the amide or amino acid, or substantially equivalent amounts of the two may be obtained from beta-propiolactone and dimethyl amine depending only on the manner in which the reactants are brought together. The liquid homologs of beta-propiolactone also react in organic medium with dimethyl amine according to the same pattern.

With dialkyl amines other than dimethyl amine, however, the product obtained is predominantly an amide regardless of the method of bringing the reactants together, but amino acids are also secured in minor amounts. For example, both the addition of beta-propiolactone to diethyl amine or a solution thereof in an organic solvent, and the addition of diethyl amine to beta-propiolactone or a solution thereof in an organic solvent result in the obtainment of a reaction product composed predominantly of N,N-diethyl hydracrylamide. Other dialkyl amines such as di-n-propyl amine, di-isopropyl amine, di-n-butyl amine, di-tert-butyl amine, di-sec-butyl amine, di-amyl amines, di-hexyl amines, di-octyl amines, etc. also react with beta-propiolactone in a completely organic medium to give a major proportion of the N,N-dialkyl hydracrylamide and a minor proportion of a beta-N,N-dialkyl-amino propionic acid, regardless of how the reactants are brought together. With homologs of beta-propiolactone these amines likewise yield a major proportion of N,N-dialkyl amide and a minor proportion of beta-N,N-dialkyl amino acid.

Although this invention is limited to reactions carried out in a completely organic liquid medium, no other special conditions are necessary. The quantities of beta-lactone and amine employed are not critical but it is generally preferred to use equimolecular proportions of lactone and amine or an excess of the amine, say from 1 to 2 moles of amine for each mole of lactone, since the presence of excess beta-lactone is of no particular advantage and in fact may be disadvantageous due to the formation of lactone polymer.

The reaction is preferably carried out at atmospheric pressure and at a temperature in the range of -30 to 60° C., more preferably at 0 to 50° C. The reaction is exothermic and liberates heat, hence it is unnecessary to supply heat externally but it often is desirable to cool the reaction mixture in order to maintain the preferred temperature. However, other temperatures and pressures may be used provided the reactants are maintained in the liquid condition during the reaction.

While presence of an inert organic solvent during the reaction is not essential, the use of such a solvent is desirable since stirring of the reaction mixture and heat removal is thereby facilitated, and the tendency for the beta-lactone to polymerize is repressed. The specific nature and amount of the solvent used, if any, are not at all critical since any polar or non-polar or-

ganic solvent may be used so long as it is capable of existing in the liquid state, and is substantially inert to the reactants, under the conditions used. It is desirable that the solvent be volatile, preferably that it have a boiling point below 150° C. since it can then be more readily recovered and reused in the process. Specific inert solvents which are effective include benzene, toluene, pentanes, hexanes, and other liquid saturated aliphatic or aromatic hydrocarbons; chlorinated liquid derivatives of such hydrocarbons such as chlorobenzene and ethylene dichloride; liquid ethers such as diethyl ether, dipropyl ether, etc.; liquid esters such as methyl acetate, ethyl acetate, methyl propionate and the like; liquid organic nitriles such as acetonitrile, propionitrile, benzonitrile, etc.; and liquid ketones such as acetone, methyl ethyl ketone, etc. Liquid alcohols are also substantially inert to the reactants under the preferred conditions of the reaction (that is, at temperatures of -30 to 60° C. and, since the reaction is effected in a completely organic medium, in the absence of inorganic acids and bases), despite the fact that alcohols do react with beta-lactones under other conditions. Accordingly, such alcohols may be employed as solvents if desired, examples of suitable alcohol solvents being methanol, ethanol, ethylene cyanohydrin, ethylene chlorohydrin and especially tertiary alcohols such as tert butanol, and the like.

After the beta-lactone and dialkyl amine are brought together and reaction has occurred, the products formed are recovered from the reaction mixture. When an amino-acid is formed in appreciable amount, it generally precipitates from the reaction mixture (such acids generally being substantially insoluble in organic liquids) and is removed and recovered by filtration. Amide present in the filtrate is then recovered by distillation, preferably at reduced pressures of less than about 4 mm. of mercury when it is desired to recover a product consisting essentially of beta-hydroxy amide, since distillation at higher pressures, with correspondingly higher temperatures, partially dehydrates the beta-hydroxy amide to give an N,N-dialkyl amide of an alpha-beta unsaturated acid. This is not undesirable in cases where the hydroxy amide is to be used to prepare unsaturated amide. For example, when diethyl amine is reacted with beta-propiolactone and the reaction mixture is distilled at moderately reduced pressure, the N,N-diethyl hydracrylamide formed is partially dehydrated during distillation to give a product containing some N,N-diethyl acrylamide, a quite useful polymerizable compound. Distillation is also effective in separating the amide from small amounts of amino acid since the latter does not distill in appreciable quantity and can be crystallized from the residue remaining after distillation. Other methods of recovering the products from the reaction mixture may also be employed as will be understood by those skilled in the art.

The practice of the invention is further illustrated by the following examples in which parts are by weight.

Example I

Gaseous dimethyl amine is bubbled into 234 parts of diethyl ether maintained at a temperature of 0° C. until the ether is saturated. 72 parts (1 mole) of beta-propiolactone are added to the solution with constant stirring over a period of two hours, the solution being kept saturated with the amine during the addition to insure an excess

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of the amine being present. The solution is then allowed to warm to room temperature, the ether evaporated and the product distilled at a pressure of approximately .1 mm. of mercury. A 95% yield of N,N-dimethyl hydracrylamide (B. P. 71°-74° C./17 mm.) is obtained. The residue is crystallized from methanol and a 3.2% yield of N,N-dimethyl beta-alanine (M. P. 141°-142° C.) is obtained.

Example II

72 parts (1 mole) of beta-propiolactone and an excess of gaseous dimethyl amine are added simultaneously to 284 parts of diethyl ether over a period of one hour, the reaction mixture being maintained at a temperature of 20° C. After the addition of the beta-lactone and the amine is complete, the ether is evaporated and the product distilled at reduced pressures. A 44% yield of a product boiling at 80°-82° C. at 15 mm. is obtained. This product is identified as consisting predominantly of N,N-dimethyl hydracrylamide containing some N,N-dimethyl acrylamide formed by dehydration during distillation. The residue from the distillation is taken up in methanol and crystallized. A 47% yield of a product identified as N,N-dimethyl beta-alanine (M. P. 141°-142° C.) is obtained.

Example III

72 parts (1 mole) of beta-propiolactone are dissolved in 284 parts of diethyl ether. The temperature of this solution is maintained at 20° C. while an excess of gaseous diethyl amine is added. When no more amine is absorbed, the ether is evaporated and the product distilled at 1 mm. of Hg. N,N-diethyl hydracrylamide (B. P. 80°-82° C./1 mm.) is obtained in 68% yield. The residue from the distillation is recrystallized from methanol and diethyl ether and dried. A 4% yield of N,N-diethyl beta-alanine is obtained.

Example IV

72 parts (1 mole) of beta-propiolactone are dissolved in 100 parts of diethyl ether and the resulting solution is added with stirring to 146 parts (2 moles) of diethyl amine. The resulting solution is then refluxed for 4 hours (35° C.) after which the ether and excess diethyl amine are removed by distillation. The residue is then distilled under reduced pressure whereupon there is obtained 94.7 parts (75%) of a distillate consisting almost entirely of a mixture of N,N-diethyl hydracrylamide and N,N-diethyl acrylamide, the latter resulting from dehydration of the hydracrylamide during distillation.

Example V

Example III is repeated except that the diethyl ether is replaced by 294 parts of acetonitrile and the temperature is maintained at from 30°-35° C. during the course of the reaction. There is obtained a 70% yield of N,N-diethyl hydracrylamide (B. P. 80°-82° C./1 mm.) and a 6% yield of N,N-diethyl beta-alanine. The hydrochloride prepared from the N,N-diethyl beta-alanine gave the following analysis:

	Calculated	Found
Per cent chlorine.....	19.52	19.37
Per cent nitrogen.....	7.71	7.68

Example VI

36 parts (0.5 mole) of beta-propiolactone are dissolved in 234 parts of acetonitrile. The tem-

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perature of the solution is maintained at 25 to 30° and 50.5 parts (0.5 mole) of di-n-propyl amine are added slowly and with constant stirring. The solvent is then removed by evaporation under reduced pressure. An oil remains which upon standing partially crystallizes. Ether is added and the solid filtered off. There are obtained from the solid material 22 parts (25%) of N,N-di-n-propyl-beta-alanine which after crystallization from acetone melts at 87°-88° C. Nitrogen analysis: Calculated for C₉H₁₉O₂N, 8.08%; Found, 7.97%.

The ethereal filtrate is concentrated to give an oil which is composed chiefly of N,N-di-n-propyl-hyacrylamide.

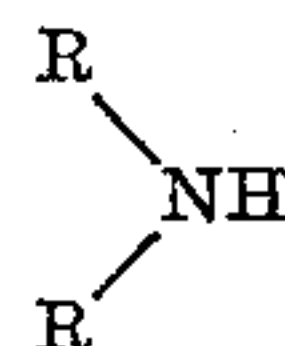
Although beta-propiolactone is employed in the above examples, it will be understood that liquid homologs thereof such as beta-n-butyrolactone, beta-n-valerolactone, beta-isovalerolactone, beta-n-caprolactone, alpha-ethyl-beta-propiolactone, alpha-isopropyl-beta-propiolactone, beta-methyl-beta-n-valerolactone, alpha-butyl-beta-propiolactone and the like, may be substituted for the beta-propiolactone and that the corresponding N,N-dialkyl beta-hydroxy amides and beta-N,N-diamino amino acids are obtained.

Accordingly, it will be understood that the invention is not intended to be limited to specific embodiments but only as required by the spirit and scope of the appended claims.

This application is a continuation-in-part of and a partial replacement for our copending application Serial No. 656,168 filed March 21, 1946, now abandoned.

We claim:

1. The method which comprises reactively adding substantially anhydrous beta-propiolactone to a completely organic liquid containing a dialkyl amine of the structure



wherein R represents a straight chain alkyl hydrocarbon radical of 1 to 12 carbon atoms, at substantially atmospheric pressure and at a temperature between 0 and 50° C. and such that the reaction mixture is maintained in the liquid state, thereby to form by reaction between beta-propiolactone and the said amine an N,N-dialkyl hydracrylamide, and distilling the reaction mixture to recover a product consisting of amide in substantially pure form.

2. The method of claim 1 wherein the dialkyl amine is dimethyl amine.

3. The method of claim 1 wherein the dialkyl amine is diethyl amine.

4. The method which comprises bringing together in a substantially anhydrous, completely organic liquid medium, at atmospheric pressure and at a temperature between 0 and 50° C., reactants consisting of beta-propiolactone and diethyl amine thereby to form a reaction product composed predominantly of N,N-diethyl hydracrylamide but containing minor amounts of N,N-diethyl beta-alanine, and then distilling the reaction product to recover the said amide substantially free from contamination by the said N,N-diethyl beta-alanine.

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