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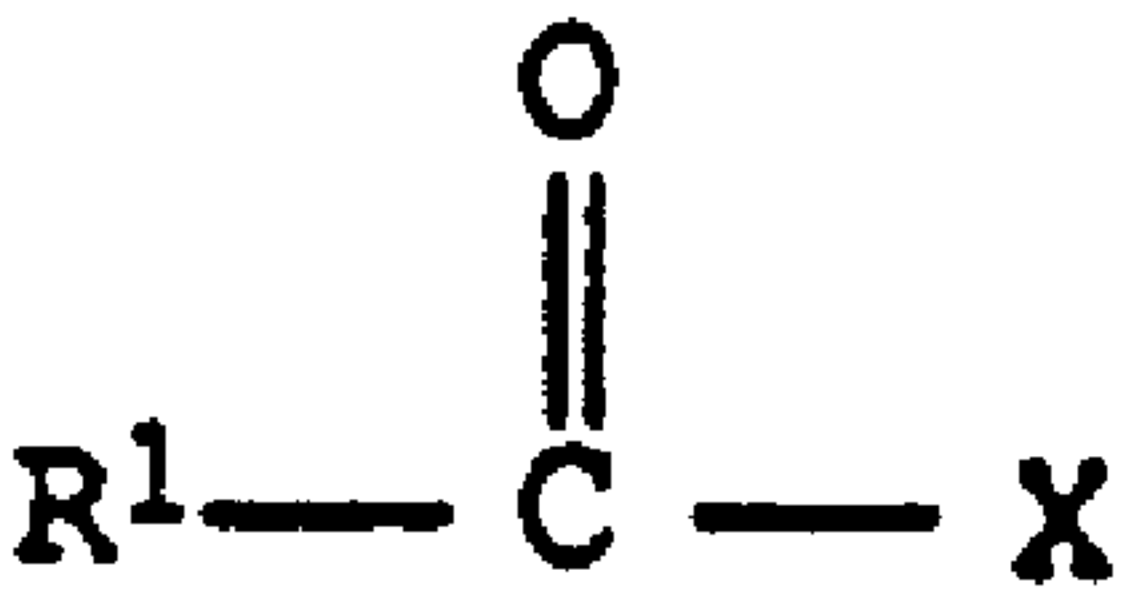
(72) **Inventeur/Inventor**:
FUCHS, EBERHARD, DE

(73) **Propriétaire/Owner**:
BASF AKTIENGESELLSCHAFT, DE

(74) **Agent**: ROBIC

(54) Titre : PROCEDE DE PREPARATION DE DERIVES D'ACIDE CARBOXYLIQUE
(54) Title: THE PREPARATION OF CARBOXYLIC ACID DERIVATIVES



$$R^1-\overset{O}{\overset{\|}{C}}-X \qquad (I)$$

(57) **Abrégé/Abstract**:

A process is disclosed for preparing carboxylic acid derivatives having the general formula (I), in which X stands for OR^2 or NH_2, R^1 stands for C_1-C_{20} alkyl, C_1-C_{20} hydroxyalkyl, C_3-C_{12}-cycloalkyl, C_4-C_{12} alkyl-cycloalkyl, C_4-C_{12}-cycloalkyl-alkyl, C_5-C_{20} alkyl-cycloalkyl-alkyl, aryl, C_7-C_{20} aralkyl, C_7-C_{20} alkylaryl, an heteroaliphatic or heteroaromatic ring with 5 to 8 carbon atoms and R^2 stands for C_1-C_{20} alkyl, from carboxylic acid nitriles having the general formula (II) R^1-C≡N, in which R^1 has the above-mentioned meanings, and from alcohols having the general formula (III) R^2-OH, in which R^2 has the above-mentioned meanings. The reaction is carried out in the liquid phase at temperatures from 50 to 300 °C and pressures from 0.1 to 350 bars in the presence of an heterogeneous catalyst.

PCT

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(71) Anmelder *(für alle Bestimmungsstaaten ausser US)*: BASF AKTIENGESELLSCHAFT [DE/DE]; D-67056 Ludwigshafen (DE).

(72) Erfinder; und
(75) Erfinder/Anmelder *(nur für US)*: FUCHS, Eberhard [DE/DE]; Bensheimer Ring 5c, D-67227 Frankenthal (DE).

(74) Gemeinsamer Vertreter: BASF AKTIENGESELLSCHAFT; D-67056 Ludwigshafen (DE).

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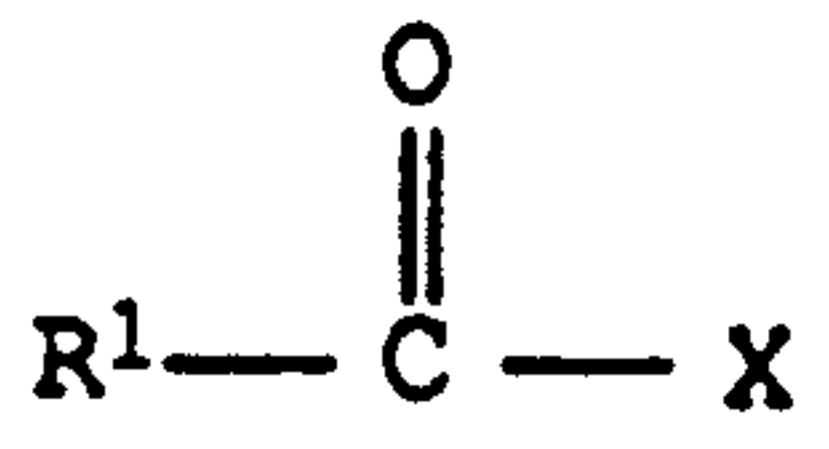
(54) Title: CARBOXYLIC ACID DERIVATIVE PREPARATION PROCESS

(54) Bezeichnung: VERFAHREN ZUR HERSTELLUNG VON CARBONSÄUREDERIVATEN

(57) Abstract



$$R^1-\overset{\overset{\displaystyle O}{\|}}{C}-X$$

(I)

A process is disclosed for preparing carboxylic acid derivatives having the general formula (I), in which X stands for OR^2 or NH_2, R^1 stands for C_1-C_{20} alkyl, C_1-C_{20} hydroxyalkyl, C_3-C_{12}-cycloalkyl, C_4-C_{12} alkyl-cycloalkyl, C_4-C_{12}-cycloalkyl-alkyl, C_5-C_{20} alkyl-cycloalkyl-alkyl, aryl, C_7-C_{20} aralkyl, C_7-C_{20} alkylaryl, an heteroaliphatic or heteroaromatic ring with 5 to 8 carbon atoms and R^2 stands for C_1-C_{20} alkyl, from carboxylic acid nitriles having the general formula (II) R^1-C≡N, in which R^1 has the above-mentioned meanings, and from alcohols having the general formula (III) R^2-OH, in which R^2 has the above-mentioned meanings. The reaction is carried out in the liquid phase at temperatures from 50 to 300 °C and pressures from 0.1 to 350 bars in the presence of an heterogeneous catalyst.

(57) Zusammenfassung

Verfahren zur Herstellung von Carbonsäurederivaten der allgemeinen Formel (I), in der X OR^2 oder NH_2, R^1 C_1- bis C_{20}-Alkyl, C_1- bis C_{20}-Hydroxyalkyl, C_3- bis C_{12}-Cycloalkyl, C_4- bis C_{12}-Alkyl-cycloalkyl, C_4- bis C_{12}-Cycloalkyl-alkyl, C_5- bis C_{20}-Alkyl-cycloalkyl-alkyl, Aryl, C_7- bis C_{20}-Aralkyl, C_7- bis C_{20}-Alkylaryl, einen heteroaliphatischen oder heteroaromatischen Ring mit 5- bis 8-Kohlenstoffatomen und R^2 C_1- bis C_{20}-Alkyl bedeuten, aus Carbonsäurenitrilen der allgemeinen Formel (II) R^1-C≡N, in der R^1 die oben genannten Bedeutungen hat, und Alkoholen der allgemeinen Formel (III) R^2-OH, in der R^2 die oben genannten Bedeutungen hat, bei Temperaturen von 50 bis 300 °C und Drücken von 0,1 bis 350 bar in Gegenwart eines Heterogenkatalysators, indem man die Umsetzung in der Flüssigphase durchführt.

PREPARATION OF CARBOXYLIC ACID DERIVATIVES

The invention relates to a process for preparing carboxylic acid derivatives from carbonitriles and alcohols at elevated temperatures on titanium oxide catalysts.

DE-A 27 14 767 discloses a process for preparing carboxylic acid derivatives by gas-phase reaction of nitriles with alcohols and water on solid, metal-containing catalysts such as copper, zinc, chromium, bismuth, manganese, iron, nickel, cadmium on carriers such as Al_2O_3, SiO_2, ZrO_2 or TiO_2. Dehydration and etherification are found as side reactions.

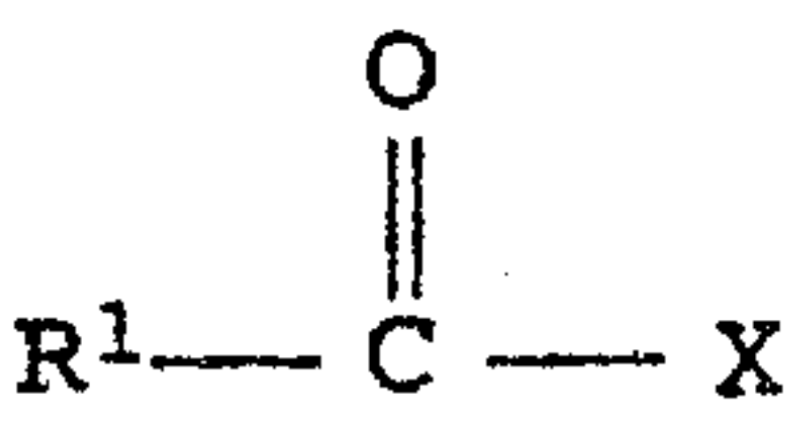
EP-A 412 310, for example, discloses a process for preparing carboxamides by hydration of nitriles with water on manganese-containing catalysts, which can subsequently be reacted with alcohols by acid catalysis, in the presence of metal salts, eg. as disclosed in US-A 4 613 684, or in the gas phase on solid catalysts, eg. as disclosed in EP-A 561 614, or with formic ester resulting in formamide formation, eg. as disclosed in EP-A 392 361, on metal oxides to give the carboxylic acid derivatives.

The disadvantages for industrial application are the two stages and the formation of byproducts, such as production of salt or formamide formation.

DE-A 43 39 648 discloses a process for preparing caprolactam (a cyclic amide) by reacting aminocapronitrile with water in an ethanolic solution on a titanium oxide catalyst.

It is an object of the present invention to remedy the abovementioned disadvantages.

More specifically, the object of the invention as broadly disclosed hereinafter is to provide an improved process for preparing carboxylic acid derivatives of the general formula I:



$$R^1-\overset{\displaystyle O}{\overset{\|}{C}}-X \qquad (I),$$

where

X is OR^2 or NH_2,

R^1 is C_1-C_{20}-alkyl, C_1-C_{20}-hydroxyalkyl, C_3-C_{12}-cycloalkyl, C_4-C_{12}-alkylcycloalkyl, C_4-C_{12}-cycloalkylalkyl, C_5-C_{20}-alkylcycloalkylalkyl, aryl, C_7-C_{20}-aralkyl, C_7-C_{20}-alkylaryl, a heteroaliphatic or heteroaromatic ring with 5 to 8 carbon atoms and

R^2 is C_1-C_{20}-alkyl,

from carbonitriles of the general formula II

$$R^1—C\equiv N \qquad (II),$$

where R^1 has the abovementioned meanings, and alcohols of the general formula III

$$R^2—OH \qquad (III),$$

where R^2 has the abovementioned meanings, at from 50 to 300°C under from 0.1 to 350 bar in the presence of a heterogeneous catalyst, wherein the reaction is carried out in liquid phase.

The invention as claimed is however restricted to the use of titanium oxide as said heterogeneous catalyst.

The process according to the invention can be carried out in the following way:

The carbonitrile II can be brought into contact with an alcohol III, preferably dissolved in the alcohol III, at from 50 to 300°C, preferably 100 to 290°C, particularly preferably 140 to 270°C, under from 0.1 to 350 bar, preferably 1 to 200 bar, particularly preferably 30 to 140 bar, in liquid phase with a titanium oxide catalyst, as a rule in pressure-stable apparatus such as autoclaves and tubular reactors, preferably tubular reactors. The result is, as a rule, an alcoholic solution of the carboxylic ester and of the carboxamide I, from which the carboxylic ester and the carboxamide I can be obtained by conventional methods, for example by distillation, extraction or crystallization.

The carboxamide can be returned to the reactor together with fresh carbonitrile II.

The reaction of solid carbonitriles II or solid alcohols III can be carried out in inert solvents, for example in ethers, preferably ethers with 2 to 20 carbon atoms, particularly preferably ethers with 4 to 12 carbon atoms, such as diethyl ether, methyl tert-butyl ether or tetrahydrofuran, hydrocarbons, preferably hydrocarbons with 5 to 30 carbon atoms, particularly preferably hydrocarbons with 5 to 12 carbon atoms, such as toluene and xylene or, advantageously, in the appropriate carboxylic ester I.

Examples of suitable heterogeneous catalysts are acidic, basic or amphoteric oxides of elements of groups IIA, IIIA, IVA of the Periodic Table of the Elements, such as calcium oxide, magnesium oxide, boron oxide, aluminum oxide, tin oxide or silicon dioxide, pyrogenic silica, as silica gel, kieselguhr, quartz, furthermore oxides of metals of groups IIB, IIIB, IVB, VB, VIB and VIIB of the Periodic Table of the Elements, such as titanium oxide, especially titanium dioxide, eg. amorphous, as anatase or rutile, zirconium oxide, zinc oxide, manganese oxide, vanadium oxide, niobium oxide, iron oxide, chromium oxide, molybdenum oxide, tungsten oxide, oxides of the lanthanides and actinides such as cerium oxide, thorium oxide, praseodymium oxide, samarium oxide, rare earth mixed oxides or mixtures thereof. Some sulfides, selenides and tellurides such as zinc telluride, tin selenide, molybdenum sulfide, tungsten sulfide, sulfides of nickel, zinc and chromium, can also be used.

The abovementioned compounds can be doped with compounds of groups IA, IIA, IIIA, IVA, VA, VIA and VIIA of the Periodic Table of the Elements or contain the later.

Further suitable catalysts are zeolites, phosphates and heteropolyacids, and acidic and alkaline ion exchangers such as Naphion [sic].

These catalysts may, where appropriate, in each case contain up to 50% by weight of copper, tin, zinc, manganese, iron, cobalt, nickel, ruthenium, palladium, platinum, silver or rhodium.

The catalysts can, depending on the composition of the catalyst, be used as unsupported or supported catalyst. Thus, for example, titanium dioxide can be used as titanium dioxide pellets or as titanium dioxide applied in a thin layer to a support. The methods used for applying TiO_2 to a support such as silicon dioxide, aluminum oxide or zirconium dioxide can be all those described in the literature. Thus, a thin TiO_2 layer can be applied by hydrolyzing organotitanium compounds such as titanium isopropoxide or butoxide or by hydrolyzing $TiCl_4$ or other inorganic Ti-containing compounds. It is also possible to use brines containing titanium oxide.

The reaction can be carried out, for example, in suspension, preferably in a fixed bed. The reaction is preferably carried out in a fixed bed because this makes it easy to carry out continuously, the yields and selectivities in the fixed bed are, as a rule, very high and thus result in short holdup times with very high throughputs. Since the heterogeneous catalysts used have, according to observations to date, a long useful life, the consumption of catalyst is extremely low.

The substituents X, R^1 and R^2 in the compounds I, II and III have the following meanings:

X

- OR^2
- NH_2

R^1,R^2

- C_1–C_{20}-alkyl, preferably C_1–C_{12}-alkyl, particularly preferably C_1–C_8-alkyl such as methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, tert-butyl, n-pentyl, isopentyl, n-hexyl, isohexyl, n-heptyl, isoheptyl, n-octyl and isooctyl, especially C_1–C_4-alkyl such as methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl and tert-butyl,
- C_1–C_{20}-hydroxyalkyl, preferably C_1–C_8-hydroxyalkyl, particularly preferably C_1–C_4-hydroxyalkyl such as hydroxymethyl, 1-hydroxyethyl, 2-hydroxyethyl and 1-methyl-1-hydroxyethyl,
- C_3–C_{12}-cycloalkyl, preferably C_5–C_8-cycloalkyl such as cyclopentyl, cyclohexyl, cycloheptyl and cyclooctyl, particularly preferably cyclopentyl and cyclohexyl,
- C_4–C_{12}-alkylcycloalkyl, preferably C_5–C_{10}-alkylcycloalkyl, particularly preferably C_5–C_8-alkylcycloalkyl,
- C_4–C_{12}-cycloalkylalkyl, preferably C_5–C_{10}-cycloalkylalkyl, particularly preferably C_5–C_8-cycloalkylalkyl,
- C_5–C_{20}-alkylcycloalkylalkyl, preferably C_6–C_{16}-alkylcycloalkylalkyl, particularly preferably C_7–C_{12}-alkylcycloalkylalkyl,
- aryl such as phenyl, 1-naphthyl and 2-naphthyl, preferably phenyl,
- C_7–C_{20}-alkylaryl, preferably C_7–C_{16}-alkylaryl, [lacuna] preferably C_7–C_{12}-alkylphenyl such as 2-methylphenyl, 3-methylphenyl, 4-methylphenyl, 2-ethylphenyl, 3-ethylphenyl and 4-ethylphenyl,
- C_7–C_{20}-aralkyl, preferably C_7–C_{16}-aralkyl, [lacuna] preferably C_7–C_{12}-phenalkyl [sic] such as phenylmethyl, 1-phenylethyl and 2-phenylethyl,
- a heteroaliphatic ring with 5 to 8 carbon atoms such as 2-morpholinyl, 3-morpholinyl, 2-piperidinyl, 3-piperidinyl and 4-piperidinyl,
- a heteroaromatic ring with 5 to 8 carbon atoms such as 2-pyridyl, 3-pyridyl, 4-pyridyl, 2-pyrazolyl, 2-imidazolyl, 4(5)-imidazolyl, preferably 3-pyridyl.

The carboxylic esters and carboxamides I are suitable as as [sic] intermediates, plastics precursors and in crop protection and pharmacy.

Examples

Example 1

A 20% by weight ethanolic solution of nicotinonitrile was passed with the addition of 1 mol of water (3.5% by weight based on the solution) at 220°C and 80 bar through a tube packed with titanium oxide (1.5 mm pellets). The holdup time was set variably via the flow rate.

The composition of the discharge from the reaction is summarized in Table 1.

Table 1

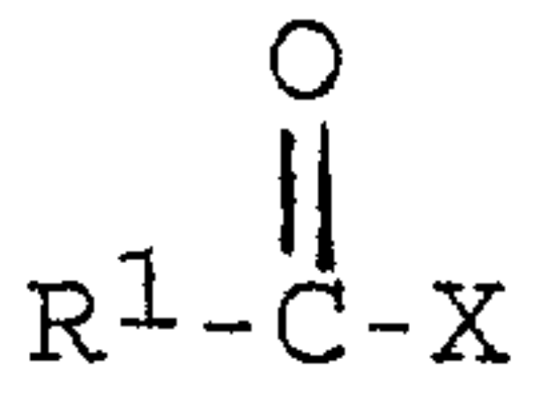
Holdup time	Nicotinonitrile	Ethyl nicotinate	Nicotinamide	Others
[min]	[%]	[%]	[%]	[%]
15	5.1	5.4	9.4	0.1
30	1.9	8.6	9.1	0.4
60	0.6	11.3	7.4	0.7

Example 2

A 20% by weight ethanolic solution of nicotinonitrile was pumped as in Example 1 in the presence of 1 mol of water at 220°C at 80 bar through an empty tube. No reaction took place.

CLAIMS

1. A process for preparing a carboxylic acid derivative of the general formula (I):



$$R^1-\overset{\overset{O}{\|}}{C}-X \qquad (I),$$

where:

X is OR^2 or NH_2,

R^1 is C_1-C_{20}-alkyl, C_1-C_{20}-hydroxyalkyl, C_3-C_{12}-cycloalkyl, C_4-C_{12}-alkylcycloalkyl, C_4-C_{12}-cycloalkylalkyl, C_5-C_{20}-alkylcycloalkylalkyl, aryl, C_7-C_{20}-aralkyl, C_7-C_{20}-alkylaryl or a heteroaliphatic or heteroaromatic ring with 5 to 8 carbon atoms and

R^2 is C_1-C_{20}-alkyl,

from a carbonitrile of the general formula II:

$$R^1-C{\equiv}N \qquad (II),$$

where R^1 has the abovementioned meanings, and an alcohol of the general formula (III):

$$R^2-OH \qquad (III),$$

where R^2 has the avovementioned meanings, at from 50 to 300°C under from 0.1 to 350 bar in the presence of a heterogeneous catalyst in liquid phase,
wherein said heterogeneous catalyst is titanium dioxide.

2. A process for preparing a carboxylic acid derivative as claimed in claim 1, wherein anatase, rutile or mixtures thereof is used as titanium dioxide.

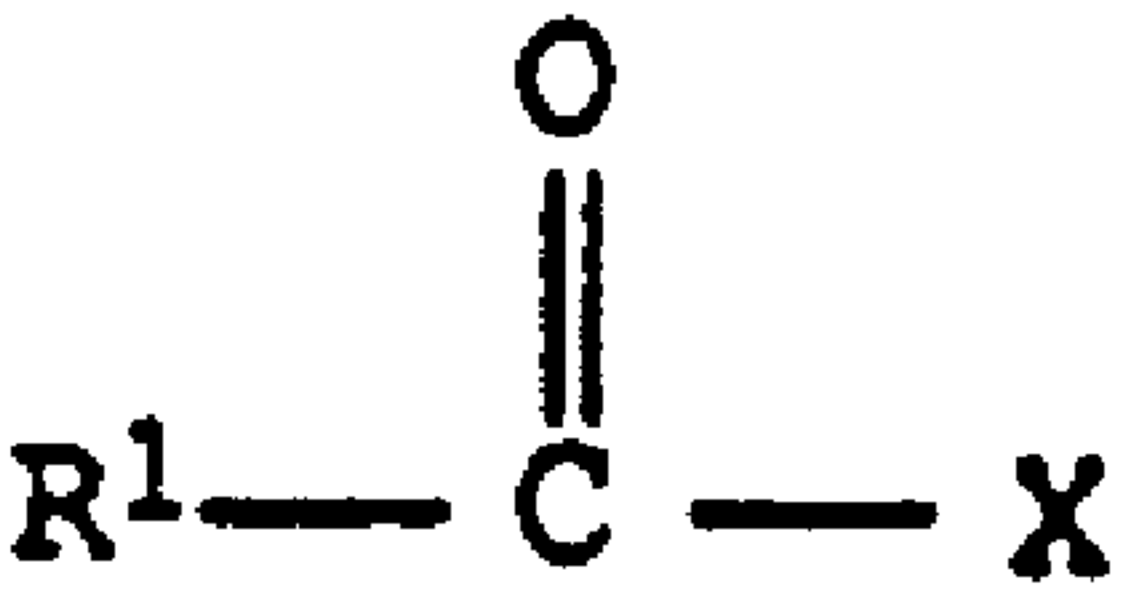
3. A process for preparing a carboxylic acid derivative as claimed in any one of claims 1 to 2, wherein the reaction is carried out at from 100 to 290°C.

4. A process for preparing a carboxylic acid derivative as claimed in claim 3, wherein the reaction is carried out at from 140 to 270°C.

5. A process for preparing a carboxylic acid derivatives as claimed in any one of claims 1 to 4, wherein the reaction is carried out in liquid phase under from 1 to 200 bar.

6. A process for preparing a carboxylic acid derivatives as claimed in claim 5, wherein the reaction is carried out under from 30 to 140 bar.

7. A process for preparing a carboxylic acid derivative as claimed in any one of claims 1 to 6, wherein R^1 is 3-pyridyl, 1-methyl-1-hydroxyethyl, 1-hydroxyethyl or 2-hydroxyethyl.



$$R^1-\overset{\overset{\displaystyle O}{\|}}{C}-X$$

(I)