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PROCESS OF PRODUCING PRIMARY Δ_1-ALKENYL MALONIC ESTERS

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This invention relates to a new process for the production of primary Δ_1-alkenyl alkyl malonic and cyanoacetic esters. It relates more particularly to a process for the conversion of primary alkylidene malonic and cyanoacetic esters into the corresponding alkyl Δ_1-alkenyl esters.

The products which are produced by this novel process, the primary Δ_1-alkenyl alkyl malonic esters and cyanoacetic esters, are valuable as intermediates for the production of corresponding primary Δ_1-alkenyl alkyl thiobarbituric acids and barbituric acids, and also for the production of unsaturated monobasic acids, which may be prepared by the de-carboxylation of the malonic esters or by the removal of the nitrile group from the cyanoacetic esters.

In accordance with the process of the present invention, the primary alkylidene malonic esters or cyanoacetic esters are alkylated by means of an alkylating agent, such as an alkyl sulfate, halide, or other alkyl salt, in an inert solvent in the presence of metallic sodium. Apparently the metallic sodium reacts with the primary alkylidene compound to produce a sodio-derivative, which in turn reacts with the alkyl salt, with the elimination of an inorganic sodium salt, and the production of the desired primary Δ_1-alkenyl alkyl ester. In the course of the reaction, the double bond uniting the cyanoacetic or the malonic ester radical with the alkylidene radical is shifted to the Δ_1 position in the alkenyl group, so that the alkylidene group is changed to a Δ_1-alkenyl group, and the alkyl group of the alkylating agent becomes attached to the methylene carbon of the malonic or cyanoacetic ester. As the reaction is carried out with metallic sodium in an inert solvent, side reactions are minimized, and the reaction proceeds smoothly, and with good yields.

In carrying out the process, any available primary alkylidene malonic ester or cyanoacetic ester may be used. The primary alkylidene compounds may be prepared advantageously by the condensation of the corresponding aldehydes with malonic ester or cyanoacetic ester in the presence of a suitable condensing agent, such as a soluble salt, such as piperidene acetate, as described in my copending application Serial No. 105,825, filed October 15, 1936. Other methods of preparing these primary alkylidene esters may be used, of course, but the process described in my said prior application is of particular advantage, inasmuch as it is applicable to the production of the alkylidene esters from any available aldehyde, and enables a wide range of the primary alkylidene esters to be prepared.

The invention will be further illustrated by the following specific example, but it is not limited thereto.

Example.—11.5 parts of sodium are powdered under xylene and rinsed into a suitable reaction vessel equipped with a mechanical stirrer, a reflux condenser, and a dropping funnel, with 350 parts of dry ether. The vessel is cooled in an ice bath while 107 parts of n-butylidene malonic ester is added, with stirring, over a period of 10 minutes. The resulting solution (the sodio derivative of the ester is formed slowly is refluxed for about 6 hours, after which 85 parts of diethyl sulfate are added over a period of 10 minutes, and the refluxing is continued for another 24 hours. The n-butylidene malonic ester and sodium are used in about equal molar proportions, and the alkylating agent, the diethyl sulfate, is used in an amount somewhat in excess of equal molar proportions. After the reaction mixture has refluxed for about 24 hours, it is acidified with dilute hydrochloric acid, the ethereal layer is removed, and the aqueous layer is extracted with ether. The ethereal layer and extract are combined, and the ether removed by evaporation at reduced pressure. The residue is then shaken for about 24 hours with aqueous ammonia to remove any unalkylated material, and the desired ester is extracted from the ammonia with ether, washed with water, and distilled. The resulting product ethyl n-Δ_1-butenyl malonic ester, boils at 104–107° C./2–3 mm.

The ethyl sulfate used in the above example may be replaced by an equivalent amount of any other alkyl sulfate, or alkyl halide, or other alkyl salts, with the introduction of corresponding alkyl groups into the final product. If alkyl halides are used, it is advantageous to use the bromides or the iodides, as these are somewhat more reactive than the chlorides, and increase the efficiency of the reaction.

Similarly, in place of the n-butylidene malonic ester, other primary alkylidene malonic esters, such as n-propylidene, isobutylidene, n-pentylidene, citronellylidene, and other malonic esters may be used as all of the primary alkylidene malonic esters, or aralkylidene malonic esters, react in an analogous manner.

The primary alkylidene and aralkylidene cyanoacetic esters may be alkylated by a procedure similar to that outlined in the example, with the use of metallic sodium in an inert solvent, and, as an alkylating agent, an alkyl salt, such

as an alkyl halide or sulfate. Some of the primary alkylidene cyanoacetic esters tend to polymerize, in contrast to the corresponding primary alkylidene malonic esters, which are quite stable. In such cases it is advantageous to employ the more stable alkylidene malonic esters.

Various inert solvents, i. e., solvents which do not react with the sodium or other reactants, may be used, including such solvents as dry ether, benzene, toluene, etc. In general, the solvent most advantageous for the production of a given primary Δ_1-alkenyl malonic or cyanoacetic ester is the solvent in which the intermediate sodium derivative is the most soluble. Thus, for some products, ether is the best solvent, whereas for others, benzene or toluene may give better results. Other inert solvents may also be used, and particularly solvents in which the intermediate sodium derivatives are relatively soluble.

Sodamide may be used in place of the metallic sodium, in an inert solvent, with about the same high conversion; but, if sodamide is used, it must be handled with due precautions, as, if not properly handled, it is explosive. One way in which it may be used safely involves dissolving it in liquid ammonia, admixing the solution with an inert solvent, such as benzene, ether or the like, and removing the liquid ammonia by vaporization. The inert solvent, containing the sodamide, may then be used in the process.

Among the primary Δ_1-alkenyl malonic and cyanoacetic esters which may be readily prepared by the process, with good yields, and with a minimum of undesirable side reactions, are the following:

n-Propyl Δ_1-n-propenyl malonic ester
Ethyl Δ_1-n-butenyl malonic ester
n-Propyl Δ_1-n-butenyl malonic ester
Isopropyl Δ_1-n-butenyl malonic ester
Allyl Δ_1-n-butenyl malonic ester
Ethyl Δ_1-isobutenyl malonic ester
Methyl Δ_1-n-heptenyl malonic ester
Ethyl isobutenyl cyanoacetic ester
Allyl Δ_1-n-butenyl cyanoacetic ester
Isopropyl Δ_1-n-butenyl cyanoacetic ester
Ethyl Δ_1-n-heptenyl cyanoacetic ester
Methyl Δ_1-n-pentenyl cyanoacetic ester

It will thus be seen that by the present invention, I provide a novel and advantageous process for the production of primary Δ_1-alkenyl alkyl malonic esters and cyanoacetic esters, by the alkylation of the corresponding primary alkylidene malonic or cyanoacetic ester, with the production of the desired product with high yields and in a condition such that it can be readily purified and isolated.

I claim:

1. The process of preparing esters of primary Δ_1-alkenyl alkyl malonic acids which comprises reacting a primary alkylidene malonic ester with a substance of the class consisting of metallic sodium and sodamide in an inert solvent, and replacing the sodium in the resulting sodio-derivative with an alkyl group by means of an alkyl salt.

2. The process of producing esters of primary Δ_1-alkenyl alkyl malonic acids which comprises reacting an alkyl halide with a primary alkylidene malonic ester in the presence of metallic sodium in an inert solvent.

3. The process of producing esters of primary Δ_1-alkenyl alkyl malonic acids which comprises reacting an alkyl sulfate with a primary alkylidene malonic ester in the presence of metallic sodium in an inert solvent.

4. The process of producing esters of primary Δ_1-alkenyl alkyl malonic acids which comprises reacting an alkyl salt with a primary alkylidene malonic ester in the presence of metallic sodium in an inert solvent.

5. The process of producing esters of primary Δ_1-alkenyl alkyl malonic acids which comprises reacting an alkyl salt with a primary alkylidene malonic ester in the presence of a substance of the class consisting of metallic sodium and sodamide in ether.

6. The process of producing esters of primary Δ_1-alkenyl alkyl malonic acids which comprises reacting an alkyl salt with a primary alkylidene malonic ester in the presence of a substance of the class consisting of metallic sodium and sodamide in benzene.

7. The process of producing esters of primary Δ_1-alkenyl alkyl malonic acids which comprises reacting an alkyl salt with a primary alkylidene malonic ester in the presence of a substance of the class consisting of metallic sodium and sodamide in toluene.

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