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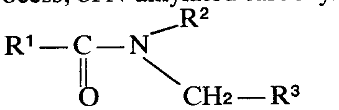
(54) ω-ALKOXY DERIVATIVES OF LACTAMS AND PROCESS FOR THEIR MANUFACTURE

(71) We, HOECHST AKTIENGESELLSCHAFT, a body corporate, organised according to the laws of the Federal Republic of Germany, of 6230 Frankfurt/Main 80, Postfach 80 03 20, Federal Republic of Germany, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:-

This invention relates to ω-alkoxy derivatives of lactams and to their manufacture.

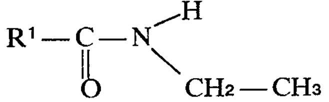
German Offenlegungsschrift No. 2,113,338 discloses the reaction by an electrochemical process, of N-alkylated carboxylic acid amides of the general formula



$$R^1-\underset{\underset{O}{\|}}{C}-N\begin{matrix}\nearrow R^2\\ \searrow CH_2-R^3\end{matrix}$$

in which each of R¹, R² and R³ represents a hydrogen atom or an organic radical and R¹ and R² may be linked to each other forming a lactam, with alcohols, to give the corresponding N-α-alkoxyalkyl carboxylic acid amides. In this process the alcohol is used in excess and the reaction carried out in the presence of a conducting salt, for example an alkali metal- or a tetraalkylammonium-tetra-fluoroborate, hexafluorophosphate or nitrate, at a temperature of up to about 100°C. The electrolytic cell may contain a stationary or a flowing electrolyte and the quantity of electricity used does not exceed 2.4 Faradays per mol of amide.

Belgian patent No. 837,906 proposes the electrolysis of particular compounds from the DOS 2,113,338 (N-alkylcarboxylic acid amides of the formula

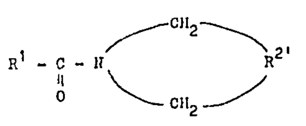


$$R^1-\underset{\underset{O}{\|}}{C}-N\begin{matrix}\nearrow H\\ \searrow CH_2-CH_3\end{matrix}$$

in which R¹ has the above-mentioned meaning) in the presence of specific conducting salts and uses higher quantities of electricity, thus obtained improved yields and, moreover, easier work-up of the reaction mixture.

In the aforesaid processes the starting materials used are N-alkylcarboxylic acid amides which, in at least one N-alkyl group, carry 2 hydrogen atoms, in the α-position to the nitrogen and which, especially when R¹ and R² are linked to each other, carry the group CH_2-R³ on the nitrogen.

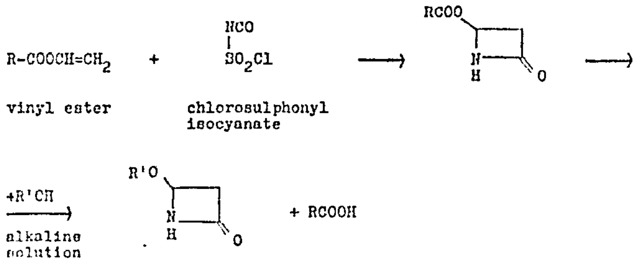
It has also been proposed to alkoxylize at the anode in substantially the same manner compounds of the formula



in which R^1 has the above meaning and $R^{2'}$ represents a linear or branched alkylene radical having from 1 to 4 carbon atoms in the chain. (cf. German offenlegungsschrift 2,539,777). Depending on the quantity of electricity used, the alkoxylation is effected on one or on both of the CH_2 groups linked to the nitrogen atom.

In the anodic alkoxylation in DOS 2,113,338 it is practically always the CH_2 group of the CH_2-R^3 substituent which is alkoxylated even if the radicals R^1 and R^2 are linked to each other to form a lactam; products alkoxylated on the nucleus; that is to say in the lactam ring, are practically not formed.

Purely chemical reactions for the preparation of lactams which carry an alkoxy group on the carbon atom adjacent to the nitrogen atom on the side remote from the carbonyl group, are known. Compounds of this type can also be considered N,O-acetals. A chemical method of preparing these compounds is described, for example in Liebigs Ann. Chem. 1974, pages 539-560, according to which four-membered ring compounds are prepared according to the following reaction scheme:



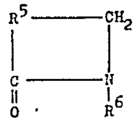
in which R and R^1 represent organic radicals.

A generalization of this method for the preparation of N,O-acetals with larger ring sizes has not yet become known.

However, in view of the fact that N,O-acetals of this type are important intermediates, it would be desirable to develop a process for the preparation of all such compounds irrespective of the size of the lactam ring.

We have therefore further developed the alkoxylation reaction described in German Offenlegungsschrift No. 2,113,338 and in Belgian Patent No. 837,906.

We have found that an electrochemical alkoxylation may be carried out on a lactam in which the nitrogen atom carries as substituent not in the ring a hydrogen atom or an alkyl radical having a secondary or tertiary N-α-carbon atom, of the general formula



I

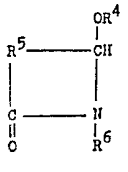
in which

R^5 represents a linear or branched alkylene radical having from 1 to 10 carbon atoms in the chain which forms part of the ring, and which may be unsubstituted or substituted by one or more groups which are unreactive under the conditions used, for example hydroxyl groups or halogen atoms,

R^6 represents a hydrogen atom or an alkyl radical which is branched at the carbon atom joined to the nitrogen atom, and which may be substituted or unsubstituted. A secondary or tertiary N-αC atom as in R^6 is difficult to alkoxylate.

The present invention provides a process for the anodic alkoxylation of a lactam of the general formula I shown above in which R^5 and R^6 have the meanings given above with an alcohol of the general formula R^4OH in which R^4 represents an alkyl radical having from 1 to 4 carbon atoms, in the presence of at least one conducting salt, which is an alkali metal- or tetra-alkylammonium-tetrafluoroborate, hexafluorophosphate or nitrate, preferably at a temperature of up to 100°C in an electrolytic cell with stationary or flowing electrolyte.

The reaction yields a nuclear-alkoxylated lactam having the general formula



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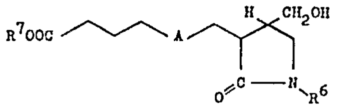
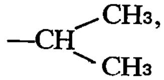
in which R^4, R^5 and R^6 have the meanings given above.

Preferred substituents of R^5 are, for example, $-CH_2OH$, and $-CH_2-A-CH_2-CH_2CH_2-COOR^7$ in which A represents $-C{\equiv}C-$, $-CH{=}CH-$ or $-CH_2-CH_2-$ and R^7 represents a hydrogen atom or a lower aliphatic (C_1-C_4), cycloaliphatic (C_5-C_6) or araliphatic (preferably C_7 or C_8) hydrocarbon radical.

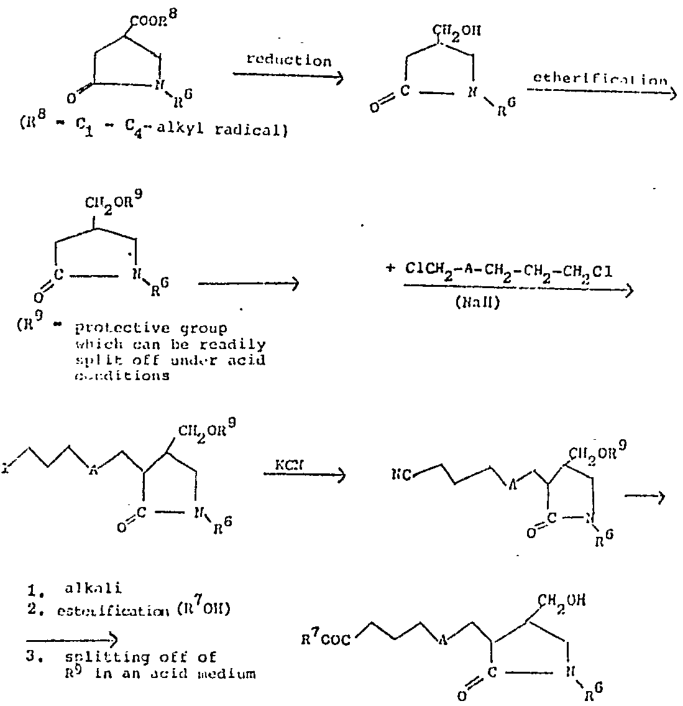
Suitable compounds of the general formula I are, for example, 2-azetidinone, 3-methyl-2-azetidinone, 1-isopropyl-1-pyrrolidone, 1-isopropyl-4-hydroxymethyl-2-pyrrolidone, 1-isopropyl-3-[6-methoxycarbonyl-hex-2-yn-1-yl]-4-hydroxymethyl-2-pyrrolidone, 1-tert.-butyl-2-pyrrolidone, 2-piperidone, ε-caprolactam, the lactams of ω-caprolactam, the lactams of ω-amino-caprylic acid, ω-amino capric acid and ω-amino lauric acid, preferably 1-isopropyl-4-hydroxymethyl-2-pyrrolidone, and compounds of the general formula



in which R^7 represents a C_1-C_4 alkyl radical, a C_5 or C_6 cycloalkyl radical or an araliphatic radical, and more preferably 1-isopropyl-3-[6-methoxycarbonyl-hex-2-yn-1-yl]-4-hydroxymethyl-2-pyrrolidone,

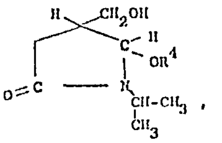
(in which A is $-C{\equiv}C-$, R^6 is  $-CH\begin{matrix}CH_3\\CH_3\end{matrix}$, R^7 is CH_3),

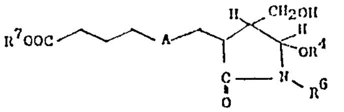
which compounds can be prepared as described in German Offenlegungsschriften, 2,452,536 and 2,528,036 according to the following reaction scheme:

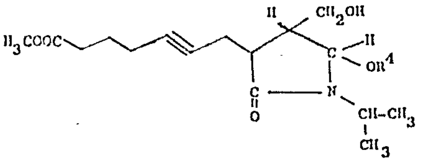


In the case of A being $-C{\equiv}C-$ the final compound can be partially hydrogenated to form the $-CH{=}CH-$ group or completely hydrogenated to $-CH_2-CH_2-$ by a method known *per se*.

With the use of the preferred starting compounds the following final compounds are obtained:

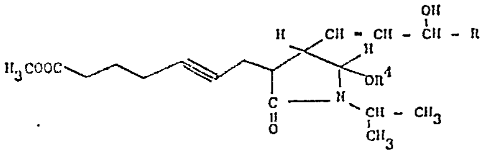


 and

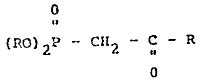


Products of this type are novel. They can be used as intermediates for the manufacture of pharmaceuticals, especially those having prostaglandine-like effects (cf. Application No. 53127/76 filed concurrently herewith).

A pharmaceutical of this type is, for example, the compound of the formula



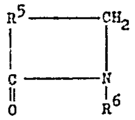
obtained by oxidation of the CH_2OH group in the latter compound to the CHO group, reaction with



$$(RO)_2\overset{O}{\overset{\|}{P}} - CH_2 - \underset{\underset{O}{\|}}{C} - R$$

in which each R stands for an alkyl radical and the radical R bound to the $\underset{\underset{O}{\|}}{C}$-group may also represent an optionally substituted phenoxy or cycloalkyl radical, and hydrogenation of the azetocarbonyl group.

Further preferred starting compounds in the process of the invention are lactams with 5 to 13 ring members of the formula



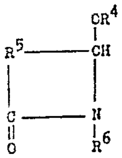
I

in which

R^5 represents $-(CH_2)_{2-10}$, preferably $-(CH_2)_3-$, $-(CH_2)_4-$ and $(CH_2)_{10}-$,

R^6 stands for hydrogen or a branched alkyl radical having from 3 to 10 carbon atoms with a secondary or tertiary N-α-C atom, preferably hydrogen.

The compounds obtained in this manner are also novel, they have the formula

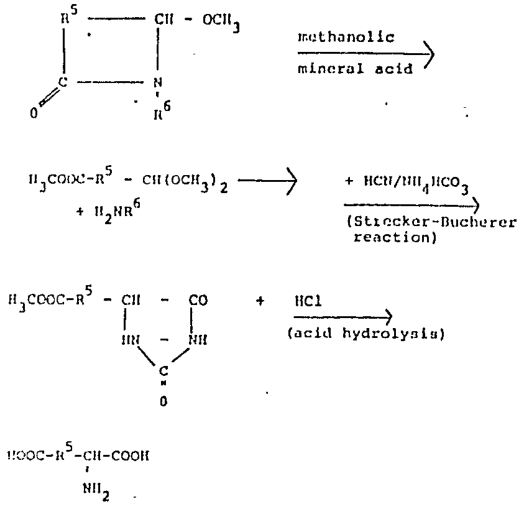


II

in which

R^5 and R^6 have the aforesaid meaning, R^4 represents an alkyl radical with 1 to 4 carbon atoms preferably CH_3.

Compounds of this type can be used as antistatic agents in textile industries and as intermedites in polymerization reactions and in the preparation of α-amino-α,ω-dicarboxylic acids according to the following reaction scheme:



Suitable alcohols R^4OH to carry out the process of the invention are methanol, ethanol, n-propanol, isopropanol, n-butanol, sec.-butanol, preferably, however, methanol and ethanol and more preferably methanol.

The conducting salt to be used in the process of the invention are alkali metal salts (Li, Na, K, Rb, Cs) and tetraalkyl ammonium salts of tetrafluoroboric acid, hexafluorophosphoric acid and nitric acid. They are used either singly or in admixture with one another. The alkyl radicals in the tetraalkyl ammonium group preferably have 1 to 6 and more preferably 1 to 4 carbon atoms, especially the methyl and ethyl radical. The following conducting salts are mentioned by way of example:

Na-tetrafluoroborate, Na-nitrate, K-tetrafluoroborate, K-hexafluorophosphate, Rb-nitrate, tetramethylammonium tetrafluoroborate, tetraethylammonium tetrafluoroborate, tetra-n-butyl-ammonium tetrafluoroborate, tetraethylammonium hexafluorophosphate, tetra-n-propylammonium hexafluorophosphate tetra-n-butyl-ammonium hexafluorophosphate, or tetramethylammonium nitrate. Preferred conducting salt sare the alkali metal and tetraalkyl ammonium tetrafluoroborates especially $NaBF_4$, KBF_4 and $(CH_3)_4-NBF_4$.

The concentration of conducting salt in the electrolysis solution should preferably be in the range of from about 0.01 to about 2.0 mol/l, preferably about 0.02 to 1.0 mol/l. The temperature of the electrolysis solution should preferably be in the range of from about −10 to −100°C, preferably about 0 to 60°C.

In the electrolytic solution the molar proportion of starting acid amide to alcohol is suitably in the range of from about 1:1 to about 1:100, preferably 1:2 to 1:60 and more preferably 1:5 to 1:50.

The electrochemical alkoxylation according to the invention may be carried out discontinuously or continuously.

The process will now be described in further detail by way of example only, with reference to the accompanying drawing which is a view, partly in section, of an electrolysis cell suitable for carrying out the process of the invention in discontinuous manner.

Referring to the drawing, an electrolytic cell (1) is equipped with a tightly sealing cover or lid (2), through which the power supply lines for electrodes (3) and (4) are led and in which an opening (5) for the supply of the electrolysis solution, an opening (6) for the discharge of gas and a thermometer (9) are fitted. The orifice (6) for the discharge of gas may be equipped with a reflux condenser, in which evaporating portions of the electrolysis mixture may be recovered by condensation. The electrolytic cell (1) is encased and may be connected to a heating or cooling liquid circuit by means of inlet and outlet sockets (7 and 8). The temperature of the electrolysis solution is controlled by the thermometer (9) or a thermosensor. The two electrodes (3) (anode) and (4) (cathode) are set up at a distance of from 0.5 to 50 mm, preferably from 1 to 15 mm.

As electrodes there are used nets or sheets of palladium or platinum or noble metal-coated metal electrodes, preferably titanium electrodes, mixed oxide-coated metal electrodes (as anodes), preferably titanium anodes, or graphite plates provided with slits or not. The use of electrode nets is especially advantageous, because these facilitate the discharge of the gaseous hydrogen formed during the electrolysis, and the uniform and thorough mixture of the electrolysis solution is additionally favoured by the gas current formed. The vertical disposition of the electrodes may be replaced, if desired, by a horizontal one. it is also possible to use several electrode pairs; a block-like combination of angular or non-angular capillary split electrodes, optional with vibration of the electrodes, has proved especially efficient. The solution is mixed vigorously during electrolysis by means of an agitator, for example a magnetic stirrer (10) or by circulation by pumping, especially in case of the block-like combinations.

If the process is carried out continuously, an additional orifice may be set in the cover (2) of the electrolysis vessel (1) for pump-circulating the electrolysis solution continuously. A portion of the electrolysis solution which is circulated by pumping is separated for work up of the product. After determination of the ratio of the desired reaction product to the starting material in the electrolysis solution by the nuclear magnetic resonance spectrum or by gas chromatography, the solution is worked up in known manner. The starting materials, recovered upon distillation, may be adjusted to the molar ratio employed and then metered into the continuously recirculating electrolysis solution together with the required quantity of the conducting salt or salts.

The electrolysis may be carried out under normal pressure, but may be performed under reduced pressure. So as to avoid the formation of explosive gas mixtures of hydrogen and air, the addition of an inert gas, e.g. nitrogen, is advantageous.

The conducting salt is suitably added after having prepared the alcoholic solution. However, this order may be changed.

There is no need to exclude water strictly from the electrolyte since minor amounts thereof do not affect the course of reaction.

The process gives an especially high yield and is especially efficient with respect to energy consumed, if the conversion of cyclic carboxylic acid amide is increased, e.g. to more than 99%, this step being also advantageous for a better work up of the electrolysis solution. Therefore, the electrolysis is advantageously continued until practically the total starting material is converted so that there is no need later to separate this from the reaction product.

The electrolysis current is switched off after having led through the quantity of electricity desired, and the electrolysis discharge is then freed from the conducting salt and worked up in known manner, preferably by distillation. The degree of purity of the product may be determined by a nuclear magnetic resonance spectrum.

The current density is chosen in the range of from about 1 to 50 A/dm^2, preferably 2 to 30 A/dm^2. Lower current densities are also possible, though they diminish the rate at which the product is formed. The quantity of electricity should be about 2 to 4, preferably 2 to 3.5 and especially 2 to 3 Faradays/mol of starting lactam.

The α-alkoxy derivatives of cyclic carboxylic acid amides prepared according to the electrochemical process of the invention are valuable intermediate products, especially for the manufacture of pharmaceuticals, having, in the first place, prostaglandine like effects and also luteolytic, bronchospasmolytic and/or antihypertensive properties and properties to inhibit the secretion of gastric juice.

The following Examples illustrate the invention.

Example 1

17.6 g of azetidinone-2- and
39.6 g of methanol

are electrolyzed in an electrolytic cell having a capacity of approximately 60 ml in the presence of 0.82 g of tetra-m-propyl-ammonium hexafluorophosphate as conducting salts. As electrodes two concentrically placed platinum net cylinders having 225 meshes per cm^2 and diameters of 15 and 30 mm, respectively, and a height of 50 mm are immersed in the solution, the outer electrode being connected as anode. During electrolysis the temperature is maintained at about 10°C. After having switched on the electrolysis direct current, the current density at the anode is 1 A/dm^2. The current is switched off after passage of 2.5 Faradays per mol of azetidinone-2. The calculated average cell tension is 29.6 volts. After working up by molecular distillation there are obtained 12.7 g of 4-methoxy-azetidinone-2 (boiling point 41°C under 0.013 millibar, melting point 62-63°C), corresponding to a material yield of 50.9% and a current efficiency of 40.7%.

Example 2:

In an electrolytic cell as described in Example 1
21.0 g of pyrrolidone-2 and
39.6 g of methanol

are electrolyzed in the presence of 0.40 g of tetramethyl-ammonium tetrafluoroborate as conducting salt. After having switched on the electrolysis direct current, the density at the anode is 3 A/dm^2. The current is switched off after the passage of 2.0 Faradays per mol of pyrrolidone-2. The calculated average cell tension is 35.2 volts. After working up by molecular distillation, 14.3 g of 5-methoxypyrrolidone-2 are obtained (boiling point 87-90°C under 0.14 millibar, melting point 56-58°C), corresponding to a material yield and a current efficiency of 50.1% each.

Example 3:

In an electrolytic cell as described in Example 1
14.7 g of pyrrolidone-2 and
39.5 g of ethanol
are electrolyzed in the presence of 0.28 g of tetramethyl ammonium tetrafluoroborate as conducting salt. After having switched on the electrolysis direct current, the anode current density is 3 A/dm^2. After having passed 2.0 Faradays per mol of pyrrolidone-2 the current is switched off. The calculated average cell tension is 48.2 volts.

Working up by molecular distillation yields 12.0 g of 5-ethoxypyrrolidone-2 (melting point 54-56°C), corresponding to a material yield and a current efficiency of 54.2% each.

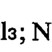
Example 4:

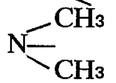
In an electrolytic cell as described in Example 1
10.0 of 1-isopropyl-4-hydroxymethylpyrrolidone and
54.6 g of methanol
are electrolyzed in the presence of 0.34 g of tetramethylammonium tetrafluoroborate as conducting salt. After having switched on the electrolysis direct current, the anode current density is 2 A/dm^2. After the passage of 2.2 Faradays per mol of 1-isopropyl-4-hydroxymethylpyrrolidone, the current is switched off. The calculated average cell tension is 48.5 volts.

After separation of the methanol and separation by column chromatography (silica gel/chloroform + ethanol [9:1]).

9.0 g of 1-isopropyl-4-hydroxymethyl-5-methoxypyrrolidone-2- are obtained, corresponding to a material yield of 75.6% and a current efficiency of 68.7%.

NMR characteristics of the compound:

NMR 100 millicycles per second; solvent: $CDCl_3$;  $N\text{-}\overset{/}{\underset{\backslash}{C}}H$: 4.1 ppm


$N{<}^{CH_3}_{CH_3}$: 1.2 ppm

—O—CH_3: 3.3 ppm

Example 5:

a) *Preparation of 1-methyl- and 1-isopropyl-3-*[6-carbomethoxy-2-hexyn-yl(1)]-4-hydroxymethyl-pyrrolidone 1-methyl compound

α) 29.4 g (138 mols) of 1-methyl-4(2-tetrahydropyranyloxymethyl—pyrrolidone dissolved in 90 ml of diethyl ether are added over a period of 20 minutes while stirring at -70°C to 150 mols of $LiN(i\text{-}C_3H_7)_2$ in 150 ml of diethyl ether. Stirring is continued for 45 minutes whereupon the solution is transferred to a coolable dropping funnel (-35 to -40°C) and added, while stirring over a period of 60 minutes, to a solution cooled to −70°C of 29.1 g (149 mols) of 1-bromo-6-chloro-hexyne (2) in 135 ml of ether. Stirring is continued for another 90 minutes, the mixture is slowly heated to room temperature, 75 ml of water are added dropwise, the organic phase is separated and the aqueous phase is extracted three times, each time with 50 ml of diethyl ether. The combined ether phases are washed three times with 40 ml each of cold sulfuric acid and once with 50 ml of water. After drying and concentrating under reduced pressure the organic phase,46.6 g of crude 1-methyl-3-[6-chloro-2-hexyn-yl(1)]-4-(2-tetrahydropyranyl-oxy-methyl— pyrrolidone (R_F 0.42 (ethyl acetate)) are obtained. The compound is used for the following reaction stage without further purification.

ß) 7.5 g (153 mols) of sodium cyanide are dissolved in 90 ml of dimethyl sulfoxide and the solution is heated to 80°C. 46.6 g (142.5 mmols) of crude 1-methyl-3-[6-chloro-2-hexyn-yl(1)]-4-(2-tetrahydropyranyl-oxymethyl)-pyrrolidone dissolved in 40 ml dimethyl sulfoxide are then added dropwise while stirring and the mixture is stirred for 3 to 6 hours at 80°C. The course of the reaction is followed by thin layer chromatography (ethyl acetate). When the reaction is terminated, the mixture is cooled to 10°C, 200 ml of water are added and the mixture is extracted three times, each time with 200 ml of diethyl ether. The combined ether phases are washed three times with saturated sodium chloride solution and dried. After concentration under reduced pressure 43.7 g of crude 1-methyl-3-[6-cyano-2-hexyn-yl(1)]-4-(2-tetrahydropyranyl-oxymethyl)-pyrrolidone [R_F 0.39 (ethyl acetate)] are obtained, which are used for the next reaction without further purification.

11 g (0.275 mol) of sodium hydroxide are dissolved in 33 ml of water, 43.7 g (137.5 mols) of 1-methyl-3-[6-cyano-2-hexyn-yl(1)]-4-(2-tetrahydropyranyl-oxymethyl)-pyrrolidone

dissolved in 135 ml of ethyl alcohol are added and the whole is refluxed for 18 hours. The alcohol is removed under pressure, 150 ml of icecold 2N sulfuric acid are added to the residue while cooling with ice and the whole is extracted ten times, each time with 100 ml of diethyl ether. After drying and concentrating the combined ether phases, 47.4 g of crude 1-methyl-3-[6-carboxy-2-hexyn-yl)]-4-(2-tetrahydropyranyl-oxymethyl)-pyrrolidone are obtained which are directly taken up in 250 ml of methylene chloride and to which 380 ml of a 0.5 molar ethereal diazomethane solution are added at 0°C. The mixture is allowed to stand for 30 minutes at 0°C and for 1 hour at room temperature. After concentration under reduced pressure, 43.7 g of crude 1-methyl-3-[6-carbomethoxy-2-hexyn-yl(1)]-4-(2-tetrahydropyranyl-oxymethyl)-pyrrolidone [R_F 0.45 (ethyl acetate)] are obtained.

The product obtained is dissolved in 200 ml of methanol, 3 drops of concentrated hydrochloric acid are added and the mixture is refluxed for 75 minutes. After concentrating under reduced pressure, the remaining oil is purified by column chromatography (silica gel/ethyl acetate) to remove by-products, then ethyl acetate:ethanol 10:1.5). 25 g of 1-methyl-3-[6-carbomethoxy-2-hexyn-yl(1)]-4-hydroxymethyl-pyrrolidone [R_F 0.14 (ethyl acetate)] are obtained.

$n_D^{20} = 1.5005$

IR(CH_2Cl_2): = 3450 (OH), 1740 (C=O), 1690 (C=O) cm^{-1}

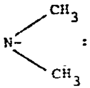
NMR: solvent: $CDCl_3$:N-CH_3: 2.82 ppm; 0-CH_3: 3.64 ppm.

The described preparation of the 1-methyl compound (which is not a starting material for the process of the invention) is nevertheless analogous to, and illustrative of, the preparation of such starting materials.

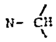
1-isopropyl compound

This compound is prepared in analogous manner using as starting compound 1-isopropyl-4-(tetrahydropyranyl-hydroxymethyl)-pyrrolidone.

n20/D = 1.4945

NMR: solvent: $CDCl_3$; OCH_3 3.63 ppm 

$N\!-\!\overset{CH_3}{\underset{CH_3}{<}}$: 1.14 ppm;



$N\!-\!CH$: 4.23 ppm.

b) *Anodic oxidation of the 1-isopropyl compound*

In an electrolytic cell having a capacity of about 60 ml of 1-isopropyl-3-[6-carbomethoxy-2-hexyn-yl(1)]-4-hydroxymethylpyrrolidone-2- and

57.7 g of methanol

are electrolyzed in the presence of 0.09 g of tetramethyl-ammonium tetrafluoroborate as conducting salt. As electrodes two concentrically diposed platinum net cylinders having 225 meshes per cm^2 and diameters of 15 and 30 mm, respectively, and a height of 50 mm are immersed in the solution. The outer electrode is connected as anode. During electrolysis the temperature is maintained at about 10°C. After having switched on the electrolysis direct current, the anode current density is found to be 1 A/dm^2. After having passed 2.44 Faradays per mol of starting lactam the current is switched off. The calculated average cell tension is 31.2 volts.

After separation of the methanol by distillation under reduced pressure there are obtained by column chromatography (silica gel/ethyl acetate) 3.35 g of 1-isopropyl-3-[carbo-methoxy-2-hexyn-yl(1)]-4-oxymethyl-5-methoxypyrrolidone-2 (R_{F1} 0.61; R_{F2} 0.55 (ethyl acetate), corresponding to a material yield of 60.8% and to a current efficiency of 50.1% of the theory.

Example 6:

In an electrolytic cell as described in Example 1, but having a capacity of 400 ml

87.3 g of caprolactam and

247.1 g of methanol

are electrolyzed in the presence of 1.24 g of tetramethylammonium tetrafluoroborate as conducting salt. The platinum net cylinders have a height of 100 mm. After having switched on the electrolysis direct current, the anode current density is found to be 3 A/dm^2. After having passed 3.0 Faradays per mole of ϵ-caprolactam, the current is switched off. The calculated average cell tension is 26.8 volts.

After working up by molecular distillation, 61.1 g of ϵ-methoxy-caprolactam (boiling point 106-108°C under 0.6 millibar; melting point 65-66°C) are obtained, corresponding to a material yield of 55.3% and a current efficiency of 36.9%.

Example 7:

In an electrolytic cell as described in Example 6

87.3 g of caprolactam and

247.1 g of methanol

are electrolyzed in the presence of 9.7 g of potassium tetrafluoroborate as conducting salt. After having switched on the electrolysis direct current, the anode current density is 1 A/dm^2.

The current is switched off after passage of 3.0 Faradays per mol of ϵ-caprolactam. The calculated average cell tension is 30.3 volts.

After working up by molecular distillation, 59.0 g of ϵ-methoxy-caprolactam (boiling point 106-108°C under 0.6 millibar; melting point 65-66°C) are obtained, corresponding to a material yield of 53.4% and a current efficiency of 35.6%.

Example 8:

In an electrolytic cell as described in Example 6
78.6 g of piperidone-2 and
253.9 g of methanol
are electrolyzed in the presence of 1.28 g of tetramethylammonium tetrafluoroborate as conducting salt. After having switched on the electrolysis direct current, the anode current density is found to be 2 A/dm^2. After passage of 2.4 Faradays per mol of piperidone-2, the current is switched off. The calculated average cell tension is 12.4 volts.

After removal of the methanol and twofold recrystallization in di-isopropyl ether, 73.4 g of 6-methoxypiperidone-2 (melting point 110-111°C) are obtained, corresponding to a material yield of 71.1% and a current efficiency of 59.2%.

Example 9:

In an electrolytic cell as described in Example 6
87.3 g of ϵ-caprolactam and
247.1 g of methanol
are electrolyzed in the presence of 8.4 g of sodium tetrafluoroborate as conducting salt. After having switched on the electrolysis direct current, the anode current density is found to be 3 A/dm^2. After passage of 3.0 Faradays per mol of ϵ-caprolactam the current is disconnected. The average cell tension is calculated to be 12.9 volts. After working up by molecular distillation, 80.0 g of ϵ-methoxy-ϵ-caprolactam are obtained, corresponding to a material yield of 72.4% and a current efficiency of 48.3%.

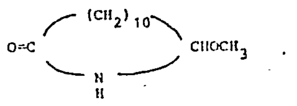
Example 10:

A test is carried out under the conditions of Example 9 with the exception, however, that a mixture of 4.2 g of sodium tetrafluoroborate and 5.9 g of tetramethylammonium tetrafluoroborate is used as conducting salt. After disconnection of the current, the average cell tension is calculated to be 18.7 volts. By working up by molecular distillation 78.4 g of ϵ-methoxy-ϵ-caprolactam are obtained, corresponding to a material yield of 71.0% and to a current efficiency of 47.3%.

Example 11:

In an electrolytic cell as described in Example 6
72.24 g of laurinolactam and
293.33 g of methanol
are electrolyzed in the presence of 0.6 g of tetramethylammonium tetrafluoroborate as conducting salt. After having switched on the electrolysis direct current, the anode current density is found to be 2 A/dm^2. After having passed 3.5 Faradays per mol of laurinolactam, the current is disconnected. The calculated average cell tension is 48.1 volts.

After working up and recrystallization 42.4 g of ϵ-methoxy-laurinolactam of the formula

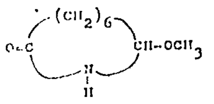


(melting point 153.5 — 154.5°C) are obtained, corresponding to a material yield of 50.9% and a current efficiency of 29.1%.

Example 12:

In an electrolytic cell as described in Example 1
16.7 g of caprylolactam and
75.8 g of methanol
are electrolyzed in the presence of 0.19 g of tetramethylammonium tetrafluoroborate as conducting salt. After having switched on the electrolysis direct current, the anode current density is 1 A/dm^2. The current is disconnected after having passed 3.0 Faradays per mol of caprylolactam. The calculated average cell tension is 35.2 volts.

After working up by molecular distillation 11.6 g of ω-methoxycaprylolactam of the formula

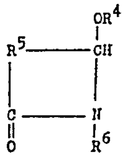


$n_D^{25} = 1.4980$
(boiling point 55°C under
0.013 millibar

are obtained, corresponding to a material yield of 57.2% and a current efficiency of 38.3%.

WHAT WE CLAIM IS:

1. A process for the preparation of a compound of the general formula



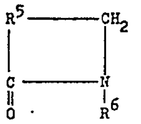
II

in which

R^4 represents an alkyl radical having from 1 to 4 carbon atoms,

R^5 represents a linear or branched alkylene radical having from 1 to 10 carbon atoms in the chain which forms part of the ring and which may be unsubstituted or substituted by one or more of the same or different groups which are not reactive under the reaction conditions, and

R^6 represents a hydrogen atom or an alkyl radical which is branched at the carbon atom joined to the nitrogen atom, and which may be substituted or unsubstituted, which comprises the anodic alkoxylation of a lactam of the general formula



I

in which R^5 and R^6 have the meanings given above, with an alcohol of the general formula R^4OH in which R^4 has the meaning given above, in the presence of at least one conducting salt, selected from alkali metal and tetraalkylammonium-tetrafluoroborates, hexafluorophosphates and nitrates, in an electrolytic cell with stationary or flowing electrolyte.

2. A process as claimed in claim 1, which is carried out at a temperature of up to 100°C.

3. A process as claimed in claim 2, which is carried out at a temperature in the range of from -10 to 100°C.

4. A process as claimed in claim 3, which is carried out at a temperature in the range of from 0 to 60°C.

5. A process as claimed in claim 4, wherein the tetraalkylammonium salt has from 1 to 6 carbon atoms in each alkyl group.

6. A process as claimed in claim 5, wherein the tetraalkylammonium salt has from 1 to 4 carbon atoms in each alkyl group.

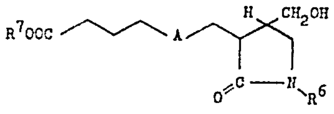
7. A process as claimed in claim 6, wherein the tetraalkylammonium salt is the tetramethyl or tetraethyl salt.

8. A process as claimed in claim 7, wherein the conducting salt is $NaBF_4$, KBF_4 or $(CH_3)_4NBF_4$.

9. A process as claimed in any one of claims 1 to 8, wherein R^6 represents an alkyl radical having from 3 to 10 carbon atoms.

10. A process as claimed in any one of claims 1 to 9, wherein the R^5 radical is substituted by one or more substituents, any two or more of which may be the same or different, selected from hydroxyl groups, halogen atoms and groups of the formula $-CH_2OH$ and $-CH_2-A-CH_2CH_2CH_2-COOR^7$ in which A represents $-C{\equiv}C-$, $-CH{=}CH-$ or $-CH_2-CH_2$ and R^7 represents a hydrogen atom or a lower aliphatic radical, a cycloaliphatic radical having 5 or 6 carbon atoms or an araliphatic radical having 7 or 8 carbon atoms.

11. A process as claimed in any one of claims 1 to 8, wherein the starting material is 2-azetidinone, 3-methyl-2-azetidinone, 1-isopropyl-2-pyrrolidone, 1-isopropyl-4-hydroxymethyl-2-pyrrolidone, 1-tert.-butyl-2-pyrrolidone, 2-piperidone, ϵ-caprolactam, a lactam of ω-amino-caprylic acid, ω-amino-capric acid or ω-amino-lauric acid, or a compound of the general formula



in which R^7 represents a C_1-C_4 alkyl radical, a C_5 or C_6 cycloalkyl radical or an araliphatic radical, and R_6 and A are as defined in claims 1 and 10 respectively.

12. A process as claimed in any one of claims 1 to 8, wherein the starting material is 1-isopropyl-4-hydroxymethyl-2-pyrrolidone or 1-isopropyl-3[6-methoxycarbonyl-hex-2-yn-1-yl]-4-hydroxymethyl-2-pyrrolidone.

13. A process as claimed in claim 11 or claim 12, wherein in the case where A is -C≡C- the final compound is partially hydrogenated to form the group -CH=CH- completely hydrogenated to $-CH_2$- CH_2- by a method known *per se*.

14. A process as claimed in any one of claims 1 to 9, wherein the starting material is a compound of the general formula I in which R_5 represents $(CH_2)_{2-100}$.

15. A process as claimed in claim 14, in which R_5 represents $-(CH_2)_3-$, $-(CH_2)_4-$ or $-(CH_2)_{10}-$.

16. A process as claimed in any one of claims 1 to 15, wherein R_4 represents a methyl group.

17. A process as claimed in any one of claims 1 to 16, wherein the conducting salt component is present in an amount of from 0.01 to 2 mols per litre.

18. A process as claimed in claim 17, wherein the conducting salt component is present in an amount of from 0.02 to 1 mol per litre.

19. A process as claimed in any one of claims 1 to 18, wherein the molar ratio of the compound I to the alcohol is in the range of from 1 : 1 to 1 : 100.

20. A process as claimed in claim 19, wherein the molar ratio is in the range of from 1 : 2 to 1 : 60.

21. A process as claimed in claim 20, wherein the molar ratio is in the range of from 1 : 5 to 1 : 50.

22. A process as claimed in any one of claims 1 to 21, wherein the current density is in the range of from 1 to 50 A/dm^2.

23. A process as claimed in claim 22, wherein the current density is in the range of from 2 to 30 A/dm^2.

24. A process as claimed in any one of claims 1 to 23, wherein the quantity of electricity is in the range of from 2 to 4 F per mol of starting lactam.

25. A process as claimed in claim 24, wherein the quantity of electricity is in the range of from 2 to 3.5 F per mol of starting lactam.

26. A process as claimed in claim 25, wherein the quantity of electricity is in the range of from 2 to 3 F per mol of starting lactam.

27. A process as claimed in claim 1, which is carried out substantially as described herein with reference to, and as illustrated by, the accompanying drawing.

28. A process as claimed in claim 1, carried out substantially as described in any one of the Examples 1 to 12 herein.

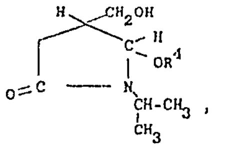
29. A compound of the general formula II shown in claim 1, wherein R^4, R^5 and R^6 have the meanings given in claim 1, whenever prepared by a process as claimed in any one of claims 1 to 28.

30. A compound of the general formula II shown in claim 1, wherein R^4, R^5 and R^6 have the meanings given in claim 1, except that R^6 does not represent a hydrogen atom.

31. A compound as claimed in claim 30, wherein R^6 represents an alkyl radical having from 3 to 10 carbon atoms.

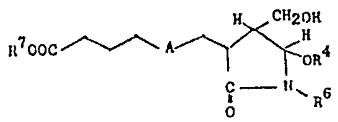
32. A compound as claimed in claim 30 or claim 31, wherein R^5 is substituted by one or more substituents, any two or more of which may be the same or different, selected from hydroxyl groups, halogen atoms and groups of the formula-CH_2OH and $-CH_2$-A-$CH_2CH_2CH_2$-$COOR^7$ in which A represents -C≡C-, -CH=CH- or $-CH_2$-CH_2- and R^7 represents a hydrogen atom or a lower aliphatic radical, a cycloaliphatic radical having 5 or 6 carbon atoms or an araliphatic radical having 7 or 8 carbon atoms.

33. A compound of the formula



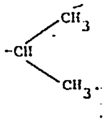
in which R^4 represents an alkyl radical having from 1 to 4 carbon atoms.

34. A compound of the formula

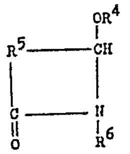


in which A, and R_7 are as defined in claim 32 and R_4, and R_6 are as defined in claim 1.

35. A compound as claimed in claim 35, in which A stands for -C≡C-, R^4 and R^7 stand for CH_3 and R^6 stands for



36. A compound of the formula



II

in which R^4 represents an alkyl radical having from 1 to 4 carbon atoms, R^5 stands for $-(CH_2)_{2-10}$ and R^6 is a branched alkyl radical having from 3 to 10 carbon atoms with a secondary or tertiary N-α-C atom.

37. A compound as claimed in claim 30, which is described in any one of the Examples herein.

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1571900 COMPLETE SPECIFICATION

1 SHEET *This drawing is a reproduction of the Original on a reduced scale*