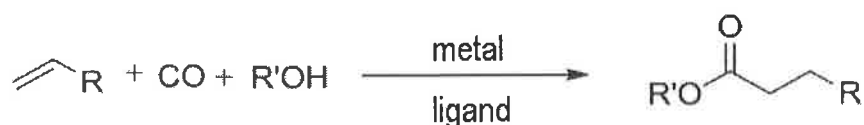


Process for the alkoxycarbonylation of alcohols

The present invention relates to a novel process for the alkoxycarbonylation of alcohols.

- 5 The alkoxycarbonylation of ethylenically unsaturated compounds is a known process for preparing esters. This method is used to react ethylenically unsaturated compounds (olefins) with carbon monoxide and alcohols in the presence of a metal-ligand complex to give the corresponding esters. Typically, the metal used is palladium. The following scheme shows the general reaction equation of an alkoxycarbonylation:

10



- A very good catalytic system for this process was developed by Lucite – now Mitsubishi Rayon – and uses a ligand based on 1,2-bis(di-tert-butylphosphinomethyl)benzene (DTBPMB) (W. Clegg, G. R. Eastham, M. R. J. Elsegood, R. P. Tooze, X. L. Wang, K. Whiston, Chem. Commun. 1999, 1877-1878).
- 15

- The possibility of using compounds other than ethylenically unsaturated compounds and reacting them with alcohols and CO to give the corresponding esters, in the form of an alkoxycarbonylation reaction, is hitherto unknown.
- 20

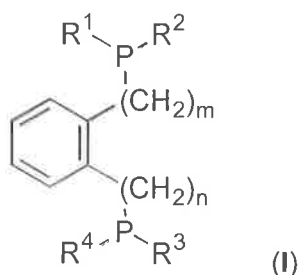
- Against this background, the problem addressed by the present invention is that of providing an alkoxycarbonylation process for the preparation of esters, which uses raw materials other than ethylenically unsaturated compounds as a starting product. Of particular interest here is the use of alcohols as a starting product for the alkoxycarbonylation.
- 25

- It has surprisingly emerged that this problem is solved by an alkoxycarbonylation process wherein particular benzene-based diphosphine ligands are used, in which at least one phosphine group is substituted by a heteroaryl radical. The process of the invention is notable for high yields, based on the alcohols used as reactants.
- 30

The invention therefore relates to a process comprising the following process steps:

- a) introducing a first alcohol, the first alcohol having 2 to 30 carbon atoms;
 b) adding a phosphine ligand and a compound which comprises Pd,
 or adding a complex comprising Pd and a phosphine ligand;
 c) adding a second alcohol;
 5 d) supplying CO;
 e) heating the reaction mixture, the first alcohol reacting with CO and the second alcohol
 to form an ester;

where the phosphine ligand is a compound of formula (I)



10 where

m and n are each independently 0 or 1;

R¹, R², R³, R⁴ are each independently selected from -(C₁-C₁₂)-alkyl, -(C₃-C₁₂)-cycloalkyl, -(C₃-C₁₂)-heterocycloalkyl, -(C₆-C₂₀)-aryl, -(C₃-C₂₀)-heteroaryl;

at least one of the R¹, R², R³, R⁴ radicals is a -(C₃-C₂₀)-heteroaryl radical;

15 and

R¹, R², R³, R⁴, if they are -(C₁-C₁₂)-alkyl, -(C₃-C₁₂)-cycloalkyl, -(C₃-C₁₂)-heterocycloalkyl, -(C₆-C₂₀)-aryl or -(C₃-C₂₀)-heteroaryl,

may each independently be substituted by one or more substituents selected from

20 -(C₁-C₁₂)-alkyl, -(C₃-C₁₂)-cycloalkyl, -(C₃-C₁₂)-heterocycloalkyl, -O-(C₁-C₁₂)-alkyl, -O-(C₁-C₁₂)-alkyl-(C₆-C₂₀)-aryl, -O-(C₃-C₁₂)-cycloalkyl, -S-(C₁-C₁₂)-alkyl, -S-(C₃-C₁₂)-cycloalkyl, -COO-(C₁-C₁₂)-alkyl, -COO-(C₃-C₁₂)-cycloalkyl, -CONH-(C₁-C₁₂)-alkyl, -CONH-(C₃-C₁₂)-cycloalkyl, -CO-(C₁-C₁₂)-alkyl, -CO-(C₃-C₁₂)-cycloalkyl, -N-[(C₁-C₁₂)-alkyl]₂, -(C₆-C₂₀)-aryl, -(C₆-C₂₀)-aryl-(C₁-C₁₂)-alkyl, -(C₆-C₂₀)-aryl-O-(C₁-C₁₂)-alkyl, -(C₃-C₂₀)-heteroaryl, -(C₃-C₂₀)-heteroaryl-(C₁-C₁₂)-alkyl, -(C₃-C₂₀)-heteroaryl-O-(C₁-C₁₂)-alkyl, -COOH, -OH, -SO₃H, -NH₂, halogen.

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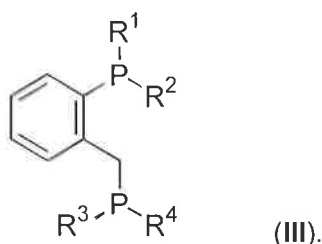
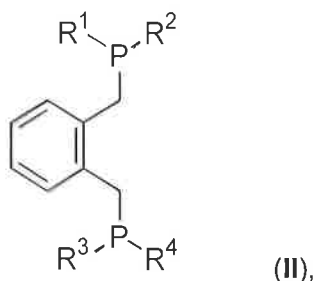
The first and second alcohols may be identical or different, but preferably the first and second alcohols are different. In one embodiment, the first alcohol is a secondary or tertiary alcohol and the second alcohol is a primary alcohol.

In this process, process steps a), b), c) and d) can be effected in any desired sequence.

30 Typically, however, the addition of CO is effected after the co-reactants have been initially

charged in steps a) to c). Steps d) and e) can be effected simultaneously or successively. In addition, CO can also be fed in in two or more steps, in such a way that, for example, a portion of the CO is first fed in, then the mixture is heated, and then a further portion of CO is fed in.

- 5 In one embodiment, the phosphine ligands according to the invention are compounds of one of the formulae (II) and (III)



In these formulae, the R^1 , R^2 , R^3 , R^4 radicals are each as defined above.

10

In one particularly preferred embodiment, the phosphine ligand according to the invention is a compound of the formula (II) where the radicals R^1 , R^2 , R^3 and R^4 are as defined above.

- The expression (C₁-C₁₂)-alkyl encompasses straight-chain and branched alkyl groups having 1 to 12 carbon atoms. These are preferably (C₁-C₈)-alkyl groups, more preferably (C₁-C₆)-alkyl, most preferably (C₁-C₄)-alkyl.
- 15

- Suitable (C₁-C₁₂)-alkyl groups are especially methyl, ethyl, propyl, isopropyl, *n*-butyl, *iso*-butyl, *sec*-butyl, *tert*-butyl, *n*-pentyl, 2-pentyl, 2-methylbutyl, 3-methylbutyl, 1,2-dimethylpropyl, 1,1-dimethylpropyl, 2,2-dimethylpropyl, 1-ethylpropyl, *n*-hexyl, 2-hexyl, 2-methylpentyl, 3-methylpentyl, 4-methylpentyl, 1,1-dimethylbutyl, 1,2-dimethylbutyl, 2,2-dimethylbutyl, 1,3-dimethylbutyl, 2,3-dimethylbutyl, 3,3-dimethylbutyl, 1,1,2-trimethylpropyl, 1,2,2-trimethylpropyl, 1-ethylbutyl, 1-ethyl-2-methylpropyl, *n*-heptyl, 2-heptyl, 3-heptyl, 2-ethylpentyl, 1-propylbutyl, *n*-octyl, 2-ethylhexyl, 2-propylheptyl, nonyl, decyl.
- 20

25

The elucidations relating to the expression (C₁-C₁₂)-alkyl also apply particularly to the alkyl groups in -O-(C₁-C₁₂)-alkyl, -S-(C₁-C₁₂)-alkyl, -COO-(C₁-C₁₂)-alkyl, -CONH-(C₁-C₁₂)-alkyl, -CO-(C₁-C₁₂)-alkyl and -N-[(C₁-C₁₂)-alkyl]₂.

- 5 The expression (C₃-C₁₂)-cycloalkyl encompasses mono-, bi- or tricyclic hydrocarbyl groups having 3 to 12 carbon atoms. Preferably, these groups are (C₅-C₁₂)-cycloalkyl.

The (C₃-C₁₂)-cycloalkyl groups have preferably 3 to 8, more preferably 5 or 6, ring atoms.

- 10 Suitable (C₃-C₁₂)-cycloalkyl groups are especially cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, cyclododecyl, cyclopentadecyl, norbornyl, adamantyl.

- The elucidations relating to the expression (C₃-C₁₂)-cycloalkyl also apply particularly to the cycloalkyl groups in -O-(C₃-C₁₂)-cycloalkyl, -S-(C₃-C₁₂)-cycloalkyl, -COO-(C₃-C₁₂)-cycloalkyl, -
15 CONH-(C₃-C₁₂)-cycloalkyl, -CO-(C₃-C₁₂)-cycloalkyl.

- The expression (C₃-C₁₂)-heterocycloalkyl encompasses nonaromatic, saturated or partly unsaturated cycloaliphatic groups having 3 to 12 carbon atoms, where one or more of the ring carbon atoms are replaced by heteroatoms. The (C₃-C₁₂)-heterocycloalkyl groups have
20 preferably 3 to 8, more preferably 5 or 6, ring atoms and are optionally substituted by aliphatic side chains. In the heterocycloalkyl groups, as opposed to the cycloalkyl groups, one or more of the ring carbon atoms are replaced by heteroatoms or heteroatom-containing groups. The heteroatoms or the heteroatom-containing groups are preferably selected from O, S, N, N(=O), C(=O), S(=O). A (C₃-C₁₂)-heterocycloalkyl group in the context of this
25 invention is thus also ethylene oxide.

Suitable (C₃-C₁₂)-heterocycloalkyl groups are especially tetrahydrothiophenyl, tetrahydrofuryl, tetrahydropyranyl and dioxanyl.

- 30 The expression (C₆-C₂₀)-aryl encompasses mono- or polycyclic aromatic hydrocarbyl radicals having 6 to 20 carbon atoms. These are preferably (C₆-C₁₄)-aryl, more preferably (C₆-C₁₀)-aryl.

Suitable (C₆-C₂₀)-aryl groups are especially phenyl, naphthyl, indenyl, fluorenyl, anthracenyl, phenanthrenyl, naphthacenyl, chrysenyl, pyrenyl, coronenyl. Preferred (C₆-C₂₀)-aryl groups are phenyl, naphthyl and anthracenyl.

- 5 The expression (C₃-C₂₀)-heteroaryl encompasses mono- or polycyclic aromatic hydrocarbyl radicals having 3 to 20 carbon atoms, where one or more of the carbon atoms are replaced by heteroatoms. Preferred heteroatoms are N, O and S. The (C₃-C₂₀)-heteroaryl groups have 3 to 20, preferably 6 to 14 and more preferably 6 to 10 ring atoms.
- 10 Suitable (C₃-C₂₀)-heteroaryl groups are especially furyl, thienyl, pyrrolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, imidazolyl, pyrazolyl, furazanyl, tetrazolyl, pyridyl, pyridazinyl, pyrimidyl, pyrazinyl, benzofuranyl, indolyl, isoindolyl, benzimidazolyl, quinolyl, isoquinolyl.

The expression halogen especially encompasses fluorine, chlorine, bromine and iodine.

- 15 Particular preference is given to fluorine and chlorine.

In one embodiment, the R¹, R², R³, R⁴ radicals, if they are -(C₁-C₁₂)-alkyl, -(C₃-C₁₂)-cycloalkyl, -(C₃-C₁₂)-heterocycloalkyl, -(C₆-C₂₀)-aryl, or -(C₃-C₂₀)-heteroaryl, may each independently be substituted by one or more substituents selected from -(C₁-C₁₂)-alkyl, -(C₃-C₁₂)-

- 20 cycloalkyl, -(C₃-C₁₂)-heterocycloalkyl, -O-(C₁-C₁₂)-alkyl, -O-(C₁-C₁₂)-alkyl-(C₆-C₂₀)-aryl, -O-(C₃-C₁₂)-cycloalkyl, -S-(C₁-C₁₂)-alkyl, -S-(C₃-C₁₂)-cycloalkyl, -(C₆-C₂₀)-aryl, -(C₆-C₂₀)-aryl-(C₁-C₁₂)-alkyl, -(C₆-C₂₀)-aryl-O-(C₁-C₁₂)-alkyl, -(C₃-C₂₀)-heteroaryl, -(C₃-C₂₀)-heteroaryl-(C₁-C₁₂)-alkyl, -(C₃-C₂₀)-heteroaryl-O-(C₁-C₁₂)-alkyl, -COOH, -OH, -SO₃H, -NH₂, halogen.

- 25 In one embodiment, the R¹, R², R³, R⁴ radicals, if they are -(C₁-C₁₂)-alkyl, -(C₃-C₁₂)-cycloalkyl, -(C₃-C₁₂)-heterocycloalkyl, -(C₆-C₂₀)-aryl, or -(C₃-C₂₀)-heteroaryl, may each independently be substituted by one or more substituents selected from -(C₁-C₁₂)-alkyl, -(C₃-C₁₂)-cycloalkyl, -O-(C₁-C₁₂)-alkyl, -O-(C₁-C₁₂)-alkyl-(C₆-C₂₀)-aryl, -O-(C₃-C₁₂)-cycloalkyl, -(C₆-C₂₀)-aryl, -(C₆-C₂₀)-aryl-(C₁-C₁₂)-alkyl, -(C₆-C₂₀)-aryl-O-(C₁-C₁₂)-alkyl, -(C₃-C₂₀)-heteroaryl, -(C₃-C₂₀)-heteroaryl-
- 30 (C₁-C₁₂)-alkyl, -(C₃-C₂₀)-heteroaryl-O-(C₁-C₁₂)-alkyl.

In one embodiment, the R¹, R², R³, R⁴ radicals, if they are -(C₁-C₁₂)-alkyl, -(C₃-C₁₂)-cycloalkyl, -(C₃-C₁₂)-heterocycloalkyl, -(C₆-C₂₀)-aryl, or -(C₃-C₂₀)-heteroaryl, may each independently be substituted by one or more substituents selected from -(C₁-C₁₂)-alkyl, -O-(C₁-C₁₂)-alkyl-(C₆-

35 C₂₀)-aryl, -(C₃-C₂₀)-heteroaryl, -(C₃-C₂₀)-heteroaryl-(C₁-C₁₂)-alkyl, -(C₃-C₂₀)-heteroaryl-O-(C₁-C₁₂)-alkyl.

In one embodiment, the R^1 , R^2 , R^3 , R^4 radicals, if they are $-(C_1-C_{12})$ -alkyl, $-(C_3-C_{12})$ -cycloalkyl, $-(C_3-C_{12})$ -heterocycloalkyl, $-(C_6-C_{20})$ -aryl, or $-(C_3-C_{20})$ -heteroaryl, may each independently be substituted by one or more substituents selected from $-(C_1-C_{12})$ -alkyl and $-(C_3-C_{20})$ -heteroaryl.

In one embodiment, the R^1 , R^2 , R^3 , R^4 radicals are unsubstituted if they are $-(C_1-C_{12})$ -alkyl, $-(C_3-C_{12})$ -cycloalkyl, or $-(C_3-C_{12})$ -heterocycloalkyl, and may be substituted as described if they are $-(C_6-C_{20})$ -aryl, or $-(C_3-C_{20})$ -heteroaryl.

In one embodiment, the R^1 , R^2 , R^3 , R^4 radicals are unsubstituted if they are $-(C_1-C_{12})$ -alkyl, $-(C_3-C_{12})$ -cycloalkyl, $-(C_3-C_{12})$ -heterocycloalkyl, $-(C_6-C_{20})$ -aryl, or $-(C_3-C_{20})$ -heteroaryl.

In one embodiment, R^1 , R^2 , R^3 , R^4 are each independently selected from $-(C_1-C_{12})$ -alkyl, $-(C_6-C_{20})$ -aryl, $-(C_3-C_{20})$ -heteroaryl; where at least one of the R^1 , R^2 , R^3 , R^4 radicals is a $-(C_3-C_{20})$ -heteroaryl radical; and R^1 , R^2 , R^3 , R^4 , if they are $-(C_1-C_{12})$ -alkyl, $-(C_6-C_{20})$ -aryl or $-(C_3-C_{20})$ -heteroaryl, may each independently be substituted by one or more of the above-described substituents.

In one embodiment, at least two of the R^1 , R^2 , R^3 , R^4 radicals are a $-(C_3-C_{20})$ -heteroaryl radical.

In one embodiment, the R^1 and R^3 radicals are each a $-(C_3-C_{20})$ -heteroaryl radical and may each independently be substituted by one or more of the substituents described above. Preferably, R^2 and R^4 are independently selected from $-(C_1-C_{12})$ -alkyl, $-(C_3-C_{12})$ -cycloalkyl, $-(C_3-C_{12})$ -heterocycloalkyl, $-(C_6-C_{20})$ -aryl, more preferably from $-(C_1-C_{12})$ -alkyl, $-(C_3-C_{12})$ -cycloalkyl, $-(C_6-C_{20})$ -aryl, most preferably from $-(C_1-C_{12})$ -alkyl. R^2 and R^4 may independently be substituted by one or more of the above-described substituents.

In one embodiment, the R^1 , R^2 , R^3 and R^4 radicals are a $-(C_6-C_{20})$ -heteroaryl radical and may each independently be substituted by one or more of the substituents described above.

In one embodiment, the R^1 , R^2 , R^3 and R^4 radicals, if they are a heteroaryl radical, are each independently selected from heteroaryl radicals having five to ten ring atoms, preferably five or six ring atoms.

In one embodiment, the R¹, R², R³ and R⁴ radicals, if they are a heteroaryl radical, are a heteroaryl radical having five ring atoms.

- 5 In one embodiment, the R¹, R², R³ and R⁴ radicals, if they are a heteroaryl radical, are each independently selected from heteroaryl radicals having six to ten ring atoms.

In one embodiment, the R¹, R², R³ and R⁴ radicals, if they are a heteroaryl radical, are a heteroaryl radical having six ring atoms.

10

In one embodiment, the R¹, R², R³ and R⁴ radicals, if they are a heteroaryl radical, are selected from furyl, thienyl, pyrrolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, imidazolyl, pyrazolyl, furazanyl, tetrazolyl, pyridyl, pyridazinyl, pyrimidyl, pyrazinyl, benzofuranyl, indolyl, isoindolyl, benzimidazolyl, quinolyl, isoquinolyl, where the heteroaryl radicals mentioned may
15 be substituted as described above.

In one embodiment, the R¹, R², R³ and R⁴ radicals, if they are a heteroaryl radical, are selected from furyl, thienyl, pyrrolyl, imidazolyl, pyridyl, pyrimidyl, indolyl, where the heteroaryl radicals mentioned may be substituted as described above.

20

In one embodiment, the R¹, R², R³ and R⁴ radicals, if they are a heteroaryl radical, are selected from 2-furyl, 2-thienyl, 2-pyrrolyl, 2-imidazolyl, 2-pyridyl, 2-pyrimidyl, 2-indolyl, where the heteroaryl radicals mentioned may be substituted as described above.

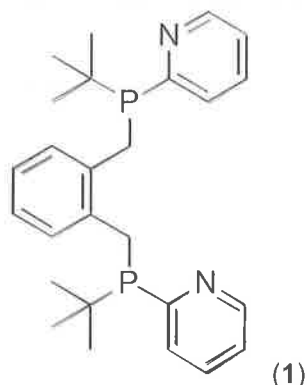
- 25 In one embodiment, the R¹, R², R³ and R⁴ radicals, if they are a heteroaryl radical, are selected from 2-furyl, 2-thienyl, N-methyl-2-pyrrolyl, N-phenyl-2-pyrrolyl, N-(2-methoxyphenyl)-2-pyrrolyl, 2-pyrrolyl, N-methyl-2-imidazolyl, 2-imidazolyl, 2-pyridyl, 2-pyrimidyl, N-phenyl-2-indolyl, 2-indolyl, where the heteroaryl radicals mentioned have no further substitution.

30

More preferably, the R¹, R², R³ and R⁴ radicals, if they are a heteroaryl radical, are pyridyl, especially 2-pyridyl.

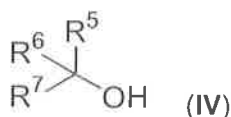
- In one embodiment, R¹ and R³ are a pyridyl radical, preferably 2-pyridyl, and R² and R⁴
35 are -(C₁-C₁₂)-alkyl, where R¹, R², R³ and R⁴ may each be substituted as described above.

In one embodiment, the phosphine ligands are a compound of formula (1):



- 5 The alcohols used in step a) as a starting product in the process according to the invention comprise 2 to 30 carbon atoms, preferably 3 to 22 carbon atoms, more preferably 4 to 12 carbon atoms. They may be primary, secondary or tertiary alcohols. The alcohols may also comprise aromatic groups.
- 10 The alcohol used in step a) is preferably a secondary or tertiary alcohol.

In one embodiment, the first alcohol used in step a) is a compound of the formula (IV)



- where R⁵ is selected from -(C₁-C₁₂)-alkyl, -(C₃-C₁₂)-cycloalkyl, -(C₆-C₂₀)-aryl;
 15 and R⁶ and R⁷ are each independently selected from -H, -(C₁-C₁₂)-alkyl, -(C₃-C₁₂)-cycloalkyl, -(C₆-C₂₀)-aryl.

- In one preferred embodiment, R⁵ is -(C₁-C₁₂)-alkyl. Preferably R⁵ is selected from methyl, ethyl, n-propyl, 2-propyl, n-butyl, 2-butyl, *sec*-butyl, *tert*-butyl, n-pentyl, 2-pentyl, 3-pentyl, 2-methylbutyl, 3-methylbutyl, 3-methylbut-2-yl, 2-methylbut-2-yl, 2,2-dimethylpropyl. More
 20 preferably R⁵ is selected from methyl and ethyl. Most preferably R⁵ is methyl.

- In one preferred embodiment, R⁶ and R⁷ are each independently selected from -H, -(C₁-C₁₂)-alkyl and -(C₆-C₂₀)-aryl. Preferably R⁶ and R⁷ are each independently selected from -H,
 25 methyl, ethyl, n-propyl, 2-propyl, n-butyl, 2-butyl, *sec*-butyl, *tert*-butyl, n-pentyl, 2-pentyl, 3-

pentyl, 2-methylbutyl, 3-methylbutyl, 3-methylbut-2-yl, 2-methylbut-2-yl, 2,2-dimethylpropyl and phenyl.

More preferably R^6 and R^7 are each independently selected from -H, methyl, ethyl, n-propyl,
 5 2-propyl, n-butyl, 2-butyl, *sec*-butyl, *tert*-butyl and phenyl.

Preferably not more than one of the radicals R^6 and R^7 is -H.

In one embodiment, R^5 is methyl and R^6 and R^7 are selected independently from -H, methyl,
 10 *tert*-butyl and phenyl, with not more than one of the radicals R^6 and R^7 being -H.

In an alternative embodiment, R^6 and R^7 are each independently selected from $-(C_1-C_{12})$ -alkyl and $-(C_6-C_{20})$ -aryl. Preferably R^6 and R^7 in this case are each independently selected from methyl, ethyl, n-propyl, 2-propyl, n-butyl, 2-butyl, *sec*-butyl, *tert*-butyl, n-pentyl, 2-pentyl, 3-
 15 pentyl, 2-methylbutyl, 3-methylbutyl, 3-methylbut-2-yl, 2-methylbut-2-yl, 2,2-dimethylpropyl and phenyl.

More preferably R^6 and R^7 in this case are each independently selected from methyl, ethyl, n-propyl, 2-propyl, n-butyl, 2-butyl, *sec*-butyl, *tert*-butyl and phenyl. In this embodiment, in
 20 particular, R^5 may be methyl, and R^6 and R^7 are each independently selected from methyl, *tert*-butyl and phenyl.

In one preferred embodiment, the first alcohol is selected from *tert*-butanol, 3,3-dimethylbutan-2-ol and 1-phenylethanol.

25

The alkoxycarbonylation according to the invention is catalysed by a Pd complex. The Pd complex may either be added in process step b) as a preformed complex comprising Pd and the phosphine ligands or be formed *in situ* from a compound comprising Pd and the free phosphine ligand. In this context, the compound comprising Pd is also referred to as catalyst
 30 precursor.

The preformed complexes may also comprise further ligands which coordinate to the metal atom. These are, for example, ethylenically unsaturated compounds or anions. Suitable additional ligands are, for example, styrene, acetate anions, maleimides (e.g. N-methylmaleimide), 1,4-naphthoquinone, trifluoroacetate anions or chloride anions.
 35

In the case that the catalyst is formed *in situ*, the ligand can be added in excess, such that the unbound ligand is also present in the reaction mixture.

- 5 In the case of the complex which is added right at the start as well, it is additionally possible to add further ligand, such that unbound ligand is also present in the reaction mixture.

In one variant, the compound comprising Pd is selected from palladium chloride (PdCl_2), palladium(II) acetylacetonate [$\text{Pd}(\text{acac})_2$], palladium(II) acetate [$\text{Pd}(\text{OAc})_2$], dichloro(1,5-cyclooctadiene)palladium(II) [$\text{Pd}(\text{cod})_2\text{Cl}_2$], bis(dibenzylideneacetone)palladium [$\text{Pd}(\text{dba})_2$], bis(acetonitrile)dichloropalladium(II) [$\text{Pd}(\text{CH}_3\text{CN})_2\text{Cl}_2$], palladium(cinnamyl) dichloride [$\text{Pd}(\text{cinnamyl})\text{Cl}_2$].

10

Preferably, the compound comprising Pd is PdCl_2 , $\text{Pd}(\text{acac})_2$ or $\text{Pd}(\text{OAc})_2$. $\text{Pd}(\text{acac})_2$ is particularly suitable.

15

The second alcohol in process step c) may be branched or linear, cyclic, alicyclic or partly cyclic, and is especially a C_1 - to C_{30} -alkanol. It is possible to use monoalcohols or polyalcohols.

20

Preferably, the alcohol used in step c) is a primary alcohol.

The alcohol used is preferably an aliphatic alcohol. An aliphatic alcohol in the context of this invention refers to an alcohol which does not comprise any aromatic groups, i.e., for example, an alkanol, alkenol or alkynol. Therefore, unsaturated nonaromatic alcohols are also permitted.

25

The alcohol in process step c) comprises preferably 1 to 30 carbon atoms, more preferably 1 to 22 carbon atoms, especially preferably 1 to 12 carbon atoms. It may be a monoalcohol or a polyalcohol.

30

The alcohol may, in addition to the one or more hydroxyl groups, contain further functional groups. Preferably, the alcohol may additionally comprise one or more functional groups selected from carboxyl, thiocarboxyl, sulfo, sulphonyl, carboxylic anhydride, imide,

carboxylic ester, sulphonic ester, carbamoyl, sulphamoyl, cyano, carbonyl, carbonothioyl, sulphhydryl, amino, ether, thioether, or silyl groups and/or halogen substituents.

5 In one embodiment, the alcohol does not comprise any further functional groups except for hydroxyl groups.

In one variant of the process, the alcohol in process step c) is selected from the group of the monoalcohols.

10 In one variant of the process, the alcohol in process step c) is selected from: methanol, ethanol, 1-propanol, 2-propanol, 1-butanol, 2-butanol, sec-butanol, tert-butanol, 1-pentanol, 2-pentanol, 3-pentanol, 1-hexanol, cyclohexanol, 2-ethylhexanol, isononanol, 2-propylheptanol, phenol, benzyl alcohol.

15 In a preferred variant, the alcohol in process step c) is selected from methanol, ethanol, 1-propanol, 1-butanol, 1-pentanol, 1-hexanol, 2-propanol, *tert*-butanol, 3-pentanol, cyclohexanol, and mixtures thereof.

20 In one variant of the process, the alcohol in process step c) is selected from the group of the polyalcohols.

In one variant of the process, the alcohol in process step c) is selected from: diols, triols, tetraols.

25 In one variant of the process, the alcohol in process step c) is selected from: cyclohexane-1,2-diol, ethane-1,2-diol, propane-1,3-diol, glycerol, butane-1,2,4-triol, 2-hydroxymethylpropane-1,3-diol, 1,2,6-trihydroxyhexane, pentaerythritol, 1,1,1-tri(hydroxymethyl)ethane, catechol, resorcinol and hydroxyhydroquinone.

30 In one variant of the process, the alcohol in process step c) is selected from: sucrose, fructose, mannose, sorbose, galactose and glucose.

In a preferred embodiment of the process, the alcohol in process step c) is selected from methanol, ethanol, 1-propanol, 1-butanol, 1-pentanol, 1-hexanol.

35

In a particularly preferred variant of the process, the alcohol in process step c) is selected from methanol and ethanol.

In a particularly preferred variant of the process, the alcohol in process step c) is methanol.

5

In one variant of the process, the alcohol in process step c) is used in excess.

In one variant of the process, the alcohol in process step c) is used simultaneously as solvent.

10

In one variant of the process, a further solvent is used, selected from: toluene, xylene, tetrahydrofuran (THF) and methylene chloride (CH_2Cl_2).

CO is fed in in step d) preferably at a partial CO pressure between 0.1 and 10 MPa (1 to 100 bar), preferably between 1 and 8 MPa (10 to 80 bar), more preferably between 2 and 4 MPa (20 to 40 bar).

15

The reaction mixture is heated in step e) of the process according to the invention preferably to a temperature between 10°C and 180°C, preferably between 20 and 160°C, more preferably between 40 and 120°C, in order to convert the alcohol to an ester.

20

The molar ratio of the alcohol initially charged in step a) to the alcohol added in step c) is preferably between 1:1 and 1:20, more preferably 1:2 to 1:10, more preferably 1:3 to 1:4.

The mass ratio of Pd to the alcohol initially charged in step a) is preferably between 0.001% and 0.5% by weight, preferably between 0.01% and 0.1% by weight, more preferably between 0.01% and 0.05% by weight.

25

The molar ratio of the phosphine ligand to Pd is preferably between 0.1:1 and 400:1, preferably between 0.5:1 and 400:1, more preferably between 1:1 and 100:1, most preferably between 2:1 and 50:1.

30

Preferably, the process is conducted with addition of an acid. In one variant, the process therefore additionally comprises step c'): adding an acid to the reaction mixture. This may preferably be a Brønsted or Lewis acid.

35

Suitable Brønsted acids preferably have an acid strength of $pK_a \leq 5$, preferably an acid strength of $pK_a \leq 3$. The reported acid strength pK_a is based on the pK_a determined under standard conditions (25°C, 1.01325 bar). In the case of a polyprotic acid, the acid strength pK_a in the context of this invention relates to the pK_a of the first protolysis step.

5

Preferably, the acid is not a carboxylic acid.

Suitable Brønsted acids are, for example, perchloric acid, sulphuric acid, phosphoric acid, methylphosphonic acid and sulphonic acids. Preferably, the acid is sulphuric acid or a
 10 sulphonic acid. Suitable sulphonic acids are, for example, methanesulphonic acid, trifluoromethanesulphonic acid, tert-butanesulphonic acid, p-toluenesulphonic acid (PTSA), 2-hydroxypropane-2-sulphonic acid, 2,4,6-trimethylbenzenesulphonic acid and dodecylsulphonic acid. Particularly preferred acids are sulphuric acid, methanesulphonic acid, trifluoromethanesulphonic acid and p-toluenesulphonic acid.

15

A Lewis acid used may, for example, be aluminium triflate.

In one embodiment, the amount of acid added in step c') is 0.3 to 40 mol%, preferably 0.4 to 15 mol%, more preferably 0.5 to 5 mol%, most preferably 0.6 to 4 mol%, based on the molar
 20 amount of the alcohol used in step a).

It is also possible for a molecular sieve to be added to the reaction mixture. In certain cases, this measure increases the yield of ester. Suitable for this purpose, for example, are molecular sieves comprising zeolite or comprising carbon, preferably molecular sieves
 25 comprising zeolite. The pore size of the molecular sieve is preferably in the range from 1 to 10 Å, more preferably in the range from 2 to 6 Å, most preferably in the range from 3 to 5 Å.

Examples

30 The examples which follow illustrate the invention.

General procedures

All the preparations which follow were carried out under protective gas using standard
 35 Schlenk techniques. The solvents were dried over suitable desiccants before use

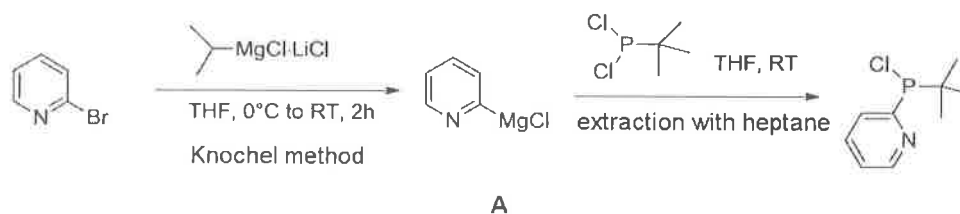
(Purification of Laboratory Chemicals, W. L. F. Armarego (Author), Christina Chai (Author), Butterworth Heinemann (Elsevier), 6th edition, Oxford 2009).

Phosphorus trichloride (Aldrich) was distilled under argon before use. All preparative
 5 operations were effected in baked-out vessels. The products were characterized by means of NMR spectroscopy. Chemical shifts (δ) are reported in ppm. The ^{31}P NMR signals were referenced as follows: $\text{SR}_{31\text{P}} = \text{SR}_{1\text{H}} * (\text{BF}_{31\text{P}} / \text{BF}_{1\text{H}}) = \text{SR}_{1\text{H}} * 0.4048$. (Robin K. Harris, Edwin D. Becker, Sonia M. Cabral de Menezes, Robin Goodfellow, and Pierre Granger, Pure Appl. Chem., 2001, 73, 1795-1818; Robin K. Harris, Edwin D. Becker,
 10 Sonia M. Cabral de Menezes, Pierre Granger, Roy E. Hoffman and Kurt W. Zilm, Pure Appl. Chem., 2008, 80, 59-84).

The recording of nuclear resonance spectra was effected on Bruker Avance 300 or Bruker Avance 400, gas chromatography analysis on Agilent GC 7890A, elemental analysis on
 15 Leco TruSpec CHNS and Varian ICP-OES 715, and ESI-TOF mass spectrometry on Thermo Electron Finnigan MAT 95-XP and Agilent 6890 N/5973 instruments.

Preparation of chloro-2-pyridyl-tert-butylphosphine (precursor A)

20 The Grignard for the synthesis of chloro-2-pyridyl-t-butylphosphine is prepared by the "Knochel method" with isopropylmagnesium chloride (Angew. Chem. 2004, 43, 2222-2226). The workup is effected according to the method of Budzelaar (Organometallics 1990, 9, 1222-1227).



25

Scheme 1: Synthesis of precursor A

8.07 ml of a 1.3 M isopropylmagnesium chloride solution (Knochel's reagent) are introduced into a 50 ml round-bottom flask with magnetic stirrer and septum, and cooled to -15°C .
 30 Thereafter, 953.5 μl (10 mmol) of 2-bromopyridine are rapidly added dropwise. The solution immediately turns yellow. It is allowed to warm up to -10°C . The conversion of the reaction is

determined as follows: about 100 μ l solution are taken and introduced into 1 ml of a saturated ammonium chloride solution. If the solution "bubbles", not much Grignard has formed yet. The aqueous solution is extracted with a pipette of ether and the organic phase is dried over Na_2SO_4 . A GC of the ethereal solution is recorded. When a large amount of pyridine has formed compared to 2-bromopyridine, conversions are high. At -10°C , there has been little conversion. After warming up to room temperature and stirring for 1-2 hours, the reaction solution turns brown-yellow. A GC test shows complete conversion. Now the Grignard solution can be slowly added dropwise with a syringe pump to a solution of 1.748 g (11 mmol) of dichloro-tert-butylphosphine in 10 ml of THF which has been cooled to -15°C beforehand. It is important that the dichloro-tert-butylphosphine solution is cooled. At room temperature, considerable amounts of dipyrityl-tert-butylphosphine would be obtained. A clear yellow solution is initially formed, which then turns cloudy. The mixture is left to warm up to room temperature and to stir overnight. According to GC-MS, a large amount of product has formed. The solvent is removed under high vacuum and a whitish solid which is brown in places is obtained. The solid is suspended with 20 ml of heptane and the solid is comminuted in an ultrasound bath. After allowing the white solid to settle out, the solution is decanted. The operation is repeated twice with 10-20 ml each time of heptane. After concentration of the heptane solution under high vacuum, it is distilled under reduced pressure. At 4.6 mbar, oil bath 120°C and distillation temperature 98°C , the product can be distilled. 1.08 g of a colourless oil are obtained. (50%).

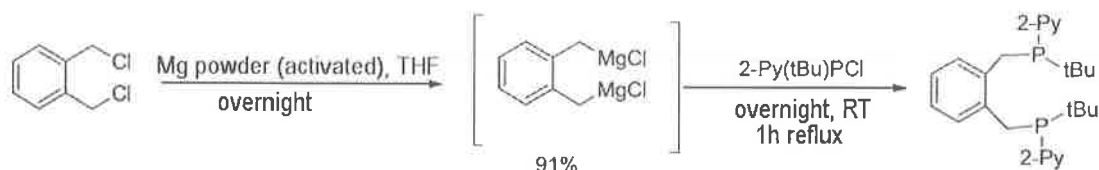
Analytical data: ^1H NMR (300 MHz, C_6D_6): δ 8.36 (m, 1H, Py), 7.67 (m, 1H, Py), 7.03-6.93 (m, 1H, Py), 6.55-6.46 (m, 1H, Py), 1.07 (d, $J = 13.3$ Hz, 9H, t-Bu).

^{13}C NMR (75 MHz, C_6D_6): δ 162.9, 162.6, 148.8, 135.5, 125.8, 125.7, 122.8, 35.3, 34.8, 25.9 and 25.8.

^{31}P NMR (121 MHz, C_6D_6) δ 97.9.

MS (EI) m/z (relative intensity) 201 (M^+ , 2), 147(32), 145 (100), 109 (17), 78 (8), 57.1 (17).

Preparation of ligand 1 (α,α' -bis(2-pyridyl)(t-butyl)phosphino)o-xylene)



Scheme 2: Synthesis of ligand 1

5 (Lit: Graham Eastham et al., Patent US 6335471)

675 mg (27.8 mmol, 4 eq) of Mg powder are weighed out in a glovebox in a 250 ml round-bottom flask with a nitrogen tap and magnetic stirrer bar, and the flask is sealed with a septum. High vacuum is applied to the round-bottom flask (about 5×10^{-2} mbar) and it is
 10 heated to 90°C for 45 minutes. After cooling down to room temperature, 2 grains of iodine are added and the mixture is dissolved in 20 ml of THF. The suspension is stirred for about 10 minutes until the yellow colour of the iodine has disappeared. After the magnesium powder has settled out, the cloudy THF solution is decanted and the activated magnesium powder is washed twice with 1-2 ml of THF. Then another 20 ml of fresh THF are added. At
 15 room temperature, a solution of 1.21 g (6.9 mmol) of α,α' -dichloro-o-xylene in 70 ml of THF is slowly added dropwise with a syringe pump. The THF solution gradually turns a darker colour. The next day, the THF suspension is filtered to remove the unconverted magnesium powder and the content of Grignard compound is determined as follows:

20 1 ml of Grignard solution is quenched in a saturated aqueous solution of NH_4Cl and extracted with ether. After drying over Na_2SO_4 , a GC of the ether solution is recorded. In qualitative terms, it is observed that exclusively o-xylene has formed.

Quantitative determination of the content of the Grignard solution:

25

1 ml of Grignard solution is quenched with 2 ml of 0.1 M HCl and the excess acid is titrated with 0.1 M NaOH. A suitable indicator is an aqueous 0.04% bromocresol solution. The colour change goes from yellow to blue. 0.74 ml of 0.1 M NaOH has been consumed. 2 ml - 0.74 ml = 1.26 ml, corresponding to 0.126 mmol of Grignard compound. Since a di-Grignard is
 30 present, the Grignard solution is 0.063 M. This is a yield exceeding 90%.

In a 250 ml three-neck flask with reflux condenser and magnetic stirrer, under argon, 1.8 g (8.66 mmol) of chlorophosphine (2-Py(tBu)PCl) are dissolved in 10 ml of THF and cooled to -60°C. Then 55 ml of the above-stipulated Grignard solution (0.063 M, 3.46 mmol) are slowly added dropwise at this temperature with a syringe pump. The solution at first remains clear and then turns intense yellow. After 1.5 hours, the solution turns cloudy. The mixture is left to warm up to room temperature overnight and a clear yellow solution is obtained. To complete the reaction, the mixture is heated under reflux for 1 hour. After cooling, 1 ml of H₂O is added and the solution loses colour and turns milky white. After removing THF under high vacuum, a stringy, pale yellow solid is obtained. 10 ml of water and 10 ml of ether are added thereto, and two homogeneous clear phases are obtained, which have good separability. The aqueous phase is extracted twice with ether. After the organic phase has been dried with Na₂SO₄, the ether is removed under high vacuum and a stringy, almost colourless solid is obtained. The latter is dissolved in 5 ml of MeOH while heating on a water bath and filtered through Celite. At -28°C, 772 mg of product are obtained in the form of white crystals overnight. (51%). After concentration, it was possible to isolate another 100 mg from the mother solution. The overall yield is 57.6%.

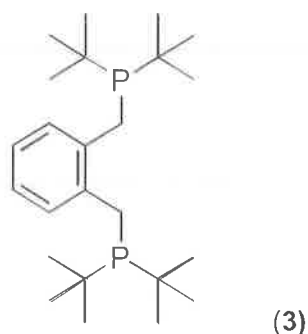
¹H NMR (300 MHz, C₆D₆): δ 8.58 (m, 2H, Py), 7.31-7.30 (m, 2H, benzene), 7.30-7.22 (m, 2H, Py), 6.85-6.77 (m, 2H, Py), 6.73 (m, 2H, benzene), 6.57-6.50 (m, 2H, py), 4.33 (dd, J = 13.3 and 4.3 Hz, 2H, CH₂), 3.72-3.62 (m, 2H, CH₂), 121(d, J = 11.8 Hz, 18H, tBu),
¹³C NMR (75 MHz, C₆D₆): δ 161.3, 161.1, 149.6, 137.8, 137.7, 134.5, 133.3, 132.7, 131.4, 131.3, 125.7, 122.9, 30.7, 30.5, 28.2, 28.0, 26.5, 26.4, 26.2, and 26.1.
³¹P NMR (121 MHz, C₆D₆) δ 8.8, EA calculated for C₂₆H₃₄N₂P₂: C, 71.54; H, 7.85; N, 6.56; P, 14.35, found: C, 71.21; H, 7.55; N, 6.56; P, 14.35.

25

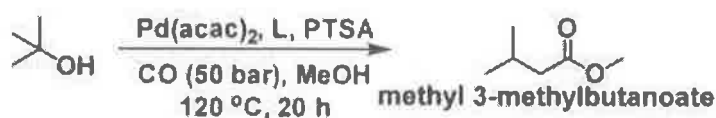
Comparative ligand

30

The comparative ligand used in the following examples is 1,2-bis(di-tert-butylphosphino-methyl)benzene (DTBMB, ligand **3**).



Methoxycarbonylation of tert-butanol



5

1) without ligand (comparative example)

A 4 ml glass reaction vessel (vial) is charged under argon with Pd(acac)_2 (3.1 mg, 0.5 mol%), PTSA (28.5 mg, 7.5 mol%) and a magnetic stirrer. Then, under argon, MeOH (2 ml) and tert-butanol (0.2 ml, 2 mmol) are added. This vial is placed in a metal plate fabricated for this purpose, and the plate with vial is transferred to a 300 ml autoclave from Parr Instruments. The autoclave is purged three times with CO and then charged with 50 bar of CO at room temperature. The reaction is carried out with magnetic stirring at 120°C for 20 hours. After cooling down to room temperature, the autoclave is cautiously decompressed. The yield was carried out by means of GC analysis with isooctane (200 μl) as internal standard (0% yield of methyl 3-methylbutanoate).

2) ligand **3** (comparative example)

A 4 ml glass reaction vessel (vial) is charged under argon with Pd(acac)_2 (3.1 mg, 0.5 mol%), **3** (15.8 mg, 2 mol%), PTSA (28.5 mg, 7.5 mol%) and a magnetic stirrer. Then, under argon, MeOH (2 ml) and tert-butanol (0.2 ml, 2 mmol) are added. This vial is placed in a metal plate fabricated for this purpose, and the plate with vial is transferred to a 300 ml autoclave from Parr Instruments. The autoclave is purged three times with CO and then charged with 50 bar of CO at room temperature. The reaction is carried out with magnetic stirring at 120°C for 20 hours. After cooling down to room temperature, the autoclave is cautiously

decompressed. The yield was carried out by means of GC analysis with isooctane (200 μ l) as internal standard (0% yield of methyl 3-methylbutanoate).

3) ligand 1

5

A 4 ml glass reaction vessel (vial) is charged under argon with Pd(acac)₂ (3.1 mg, 0.5 mol%), 1 (17.5 mg, 2 mol%), PTSA (28.5 mg, 7.5 mol%) and a magnetic stirrer. Then, under argon, MeOH (2 ml) and tert-butanol (0.2 ml, 2 mmol) are added. This vial is placed in a metal plate fabricated for this purpose, and the plate with vial is transferred to a 300 ml autoclave from
10 Parr Instruments. The autoclave is purged three times with CO and then charged with 50 bar of CO at room temperature. The reaction is carried out with magnetic stirring at 120°C for 20 hours. After cooling down to room temperature, the autoclave is cautiously decompressed. The yield was carried out by means of GC analysis with isooctane (200 μ l) as internal standard (99% yield of methyl 3-methylbutanoate).

15

The results are summarized in the following table:

Example	Ligand	Yield of methyl 3-methylbutanoate (%)
1 (CE)	none	0
2*	3	0
3 (CE)	1	99

CE: comparative example

*: inventive example

20

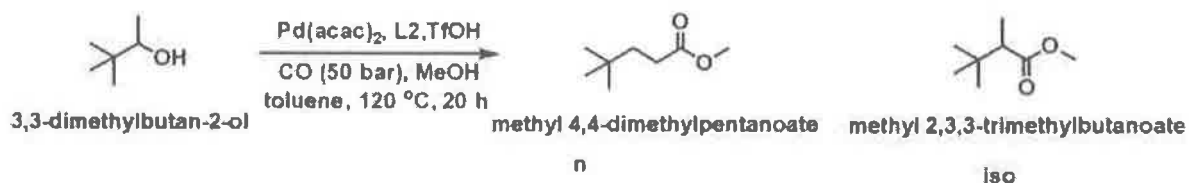
Methoxycarbonylation of 1-phenylethanol

A 4 ml glass reaction vessel (vial) is charged under argon with Pd(acac)₂ (3.1 mg, 0.5 mol%), PTSA (28.5 mg, 7 mol%), ligand 1 (8.7 mg, 1 mol%) and a magnetic stirrer. Then, under
25 argon, MeOH (2 ml) and 2 mmol of 1-phenylethanol are added. This vial is placed in a metal plate fabricated for this purpose, and the plate with vial is transferred to a 300 ml autoclave from Parr Instruments. The autoclave is purged three times with CO and then charged with 50 bar of CO at room temperature. The reaction is carried out with magnetic stirring at 120°C for 20 hours. After cooling down to room temperature, the autoclave is cautiously
30 decompressed. The product obtained was a mixture of methyl 3-phenylpropanoate (n product) and methyl 2-phenylpropanoate (iso product). The yield was carried out by means

of GC analysis with isooctane (200 μ l) as internal standard (40% overall yield, n/iso ratio 70/30).

Methoxycarbonylation of 3,3-dimethylbutan-2-ol

5



Example 1: ligand **3**

A 4 ml glass reaction vessel (vial) is charged under argon with Pd(acac)₂ (3.1 mg, 0.5 mol%), **3** (15.8 mg, 2 mol%), CF₃SO₂OH (48.0 mg, 16 mol%) and a magnetic stirrer. Then, under argon, toluene (2 ml) and 3,3-dimethylbutan-2-ol (0.25 ml, 2 mmol) are added. This vial is placed in a metal plate fabricated for this purpose, and the plate with vial is transferred to a 300 ml autoclave from Parr Instruments. The autoclave is purged three times with CO and then charged with 50 bar of CO at room temperature. The reaction is carried out with magnetic stirring at 120°C for 20 hours. After cooling down to room temperature, the autoclave is cautiously decompressed. The yield was carried out by means of GC analysis with isooctane (200 μ l) as internal standard (0% yield).

Example 2: ligand **3** with 4 Å molecular sieve

20

A 4 ml glass reaction vessel (vial) is charged under argon with Pd(acac)₂ (3.1 mg, 0.5 mol%), **3** (15.8 mg, 2 mol%), CF₃SO₂OH (48.0 mg, 16 mol%), 4 Å zeolite molecular sieve (4 Å MS, 20 mg) and a magnetic stirrer. Then, under argon, toluene (2 ml) and 3,3-dimethylbutan-2-ol (0.25 ml, 2 mmol) are added. This vial is placed in a metal plate fabricated for this purpose, and the plate with vial is transferred to a 300 ml autoclave from Parr Instruments. The autoclave is purged three times with CO and then charged with 50 bar of CO at room temperature. The reaction is carried out with magnetic stirring at 120°C for 20 hours. After cooling down to room temperature, the autoclave is cautiously decompressed. The yield was carried out by means of GC analysis with isooctane (200 μ l) as internal standard (0% yield).

30

Example 3: ligand **1**

A 4 ml glass reaction vessel (vial) is charged under argon with Pd(acac)₂ (3.1 mg, 0.5 mol%), **1** (17.5 mg, 2 mol%), CF₃SO₂OH (48.0 mg, 16 mol%) and a magnetic stirrer. Then, under
 5 argon, toluene (2 ml) and 3,3-dimethylbutan-2-ol (0.25 ml, 2 mmol) are added. This vial is placed in a metal plate fabricated for this purpose, and the plate with vial is transferred to a 300 ml autoclave from Parr Instruments. The autoclave is purged three times with CO and then charged with 50 bar of CO at room temperature. The reaction is carried out with magnetic stirring at 120°C for 20 hours. After cooling down to room temperature, the
 10 autoclave is cautiously decompressed. The yield was carried out by means of GC analysis with isooctane (200 µl) as internal standard (10% yield).

Example 4: ligand **1** with 4 Å molecular sieve

A 4 ml glass reaction vessel (vial) is charged under argon with Pd(acac)₂ (3.1 mg, 0.5 mol%), **1** (17.5 mg, 2 mol%), CF₃SO₂OH (48.0 mg, 16 mol%), 4 Å MS (20 mg) and a magnetic stirrer. Then, under argon, toluene (2 ml) and 3,3-dimethylbutan-2-ol (0.25 ml, 2 mmol) are added. This vial is placed in a metal plate fabricated for this purpose, and the plate with vial is transferred to a 300 ml autoclave from Parr Instruments. The autoclave is purged three
 20 times with CO and then charged with 50 bar of CO at room temperature. The reaction is carried out with magnetic stirring at 120°C for 20 hours. After cooling down to room temperature, the autoclave is cautiously decompressed. The yield was carried out by means of GC analysis with isooctane (200 µl) as internal standard (20% yield).

25 The results are summarized in the following table:

Example	Ligand	Additive	Yield	n/iso ratio
1 (CE)	3		0%	-
2 (CE)	3	4 Å MS	0%	-
3*	1		10%	75/25
4*	1	4 Å MS	20%	74/26

CE: comparative examples

*: inventive examples

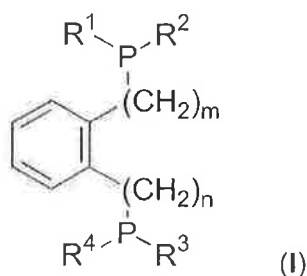
The above experiments show that by means of the process of the invention, using the ligands according to the invention, a series of structurally different alcohols can be reacted as substrate in an alkoxycarbonylation reaction with CO and a further alcohol to form esters. Conversely, the ligand known from the prior art is not suitable for the reaction of alcohols in

5 an alkoxycarbonylation reaction.

Claims

1. Process comprising the following process steps:
 - a) introducing a first alcohol, the first alcohol having 2 to 30 carbon atoms;
 - 5 b) adding a phosphine ligand and a compound which comprises Pd, or adding a complex comprising Pd and a phosphine ligand;
 - c) adding a second alcohol;
 - d) supplying CO;
 - 10 e) heating the reaction mixture, the first alcohol reacting with CO and the second alcohol to form an ester;

where the phosphine ligand is a compound of formula (I)



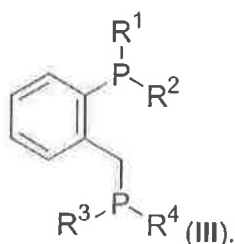
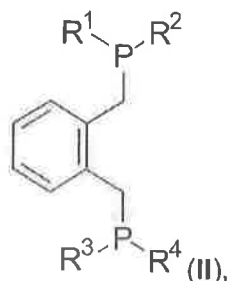
where

m and n are each independently 0 or 1;

- 15 R¹, R², R³, R⁴ are each independently selected from -(C₁-C₁₂)-alkyl, -(C₃-C₁₂)-cycloalkyl, -(C₃-C₁₂)-heterocycloalkyl, -(C₆-C₂₀)-aryl, -(C₃-C₂₀)-heteroaryl; at least one of the R¹, R², R³, R⁴ radicals is a -(C₃-C₂₀)-heteroaryl radical; R¹, R², R³, R⁴, if they are -(C₁-C₁₂)-alkyl, -(C₃-C₁₂)-cycloalkyl, -(C₃-C₁₂)-heterocycloalkyl, -(C₆-C₂₀)-aryl or -(C₃-C₂₀)-heteroaryl,
 - 20 may each independently be substituted by one or more substituents selected from -(C₁-C₁₂)-alkyl, -(C₃-C₁₂)-cycloalkyl, -(C₃-C₁₂)-heterocycloalkyl, -O-(C₁-C₁₂)-alkyl, -O-(C₁-C₁₂)-alkyl-(C₆-C₂₀)-aryl, -O-(C₃-C₁₂)-cycloalkyl, -S-(C₁-C₁₂)-alkyl, -S-(C₃-C₁₂)-cycloalkyl, -COO-(C₁-C₁₂)-alkyl, -COO-(C₃-C₁₂)-cycloalkyl, -CONH-(C₁-C₁₂)-alkyl, -CONH-(C₃-C₁₂)-cycloalkyl, -CO-(C₁-C₁₂)-alkyl, -CO-(C₃-C₁₂)-cycloalkyl, -N-[(C₁-C₁₂)-alkyl]₂, -(C₆-C₂₀)-aryl, -(C₆-C₂₀)-aryl-(C₁-C₁₂)-alkyl, -(C₆-C₂₀)-aryl-O-(C₁-C₁₂)-alkyl,
 - 25 -(C₃-C₂₀)-heteroaryl, -(C₃-C₂₀)-heteroaryl-(C₁-C₁₂)-alkyl, -(C₃-C₂₀)-heteroaryl-O-(C₁-C₁₂)-alkyl, -COOH, -OH, -SO₃H, -NH₂, halogen;
- and further where

the $-(C_3-C_{12})$ -heterocycloalkyl comprises non-aromatic, saturated or partly unsaturated cycloaliphatic groups having 3 to 12 carbon atoms, where one or more of the ring carbon atoms of the cycloaliphatic groups are replaced by heteroatoms.

- 5 2. Process according to Claim 1,
where the phosphine ligand is a compound of one of the formulae (II) and (III)

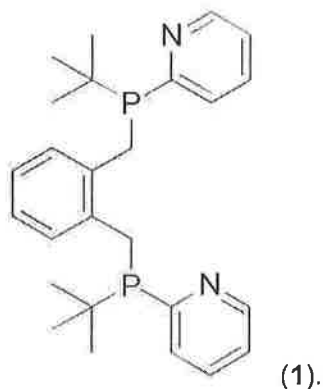


- 10 3. Process according to either of Claims 1 and 2,
where at least two of the R^1 , R^2 , R^3 , R^4 radicals are a $-(C_3-C_{20})$ -heteroaryl radical.
4. Process according to any of Claims 1 to 3,
where the R^1 and R^3 radicals are each a $-(C_3-C_{20})$ -heteroaryl radical.
- 15 5. Process according to any of Claims 1 to 4,
where the R^1 and R^3 radicals are each a $-(C_3-C_{20})$ -heteroaryl radical;
and R^2 and R^4 are each independently selected from $-(C_1-C_{12})$ -alkyl, $-(C_3-C_{12})$ -
cycloalkyl, $-(C_3-C_{12})$ -heterocycloalkyl, $-(C_6-C_{20})$ -aryl.
- 20 6. Process according to any of Claims 1 to 5,
where the R^1 and R^3 radicals are each a $-(C_3-C_{20})$ -heteroaryl radical;
and R^2 and R^4 are each independently selected from $-(C_1-C_{12})$ -alkyl.
- 25 7. Process according to any of Claims 1 to 6,

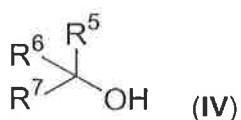
where R^1 , R^2 , R^3 , R^4 , if they are a heteroaryl radical, are each independently selected from furyl, thienyl, pyrrolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, imidazolyl, pyrazolyl, furazanyl, tetrazolyl, pyridyl, pyridazinyl, pyrimidyl, pyrazinyl, benzofuranyl, indolyl, isoindolyl, benzimidazolyl, quinolyl, isoquinolyl.

5

8. Process according to any of Claims 1 to 7,
where the phosphine ligand is a compound of formula (1)



- 10 9. Process according to any of Claims 1 to 8,
wherein the first alcohol in process step a) is a compound of formula (IV)



where R^5 is selected from $-(C_1-C_{12})$ -alkyl, $-(C_3-C_{12})$ -cycloalkyl, $-(C_6-C_{20})$ -aryl;
and R^6 and R^7 are each independently selected from -H, $-(C_1-C_{12})$ -alkyl, $-(C_3-C_{12})$ -
15 cycloalkyl, $-(C_6-C_{20})$ -aryl.

10. Process according to Claim 9,
wherein R^5 is $-(C_1-C_{12})$ -alkyl.

- 20 11. Process according to any of Claims 9 to 10,
where R^6 and R^7 are each independently selected from -H, $-(C_1-C_{12})$ -alkyl, $-(C_6-C_{20})$ -
aryl.

12. Process according to any of Claims 9 to 11,
25 wherein not more than one of the radicals R^6 and R^7 is -H.

13. Process according to any of Claims 1 to 12,
wherein the compound comprising Pd in process step b) is selected from palladium
dichloride, palladium(II) acetylacetonate, palladium(II) acetate, dichloro(1,5-
cyclooctadiene)palladium(II), bis(dibenzylideneacetone)palladium,
5 bis(acetonitrile)dichloropalladium(II), palladium(cinnamyl) dichloride.
14. Process according to any of Claims 1 to 13,
wherein the second alcohol in process step c) is selected from methanol, ethanol, 1-
propanol, 1-butanol, 1-pentanol, 1-hexanol, 2-propanol, *tert*-butanol, 3-pentanol,
10 cyclohexanol, and mixtures thereof.
15. Process according to any of Claims 1 to 14,
wherein the first alcohol in process step a) is a secondary or tertiary alcohol and the
second alcohol in process step c) is a primary alcohol.