Title: SUBSTITUTED 4-HYDROXYPYRIDINES

Abstract: The present invention relates to substituted 4-hydroxypyridines as well as their derivatives, a process for producing substituted 4-hydroxypyridines and their derivatives as well as the use of these compounds.
Substituted 4-Hydroxypyridines

The present invention relates to substituted 4-hydroxypyridines as well as their derivatives, a process for producing substituted 4-hydroxypyridines and their derivatives as well as the use of these compounds.

Substituted pyridines have been the subject of intensive attempts at synthesis on account of their great versatility and their uses as components of active substances, especially of medicinal drugs and plant protection agents. It has been conjectured as regards their use as medicinal drugs that pyridine derivatives can be used as anticoagulants, antihistamines, antiseptics, antiarrythmic agents and antirheumatic agents. Also, various attempts have been undertaken to chemically synthesize pyridines (cf. e.g., Konakahara et al., 1999, J. Chem. Soc, Perkin Transp. 1, 2803-2806; Lee et al., 1990, J. Org. Chem., 55, 2964-2967; Hedge S., 1991, J. Org. Chem., 56, 5726-5729). However, the previously known synthesis paths were complicated or supplied substituted pyridines only in small yields. In particular, they do not permit the synthesis of 2- and/or 6-fluoroalkyl-substituted pyridines. However, precisely the latter group is of special interest since, e.g., 2-trifluoromethylpyridine can be used as insecticide and herbicide (Riyuuozou, JP 58010569, 1983).

Accordingly, the present invention has the task of making available a new synthesis path for the production of substituted 4-hydroxypyridines. Furthermore, the present invention has the task of making a synthesis available that supplies the named compounds in a high yield.

Furthermore, the present invention has the task of making available a synthesis that starts from readily accessible initial substances and can therefore be carried out very economically. Furthermore, the present invention has the task of making available new, highly-substituted pyridines.

The tasks of the present invention are solved by a process for producing a compound in accordance with the present invention with the formula (I)
wherein

$R^1$ is selected from the group comprising substituted and non-substituted alkyl, substituted and non-substituted aryl, substituted and non-substituted heteroaryl, substituted and non-substituted alkenyl, substituted and non-substituted alkinyl,

$R^2$ is selected from the group comprising H, substituted and non-substituted alkyl, substituted and non-substituted aryl, in particular substituted and non-substituted C$_1$-C$_2$ aryl, especially methyl, ethyl, $\alpha$-propyl, isopropyl, n-butyl, t-butyl,

$R^3$ is selected from the group comprising H, substituted and non-substituted alkyl, substituted and non-substituted cycloalkyl, substituted and non-substituted aryl, substituted and non-substituted heteroaryl, especially substituted and non-substituted Q-C$_2$ aryl, especially methyl, ethyl, $\alpha$-propyl, isopropyl, n-butyl, t-butyl, substituted and non-substituted perhalogenated aryl, wherein the halogenide is selected from the group consisting of F, Cl, Br and I, especially F, and

$R^4$ is selected from the group comprising substituted and non-substituted alkyl, especially substituted and non-substituted C$_1$-C$_{12}$ alkyl, perhalogenated alkylsulfonyl, especially perhalogenated C$_1$-C$_{12}$ alkylsulfonyl, wherein the halogenide is selected from the group consisting of F, Cl, Br and I, especially F, e.g., trifluoromethanesulfonyl,
nonafluorobutanesulfonyl, p-toluenesulfonyl, p-bromobenzenesulfonyl, p-nitrobenzenesulfonyl, methanesulfonyl, 2,2,2-trifluoroethanesulfonyl,

with the steps:

a) Conversion of 1,3-diketones (1) with ammonia to a compound (2) of an $\alpha,\beta$-unsaturated $\beta$-aminoketone, wherein $R^1$ and $R^2$ are defined as above,

\[ R^1\overset{\text{O}}{\text{C}}\overset{\text{O}}{\text{C}}\overset{\text{R}^2}{\text{R}} \xrightarrow{\text{NH}_3} \overset{\text{H}}{\text{N}}\overset{\text{C}}{\text{O}}\overset{\text{R}^1}{\text{C}}\overset{\text{O}}{\text{C}}\overset{\text{R}^2}{\text{R}} \]

b) Conversion of (2) by treatment with a carbonic acid anhydride or carbonic acid halogenide into an N-acetylated $\alpha,\beta$-unsaturated $\beta$-aminoketone (3), wherein $R^3$ is defined as above and $X$ is an anhydride or halogenide, wherein the halogenide is selected from the group consisting of F, Cl, Br and I, especially Cl,

\[ R^1\overset{\text{O}}{\text{C}}\overset{\text{X}}{\text{X}}\overset{\text{R}^3}{\text{R}} \xrightarrow{\text{H}}\overset{\text{N}}{\text{H}}\overset{\text{C}}{\text{O}}\overset{\text{R}^1}{\text{C}}\overset{\text{O}}{\text{C}}\overset{\text{R}^2}{\text{R}} \]

c) Ring formation by intramolecular aldol condensation of the N-acetylated $\alpha,\beta$-unsaturated $\beta$-aminoketone (3) produced at b) with a condensation agent to 2,6-di-substituted or 2,3,6-tri-substituted 4-hydroxypyridines (4b),
and

(d) O-alkylation or O-sulfonylation of the 4-hydroxy group of (4b) with a compound with the formula R^4-X to 4-alkoxypyridines (I) or pyridinyl-4-sulfonic acid esters (I), wherein R^4 is defined as above, comprising the following scheme

In one embodiment the process comprises compounds, in which

R^1 is selected from the group comprising substituted and non-substituted C_i-C_{i+2} alkyl, especially methyl, ethyl, α-propyl, isopropyl, n-butyl, t-butyl, substituted and non-substituted phenyl, substituted and non-substituted C_5-C_6 heteroaryl, substituted and non-substituted naphthyl, substituted and non-substituted C_7-C_{11} alkylphenyl, substituted and non-substituted C_5-C_7 cycloalkyl, substituted and non-substituted C_5-C_7 cycloalkenyl, halogenated alkyl or aryl.
R\textsuperscript{2} is selected from the group comprising H, substituted and non-substituted C\textsubscript{i}-C\textsubscript{2} alkyl, especially methyl, ethyl, α-propyl, isopropyl, n-butyl, t-butyl, substituted and non-substituted phenyl, substituted and non-substituted C\textsubscript{7}-C\textsubscript{8} alkylphenyl.

R\textsuperscript{3} is selected from the group comprising H, substituted and non-substituted C\textsubscript{i}-C\textsubscript{2} alkyl, especially methyl, ethyl, α-propyl, isopropyl, n-butyl, t-butyl, substituted and non-substituted perhalogenated C\textsubscript{1}-C\textsubscript{2} alkyl, wherein the halogenide is selected from the group consisting of F, Cl, Br and I, especially F, substituted and non-substituted phenyl, substituted and non-substituted heteroaryl, substituted and non-substituted naphthyl, substituted and non-substituted C\textsubscript{7}-C\textsubscript{8} alkylphenyl, substituted and non-substituted C\textsubscript{3}-C\textsubscript{7} cycloalkyl, and

R\textsuperscript{4} is selected from the group comprising substituted and non-substituted C\textsubscript{i}-C\textsubscript{12} alkyl, especially methyl, ethyl, α-propyl, isopropyl, n-butyl, t-butyl, perhalogenated alkylsulfonyl, especially perhalogenated C\textsubscript{1}-C\textsubscript{2} alkylsulfonyl, wherein the halogenide is selected from the group consisting of F, Cl, Br and I, especially F, e.g., trifluoromethanesulfonyl, nonafluorobutanesulfonyl, p-toluenesulfonyl, p-bromobenzenesulfonyl, p-nitrobenzenesulfonyl, methanesulfonyl, 2,2,2-trifluoroethanesulfonyl.

In one embodiment the process comprises compounds wherein

R\textsuperscript{1} is selected from the group comprising substituted and non-substituted C\textsubscript{i}-C\textsubscript{12} alkyl, especially methyl, ethyl, α-propyl, isopropyl, n-butyl, t-butyl, substituted and non-substituted phenyl, substituted and non-substituted naphthyl,

R\textsuperscript{2} is selected from the group comprising H, methyl, ethyl, α-propyl, isopropyl, n-butyl, t-butyl, substituted and non-substituted phenyl,

R\textsuperscript{3} is selected from the group comprising H, substituted and non-substituted C\textsubscript{4} alkyl, especially methyl, ethyl, α-propyl, isopropyl, n-butyl, t-butyl, substituted and non-substituted perhalogenated C\textsubscript{1}-C\textsubscript{9} alkyl, especially CF\textsubscript{3}, C\textsubscript{2}F\textsubscript{5}, C\textsubscript{3}F\textsubscript{7}, C\textsubscript{4}F\textsubscript{9}, C\textsubscript{5}Fn, C\textsubscript{6}F\textsubscript{13}, C\textsubscript{7}Fi\textsubscript{5}, C\textsubscript{8}F\textsubscript{17}, and C\textsubscript{9}F\textsubscript{19}, wherein the halogenide is selected from the group consisting of F, Cl, Br and I, especially F, substituted and non-substituted phenyl, substituted and non-substituted naphthyl, substituted and non-substituted pyridinyl, and
R4 is selected from the group comprising substituted and non-substituted C1-C4 alkyl, especially methyl, ethyl, α-propyl, isopropyl, n-butyl, t-butyl, perhalogenated C1-C9 alkylsulfonyl, wherein the halogenide is selected from the group consisting of F, Cl, Br and I, especially F, e.g., trifluoromethanesulfonyl, nonafluorobutanesulfonyl, p-toluenesulfonyl, p-bromobenzenesulfonyl, p-nitrobenzenesulfonyl, methanesulfonyl, 2,2,2-trifluoroethanesulfonyl.

One embodiment comprises compounds, characterized in that

R1 is selected from the group comprising methyl, ethyl, α-propyl, isopropyl, n-butyl, t-butyl,

R2 is selected from the group comprising H, methyl, ethyl, α-propyl, isopropyl, n-butyl, t-butyl, phenyl

R3 is selected from the group comprising H, methyl, ethyl, α-propyl, isopropyl, n-butyl, t-butyl, CF3, C2F5, C3F7, C4F9, C5Fn, C6Fi3, C7Fi5, C8Fi7, and C9Fi9, phenyl, halogenated phenyl, wherein the halogenide is selected from the group consisting of F, Cl, Br and I, especially F, substituted and non-substituted pyridinyl, and

R4 is selected from the group comprising methyl, ethyl, α-propyl, isopropyl, n-butyl, t-butyl, trifluoromethanesulfonyl, nonafluorobutanesulfonyl, p-toluenesulfonyl, p-bromobenzenesulfonyl, p-nitrobenzenesulfonyl, methanesulfonyl, 2,2,2-trifluoroethanesulfonyl.

One embodiment comprises compounds, characterized in that

R1 is methyl.

In one embodiment the process comprises compounds, wherein R2 is H.

In one embodiment the process comprises compounds, wherein R3 is phenyl, C5F5 or pyridinyl.
In one embodiment the process comprises compounds, wherein $R^4$ is trifluoromethanesulfonyl or nonafluorobutanesulfonyl.

In one embodiment the process comprises compounds, wherein the conversion carried out in step a) is carried out with the aid of silica gel.

In one embodiment the process comprises compounds, wherein the halogenide or anhydride reacted in step b) is produced by activating a carboxylic acid.

In one embodiment the process comprises compounds, wherein the activation of the carboxylic acid is an in situ activation selected from the carbodiimide method, the Mitsunobu reaction and the Yamaguchi esterification.

The carbodiimide method, the Mitsunobu reaction and the Yamaguchi esterification are organic synthesis steps that are well known to those skilled in the art and are described more precisely, e.g., in the following references (Handbook of Reagents for Organic Synthesis, Activating Agents and Protecting Groups (eds. A. J. Pearson, W. J. Roush), John Wiley & Sons, Chichester 1999; pages 133-136, 402-404, 454-464; D. L. Hughes, Organic Reactions, 1992, 42, 335).

In one embodiment the process comprises compounds, wherein the carboxylic acid used for the conversion to a halogenide or anhydride in step b) is reacted with a halogenation agent, the halogenation agent being a chlorination agent or a bromination agent, especially $\text{SOCl}_2$, $\text{SOBr}_2$, $\text{POCl}_3$, $\text{POBr}_3$.

In one embodiment the process comprises compounds, wherein the chlorination agent is $\text{SOCl}_2$.

In one embodiment the process comprises compounds, wherein the condensation agent used for the ring formation is an alkylsilyltriflate, especially trialkylsilyltriflate ($\text{alkyl}_3\text{SiOTf}$), preferably trimethylsilyltriflate ($\text{Me}_3\text{SiOTf}$) in the presence of a base, especially of a tertiary amine, especially triethylamine ($\text{Et}_3\text{N}$) or diisopropylethylamine ($\text{t-Pr}_2\text{NEt}$).
In one embodiment the process comprises compounds, wherein the acid used for the production of the halogenide converted in step d) is selected from the group comprising p-toluenesulfonic acid, p-bromobenzenesulfonic acid, p-nitrobenzenesulfonic acid, methanesulfonic acid, trifluoromethanesulfonic acid, nonafluorobutanesulfonic acid or 2,2,2-trifluoroethanesulfonic acid, and wherein the halogenation agent is a chlorination agent or a bromination agent, especially SOCl₂, SOBr₂, POCl₃, POBr₃.

In one embodiment the process comprises compounds, wherein the halogenide used in step d) is nonafluorobutanesulfonylfluoride (NfF).

In one embodiment a coupling reaction is carried out in the presence of a palladium catalyst following step d), wherein OR₄ is a sulfonic acid ester, preferably a sulfonic acid ester as defined above.

One embodiment of the process is characterized in that the coupling reaction is carried out as a Suzuki coupling, Sonogashira coupling, Negishi coupling, Stille coupling and/or Heck coupling.

The Suzuki coupling, Sonogashira coupling, Negishi coupling, Stille coupling and Heck coupling are organic synthesis steps that are well known to those skilled in the art that are described more precisely in the following references (Metal-Catalyzed Cross-Coupling Reactions (eds. A. de Meijere, F. Diederich), Wiley-VCH, Weinheim 2004).

The tasks of the present invention are also solved by compounds of formula (I),
wherein

$R^1$ is selected from the group comprising substituted and non-substituted alkyl, substituted and non-substituted aryl, substituted and non-substituted heteroaryl, substituted and non-substituted alkenyl, substituted and non-substituted alkinyl,

$R^2$ is selected from the group comprising substituted and non-substituted alkyl, substituted and non-substituted aryl, especially substituted and non-substituted $C_1- C_2$ alkyl, especially methyl, ethyl, $\alpha$-propyl, isopropyl, n-butyl, t-butyl,

$R^3$ is selected from the group comprising H, substituted and non-substituted alkyl, substituted and non-substituted cycloalkyl, substituted and non-substituted aryl, substituted and non-substituted heteroaryl, especially substituted and non-substituted $C_1-C_{12}$ alkyl, especially methyl, ethyl, $\alpha$-propyl, isopropyl, n-butyl, t-butyl, substituted and non-substituted perhalogenated alkyl, wherein the halogenide is selected from the group consisting of F, Cl, Br and I, especially F,

$R^4$ is selected from the group comprising substituted and non-substituted alkyl, especially substituted and non-substituted $C_1-C_{12}$ alkyl, perhalogenated alkylsulfonyl, especially perhalogenated $C_1-C_{12}$ alkylsulfonyl, wherein the halogenide is selected from the group consisting of F, Cl, Br and I, especially F, e.g., trifluoromethanesulfonyl,
nonafluorobutanesulfonyl, p-toluenesulfonyl, p-bromobenzenesulfonyl, p-nitrobenzenesulfonyl, methanesulfonyl, 2,2,2-trifluoroethanesulfonyl.

In one embodiment

R\(^1\) is selected from the group comprising substituted and non-substituted Ci-C\(_2\) alkyl, especially methyl, ethyl, \(\alpha\)-propyl, isopropyl, n-butyl, t-butyl, substituted and non-substituted phenyl, substituted and non-substituted C\(_5\)-C\(_6\) heteroaryl, substituted and non-substituted naphthyl, substituted and non-substituted C\(_7\)-Ci\(_8\) alkylphenyl, substituted and non-substituted C\(_3\)-C\(_7\) cycloalkyl, substituted and non-substituted C\(_5\)-C\(_7\) cycloalkenyl, halogenated alkyl or aryl,

R\(^2\) is selected from the group comprising H, substituted and non-substituted Ci-C\(_2\) alkyl, especially methyl, ethyl, \(\alpha\)-propyl, isopropyl, n-butyl, t-butyl, substituted and non-substituted phenyl, substituted and non-substituted C\(_7\)-Ci\(_8\) alkylphenyl,

R\(^3\) is selected from the group comprising H, substituted and non-substituted Ci-C\(_{12}\) alkyl, especially methyl, ethyl, \(\alpha\)-propyl, isopropyl, n-butyl, t-butyl, substituted and non-substituted perhalogenated Ci-C\(_2\) alkyl, wherein the halogenide is selected from the group consisting of F, Cl, Br and I, especially F, substituted and non-substituted phenyl, substituted and non-substituted C\(_7\)-Ci\(_8\) alkylphenyl, substituted and non-substituted heteroaryl, substituted and non-substituted naphthyl, substituted and non-substituted C\(_7\)-Ci\(_8\) alkylphenyl, substituted and non-substituted C\(_3\)-C\(_7\) cycloalkyl, and

R\(^4\) is selected from the group comprising substituted and non-substituted Ci-C\(_2\) alkyl, especially methyl, ethyl, \(\alpha\)-propyl, isopropyl, n-butyl, t-butyl, perhalogenated alkylsulfonyl, especially perhalogenated Ci-C\(_2\) alkylsulfonyl, wherein the halogenide is selected from the group consisting of F, Cl, Br and I, especially F, e.g., trifluoromethanesulfonyl, nonafluorobutanesulfonyl, p-toluenesulfonyl, p-bromobenzenesulfonyl, p-nitrobenzenesulfonyl, methanesulfonyl, 2,2,2-trifluoroethanesulfonyl.

One embodiment is characterized in that
R\(^1\) is selected from the group comprising substituted and non-substituted Ci-C\(_2\) alkyl, especially methyl, ethyl, \(\alpha\)-propyl, isopropyl, n-butyl, t-butyl, substituted and non-substituted phenyl, substituted and non-substituted naphthyl,

R\(^2\) is selected from the group comprising H, methyl, ethyl, \(\alpha\)-propyl, isopropyl, n-butyl, t-butyl, substituted and non-substituted phenyl,

R\(^3\) is selected from the group comprising H, substituted and non-substituted C\(_1\)-C\(_4\) alkyl, especially methyl, ethyl, \(\alpha\)-propyl, isopropyl, n-butyl, t-butyl, substituted and non-substituted perhalogenated Ci-C\(_9\) alkyl, especially CF\(_3\), C\(_2\)F\(_5\), C\(_3\)F\(_7\), C\(_4\)F\(_9\), C\(_5\)F\(_n\), C\(_6\)F\(_3\), C\(_7\)F\(_{15}\), C\(_8\)F\(_{17}\), and C\(_9\)F\(_{59}\), wherein the halogenide is selected from the group consisting of F, Cl, Br and I, especially F, substituted and non-substituted phenyl, substituted and non-substituted naphthyl, substituted and non-substituted pyridinyl, and

R\(^4\) is selected from the group comprising substituted and non-substituted C\(_1\)-C\(_4\) alkyl, especially methyl, ethyl, \(\alpha\)-propyl, isopropyl, n-butyl, t-butyl, substituted and non-substituted perhalogenated Ci-C\(_9\) alkylsulfonyl, wherein the halogenide is selected from the group consisting of F, Cl, Br and I, especially F, e.g., trifluoromethanesulfonyl, nonafluorobutanesulfonyl, p-toluenesulfonyl, p-bromobenzenesulfonyl, p-nitrobenzenesulfonyl, methanesulfonyl, 2,2,2-trifluoroethanesulfonyl.

One embodiment is characterized in that

R\(^1\) is selected from the group comprising methyl, ethyl, \(\alpha\)-propyl, isopropyl, n-butyl, t-butyl, phenyl

R\(^2\) is selected from the group comprising H, methyl, ethyl, \(\alpha\)-propyl, isopropyl, n-butyl, t-butyl, phenyl

R\(^3\) is selected from the group comprising H, methyl, ethyl, \(\alpha\)-propyl, isopropyl, n-butyl, t-butyl, CF\(_3\), C\(_2\)F\(_5\), C\(_3\)F\(_7\), C\(_4\)F\(_9\), C\(_5\)F\(_n\), C\(_6\)F\(_3\), C\(_7\)F\(_{15}\), C\(_8\)F\(_{17}\), and C\(_9\)F\(_{59}\), phenyl, halogenated phenyl, wherein the halogenide is selected from the group consisting of F, Cl, Br and I, especially F, substituted and non-substituted pyridinyl, and

R\(^4\) is selected from the group comprising methyl, ethyl, \(\alpha\)-propyl, isopropyl, n-butyl, t-butyl, trifluoromethanesulfonyl, nonafluorobutanesulfonyl, p-toluenesulfonyl, p-
bromobenzenesulfonyl, p-nitrobenzene-sulfonyl, methanesulfonyl, 2,2,2-trifluoroethanesulfonyl.

One embodiment is characterized in that $R^1$ is methyl.

One embodiment is characterized in that $R^2$ is H.

One embodiment is characterized in that $R^3$ is phenyl, $C_5F_5$ or pyridinyl.

One embodiment is characterized in that $R^4$ is trifluoromethanesulfonyl or nonafluorobutanesulfonyl.

The tasks of the invention are also solved by using a compound of the present invention as initial material for the production of medicinal drugs and/or plant protective agents and/or for molecular electronics and/or for optical applications.

The inventors surprisingly found that starting from three readily accessible components, namely, a 1,3-diketone, ammonia and a carboxylic acid anhydride or carboxylic acid halogenide, highly substituted pyridine derivatives can be prepared. Based on a skillful selection of the components, aliphatic and aromatic groups can be attached in high yields as substituents on the pyridine ring. The pyridinyl derivatives produced at first can be made accessible for further reactions (alkylation, alkenylation, alkinylation, arylation, etc.) by the conversion of the 4-OH group into a better leaving group such as, e.g., triflate, nonaflate, tresylate, etc. The synthesis in accordance with the invention can be readily carried out and yields the desired pyridine derivatives in high yields.

The concept "alkyl" as it is used here designates hydrocarbon radicals, preferably hydrocarbon radicals with 1-24 C atoms (C$_1$-C$_{24}$), more preferably hydrocarbon radicals with C$_1$-C$_{12}$ atoms (C$_1$-C$_2$alkyl).

The concept "substituted", used with "alkyl", "alkenyl", "aryl", etc., designates the substitution of one or more atoms, as a rule H atoms, by one or more of the following substituents: halogen, hydroxy, protected hydroxy, oxo, protected oxo, C$_3$-C$_7$ cycloalkyl, phenyl, naphthyl, amino, protected amino, mono-substituted amino, protected mono-
substituted amino, di-substituted amino, guanidino, protected guanidino, a heterocyclic ring, 
a substituted heterocyclic ring, imidazolyl, indolyl, pyrrolidinyl, CpCi₂alkoxy, Ci-Ci₂acyl, C₁-C₁₂ acyloxy, nitro, carboxy, protected carboxy, carbamoyl, carboxamid, protected carboxamid, N-(Ci-Ci₂alkyl)carboxamid, protected N-(Ci-Ci₂alkyl)carboxamid, N,N-Di(C₁-Ci₂alkyl)carboxamid, cyano, methylsulfonylamino, thiol, Ci-Ci₀alkylthio and Ci-Ci₀alkylsulfonyl. The substituted alkyl groups, aryl groups, alkenyl groups can be substituted once or multiply and preferably 1 time or 2 times with the same or different substituents.

Examples for the above-named substituted alkyl groups include 2-oxo-prop-1-yl, 3-oxo-but-1-yl, cyanomethyl, nitromethyl, chloromethyl, hydroxymethyl, tetrahydropyranloxyethyl, trityloxyethyl, propionyloxymethyl, aminomethyl, carboxymethyl, allyloxycarbonylmethyl, allyloxycarbonylaminomethyl, methoxymethyl, ethoxymethyl, t-butoxymethyl, acetoxyethyl, chloromethyl, bromomethyl, iodomethyl, trifluoromethyl, 6-hydroxyhexyl, 2,4-dichloro(n-butyl), 2-aminopropyl, 1-chloroethyl, 2-chloroethyl, 1-bromoethyl, 2-bromoethyl, 1-fluoroethyl, 2-fluoroethyl, 1-idoethyl, 2-idoethyl, 1-chloropropyl, 2-chloropropyl, 3-chloropropyl, 1-bromopropyl, 2-bromopropyl, 3-bromopropyl, 1-fluoropropyl, 2-fluoropropyl, 3-fluoropropyl, 1-iodopropyl, 2-iodopropyl, 3-iodopropyl, 2-aminoethyl, 1-aminoethyl, N-benzoyle-2-aminoethyl, N-acetyl-2-aminoethyl, N-benzyloyle-1-aminoethyl, N-acetyl-1-aminoethyl and the like.

The concept "cycloalkyl" comprises the groups cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl und cycloheptyl.

The concept "Ci-Ci₂alkyl" designates radicals such as methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, s-butyl, t-butyl, amyl, t-amyl, hexyl, heptyl, octyl, nonyl, decyl, undecyl, dodecyl, and the like. Preferred "Ci-Ci₂alkyl" groups are methyl, ethyl, isobutyl, s-butyl and isopropyl.

Examples for the above-named substituted alkenyl groups include styryl, 3-chloro-propen-1-yl, 3-chloro-butene-1-yl, 3-methoxy-propen-2-yl, 3-phenyl-butene-2-yl, 1-cyano-butene-3-yl and the like. The stereometry is not essential and all stereoisomers can be used for a particular substituted alkenyl.
The concept "alkinyl", as it is used here, designates a group with the formula R-C≡C-, in particular a group with the formula R*-C≡C-, as defined above, in particular "C₂-C₂ alkynyl". Examples for "C₂-C₂ alkynyls" include: ethinyl, propinyl, 2-butinyl, 2-pentinyl, 3-pentinyl, 2-hexinyl, 3-hexinyl, 4-hexinyl, 2-heptinyl, 3-heptinyl, 4-heptinyl, 5-heptinyl, as well as octinyl, noninyl, decinyl, undecinyl, dodecinyl, as well as diines and triines of straight and branched alkyl chains. Those alkinyl groups are preferred in which the triple bond is terminal so that if the alkinyl group occurs in the compounds in accordance with the invention, the triple bond comes to be located in the resulting pyridine product directly on the pyridine ring, that is, one of the two carbon atoms participating in the triple bond is directly connected to the pyridine ring via a single bond.

The concept "aryl", as used herein, designates aromatic hydrocarbon groups, e.g., phenyl, benzyl, naphthyl, anthryl.

"Substituted aryl groups" are aryl groups, as defined above, that are substituted with one or several substituents.

The concept "heterocyclic compound" or "heterocyclic ring" designates facultatively substituted five-member to eight-member rings that have 1 to 4 heteroatoms such as, e.g., oxygen, sulfur and/or nitrogen, especially nitrogen, either alone or in association with sulfur or oxygen ring atoms. These five-member to eight-member rings can be saturated or completely unsaturated or partially unsaturated but completely saturated rings are preferred. Preferred heterocyclic rings include morpholino, piperidinyl, piperazinyl, 2-amino-imidazoyl, tetrahydrofurano, pyrrolo, tetrahydrothiophen-yl, hexylmethylene imino and heptylmethylene imino.

Highly substituted pyridines, especially substituted 4-hydroxypyridines, can be synthesized in good yields with the process in accordance with the invention that can serve as starting point for further reactions and the synthesis of pyridines that have not yet been described.

The inventors were surprisingly able to show that, starting from readily available initial substances, namely, 1,3-diketones, ammonia and an organic carboxylic acid anhydride or carboxylic acid halogenide, highly substituted pyridine derivatives can be prepared. According to the present state of knowledge, this has not yet been described in the state of the
Various aspects are very interesting and surprising in the synthesis path in accordance with the invention:

Highly substituted pyridines can be produced from readily available starting substances that subsequently make possible the access to further interesting, highly substituted pyridine derivatives. These pyridine derivatives can then serve as initial substances for medicinal drugs, plant protection agents. They can also be used in molecular electronics and/or for optical applications.

The process of the present invention is characterized in particular in that it was able to reduce the previously current synthesis process with at least 6 synthesis steps for the production of highly substituted pyridine compounds to a distinctly simplified three-stage synthesis process. The resulting savings of cost and time make the process of the present invention highly attractive.

Reference is now made to the figures, in which

**Figure 1** shows the synthesis of the pyridine derivative (4),

**Figure 2** shows the synthesis of the pyridine derivative 4-methoxy-6-methyl-[2,2′]bipyridinyl,

**Figure 3** the conversion of 4-amino-pent-3-en-2-one with pentafluorobenzoic acid to 2,3,4,5,6-pentafluoro-N-(1-methyl-3-oxo-but-1-enyl)benzamide with subsequent cyclization to 2-methyl-6-(pentafluorophenyl)pyridine-4-nonaflate,

The invention will be described using the following examples that are presented for purposes of illustration and not to limit the invention.

**EXAMPLES**

**Example 1**

Synthesis of pyridine derivatives 4

a) **Conversion of ammonia with acetylacetone to a 4-amino-pent-3-en-2-one (2)**
The conversion was carried out according to published processes. An aqueous solution of ammonia (25%, 52 ml, 0.76 mol) was slowly added to a suspension of acetylacetone (19.4 g, 0.19 mol) and SiO₂ (4 g, 0.040-0.063 mm, Fluka) added. The reaction mixture was agitated at room temperature for two days and extracted with CH₂Cl₂ (3 x 25 ml), dried with Na₂SO₄ and concentrated until dry, in order to obtain 2 (18.8 g, 98%) as a colorless solid (mp = 32-33 °C, lit.[¹] 30-32 °C). The raw product was pure enough for the subsequent reactions.

b) Production of N-(1-methyl-3-oxo-but-1-enyl)benzamide (3) [²]

Thionyl chloride (0.88 ml, 12.00 mmol) was added drop by drop at 0 °C to an agitated solution of benzoic acid (1.46 g, 12.00 mmol) and Et₃N (2.53 ml, 18.00 mmol) in 20 ml CH₂Cl₂. The reaction was agitated for 30 minutes and then a solution of 4-amino-pent-3-en-2-one (2) (990 mg, 10.00 mmol) in 10 ml CH₂Cl₂ was added at 0 °C to the reaction mixture. The reaction mixture was able to warm up to room temperature overnight. The reaction mixture was compounded with a saturated solution of NaHCO₃ and extracted with CH₂Cl₂ (3 x 10 ml), dried with Na₂SO₄ and concentrated until dry. The residue was purified chromatographically over silica gel (hexane/ethylacetate = 8:1), in order to obtain 1.68 g (83%) of a colorless solid 3 (mp = 82-83 °C, lit.[²] 80-81 °C).

c) cyclization with the aid of TMSOTf/-Pr₂NEt [³]

The enamide 3 (406 mg, 2.00 mmol) was dissolved in 1,2-dichloroethane (10 ml). Then, /-Pr₂NEt (1.38 ml, 8.00 mmol) and trimethylsilyltriflate (1.81 ml, 10.00 mmol) were added at 0 °C. The reaction vessel was allowed to warm up to room temperature, heated 3 days under reflux and compounded with a saturated solution of NH₄Cl (10 ml). After extraction with dichloromethane (3 x 10 ml) the combined organic phases were dried with Na₂SO₄ and concentrated in order to obtain the raw pyridinol.

The raw product was dissolved in THF (20 ml) and NaH (237 mg, 60% in mineral oil, 6.00 mmol) was added under an atmosphere of argon. Nonafluorobutane sulfonylfluoride (0.88 ml, 5.00 mmol) was added drop by drop at room temperature. The mixture was agitated 7 hours at room temperature during which the reaction course was followed by TLC, and was slowly compounded with methanol and water (5 ml). It was extracted with ethylacetate (3 x 10 ml), dried with Na₂SO₄ and concentrated until dry. The residue was
chromatographically purified over silica gel (hexane/ethylacetate = 10:1) in order to obtain 663 mg (71%) of a colorless liquid 4.

$^3$H NMR (500 MHz, CDCl$_3$): $\delta$ = 7.98-7.95 (m, 2H, Ph), 7.52-7.45 (m, 3H, Ph), 7.43, 7.04 (2d, 1H each, $J = 2.1$ Hz, 5-H), 2.69 ppm (s, 3H, Me);

$^{13}$C NMR (125.8 MHz, CDCl$_3$): $\delta$ = 161.8, 160.2, 157.6 (3s, C-2, C-4, C-6), 137.8 (s, J-Ph), 130.1, 129.0, 127.2 (3d, Ph), 113.2, 109.9 (2d, C-3, C-5), 25.0 ppm (q, CH$_3$);

IR (film): $\nu$ = 3060 (-C-H), 2955-2855 (C=C), 1430, 1350, 1250 cm$^{-1}$ (SO);

MS (80 eV, EI): $m/z$ (%) = 467 (100) [M]$^+$, 184 (13) [M - C$_4$F$_9$SO$_2$]$^+$, 77 (24) [C$_6$H$_3$]$^+$, 69 (9) [CF$_3$]$^+$;

HRMS (80 eV): C$_{16}$H$_{10}$F$_9$NO$_3$S calculated 467.02377; found: 467.02437.

**Example 2**

**Synthesis of pyridine derivatives 8**

a) **Condensation of enaminone 2 with picolinic acid 5**

Thionyl chloride (2.92 ml, 39.96 mmol) was added drop by drop at 0°C to an agitated solution of picolinic acid 5 (4.92 g, 39.96 mmol) and Et$_3$N (8.42 ml, 59.94 mmol) in 60 ml CH$_2$Cl$_2$. The reaction was agitated 30 min and warmed up to room temperature and then a solution of 4-amino-pent-3-en-2-one (2) (3.29 g, 33.30 mmol) in 35 ml CH$_2$Cl$_2$ was added to the reaction mixture at 0°C. The reaction mixture was able to warm up overnight to room temperature. The reaction mixture was compounded with a saturated solution of NaHCO$_3$ (40 ml) and extracted with CH$_2$Cl$_2$ (3 x 20 ml), dried with Na$_2$SO$_4$ and concentrated until dry. The residue was chromatographically purified over silica gel (w-hexane/ethylacetate = 5:1 to 1:1) in order to obtain 5.60 g (82%) of 6 and 106 mg of 7 (1.3%).

**Compound 6**

Yield: 82%; colorless solid, mp 108-109 °C;

$^3$H NMR (500 MHz, CDCl$_3$): $\delta$ = 13.85 (sbr, IH, NH), 8.64 (ddd, IH, $J = 4.8$, 1.8, 0.9 Hz, 6-H), 8.06 (dt, IH, $J = 7.8$, 1.2 Hz, 3-H), 7.75 (td, IH, $J = 7.8$, 1.8 Hz, 4-H), 7.37 (ddd, 1H$_5$J = 7.6, 4.8, 1.1 Hz, 5-H), 5.37 (d, IH, $J = 1.0$ Hz, 2''-H), 2.41 (d, 3H, $J = 1.0$ Hz, CH$_3$), 2.08 ppm (s, 3H, CH$_3$);
$^{13}$C NMR (125.8 MHz, CDCl$_3$): $\delta$ = 199.2 (s, C-3"), 164.3 (s, C-I'), 153.4, 149.7 (2s, C-2, C-1"), 148.8, 137.4, 126.8, 123.0 (4d, C-6, C-4, C-5, C-3), 107.3 (d, C-2"), 30.5, 21.9 ppm (2q, CH$_3$);

IR (KBr): $\nu$ = 3360 (N-H), 3100-3060 (C=C), 2990-2840 (C=O), 1690 (C=O), 1650, 1590, 1580, 1460 cm$^{-1}$ (C=C);

MS (80 eV, Ei): m/z (%) = 204 (6) [M]+, 189 (3) [M - CH$_3$]+, 161 (100) [M - C$_2$H$_3$O]$^+$, 78 (50) [C$_2$H$_6$N]$^+$, 43 (19) [C$_2$H$_4$O]$^+$;

HRMS (80 eV): C$_n$H$_{12}$N$_2$O$_2$ calculated 204.08987; found: 204.0894.

b) **Production of 4-methoxy-6-methyl-[2,2']bipyridinyl** (8)[4]

The enamide 6 (1.59 g, 7.80 mmol) was dissolved in 1,2-dichloroethane (40 ml) and cooled to 0°C. Then, $\alpha$-Pr$_2$NEt (5.37 ml, 31.20 mmol) and trimethylsilyl triflate (7.32 ml, 39.00 mmol) were added. The reaction vessel was allowed to warm up to room temperature, was heated 3 days under reflux and compounded with a saturated solution of NH$_4$Cl (20 ml). After extraction with CH$_2$Cl$_2$ (3 x 15 ml) the combined organic phases were dried with Na$_2$SO$_4$ and concentrated in order to obtain the raw pyridinol.

The raw product was dissolved in acetone (30 ml) and K$_2$CO$_3$ (2.11 g, 15.60 mmol) and Mel (1.22 ml, 16.00 19.50 mmol) were added under an atmosphere of argon. The mixture was maintained under reflux for 7 hours (TLC control) and diluted with water (15 ml). It was extracted with ethylacetate (3 x 15 ml), dried with Na$_2$SO$_4$ and concentrated until dry. The residue was chromatographically purified over silica gel (hexane/ethylacetate = 20:1) in order to obtain a colorless solid 8 (mp 53-54 °C; Lit.$^{[4]}$ 57 °C).

$^1$H NMR (500 MHz, CDCl$_3$): $\delta$ = 8.65 (ddd, IH, $J$= 4.8, 1.8, 1.0 Hz, 6'-H), 8.38 (dt, 1H, $J$= 8.0, 1.1 Hz, 5-H), 7.78 (cq, IH, $J$= 8.0, 1.7 Hz, 4'-H), 7.75 (d, IH, $J$= 2.3 Hz, 3-H), 7.27 (ddd, IH, $J$= 8.0, 4.8, 1.1 Hz, 5'-H), 6.69 (d, IH, $J$= 2.3 Hz, 5-H), 3.91 (s, 3H, OCH$_3$), 2.56 ppm (s, 3H, CH$_3$);

$^{13}$C NMR (125.8 MHz, CDCl$_3$): $\delta$ = 167.1, 159.4, 157.5, 156.4 (4s, C-2, C-6, C-T, C-I), 149.1, 136.9, 123.7, 121.5 (4d, C-3, C-4, C-5, C-6, 4-methoxy), 110.0, 103.6 (2d, C-3, C-5), 55.3 (q, OCH$_3$), 24.8 ppm (s, CH$_3$);

IR (KBr): $\nu$ = 3350 (N-H), 3080-2965 (C=H), 2940-2850 (C=H), 1640, 1580, 1560, 1460 cm$^{-1}$ (C=C);

MS (80 eV, EI): m/z (%) = 201 (14) [M + H]$^+$, 200 (100) [M]$^+$, 185 (3) [M - CH$_3$]$^+$, 170 (56) [M - CH$_2$O]$^+$;
HRMS (80 eV): $C_{12}H_{12}N_2O$ calculated 200.09497; found: 200.09388.

Example 3

Synthesis of pentafluorophenyl-substituted pyridine derivatives 11 and 12

a) Production of $2,3,4,5,6$-pentafluoro-$N$-(1-methyl-3-oxo-but-1-enyl)benzamide

Thionyl chloride (0.66 ml, 39.96 mmol) was added drop by drop at 0°C to an agitated solution of pentafluorobenzoic acid (9) (1.93 g, 9.10 mmol) and Et$_3$N (1.91 ml, 13.65 mmol) in 20 ml CH$_2$Cl$_2$. The reaction was agitated for 30 min and then a solution of 4-amino-pent-3-en-2-one (2) (7.50 g, 7.55 mmol) in 40 ml CH$_2$Cl$_2$ was added to the reaction mixture at 0°C. The reaction mixture was able to warm up overnight to room temperature. The reaction mixture was compounded with a saturated solution of NaHCO$_3$ and extracted with CH$_2$Cl$_2$ (3 x 20 ml), dried with Na$_2$SO$_4$ and concentrated until dry. The residue was chromatographically purified over silica gel (hexane/ethylacetate = 8:1) in order to obtain 1.70 g (77%) of a colorless solid 10 (mp = 58-59 °C).

HRMS (80 eV): $C_{12}H_{12}F_5NO_2$ calculated 293.04752; found: 293.04655.

b) Production of 2-methyl-6-pentafluorophenyl-pyridin-4-ol

The enamide 10 (293 mg, 1.00 mmol) was dissolved in 1,2-dichloroethane (5 ml) in a closed tube and cooled to 0°C. Then, i-Pr$_2$NEt (0.69 ml, 4.00 mmol) und trimethylsilyltriflate (0.90 ml, 5.00 mmol) were added. The mixture was warmed to room temperature, heated 3 days under reflux and compounded with a saturated solution of NH$_4$Cl (10 ml). After extraction with CH$_2$Cl$_2$ (3 x 10 ml) the combined organic phases were dried with Na$_2$SO$_4$ and concentrated in order to obtain the crude pyridinol. The residue was purified chromatographically over silica gel (hexane/ethylacetate = 1:1 to ethylacetate) in order to obtain 187 mg (68%) of pyridine as a colorless solid, mp = 231-232 °C.

$^1$H NMR (500 MHz, CD$_3$OD): $\delta$ = 6.55 (d, IH, $J$ = 2.0 Hz, 5-H), 6.45 (d, IH, $J$ = 2.0 Hz, 3-H), 2.40 ppm (s, 3H, CH$_3$);

$^{13}$C NMR (125.8 MHz, CD$_3$OD): The signals were observed $\delta$ = 145.5, 143.5, 138.8, 136.9, 124.1 (C-4), 121.6, 119.1 (2d, C-3, C-5), 18.0 ppm (q, CH$_3$);
IR (KBr): \( v = 3435 \text{ (OH)}, 3260-3050 \text{ (=C-H)}, 2920-2590 \text{ (C-H)}, 1660, 1640, 1620, 1535, 1450 \text{ cm}^{-1} \text{ (C=C)}; \\
MS (80 \text{ eV, EI}): \text{m/z (%)} = 276 (22) [M + H]^+, 275 (100) [M]^+; \\
HRMS (80 \text{ eV}): \text{C}_{12} \text{H}_6 \text{F}_5 \text{NO} \text{ calculated } 275.03696; \text{ found: } 275.03588.

c) Production of 2-methyl-6-(pentafluorophenyl)pyridine-4-nonaflate (12)

The pyridinol 11 (100 mg, 0.36 mmol) was dissolved in THF (5 ml) and NaH (42 mg, 60% in mineral oil, 1.08 mmol) was added under an atmosphere of argon. Nonafluorobutanesulfonylfluoride (0.13 ml, 0.72 mmol) was added drop by drop at room temperature. The mixture was agitated 6 hours at room temperature (TLC control) and slowly compounded with methanol and water (5 ml). It was extracted with ethylacetate (3 x 10 ml), dried with \( \text{Na}_2\text{SO}_4 \) and concentrated until dry. The residue was purified chromatographically over silica gel (hexane/ethylacetate = 10:1) in order to obtain 146 mg (73%) of a colorless liquid 4.

\(^1\text{H NMR} (500 \text{ MHz, CDCl}_3): \delta = 7.24 \text{ (s, br, IH, 5-H)}, 7.19 \text{ (d, IH, } J = 2.1 \text{ Hz, 3-H)}, 2.69 \text{ ppm (s, 3H, CH}_3\text{);} \\
\(^{13}\text{C NMR} (125.8 \text{ MHz, CDCl}_3): \delta = 162.8, 156.9, 148.9 \text{ (3s, C-2, C-6, C-4)}, 145.6, 143.6, 138.9, 136.9 \text{ (m, Ar}, \text{F}), 115.6, 115.5 \text{ (2d, C-3, C-5)}, 24.7 \text{ ppm (q, CH}_3\text{);} \\
IR \text{ (film): } v = 3260 \text{ (=C-H)}, 2960, 2855 \text{ (C-H)}, 1655, 1590, 1520, 1500, 1435 \text{ cm}^{-1} \text{ (C=C)}; \\
MS (80 \text{ eV, EI}): \text{m/z (%)} = 557 (17) [M + H]^+, 556 (100) [M]^+; \\
HRMS (80 \text{ eV}): \text{C}_{6} \text{H}_3 \text{F}_4 \text{NO}_3\text{S calculated } 556.67668; \text{ found } 556.97668.

The features disclosed in the previous description, the claims as well as the drawings can be significant individually as well as also in any combination for the realization of the invention.

References:
Claims

1. A process for producing a compound of the formula (I)

(I)

wherein

R¹ is selected from the group comprising substituted and non-substituted alkyl, substituted and non-substituted aryl, substituted and non-substituted heteroaryl, substituted and non-substituted alkenyl, substituted and non-substituted alkinyl,

R² is selected from the group comprising H, substituted and non-substituted alkyl, substituted and non-substituted aryl, in particular substituted and non-substituted C₆-C₁₂ alkyl, especially methyl, ethyl, α-propyl, isopropyl, n-butyl, t-butyl,

R³ is selected from the group comprising H, substituted and non-substituted alkyl, substituted and non-substituted cycloalkyl, substituted and non-substituted aryl, substituted and non-substituted heteroaryl, especially substituted and non-substituted C₁-C₂ alkyl, especially methyl, ethyl, α-propyl, isopropyl, n-butyl, t-butyl, substituted and
non-substituted perhalogenated alkyl, wherein the halogenide is selected from the group consisting of F, Cl, Br and I, especially F, and

$R^4$ is selected from the group comprising substituted and non-substituted alkyl, especially substituted and non-substituted $C_1$-$C_{12}$ alkyl, perhalogenated alkylsulfonyl, especially perhalogenated $Ci$-$C_{12}$ alkylsulfonyl, wherein the halogenide is selected from the group consisting of $F$, $Cl$, $Br$ and $I$, especially $F$, e.g., trifluoromethanesulfonyl, nonafluorobutanesulfonyl, $p$-toluenesulfonyl, $p$-bromobenzenesulfonyl, $p$-nitrobenzenesulfonyl, methanesulfonyl, 2,2,2-trifluoroethanesulfonyl,

with the steps:

a) Conversion of 1,3-diketones (1) with ammonia to a compound (2) of an $\alpha,\beta$-unsaturated $\beta$-aminoketone, wherein $R^1$ and $R^2$ are defined as above,

\[
\begin{align*}
\text{O} & \quad \text{O} & \quad \text{NH}_3 \\
\text{R}^1 & \quad \text{R}^2
\end{align*}
\]

b) Conversion of (2) by treatment with a carbonic acid anhydride or carbonic acid halogenide into an N-acylated $\alpha,\beta$-unsaturated $\beta$-aminoketone (3), wherein $R^3$ is defined as above and $X$ is an anhydride or halogenide, wherein the halogenide is selected from the group consisting of $F$, $Cl$, $Br$ and $I$, especially $Cl$. 
(c) Ring formation by intramolecular aldol condensation of the N-acylated α,β-unsaturated β-aminoketone (3) produced at b) with a condensation agent to 2,6-di-substituted or 2,3,6-tri-substituted 4-hydroxypyridines (4b),

and

(d) O-alkylation or O-sulfonylation of the 4-hydroxy group of (4b) with a compound with the formula $R^4-X$ to 4-alkoxypyridines (I) or pyridinyl-4-sulfonic acid esters (I), wherein $R^4$ is defined as above, comprising the following scheme
2. The process according to Claim 1, characterized in that

R¹ is selected from the group comprising substituted and non-substituted Ci-Ci₂ alkyl, especially methyl, ethyl, α-propyl, isopropyl, n-butyl, t-butyl, substituted and non-substituted phenyl, substituted and non-substituted C₅-C₆ heteroaryl, substituted and non-substituted naphthyl, substituted and non-substituted C₇-C₈ alkylphenyl, substituted and non-substituted C₃-C₇ cycloalkyl, substituted and non-substituted C₅-C₇ cycloalkenyl, halogenated alkyl or aryl.

R² is selected from the group comprising H, substituted and non-substituted Ci-C₁₂ alkyl, especially methyl, ethyl, α-propyl, isopropyl, n-butyl, t-butyl, substituted and non-substituted phenyl, substituted and non-substituted C₇-C₁₈ alkylphenyl,

R³ is selected from the group comprising H, substituted and non-substituted C₁-Ci₂ alkyl, especially methyl, ethyl, α-propyl, isopropyl, n-butyl, t-butyl, substituted and non-substituted perhalogenated Ci-Ci₂ alkyl, wherein the halogenide is selected from the group consisting of F, Cl, Br and I, especially F, substituted and non-substituted phenyl, substituted and non-substituted heteroaryl, substituted and non-substituted naphthyl, substituted and non-substituted C₇-C₁₈ alkylphenyl, substituted and non-substituted C₃-C₇ cycloalkyl, and
R\textsuperscript{4} is selected from the group comprising substituted and non-substituted C\textsubscript{1}-C\textsubscript{12} alkyl, especially methyl, ethyl, \(\alpha\)-propyl, isopropyl, n-butyl, t-butyl, perhalogenated alkylsulfonyl, especially perhalogenated C\textsubscript{1}-C\textsubscript{12} alkylsulfonyl, wherein the halogenide is selected from the group consisting of F, Cl, Br and I, especially F, e.g., trifluoromethanesulfonyl, nonafluorobutanesulfonyl, p-toluenesulfonyl, p-bromobenzenesulfonyl, p-nitrobenzenesulfonyl, methanesulfonyl, 2,2,2-trifluoroethanesulfonyl.

3. The process according to Claim 2, characterized in that

R\textsuperscript{1} is selected from the group comprising substituted and non-substituted C\textsubscript{i}-C\textsubscript{2} alkyl, especially methyl, ethyl, \(\alpha\)-propyl, isopropyl, n-butyl, t-butyl, substituted and non-substituted phenyl, substituted and non-substituted naphthyl, substituted and non-substituted pyridinyl, and

R\textsuperscript{2} is selected from the group comprising H, methyl, ethyl, \(\alpha\)-propyl, isopropyl, n-butyl, t-butyl, substituted and non-substituted phenyl,

R\textsuperscript{3} is selected from the group comprising H, substituted and non-substituted C\textsubscript{1}-C\textsubscript{4} alkyl, especially methyl, ethyl, \(\alpha\)-propyl, isopropyl, n-butyl, t-butyl, substituted and non-substituted perhalogenated C\textsubscript{1}-C\textsubscript{9} alkyl, especially CF\textsubscript{3}, C\textsubscript{2}F\textsubscript{5}, C\textsubscript{3}F\textsubscript{7}, C\textsubscript{4}F\textsubscript{9}, C\textsubscript{5}Fn, C\textsubscript{6}Fi\textsubscript{3}, C\textsubscript{7}F\textsubscript{15}, C\textsubscript{8}F\textsubscript{17}, and C\textsubscript{9}F\textsubscript{19} wherein the halogenide is selected from the group consisting of F, Cl, Br and I, especially F, substituted and non-substituted phenyl, substituted and non-substituted naphthyl, substituted and non-substituted pyridinyl, and

R\textsuperscript{4} is selected from the group comprising substituted in non-substituted C\textsubscript{i}-C\textsubscript{4} alkyl, especially methyl, ethyl, \(\alpha\)-propyl, isopropyl, n-butyl, t-butyl, perhalogenated C\textsubscript{1}-C\textsubscript{9} aikylsulfonyl, wherein the halogenide is selected from the group consisting of F, Cl, Br and I, especially F, e.g., trifluoromethanesulfonyl, nonafluorobutanesulfonyl, p-toluenesulfonyl, p-bromobenzenesulfonyl, p-nitrobenzenesulfonyl, methanesulfonyl, 2,2,2-trifluoroethanesulfonyl.

4. The process according to Claim 3, characterized in that
R\textsuperscript{1} is selected from the group comprising methyl, ethyl, \(\alpha\)-propyl, isopropyl, n-butyl, t-butyl.

R\textsuperscript{2} is selected from the group comprising H, methyl, ethyl, \(\alpha\)-propyl, isopropyl, n-butyl, t-butyl, phenyl.

R\textsuperscript{3} is selected from the group comprising H, methyl, ethyl, \(\alpha\)-propyl, isopropyl, n-butyl, t-butyl, CF\(_3\), C\(_2\)F\(_5\), C\(_3\)F\(_7\), C\(_4\)F\(_9\), C\(_5\)F\(_{11}\), C\(_6\)F\(_{13}\), C\(_7\)F\(_{15}\), C\(_8\)F\(_{17}\), and C\(_9\)F\(_{19}\), phenyl, halogenated phenyl, wherein the halogenide is selected from the group consisting of F, Cl, Br and I, especially F, substituted and non-substituted pyridinyl, and

R\textsuperscript{4} is selected from the group comprising methyl, ethyl, \(\alpha\)-propyl, isopropyl, n-butyl, t-butyl, trifluoromethanesulfonyl, nonafluorobutanesulfonyl, p-toluenesulfonyl, p-bromobenzenesulfonyl, p-nitrobenzenesulfonyl, methanesulfonyl, 2,2,2-trifluoroethanesulfonyl.

5. The process according to Claim 4, characterized in that

R\textsuperscript{1} is methyl.

6. The process according to Claim 4, characterized in that

R\textsuperscript{2} is H.

7. The process according to Claim 4, characterized in that

R\textsuperscript{3} is phenyl, C\(_5\)F\(_5\) or pyridinyl.

8. The process according to Claim 4, characterized in that

R\textsuperscript{4} is trifluoromethanesulfonyl or nonafluorobutanesulfonyl.

9. The process according to any one of Claims 1 to 8, wherein the conversion carried out in step a) is carried out with the aid of silica gel.
10. The process according to any one of Claims 1 to 9, wherein the halogenide or anhydride converted in step b) is produced by activating a carboxylic acid.

11. The process according to Claim 10, wherein the activation of the carboxylic acid is an in situ activation selected from the carbodiimide method, the Mitsunobu reaction and the Yamaguchi esterification.

12. The process according to any one of Claims 1 to 11, wherein the carboxylic acid used for the conversion to a halogenide or anhydride in step b) is reacted with a halogenation agent, the halogenation agent being a chlorination agent or a bromination agent, especially \(\text{SOCl}_2\), \(\text{SOBr}_2\), \(\text{POCl}_3\), \(\text{POBr}_3\).

13. The process according to Claim 12, wherein the chlorination agent is \(\text{SOCl}_2\).

14. The process according to any one of Claims 1 to 13, wherein the condensation agent used for the ring formation is an alkylsilyltriflate, especially trialkylsilyltriflate (alkyl\(_2\)SiOTf), preferably trimethylsilyltriflate (Me\(_3\)SiOTf) in the presence of a base, especially of a tertiary amine, especially triethylamine (Et\(_3\)N) or diisopropylethylamine (\(\text{-Pr}_2\text{NEt}\)).

15. The process according to any one of Claims 1 to 14, wherein the acid used for the production of the halogenide converted in step d) is selected from the group comprising p-toluenesulfonic acid, p-bromobenzenesulfonic acid, p-nitrobenzenesulfonic acid, methanesulfonic acid, trifluoromethanesulfonic acid, nonafluorobutanesulfonic acid or 2,2,2-trifluoroethanesulfonic acid, and wherein the halogenation agent is a chlorination agent or a bromination agent, especially \(\text{SOCl}_2\), \(\text{SOBr}_2\), \(\text{POCl}_3\), \(\text{POBr}_3\).

16. The process according to any one of Claims 1 to 15, wherein the halogenide used in step d) is nonafluorobutanesulfonylfluoride (NfF).

17. The process according to any one of Claims 1 to 16, characterized in that a coupling reaction is carried out in the presence of a palladium catalyst following step d),
wherein OR^4 is a sulfonic acid ester, preferably a sulfonic acid ester as defined in any one of Claims 1 to 8.

18. The process according to Claim 17, characterized in that the coupling reaction is carried out as a Suzuki coupling, Sonogashira coupling, Stille coupling, Negishi coupling and/or Heck coupling.

19. A compound with the formula (I)

(I)

wherein

R^1 is selected from the group comprising substituted and non-substituted alkyl, substituted and non-substituted aryl, substituted and non-substituted heteroaryl, substituted and non-substituted alkenyl, substituted and non-substituted alkinyl,

R^2 is selected from the group comprising substituted and non-substituted alkyl, substituted and non-substituted aryl, especially substituted and non-substituted CpCIC_2 alkyl, especially methyl, ethyl, α-propyl, isopropyl, n-butyl, t-butyl,

R^3 is selected from the group comprising H, substituted and non-substituted alkyl, substituted and non-substituted cycloalkyl, substituted and non-substituted aryl, substituted and non-substituted heteroaryl, especially substituted and non-substituted
C₁-C₂ alkyl, especially methyl, ethyl, α-propyl, isopropyl, n-butyl, t-butyl, substituted and non-substituted perhalogenated alkyl, wherein the halogenide is selected from the group consisting of F, Cl, Br and I, especially F, and

R⁴ is selected from the group comprising substituted and non-substituted alkyl, especially substituted and non-substituted C₁-C₂ alkyl, perhalogenated alkylsulfonyl, especially perhalogenated C₁-C₁₂ alkylsulfonyl, wherein the halogenide is selected from the group consisting of F, Cl, Br and I, especially F, e.g., trifluoromethanesulfonyl, nonafluorobutanesulfonyl, p-toluenesulfonyl, p-bromobenzenesulfonyl, p-nitrobenzene-sulfonyl, methanesulfonyl, 2,2,2-trifluoroethanesulfonyl.

20. The compound according to Claim 19, characterized in that

R¹ is selected from the group comprising substituted and non-substituted C₁-C₂ alkyl, especially methyl, ethyl, α-propyl, isopropyl, n-butyl, t-butyl, substituted and non-substituted phenyl, substituted and non-substituted C₅-C₆ heteroaryl, substituted and non-substituted naphthyl, substituted and non-substituted C₇-C₁₈ alkylphenyl, substituted and non-substituted C₃-C₇ cycloalkyl, substituted and non-substituted C₅-C₇ cycloalkenyl, halogenated alkyl or aryl,

R² is selected from the group comprising H, substituted and non-substituted C₁-C₁₂ alkyl, especially methyl, ethyl, α-propyl, isopropyl, n-butyl, t-butyl, substituted and non-substituted phenyl, substituted and non-substituted C₇-C₁₈ alkylphenyl,

R³ is selected from the group comprising H, substituted and non-substituted C₁-C₁₂ alkyl, especially methyl, ethyl, α-propyl, isopropyl, n-butyl, t-butyl, substituted and non-substituted perhalogenated C₁-C₁₂ alkyl, wherein the halogenide is selected from the group consisting of F, Cl, Br and I, especially F, substituted and non-substituted phenyl, substituted and non-substituted C₇-C₁₈ alkylphenyl, substituted and non-substituted heteroaryl, substituted and non-substituted naphthyl, substituted and non-substituted C₇-C₁₈ alkylphenyl, substituted and non-substituted C₇-C₇ Cycloalkyl, and
R₄ is selected from the group comprising substituted and non-substituted alkyl, especially methyl, ethyl, α-propyl, isopropyl, n-butyl, t-butyl, perhalogenated alkylsulfonyl, especially perhalogenated C₁₋C₂ alkylsulfonyl, wherein the halogenide is selected from the group consisting of F, Cl, Br and I, especially F, e.g., trifluoromethanesulfonyl, nonafluorobutanesulfonyl, p-toluenesulfonyl, p-bromobenzenesulfonyl, p-nitrobenzene-sulfonyl, methanesulfonyl, 2,2,2-trifluoroethanesulfonyl.

21. The compound according to Claim 20, characterized in that

R¹ is selected from the group comprising substituted and non-substituted C₁₋C₂ alkyl, especially methyl, ethyl, α-propyl, isopropyl, n-butyl, t-butyl, substituted and non-substituted phenyl, substituted and non-substituted naphthyl,

R² is selected from the group comprising H, methyl, ethyl, α-propyl, isopropyl, n-butyl, t-butyl, substituted and non-substituted phenyl,

R³ is selected from the group comprising H, substituted and non-substituted C₁₋C₄ alkyl, especially methyl, ethyl, α-propyl, isopropyl, n-butyl, t-butyl, substituted and non-substituted perhalogenated C₁₋C₉ alkyl, especially C₃F₃, C₄F₅, C₅F₇, C₆F₉, C₇F₁₁, C₈F₁₃, C₉F₁₅, and C₁₀F₁₇, wherein the halogenide is selected from the group consisting of F, Cl, Br and I, especially F, substituted and non-substituted phenyl, substituted and non-substituted naphthyl, substituted and non-substituted pyridinyl, and

R⁴ is selected from the group comprising substituted and non-substituted alkyl, especially methyl, ethyl, α-propyl, isopropyl, n-butyl, t-butyl, substituted and non-substituted perhalogenated C₁₋C₉ alkylsulfonyl, wherein the halogenide is selected from the group consisting of F, Cl, Br and I, especially F, e.g., trifluoromethanesulfonyl, nonafluorobutanesulfonyl, p-toluenesulfonyl, p-bromobenzenesulfonyl, p-nitrobenzene-sulfonyl, methanesulfonyl, 2,2,2-trifluoroethanesulfonyl.

22. The compound according to Claim 21, characterized in that
R\textsuperscript{1} is selected from the group comprising methyl, ethyl, \(\alpha\)-propyl, isopropyl, n-butyl, t-butyl,

R\textsuperscript{2} is selected from the group comprising H, methyl, ethyl, \(\alpha\)-propyl, isopropyl, n-butyl, t-butyl, phenyl

R\textsuperscript{3} is selected from the group comprising H, methyl, ethyl, \(\alpha\)-propyl, isopropyl, n-butyl, t-butyl, CF\textsubscript{3}, C\textsubscript{2}F\textsubscript{5}, C\textsubscript{3}F\textsubscript{7}, C\textsubscript{4}F\textsubscript{9}, C\textsubscript{5}F\textsubscript{11}, C\textsubscript{6}F\textsubscript{13}, C\textsubscript{7}F\textsubscript{15}, C\textsubscript{8}F\textsubscript{17}, and C\textsubscript{9}F\textsubscript{19}. phenyl, halogenated phenyl, wherein the halogenide is selected from the group consisting of F, Cl, Br and I, especially F, substituted and non-substituted pyridinyl, and

R\textsuperscript{4} is selected from the group comprising methyl, ethyl, \(\alpha\)-propyl, isopropyl, n-butyl, t-butyl, trifluoromethanesulfonyl, nonafluorobutanesulfonyl, p-toluenesulfonyl, p-bromobenzenesulfonyl, p-nitrobenzene-sulfonyl, methanesulfonyl, 2,2,2-trifluoroethanesulfonyl.

23. The compound according to Claim 22, characterized in that

R\textsuperscript{1} is methyl.

24. The compound according to Claim 22, characterized in that

R\textsuperscript{2} is H.

25. The compound according to Claim 22, characterized in that

R\textsuperscript{3} is phenyl, C\textsubscript{5}F\textsubscript{5} or pyridinyl.

26. The compound according to Claim 22, characterized in that

R\textsuperscript{4} is trifluoromethanesulfonyl or nonafluorobutanesulfonyl.
27. The use of a compound according to any one of Claims 19 to 26 as initial substance for producing drugs and/or plant protection agents and/or as initial substance for molecular electronics and/or optical applications.
Figure 1

\[\text{Me} \quad \text{O} \quad \text{C} \quad \text{O} \quad \text{Me} \quad \xrightarrow{\text{SiO}_2, \text{aq. NH}_3} \quad \text{rt}, 2 \text{~d, quant.} \quad \text{Me} \quad \text{NH}_2 \quad \text{O} \quad \text{C} \quad \text{Me} \quad \xrightarrow{1) \text{PhCO}_2\text{H} (1.2 \text{~eq.}), \text{SOCl}_2 (1.2 \text{~eq.})} \quad 2) \text{Et}_3\text{N} (1.8 \text{~eq.}), 0 ^\circ \text{C} \quad \text{CH}_2\text{Cl}_2, 83\% \]

\[\text{Me} \quad \text{NH} \quad \text{C} \quad \text{O} \quad \text{Me} \quad \xrightarrow{1) \text{TMSOTf} (5.0 \text{~eq.}), \text{t-Pr}_2\text{NEt} (4.0 \text{~eq.}) \text{1,2-dichloroethane, reflux, 3d}} \quad 2) \text{NaH} (3 \text{~eq.}), \text{Nf} (2.5 \text{~eq.}, \text{rt} \quad 71\% \text{for 2 steps}}
\]

\[\text{Me} \quad \text{Me} \quad \text{OR} \quad \xrightarrow{4} \quad \text{R = Nf (Nf = C}_4\text{F}_9\text{SO}_2)} \]
Figure 2

\[
\begin{align*}
\text{Me} & \overset{\text{O}}{\text{CO}} \text{Me} & \text{SiO}_2, \text{aq. NH}_3, \text{rt, 2 d, quant.} & \text{Me} & \overset{\text{NH}_2}{\text{CO}} \text{Me} \\
\text{1} & & \rightarrow & \text{2} \\
\text{Me} & \overset{\text{O}}{\text{CO}} \text{Me} & \text{SOCl}_2, \text{Et}_3\text{N}, 0^\circ \text{C} & \text{N} & \overset{\text{O}}{\text{CO}} \\
\text{5} & & \rightarrow & \text{6} \\
\end{align*}
\]

\[
\begin{align*}
\text{6} & \quad 82\% \\
\text{7} & \quad 1.3\% \\
\end{align*}
\]

\[
\begin{align*}
\text{Me} & \overset{\text{N}}{\text{NH}} & \overset{\text{O}}{\text{CO}} \text{Me} \\
\text{6} & \quad + & \text{Me} & \overset{\text{N}}{\text{NH}} & \overset{\text{Cl}}{\text{CO}} \text{Me} \\
\text{7} & \quad 1.3\% \\
\end{align*}
\]

\[
\begin{align*}
\text{N} & \overset{\text{O}}{\text{Me}} \\
\text{8} & \quad 63\% \text{ for 2 steps}
\end{align*}
\]

1) TMSOTf (5.0 eq.), i-Pr$_2$NEt (4.0 eq.)
1,2-dichloroethane, reflux, 3d
2) K$_2$CO$_3$ (2 eq.), MeI (2.5 eq.)
Acetone, reflux, 7 h
Figure 3

\[
\begin{align*}
\text{NH}_2\text{C} = \text{O} \quad \text{Me} & \quad \text{Me} \\
\text{SOCl}_2, \text{Et}_3\text{N}, 0^\circ \text{C} & \quad \text{CH}_2\text{C}_2, 77\% \\
\end{align*}
\]

\[
\begin{align*}
\text{F} & \quad \text{F} \quad \text{F} \quad \text{F} \quad \text{CO}_2\text{H} \\
\text{F} & \quad \text{F} \quad \text{F} \quad \text{F} \quad \text{9} \\
\text{F} & \quad \text{F} \quad \text{F} \quad \text{F} \quad \text{Me} \\
\text{F} & \quad \text{F} \quad \text{F} \quad \text{F} \quad \text{10} \\
\end{align*}
\]

\[
\begin{align*}
\text{TMSOTf (5.0 eq.)} & \quad i\text{-Pr}_2\text{NEt (4.0 eq.)} \\
\text{1,2-dichloroethane} & \quad \text{pressure pipe, 110}^\circ \text{C}, 3 \text{d} \\
& \quad 68\% \\
\text{Me} & \quad \text{F} \quad \text{F} \quad \text{F} \quad \text{F} \\
\text{11} & \quad \text{OH} \\
\end{align*}
\]

\[
\begin{align*}
\text{NaH (3 eq.)} & \quad \text{NIF (2.0 eq.)} \\
\text{THF, rt, 6 h} & \quad 73\% \\
\text{Me} & \quad \text{F} \quad \text{F} \quad \text{F} \\
\text{12} & \quad \text{F} \quad \text{F} \quad \text{F} \\
R = \text{NIF (NIF = C}_4\text{F}_9\text{SO}_2) \\
\end{align*}
\]
A. CLASSIFICATION OF SUBJECT MATTER
INV. C07D213/68

According to International Patent Classification (IPC) or to both national classification and IPC.

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic database consulted during the international search (name of database and, where practical, search terms used)

EPO-Internal, WPI Data, BEILSTEIN Data, CHEMABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
<thead>
<tr>
<th>Category</th>
<th>Citation of document with indication where appropriate of the relevant passages</th>
<th>Relevant to claim No</th>
</tr>
</thead>
</table>

Further documents are listed in the continuation of Box C

Date of the actual completion of the international search: 25 April 2008

Date of mailing of the international search report: 20/05/2008

Name and mailing address of the ISA/
European Patent Office, P B 5818 Patentlaan 2
NL-2280 HV Rijswijk
Tel (+31-70) 340-2040, Tx 31 651 epo nl
Fax (+31-70) 340-3016

Authorized officer
Fazzi, Raffaela
<table>
<thead>
<tr>
<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No</th>
</tr>
</thead>
<tbody>
<tr>
<td>X</td>
<td>WO 2005/028452 A (PFIZER LTD [GB]; BROWN ALAN DANIEL [GB]; ELLIS DAVID [GB]; SMITH CHRIS) 31 March 2005 (2005-03-31) examples 54,55</td>
<td>19-26</td>
</tr>
</tbody>
</table>

Form PCT/ISA/210 (continuation of second sheet) (April 2005)
<table>
<thead>
<tr>
<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>X</td>
<td>SNIDER ET AL.: &quot;Synthesis of (+/-)-deoxysymbioimine using an intramolecular diels-Alder reaction with an N-alkoxycarbonyl 2,3-dihydropyridinium cation as the dienophile&quot;</td>
<td>19-26</td>
</tr>
<tr>
<td>X</td>
<td>OHARA ET AL.: &quot;Inhibitory action of a novel proton pump inhibitor, rabeprazole, and its thioether derivative against the growth and motility of clarithromycin-resistant helicobacter pylori&quot;</td>
<td>19-26</td>
</tr>
<tr>
<td>X</td>
<td>TYVORSKII V I ET AL.: &quot;Synthesis of 5-alkyl-4-amino-2-(trifluoromethyl)pyridines and their transformation into trifluoromethylated 1H-pyrazolo[4,3-c]pyridines&quot;</td>
<td>19-26</td>
</tr>
<tr>
<td>X</td>
<td>KONAKAHARA ET AL.: &quot;One-pot synthesis of 2-(trifluoromethyl)pyridines from N-silyl-1-aza-allyl anions with trifluoroacetylketene diethyl ketal or (E)-1,1,1-trifluoro-4-phenyl but-3-en-2-one&quot;</td>
<td>19-26</td>
</tr>
<tr>
<td>X</td>
<td>TRECOURT ET AL.: &quot;First synthesis of caerulomycin E and collismycins A and C. A new synthesis of caerulomycin A&quot;</td>
<td>19-26</td>
</tr>
<tr>
<td>Category</td>
<td>Citation of document, with indication, where appropriate, of the relevant passages</td>
<td>Relevant to claim No.</td>
</tr>
<tr>
<td>----------</td>
<td>---------------------------------------------------------------------------------</td>
<td>----------------------</td>
</tr>
<tr>
<td></td>
<td>VON AKEN ET AL.: &quot;The synthesis of 3-functionalized 5-chloro-6-methyl-2H-1,4-oxazin-2-ones and of pyridines from cycloaddition-elimination reactions with substituted acetylenic compounds&quot; TETRAHEDRON, vol. 50, no. 17, 1994, pages 5211-5224, XP002476526</td>
<td>19-26</td>
</tr>
<tr>
<td>Patent document cited in search report</td>
<td>Publication date</td>
<td>Patent family member(s)</td>
</tr>
<tr>
<td>----------------------------------------</td>
<td>------------------</td>
<td>-------------------------</td>
</tr>
<tr>
<td></td>
<td></td>
<td>JP 1551764 C</td>
</tr>
<tr>
<td>WO 2005028452 A</td>
<td>31-03-2005</td>
<td>BR P10414663 A</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CA 2539297 A1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>JP 2007505888 T</td>
</tr>
<tr>
<td></td>
<td></td>
<td>MX PA06003158 A</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NL 1027084 C2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NL 1027084 A1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>UY 28524 A1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CA 2504941 A1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>EP 1565452 A2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>JP 4234849 A</td>
</tr>
<tr>
<td></td>
<td></td>
<td>AU 6867487 A</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CA 1262137 A1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>DE 3768992 D1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ES 2037708 T3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>JP 1722804 C</td>
</tr>
<tr>
<td></td>
<td></td>
<td>JP 4005674 B</td>
</tr>
<tr>
<td></td>
<td></td>
<td>JP 62201884 A</td>
</tr>
<tr>
<td></td>
<td></td>
<td>US 4753955 A</td>
</tr>
</tbody>
</table>