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PROCESS FOR THE CYCLIZATION OF UNSATURATED ORGANIC COMPOUNDS

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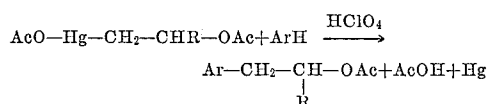
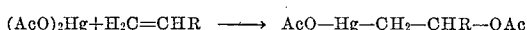
6 Claims

ABSTRACT OF THE DISCLOSURE

Organic compounds having two carbon-carbon double bonds in the 1,5- or 1,6-position are cyclized by treatment with a mercuric compound and a proton acid or Lewis acid.

This invention relates to the cyclization of organic compounds having two double bonds in the 1,5- or 1,6-positions.

It is known that olefines such as ethylene and propylene yield addition compounds with mercury salts of carboxylic acids and that under the influence of proton acids having anions which are only slightly nucleophilic (e.g. perchloric acid, sulphuric acid or phosphoric acid) or of Lewis acids (for example BF_3), these compounds can substitute aromatic nuclei to yield homobenzyl derivatives. Thus ethylene and propylene by reaction with mercuric acetate in acetic acid yield the corresponding addition derivatives which in the presence of perchloric acid and benzene or anisole yield the acetates of 2-aryl-ethanols and 1-aryl-propanols-2 according to the following scheme:



(where Ac is CH_3CO , R is H or CH_3 , and Ar is, C_6H_5 or $\text{CH}_3\text{OC}_6\text{H}_4$)

It has now been found that if organic compounds having two carbon-carbon double bonds in the 1,5- or 1,6-positions are reacted with a mercuric salt and the resulting compound is then treated with a proton acid or with a Lewis acid, cyclization of the portion of the molecule which contains the two double bonds results.

The invention accordingly provides a process for the cyclization of an organic compound having two carbon-carbon double bonds in the 1,5- or 1,6-position, which comprises mixing the said compound with a mercuric salt in an amount such as to provide one Hg^{++} ion for each pair of double bonds, adding a proton acid the anion of which is only slightly nucleophilic or a Lewis acid, and heating the mixture so obtained.

The unit which carries the two double bonds may be substituted and one or both of the double bonds may belong to a ring. However, it is essential that the carbon atoms of the double bonds in question should not be entirely substituted. With this reservation, any organic compound containing a pair of 1,5- or 1,6- carbon-carbon double bonds may be cyclized by the new process. In particular, the following may be cyclized: purely aliphatic compounds such as diallyl, 2,5-dimethyl-diallyl, and 2-methyl-2,6-heptadiene; compounds in which one of the double bonds is part of an aliphatic or aromatic ring which may optionally be substituted, for example 4-phenyl-1-butene and 5-phenyl-1-pentene; compounds in which both the double bonds are in rings, each belonging to a different ring, for example 3-[2-(3-methoxyphenyl)ethyl]cyclohex-

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ene and 3 - [2-(3,4-dimethoxyphenyl)ethyl]cyclohexene; compounds having the two double bonds in a single ring, for example 1,5-cyclooctadiene.

Depending on whether or not there are substituents on the doubly bonded carbon atoms, and on the number and nature of the substituents if any, the ring formed may have 5, 6 or 7 carbon atoms. Furthermore the anionic part of the mercuric salt used may, after addition to one of the double bonds, remain as a substituent in the resulting ring. However the cyclization may also take place so that no new substituents appear in the resulting ring; this is so when the bond to the expected substituent is too weak to withstand the working conditions, particularly when the substituent would be carried by a tertiary carbon atom. The ring obtained under these conditions is thus necessarily an unsaturated ring. If the starting materials employed and the working conditions are such that the cyclization results in a cyclohexadiene group, the latter has a greater or less tendency to aromatise into a benzene ring. The mercuric salt may in general be any salt of an organic carboxylic acid, especially a salt of a lower alkanic acid, and more particularly mercuric acetate. The mercuric salt corresponding to the proton acid may also be used. The amount of the mercuric salt is 1 Hg^{++} per unit with 1,5- or 1,6-double bonds and per mol of organic compound containing this unit.

The amount of proton acid may be a small molar fraction of the starting material or an equimolar proportion. A proportion of $\frac{1}{10}$ mol per mol of 1,5- or 1,6-diene is generally sufficient.

The reaction may be carried out in an anhydrous organic medium, especially in a lower alkanic acid or in a compound such as nitromethane. It may equally be carried out in an aqueous organic medium or even in a purely aqueous medium.

Depending on the medium in which the reaction is carried out and the reactivity of the acid used as catalyst, the reaction may take place rapidly at ambient temperature (for example 20°C .) or may, conversely, require heating to a more or less elevated temperature, possibly in an autoclave. It is generally not necessary to exceed 150°C . and most frequently it is possible to work satisfactorily at a temperature of $60-90^\circ\text{C}$.

A particularly valuable method of working consists of mixing a mercuric salt of a lower alkanic acid and a diene compound, as defined above, in a liquid organic carboxylic acid, which may be acetic acid, and then, after dissolving the salt, adding the proton acid and heating, generally to $60-90^\circ\text{C}$. When the reaction is complete the mercury metal produced is removed, and the organic compound formed is isolated by known methods; for example, water is added to the product which has been freed of the mercury metal, the mixture is extracted with an organic solvent which is inert under the working conditions, the solution obtained is washed until neutral and dried, the solvent is evaporated, and the residue is fractionally distilled. In this way a main fraction consisting of a cyclic ester, and subsidiary fractions containing unconverted diene and secondary reaction products, are obtained.

The cyclization product may optionally be converted into other compounds either after isolation or by directly treating the crude cyclization product. In particular, the products resulting from a cyclization with fixation of an acyloxy radical may be saponified to alcohols.

The following examples illustrate the invention.

EXAMPLE 1

41 g. (0.5 mol) of diallyl are added to a suspension of 160 g. (0.5 mol) of mercuric acetate in 1250 cm^3 of acetic acid. After dissolving the salt, 90 g. (0.5 mol) of 60% perchloric acid are added, and the mixture heated at 70°C . for 30 minutes. 100 g. (0.5 gram atom) of mer-

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cury are produced and separated. The liquid portion is poured into 1 l. of water, and extracted with benzene. The extract is successively washed with sodium carbonate solution and water, and dried. The solvent is evaporated and the residue then distilled under reduced pressure. In this way two fractions of the following properties are obtained:

(1) Cyclohexen-3-yl acetate, B.P. 71.5–72.5° C./15 mm. Hg; 36 g.; $n_D^{24.5}=1.4551$.

(2) Cyclohexane-1,4-diol diacetate, B.P. 135–136° C./15 mm. Hg; 8.1 g.

The same result is obtained using 1 cm.³ of 60% perchloric acid in place of the 90 g. used above.

EXAMPLE 2

21.6 g. (0.1 mol) of mercuric oxide, 200 cm.³ of water, and sufficient concentrated aqueous perchloric acid solution to dissolve all the mercuric oxide are introduced into a flask fitted with a cooling unit and a condenser cooled with a mixture of solid carbon dioxide and acetone. 8.2 g. (0.1 mol) of diallyl are then added and the mixture heated under reflux overnight. During the reaction a gas is evolved which is condensed in the condenser cooled by the solid carbon dioxide-acetone mixture. The mixture obtained at the end of the reaction is filtered to remove the mercury formed. The filter is washed with diethyl ether which is then added to the aqueous phase. The entire liquid fraction is neutralized by adding sodium bicarbonate and then saturated with sodium chloride. The mixture is extracted with diethyl ether, the ether extract is dried over anhydrous sodium sulphate and filtered, the ether is removed and the residue is distilled. In this way 4 g. (40% yield) of a product, identified as 4-cyclohexenol and having a boiling point of 80° C./20 mm. Hg, are obtained. 4 g. of a liquid consisting of approximately equal parts of diallyl and benzene are recovered from the condenser.

EXAMPLE 3

Working as in Example 2 but replacing the 200 cm.³ of water by a mixture of 100 cm.³ of water and 200 cm.³ of acetone, 5.5 g. (55%) of 4-cyclohexenol are obtained.

EXAMPLE 4

Working as in Example 2 but using 11 g. (0.1 mol) of 2,5-dimethyl-diallyl in place of diallyl, 5 g. (50% yield) of a product identified as p-xylene are obtained.

EXAMPLE 5

11 g. (0.1 mol) of 2-methyl-2,6-heptadiene are added to a solution of 32 g. of mercuric acetate in 300 cm.³ of acetic acid. 1.8 g. of 60% perchloric acid are added, and the mixture is heated to 70° C. After 40 minutes, the portion which has been separated from the 20 g. of mercury formed is poured into 300 cm.³ of water, and extracted with benzene. The extract is washed as described above and dried, the solvent is evaporated, and the residue distilled. In this way 3.4 g. of a product, B.P. 130° C./40 mm. Hg, identified as 3-isopropylidene-cyclopentyl acetate, are obtained.

EXAMPLE 6

26.4 g. (0.2 mol) of 4-phenyl-1-butene are added to a solution of 64 g. (0.2 mol) of mercuric acetate in 600 cm.³ of acetic acid. 36 g. (0.2 mol) of 60% strength perchloric acid are then added, and the mixture is heated at 65° C. for 15–20 minutes. The theoretical amount of mercury (40 g.=0.2 gram atom) is produced and separated. The liquid is poured into 600 cm.³ of water and extracted with benzene. The benzene solution is washed with a saturated aqueous solution of sodium carbonate then with water, dried over anhydrous sodium sulphate, and the solvent evaporated. The crude mixture of acetic esters so produced is then treated with 10 g. of potassium hydroxide in 100 cm.³ of ethyl alcohol under reflux for 1 hour. The greater part of the alcohol is then evaporated, 100 cm.³ of water are added, and the mixture is extracted with

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diethyl ether. The ether solution is washed with water, and dried over sodium sulphate, the solvent is evaporated, and the residue is distilled under reduced pressure. The following fractions are obtained:

(1) B.P.=85–91° C./10 mm. Hg, 9 g., whose composition, by vapour phase chromatography, is as follows:

	Percent
Phenylbutene starting material	22
Tetralin	1
Δ^1 -Dialin	46
Δ^2 -Dialin	18
Naphthalene	10

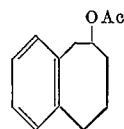
Aromatisation of the entire mixture yields 80% of naphthalene.

(2) Naphthalene, B.P.=91–110° C./10 mm. Hg, 2.8 g.

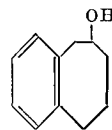
(3) An unidentified alcohol, B.P.=136–139° C./10 mm. Hg, 4.8 g.

EXAMPLE 7

14.5 g. of 5-phenyl-1-pentene (0.1 mol) are added to a suspension of 32 g. (0.1 mol) of mercuric acetate in 60 cm.³ of acetic acid. After the mercuric salt has dissolved, 18 g. (0.1 mol) of 60% perchloric acid are added and the mixture is heated at 60° C. for 1 hour. 20 g. (0.1 gram atom) of mercury are formed and are removed. The liquid portion is poured into 60 cm.³ of water, and extracted with benzene, and the benzene solution washed with sodium carbonate solution and with water. After drying over anhydrous sodium sulphate, the solvent is evaporated and the residue distilled in vacuo. In this way 12 g. of a product, B.P.=102–104° C./0.7 mm. Hg, are obtained, consisting principally of the compound of formula:



which is identified by saponification. For this, the 12 g. of product are heated for 1 hour under reflux with 6 g. of potassium hydroxide and 60 cm.³ of ethanol. The mixture is evaporated, and the residue taken up in 60 cm.³ of water, and extracted with diethyl ether. The extract is dried, the solvent is evaporated, and the residue (9.5 g.) is recrystallised from a mixture of petroleum ether and benzene (1/1). In this way an alcohol melting at 66–67° C. and identical with the product of formula:



prepared in accordance with the method of Huisgen et al., Annalen (1964) 671, 41, is obtained. The infrared spectra of the alcohols can be superposed at all points.

EXAMPLE 8

2.5 g. (0.01 mol) of 3-[2-(3,4-dimethoxyphenyl)ethyl]-cyclohexene, 3.2 g. of mercuric acetate and 20 cm.³ of acetic acid are introduced into a flask which is equipped as in the preceding examples. When the whole of the mercuric salt has dissolved, 1 cm.³ of a 60% aqueous solution of perchloric acid is added, and the mixture is heated to 80° C. After three hours heating at this temperature, the mixture is cooled and filtered, and filtrate is poured into 150 cm.³ of water, and the product is neutralised by adding 2 N caustic soda solution and extracted with chloroform. The chloroform extract is evaporated, and the residue is saponified by adding 250 cm.³ of methanol containing 4 g. of potassium hydroxide and heating under reflux for 3 hours. The product from this saponification is evaporated to drive off the alcohol and then, after adding 150 cm.³ of water, the residue is neu-

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tralised by adding 3 N aqueous hydrochloric acid. The mixture is extracted with chloroform and 0.9 g. (40% yield) of a product, melting at 142–143° C. and identified as 4 - hydroxy - 6,7 - dimethoxy - 1,2,3,4,4a,9,10,10a - octahydrophenanthrene, is isolated.

EXAMPLE 9

Working as in Example 8, but using 10.6 g. of 3-[2-(3-methoxyphenyl)ethyl]cyclohexene, 3.8 g. (36%) of a product, melting at 101° C. and identified as 4-hydroxy-7 - methoxy - 1,2,3,4,4a,9,10,10a - octahydro - phenanthrene, are obtained.

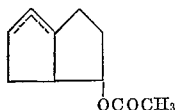
The structure of this product was confirmed by aromatisation, by heating a mixture of 100 mg. of the product in 40 cm.³ of decalin with 250 mg. of palladized charcoal containing 10% of palladium, under reflux for 24 hours.

The 3-[2-(3-methoxyphenyl)ethyl]cyclohexene used as the starting material was prepared in the following manner. The magnesium derivative of 1-bromo-2(3-methoxyphenyl)ethane is prepared and is then reacted with 3-bromocyclohexene. After hydrolysis with a saturated aqueous solution of ammonium chloride, 3-[2-(3-methoxyphenyl)ethyl]cyclohexene, B.P. 120–133° C./1 mm. Hg, is obtained.

EXAMPLE 10

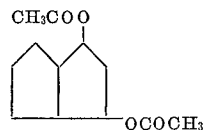
10.8 g. (0.1 mol) of cyclooctadiene are added to a suspension of 32 g. of mercuric acetate (0.1 mol) in 300 cm.³ of acetic acid. The mixture is heated to 85° C., and 18 g. (0.1 mol) of concentrated perchloric acid are added. After about 1 hour the mixture is allowed to cool, and decanted, and the precipitate is washed with benzene. 500 cm.³ of water are added to the acetic acid solution and the mixture is extracted with benzene (initially with the benzene with which the precipitate has been washed). The benzene extract is first washed with aqueous sodium bicarbonate solution, and then with water, and dried over anhydrous sodium sulphate. The precipitate, which is thoroughly washed with acetone, is mercury (20 g.=0.1 gram atom, the theoretical amount). The solution is evaporated in vacuo and the residue then distilled. This yields:

(1) a first fraction consisting of 6 g. of a product, B.P. 93–96° C./12 mm. Hg, characterised as having the formula:



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(2) a second fraction consisting of 3 g. of a product, B.P. 145–147° C./12 mm. Hg, characterised as having the formula:



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10 The yields are respectively 38% and 19% for these two fractions.

I claim:

1. Process for the cyclization and simultaneous oxidation of an organic compound having two carbon-carbon double bonds in the 1,5- or 1,6-positions and having at least one carbon atom of each double bond not entirely substituted selected from the group consisting of diallyl, 2,5-dimethyl-diallyl, 2-methyl-2,6-heptadiene, 4-phenyl-1-butene, 5 - phenyl - 1 - pentene, 3-[2-(3-methoxyphenyl)ethyl]cyclohexene, 3 - [2 - (3,4 - dimethoxyphenyl)ethyl]cyclohexene and 1,5-cyclooctadiene, which comprises mixing the said compound with a mercuric salt of a lower alkanolic acid or of perchloric, sulphuric or phosphoric acid in an amount providing one Hg⁺⁺ ion for each unit of the said organic compound containing the 1,5- or 1,6-double bonds and per mole of organic compound containing this unit, adding a proton acid selected from perchloric, phosphoric and sulphuric acid or a Lewis acid and heating the mixture so obtained to a temperature of at most 150° C.

2. Process according to claim 1, in which the mixture is heated to 60° to 90° C.

3. Process according to claim 1, in which the mercuric salt is mercuric acetate.

35 4. Process according to claim 1, in which the reaction is carried out in a lower alkanolic acid as reaction medium.

5. Process according to claim 4, in which the alkanolic acid is acetic acid.

40 6. Process according to claim 1, in which the proton acid is perchloric acid.

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