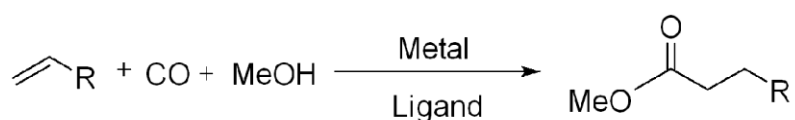


Methoxycarbonylation with formic acid and methanol

The invention relates to a process for methoxycarbonylation with formic acid and methanol.

- 5 The methoxycarbonylation of alkenes is a process of increasing importance. In classical methoxycarbonylation an olefin is reacted with CO and MeOH in the presence of a catalyst comprising a ligand and a metal:



- 10 CO is introduced into the reaction vessel as a gas.

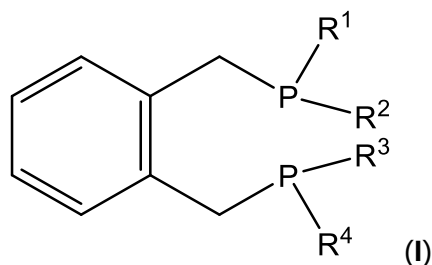
It was an object of the invention to provide a process that employs a CO source other than CO gas which is introduced into the reaction vessel. The process should achieve a high yield of methyl ester.

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The object is achieved by a process according to Claim 1.

Process comprising the process steps of:

- a) addition of an olefin;
 20 b) addition of a compound comprising Pd, wherein the Pd is capable of forming a complex;
 c) addition of a compound of general formula (I):



- wherein R¹, R², R³ and R⁴ are each independently selected from: -H, -(C₁-C₁₂)-alkyl, -O-(C₁-C₁₂)-alkyl, -(C₄-C₁₄)-aryl, -O-(C₄-C₁₄)-aryl, cycloalkyl, -(C₁-C₁₂)-heteroalkyl, -O-(C₁-C₁₂)-heteroalkyl, -(C₃-C₁₄)-heteroaryl, -O-(C₃-C₁₄)-heteroaryl, -COO-alkyl, -COO-aryl, -C-O-alkyl, -C-O-aryl, NH₂, halogen and the residues are also capable of forming a larger condensed ring;
- 25

wherein the recited alkyl groups, aryl groups, cycloalkyl, heteroalkyl groups, heteroaryl groups may be substituted as follows:

-(C₁-C₁₂)-alkyl, -O-(C₁-C₁₂)-alkyl, halogen;

and at least one of the radicals R¹, R², R³, R⁴ does not represent phenyl;

5 d) addition of MeOH;

e) addition of HCOOH,

wherein the employed volume based on 2 mmol of olefin is in the range from 0.3 ml to 0.8 ml;

f) heating of the reaction mixture to convert the olefin into the methyl ester.

10 In one variant of the process no CO gas is supplied to the reaction mixture.

In one variant of the process HCOOH serves as the only CO source for the reaction.

In one variant of the process the compound in process step b) is selected from:

15 Pd(acac)₂, PdCl₂, Pd(dba)₃*CH₃Cl (dba = dibenzylideneacetone), Pd(OAc)₂, Pd(TFA)₂, Pd(CH₃CN)Cl₂.

In one variant of the process the compound in process step b) is Pd(OAc)₂.

20 In one variant of the process the process comprises the additional process step g):

g) addition of an acid.

In one variant of the process, the acid is selected from: H₂SO₄, CH₃SO₃H, CF₃SO₃H, PTSA (p-toluenesulfonic acid).

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In one variant of the process the acid is PTSA (p-toluenesulfonic acid).

In one variant of the process the employed volume of HCOOH based on 2 mmol of olefin is in the range from 0.4 ml to 0.6 ml.

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In one variant of the process R¹, R², R³, R⁴ are each independently selected from: -(C₁-C₁₂)-alkyl, -O-(C₁-C₁₂)-alkyl, -(C₄-C₁₄)-aryl, -O-(C₄-C₁₄)-aryl, cycloalkyl, -(C₁-C₁₂)-heteroalkyl, -O-(C₁-C₁₂)-heteroalkyl, -(C₃-C₁₄)-heteroaryl, -O-(C₃-C₁₄)-heteroaryl, -COO-alkyl, -COO-aryl, -C-O-alkyl, -C-O-aryl, NH₂, halogen and the residues are also capable of forming a larger condensed ring;

wherein the recited alkyl groups, aryl groups, cycloalkyl, heteroalkyl groups, heteroaryl groups may be substituted as follows:

-(C₁-C₁₂)-alkyl, -O-(C₁-C₁₂)-alkyl, halogen;

and at least one of the radicals R¹, R², R³, R⁴ does not represent phenyl.

5

In one variant of the process R¹, R², R³, R⁴ are each independently selected from: -(C₁-C₁₂)-alkyl, -(C₄-C₁₄)-aryl, cycloalkyl, -(C₁-C₁₂)-heteroalkyl, -(C₃-C₁₄)-heteroaryl, halogen and the residues are also capable of forming a larger condensed ring;

wherein the recited alkyl groups, aryl groups, cycloalkyl, heteroalkyl groups, heteroaryl groups

10 may be substituted as follows:

-(C₁-C₁₂)-alkyl, -O-(C₁-C₁₂)-alkyl, halogen;

and at least one of the radicals R¹, R², R³, R⁴ does not represent phenyl.

In one variant of the process R¹, R², R³, R⁴ are each independently selected from: -(C₁-C₁₂)-alkyl, cycloalkyl, -(C₃-C₁₄)-heteroaryl and the residues are also capable of forming a larger condensed ring;

15

wherein the recited alkyl groups, cycloalkyl, heteroaryl groups may be substituted as follows:

-(C₁-C₁₂)-alkyl, -O-(C₁-C₁₂)-alkyl, halogen,

and at least one of the radicals R¹, R², R³, R⁴ does not represent phenyl.

20

In one variant of the process R¹, R⁴ are each independently selected from: -(C₁-C₁₂)-alkyl, cycloalkyl, and the residues are also capable of forming a larger condensed ring;

wherein the recited alkyl groups, cycloalkyl may be substituted as follows:

-(C₁-C₁₂)-alkyl, -O-(C₁-C₁₂)-alkyl, halogen.

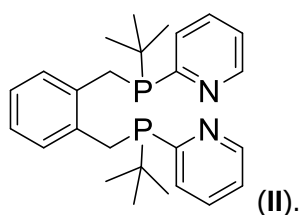
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In one variant of the process R², R³ each independently represent -(C₃-C₁₄)-heteroaryl,

wherein the recited heteroaryl groups may be substituted as follows:

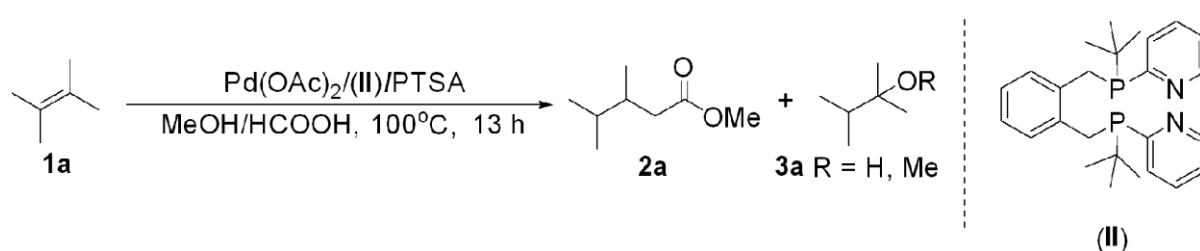
-(C₁-C₁₂)-alkyl, -O-(C₁-C₁₂)-alkyl, halogen.

30 In one variant of the process the compound of general formula (I) has the structure (II):



The invention is more particularly elucidated hereinbelow with reference to exemplary embodiments.

5 Pd-catalyzed methoxycarbonylation of tetramethylethylene **1a** with HCOOH: Effect of employed volume of HCOOH



Added to a sealed 35 ml tube were [Pd(OAc)₂] (1.12 mg, 0.25 mol%), **(II)** (8.72 mg, 1.0 mol%), p-
 10 toluenesulfonic acid (PTSA•H₂O) (15.2 mg, 4 mol%) and an oven-dried stirrer rod. The tube
 together with the lid were placed into a long Schlenk tube having a large opening. The Schlenk
 tube is evacuated three times and refilled with argon. Under an argon atmosphere **1a** (2 mmol),
 MeOH (1.5 ml) and HCOOH (X ml) (X see table 1) were injected into the 35 ml tube using a
 syringe. The 35 ml tube was then sealed with the lid. The reaction was carried out at 100°C over
 15 13 h. At the end of the reaction the tube was allowed to reach room temperature without additional
 cooling and carefully decompressed. Isooctane (100 µl) was then injected as internal standard.
 Conversion was measured by GC analysis.

The results are summarized in table 1 which follows:

Table 1:

HCOOH (volume in ml)	Conversion %	Yield of 2a %	Yield of 3a %
0.2	73	53	17
0.3	85	72	11

0.5	91	80	7
0.8	90	71	5

As is shown by the experiments described above, the problem is solved by a process according to the invention.

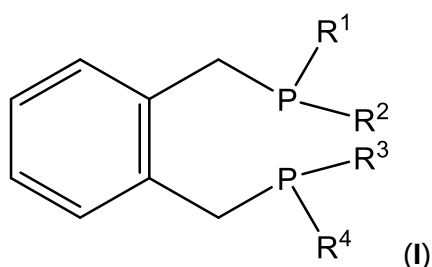
Claims

1. Process comprising the process steps of:

a) addition of an olefin;

5 b) addition of a compound comprising Pd, wherein the Pd is capable of forming a complex;

c) addition of a compound of general formula (I):



wherein R^1 , R^2 , R^3 and R^4 are each independently selected from: -H, -(C₁-C₁₂)-alkyl, -O-(C₁-C₁₂)-alkyl, -(C₄-C₁₄)-aryl, -O-(C₄-C₁₄)-aryl, cycloalkyl, -(C₁-C₁₂)-heteroalkyl, -O-(C₁-C₁₂)-heteroalkyl, -(C₃-C₁₄)-heteroaryl, -O-(C₃-C₁₄)-heteroaryl, -COO-alkyl, -COO-aryl, -C-O-alkyl, -C-O-aryl, NH₂, halogen and the residues are also capable of forming a larger condensed ring;

wherein the recited alkyl groups, aryl groups, cycloalkyl, heteroalkyl groups, heteroaryl groups may be substituted as follows:

15 -(C₁-C₁₂)-alkyl, -O-(C₁-C₁₂)-alkyl, halogen;

and at least one of the radicals R^1 , R^2 , R^3 , R^4 does not represent phenyl;

d) addition of MeOH;

e) addition of HCOOH,

wherein the employed volume based on 2 mmol of olefin is in the range from 0.3 ml to 0.8 ml;

20 f) heating of the reaction mixture to convert the olefin into the methyl ester.

2. Process according to Claim 1,

wherein no CO gas is supplied to the reaction mixture.

25 3. Process according to Claim 1 or 2,

wherein HCOOH serves as the only CO source for the reaction.

4. Process according to any of Claims 1 to 3,

wherein the compound in process step b) is selected from:

$\text{Pd}(\text{acac})_2$, PdCl_2 , $\text{Pd}(\text{dba})_3 \cdot \text{CH}_3\text{Cl}$ (dba = dibenzylideneacetone), $\text{Pd}(\text{OAc})_2$, $\text{Pd}(\text{TFA})_2$, $\text{Pd}(\text{CH}_3\text{CN})\text{Cl}_2$.

5. Process according to any of Claims 1 to 4,

- 5 wherein the process comprises the additional process step g):
g) addition of an acid.

6. Process according to Claim 5,

wherein the acid is selected from: H_2SO_4 , $\text{CH}_3\text{SO}_3\text{H}$, $\text{CF}_3\text{SO}_3\text{H}$, PTSA.

10

7. Process according to any of Claims 1 to 6,

wherein the employed volume of HCOOH based on 2 mmol of olefin is in the range from 0.4 ml to 0.6 ml.

- 15 8. Process according to any of Claims 1 to 7,

wherein R^1 , R^2 , R^3 and R^4 are each independently selected from: $-(\text{C}_1\text{-C}_{12})\text{-alkyl}$, $-\text{O}-(\text{C}_1\text{-C}_{12})\text{-alkyl}$, $-(\text{C}_4\text{-C}_{14})\text{-aryl}$, $-\text{O}-(\text{C}_4\text{-C}_{14})\text{-aryl}$, cycloalkyl, $-(\text{C}_1\text{-C}_{12})\text{-heteroalkyl}$, $-\text{O}-(\text{C}_1\text{-C}_{12})\text{-heteroalkyl}$, $-(\text{C}_3\text{-C}_{14})\text{-heteroaryl}$, $-\text{O}-(\text{C}_3\text{-C}_{14})\text{-heteroaryl}$, $-\text{COO-alkyl}$, $-\text{COO-aryl}$, $-\text{C-O-alkyl}$, $-\text{C-O-aryl}$, NH_2 , halogen and the residues are also capable of forming a larger condensed ring;

- 20 wherein the recited alkyl groups, aryl groups, cycloalkyl, heteroalkyl groups, heteroaryl groups may be substituted as follows:

$-(\text{C}_1\text{-C}_{12})\text{-alkyl}$, $-\text{O}-(\text{C}_1\text{-C}_{12})\text{-alkyl}$, halogen;

and at least one of the radicals R^1 , R^2 , R^3 , R^4 does not represent phenyl.

- 25 9. Process according to any of Claims 1 to 8,

wherein R^1 , R^2 , R^3 and R^4 are each independently selected from: $-(\text{C}_1\text{-C}_{12})\text{-alkyl}$, $-(\text{C}_4\text{-C}_{14})\text{-aryl}$, cycloalkyl, $-(\text{C}_1\text{-C}_{12})\text{-heteroalkyl}$, $-(\text{C}_3\text{-C}_{14})\text{-heteroaryl}$, halogen and the residues are also capable of forming a larger condensed ring;

wherein the recited alkyl groups, aryl groups, cycloalkyl, heteroalkyl groups, heteroaryl groups may be substituted as follows:

30

$-(\text{C}_1\text{-C}_{12})\text{-alkyl}$, $-\text{O}-(\text{C}_1\text{-C}_{12})\text{-alkyl}$, halogen;

and at least one of the radicals R^1 , R^2 , R^3 , R^4 does not represent phenyl.

10. Process according to any of Claims 1 to 9,

wherein R^1 , R^2 , R^3 and R^4 are each independently selected from: $-(C_1-C_{12})$ -alkyl, cycloalkyl, $-(C_3-C_{14})$ -heteroaryl and the residues are also capable of forming a larger condensed ring;

wherein the recited alkyl groups, cycloalkyl, heteroaryl groups may be substituted as follows:

$-(C_1-C_{12})$ -alkyl, $-O-(C_1-C_{12})$ -alkyl, halogen,

5 and at least one of the radicals R^1 , R^2 , R^3 , R^4 does not represent phenyl.

11. Process according to any of Claims 1 to 10,

wherein R^1 , R^4 are each independently selected from: $-(C_1-C_{12})$ -alkyl, cycloalkyl, and the residues are also capable of forming a larger condensed ring;

10 wherein the recited alkyl groups, cycloalkyl may be substituted as follows:

$-(C_1-C_{12})$ -alkyl, $-O-(C_1-C_{12})$ -alkyl, halogen.

12. Process according to any of Claims 1 to 11,

wherein R^2 , R^3 each independently represent $-(C_3-C_{14})$ -heteroaryl,

15 wherein the recited heteroaryl groups may be substituted as follows:

$-(C_1-C_{12})$ -alkyl, $-O-(C_1-C_{12})$ -alkyl, halogen.

13. Process according to any of Claims 1 to 12,

wherein the compound of general formula (I) has the structure (II):

