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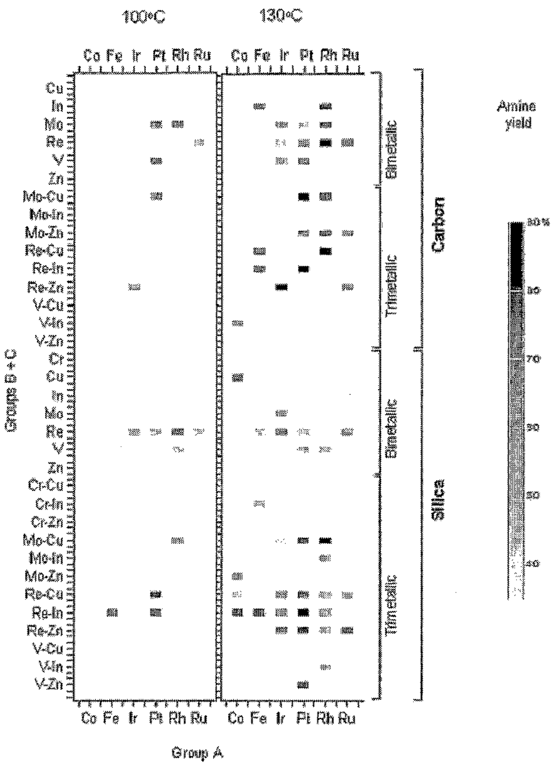
(54) Title: METHOD FOR THE CATALYTIC REDUCTION OF AMIDES



(57) Abstract: Described is a method for the catalytic reduction of an amide for the preparation of an amine at a temperature of below 200° C and a pressure of below 50 bar, the catalyst being chosen from bimetallic and trimetallic catalysts of the group consisting of ABC, AB, AC and BC, wherein: A is a metal, chosen from the group, consisting of Co, Fe, Ir, Pt, Rh and Ru, B is a metal, chosen from the group, consisting of Cr, Mo, Re and V, and, C is a metal, chosen from the group, consisting of Cu, In and Zn. Further, novel catalysts and a selection method for such catalysts is disclosed.

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Title: Method for the catalytic reduction of amides.

The invention relates to a novel method for the catalytic reduction of amides at mild reaction conditions, using novel bimetallic and trimetallic catalysts, active in the reduction of amines and to a method for the selection of such catalysts.

Amines constitute an important class of compounds with extensive use as medicines or basic raw materials for the preparation of pharmaceuticals. Therefore, economically viable and green methods of synthesising amines are important. A simple and direct approach would be catalytic reduction of amides, and, indeed, there are numerous reports claiming the reduction of amides either by using hydrogen gas or by means of hydride containing reagents.

However, known processes for the reduction of amides into the related amines using metal catalysts and hydrogen gas, require high temperatures and pressures, therewith compromising the presence of any other reducible functional groups, thermolabile groups and precluding the available methods for many practical applications. In the art, temperatures and pressures above 200°C and 200 bar are often necessary. For example, methods are known using a bimetallic copper chromium catalyst at temperatures between 200 and 260°C and pressures of 100-400 bar, see e.g. Wojcik, B.; Adkins, H. *J. Am. Chem. Soc.* 1934, *56*, 2419-2425; Paden, J.H.; Adkins, K. *J. Am. Chem. Soc.* 1936, *58*, 2487-2499; Sauer, J.C.; Adkins, H. *J. Am. Chem. Soc.* 1938, *60*, 402-406 and US-A-2,143,751.

Regarding the above, several attempts have been made to obtain amines by catalytic reduction of amides at mild reaction conditions. Hiroshawa *et al* (Hirosawa, C.; Wakasa, N.; Takamasa, F. *Tetrahedron Lett*. 1996, *37*, 6749-6752) describe such catalytic reduction using the bimetallic catalysts RhRe, RhW, RhMo, RuRe and RuMo. Primary, secondary and tertiary amides were reduced to the corresponding amines, although the reaction conditions where still moderately harsh (100 bar at 160°C).

The present inventors have now found a novel method for the catalytic reduction of amides for the preparation of amines at mild reaction conditions to obviate the above drawbacks, i.e. at a temperature of below 200°C and a pressure of below 50 bar, by performing the said reduction reaction at the above mild reaction conditions with numerous bimetallic and trimetallic catalysts. Said experiments were performed by high-throughput experimentation, as e.g is described in EP 1001846. It was found that a catalyst, chosen from bimetallic and trimetallic catalysts of the group, consisting of ABC, AB, AC and BC, wherein:

A is a metal, chosen from the group, consisting of Co, Fe, Ir, Pt, Rh and Ru,

B is a metal, chosen from the group, consisting of Cr, Mo, Re and V, and,

C is a metal, chosen from the group, consisting of Cu, In and Zn, were surprisingly suitable for the reduction of amides at mild reaction conditions.

The reduction process is preferably performed with a heterogeneous catalyst. However, it is not necessary for the metals of the catalyst to be bound on the same support. E.g., one of the metals can be present on a carbon support, whereas another metal of the said catalyst can be present on e.g. a silica, titania or carbon support. The skilled person is aware of suitable supports for the envisaged catalysts. It is also possible to provide a metal of the catalyst on different supports. It is however preferred to provide the bimetallic and/or trimetallic catalyst on similar support material, although the different metals do not necessary have to be present on the very same support particles.

Preferably, the support is chosen from carbon, titania, amorphous silica-alumina and silica or a combination thereof.

It has been found that, using the catalysts as identified above, the catalytic reduction can even be performed at pressures of 30 bar or less, even at 15 bar or less. As will be explained below, the method according to the invention can also successfully be performed at a pressure of 10 bar, preferably between 5-10 bar, more preferably between 6-10 bar.

In a preferred embodiment, the reduction is performed in a continuous flow mode. Although according to the invention such a continuous flow mode can be performed in a liquid phase, it is preferably performed in gaseous phase, i.e. wherein one or more, preferably all of the reactants are passed in gaseous phase over the catalyst at the above-mentioned reaction conditions.

It is also been found that the above method according to the invention can successfully be performed at a temperature of 160°C or less, even at a temperature of 130°C or less. Also, it has been found that the method can be suitably performed at a temperature between 70-100°C, preferably around 80°C. “About” means that a deviation of 5°C is allowed.

However, in another preferred embodiment, the method of the invention is performed at batch mode reactions, e.g. wherein at least one but preferably all of the reactants are in a liquid phase, e.g. in solution, and contacted with the catalyst. At batch mode reaction conditions, the amide substrate is dissolved in an appropriate solvent, such as an acid, an ether, an ester or an alcohol, preferably an acid, preferably a Bronsted acid, more preferably an organic acid. The term "Bronsted acid" is well known in the art. Carboxylic acid is a preferred organic acid; most preferably, the organic acid comprises acetic acid. The solvent preferably has a pKa value of 5 or less, more preferably between 3 and 5. The preferred concentration of the acid, preferably organic acid, more preferably carboxylic acid and most preferably acetic acid is up to 1.0 M, preferably between 0.2 and 0.8 M, more preferably between 0.4 and 0.5 M. An internal standard, such as n-decane can be co-added to the reaction mixture for quantitative gas-chromatography analysis.

In batch mode reactions according to the invention, the addition of an additive may be favoured. The additive preferably comprises an acid, more preferably a Lewis acid, most preferably a boron-containing compound. The term "Lewis acid" is well known in the art. The substrate:additive ratio in the reaction mixture is preferably 4 or less, more preferably 2 or less, and most preferably between 0.9-1.1. During the reaction, the reaction mixture is preferably subjected to hydrogen pressures between 1 and 17 bar, more preferably between 5 and 10 bar. The reaction temperature is preferably between 90 and 140°C, more preferably between 100 and 130°C.

According to a preferred embodiment of the method of the invention, both for flow and batch mode reactions, the catalyst is chosen from the group, consisting of:

CoCu
FeIn
FeRe
IrMo
IrRe
IrV
MoIn
IrMoCu
IrReCu
IrReZn
IrVZn
PtMoCu
PtMoIn
PtMoZn

PtMo
PtRe
PtV
ReIn
RhCu
RhIn
RhMo
RhRe
RhV
RuRe
CoMoZn
CoReCu
CoReIn
CoVIn
FeCrIn
FeReCu
FeReIn
FeReZn
PtReCu
PtReIn
PtReZn
PtVIn
PtVZn
RhMoCu
RhMoIn
RhMoZn
RhReCu
RhReIn
RhReZn
RhMoZn
RhVIn
RuReCu
RuReZn

Preferably, the catalyst is chosen from the group consisting of PtRe, IrMo, IrRe, PtRe, PtV, RhRe, RhV, FeReIn, PtReCu, PtReIn, PtReZn, RhMoCu, RuReZn, PtMo, RhMo, RuRe, IrReZn and PtMoCu, most preferably more preferably from the group consisting of PtRe, PtReCu, PtReIn, FeReIn, PtMo, PtV, RhMo, PtMoCu, RhMoCu, and RuRe, even more preferably from the group, consisting of PtReCu, PtReIn, FeReIn, PtMo, PtV, RhMo, PtMoCu, RhMoCu, PtRe and RuRe, and most preferably from the group consisting of PtReCu, PtRe, PtMo IrReZn, PtMoCu and PtReIn. As will be shown in the Examples, the above-identified catalysts can effectively be used at the mild reaction conditions according to the invention.

In a further aspect, the invention relates to novel bi- or trimetallic catalysts for the reduction of amides to amines, chosen from the group, consisting of:

CoCu
FeIn
FeRe
IrMo
IrRe
IrV
MoIn
PtMo
PtRe
PtV
ReIn
RhCu
RhIn
RhV
CoMoZn
CoReCu
CoReIn
CoVIn
IrMoCu
IrReCu
IrReZn
IrVZn
PtMoCu
PtMoIn
PtMoZn
PtReCu
PtReIn
PtReZn
PtVIn
PtVZn
RhMoCu
RhMoIn
RhMoZn
RhReCu
RhReIn
RhReZn

FeCrIn
FeReCu
FeReIn
FeReZn
RhMoZn
RhVIn
RuReCu
RuReZn

more preferably from the group, consisting of IrMo, IrRe, PtRe, PtV, RhV, FeReIn, PtReCu, PtReIn, PtReZn, RhMoCu, RuReZn, PtMo, IrReZn and PtMoCu, preferably chosen from the group, consisting of FeReIn, PtReCu, IrReZn, PtMoCu, PtRe and PtReIn, and most preferably chosen from the group, consisting of PtReCu, PtRe, PtMo IrReZn, PtMoCu and PtReIn

The catalyst is preferably supported on a carrier, as outlined above.

In a further aspect, the invention relates to a method for the selection of at least one bi- or trimetallic catalyst, active in the reduction of amides into amines from a collection of bi- and/or trimetallic catalysts, comprising the steps of

A) preparing the catalysts on separate carriers,

B) loading the catalysts prepared in step A) in separate reactor vessels, the vessels having a parallel arrangement,

C) feeding and incubating the reactor vessels with an amide and hydrogen at identical conditions regarding at least one of the quantities, chosen from reaction time, temperature and pressure,

D) measuring the conversion of amides into amines in each reactor vessel,

E) selecting one or more of the catalysts, based on the measured conversion in step D).

This method allows the rapid identification and selection of active catalysts for the reduction of amides; a large range of different catalysts, having a different metal composition or ratio between the metals can be tested in the hydrogenation reaction, wherein the reaction conditions can be controlled and optimised. Thereto, the different catalysts are prepared on separate carriers, according to methods, known in the art. Preferably, in step A) the catalysts are prepared in parallel. The carriers can be the same for the catalysts to be tested, but may also be different in order to test and select an optimal catalyst-carrier combination. Then the prepared catalysts on a carrier are loaded in reactor vessels arranged in parallel , so that the reactions to be performed with the catalysts can be done simultaneously. Preferably, after feeding of the reactants, which is preferably performed in parallel in the reactor vessels; the reaction conditions, such as reaction time, temperature and pressure are identical for the catalysts to be tested. This way, the reactions are performed at identical conditions, so that relevant selections of active catalysts can be made. Once selected, the said catalyst can be further tested at reaction conditions that differ from the first selection process to identify one or more catalysts that are optimally suitable for the envisaged reaction conditions. Further, the selection method, that is preferably performed in a gaseous phase in flow mode, can be extrapolated to batch mode reaction for industrial processes for the preparation of amines at suitably mild reaction conditions.

The invention will now be further illustrated by way of non-limiting Examples and Figures.

Figures 1 to 5 refer to the results of amide reduction in flow mode.

Figure 1 shows a gas chromatogram of a reduction reaction of 1-acetylpyrrolidine with the catalyst RhReCu on a carbon carrier at a temperature of 160°C and a pressure of 10 bar. The metal molar ratio of the catalyst was 1:1:1.

Figure 2 and Figure 3 show the performance of silica and carbon supported catalysts, respectively, in the reduction of 1-acetylpyrrolidine at several different temperatures. In these examples, the metal molar ratio of the catalysts is 1:1 or 1:1:1 for bimetallic or trimetallic catalysts, respectively.

Figure 4 shows the amine (in this case, 1-ethylpyrrolidine) formation profile at 100°C and 130°C as a function of the catalyst composition (bi- and trimetallic catalysts from groups A and B-C). The grey intensity of the squares shows the amine yield. Only yields higher than 35% were plotted.

Figure 5, like Figure 4, shows 1-ethylpyrrolidine formation profile at 100°C and 130°C as a function of the catalyst composition but for the case of bimetallic catalysts from groups B and C. The grey intensity of the squares shows the amine yield. For clarity, only yields higher than 35% were plotted.

Figures 6-10 refer to results of amide reduction in batch mode, wherein figures 6-7 show the performance of trimetallic catalysts without and with the presence of BF_3 as additive, respectively, and wherein figures 8-9 show the performance of bimetallic catalysts without and with the presence of BF_3 as additive, respectively. Figure 10 shows the performance of physical-mixture and pre-made catalysts, as well as the importance of having more than one metal element in the catalyst composition.

EXAMPLES

Equipment and Conditions

Flow Reactions

The Nanoflow Equipment

The catalyst screening in flow mode was carried out in reactors, arranged in parallel, the Avantium's Nanoflow 2b (Avantium Technologies B.V., Netherlands), designed to allow gas and liquid feeds in trickle flow mode performed for this application. The equipment consists of 64 parallel reactors divided into four blocks of 16 reactors. Each reactor can be loaded with up to 200 mg of catalyst. Temperature can be varied independently on each block. The maximum temperature of the unit is 450-500°C, and the maximum pressure is 40 bar. An evaporator is placed up-stream of each reactor, so that controlled evaporation of liquid can take place.

Typical Run Conditions in Flow Mode

After an equipment-commissioning phase, and regarding the low vapour pressure of the chosen amide, the catalyst screening was carried out in an effective manner at temperatures higher than 70°C. Thus, the experiments were performed at temperatures of 70, 100, 130, and 160°C and at 10 bar of H_2. 1-Acetylpyrrolidine (substrate) and n-nonane (internal standard) were dissolved in diisopropyl ether forming a solution containing 0.25 wt% and 0.12 wt% of each component respectively. This solution was pumped through the 64 Nanoflow reactors at a rate of 0.8 ml/min, causing the amide (mass) flow to be equal to 0.0015 g/min. Under these conditions, the estimated vapour residence time in the catalyst bed (on each reactor, and per temperature) is shown in Table 1.

Table 1. Estimated 1-acetylpyrrolidine vapour residence time (RT) used during the screening for temperatures above 90°C.

T(°C)	R_T (s)
90	0.87
100	0.81
130	0.75
160	0.70

Analysis of the reactor effluent was done using an on-line gas-chromatograph.

Batch Reactions

The QS Equipment

The catalyst screening in batch mode was carried out in 96 pressure reactors, arranged in parallel: the Avantium QS Equipment (Avantium Technologies B.V., Netherlands). This equipment is divided into eight blocks of 12 reactors that operate in the so-called gas-on-demand system. This means that gas is added as soon as it is consumed by reaction, but no gas leaves the reactor at the exit. The maximum volume of each reactor is 7 ml; the maximum operating pressure for the blocks is 17 bar, and the maximum temperature is 140°C. Stirring is provided via magnetic stirring.

Typical Run Conditions in Batch Mode

A solution of 1-acetylpiperidine in acetic acid (2 ml, 0.8 mmol) containing n-decane (0.2 mmol) was added to a reactor containing 1 mol% of reduced PtV/titania. After purging, the hydrogen pressure was brought to 10 bar and the temperature to 130°C. GC analysis of the reaction mixture after 16 h showed formation of 1-ethylpiperidine as the sole product, having a yield of 20%.

Reaction Quantification

Amine quantification was performed via on-line and off-line GC for flow and batch reactions, respectively. In both cases, a suitable internal standard was added to the reaction mixture to allow quantification of amide consumption and product formation. The gas-chromatograph was mounted with a WCOT fused silica 10 m x 0.32 mm column (coating: CP-Volamine).

Catalyst Preparation and Handling

The two or three metals forming the catalysts were deposited onto the carrier using the techniques known by the skilled person, and

preferably by incipient wetness impregnation directly from aqueous solutions containing a mixture of all desired metal salts. The total metal loading was kept between 2 and 5 wt% for the catalysts.
Catalyst reduction can be attained by several reductants, like, and not limited to, $NaBH_4$, hydrazine, and hydrogen gas. Reduction by hydrogen gas was the preferred method, mainly in case of the reactions in flow mode. Catalyst reduction can be carried out in situ (immediately before addition of the reaction mixture) or beforehand. In the latter situation, it is recommended to store and handle the reduced catalyst under an oxygen free environment (e.g. a glove box under an atmosphere of nitrogen), to prevent metal oxidation.

It is recommended, but not essential, to have the support particle size between 50 and 1000 µm, preferably between 100 and 700 µm, and most preferably between 200 and 400 µm.

RESULTS

Catalyst Performance and Best Catalysts

Table 2 shows those catalysts that formed the amine in yields higher than 35% and at temperatures lower than 160°C. An alternative and more comprehensive visualisation of these data are presented in Figure 4 and Figure 5. Figure 4 shows that many of the active species result from combinations of Pt, Rh or Ir (Group A metals) with Re (followed by Mo and V from Group B).

Figure 5 shows the amine yield obtained with catalysts containing only metals from groups B and C. As can be seen, only combinations of Re and Mo with In formed 1-ethylpyrrolidine in yields higher than 35%, and at temperature of 130°C. This result bears the important message that the presence of a metal from Group A is important in the formation of active catalytic species. Figure 4 and Figure 5 also show that the support may also affect the catalyst activity.

Table 2. List of silica- and carbon-supported catalysts that formed amine in yields equal or higher than 35%. Values lower than 35% were left blank. The table is divided into bi- and trimetallic catalysts, and within each division the content is sorted by catalyst alphabetical order.

Support: Silica

Type	Catalyst	Amine (%) 100°C	Amine (%) 130°C
Bimetallic	CoCu		72
	FeRe		40
	IrMo	35	53
	IrRe	48	70
	PtRe	45	44
	PtV	36	49
	ReIn		61
	RhRe	77	36
	RhV	42	51
	RuIn		37
	RuRe	44	63
Trimetallic	CoMoZn		59
	CoReCu		41
	CoReIn		77
	FeCrIn		48
	FeReIn	68	76
	IrMoCu		39
	IrReCu		65
	IrReIn		59
	IrReZn		66
	PtMoCu		74
	PtReCu	79	76
	PtReIn	76	86
	PtReZn	37	81
	PtVIn		37
	PtVZn		74
	RhMoCu	60	85
	RhMoIn		54
	RhReCu		51
	RhReIn		56
	RhReZn		47
	RhVIn		46
	RuReCu		48
	RuReZn	39	75

Support: Carbon

Type	Catalyst	Amine (%) 100°C	Amine (%) 130°C
Bimetallic	FeIn		66
	IrMo		62
	IrRe		40
	IrV		52
	MoIn		55
	PtMo	69	46
	PtRe		58
	PtV	67	71
	ReIn		54
	RhCu		40
	RhIn		76
	RhMo	68	77
	RhRe	38	83
	RuRe	48	69
Trimetallic	CoVIn		54
	FeReCu		71
	FeReIn		73
	FeReZn		35
	IrReZn	57	84
	IrVZn		38
	PtMoCu	64	85
	PtMoIn		35
	PtMoZn		63
	PtReIn		86
	PtReZn		35
	RhMoCu	36	73
	RhMoIn		37
	RhMoZn		77
	RhReCu		83
	RhReZn		37
	RuMoZn		58
	RuReZn	41	58

Performance of Related Bi- and Trimetallic Catalysts

In a number of situations, trimetallic catalysts performed better than related bimetallic species. This synergistic effect has been noticed with carbon and silica supports, and Table 3 gives two examples of such situation (both with silica supported catalysts). Thus, in case of PtReIn/Silica and PtReCu/Silica, none of the related bimetallic species performed as well as the trimetallic ones. Conversely, the catalyst IrRe/Silica gave higher yields of amine than any other trimetallic species containing Ir and Re (i.e., IrReCu, IrReIn and IrReZn on silica, Table 6).

Table 3. Examples of the performance of bi- and trimetallic catalysts.

Catalyst [a]	Amine (%)	
	100°C	130°C
PtReIn	76	86
PtRe	45	44
PtIn	10	67
ReIn	60	70
PtReCu	79	76
PtRe	45	44
PtCu	>10	>10
ReCu	>10	27
IrReCu	26	65
IrReIn	15	59
IrReZn	24	66
IrRe	48	70

a) Support: silica.

Amide reduction in Batch Mode

Figures 6 to 9 show the performance of several bi- and trimetallic catalysts in the reduction of 1-acetylpiperidine at 10 bar and 130°C having acetic acid as solvent. The amount of catalyst on each reaction was kept constant at 5 mol% (calculated considering the total number of moles of metals on each catalyst). The ratio in front of each catalyst name refers to the molar fraction of each metal in the catalyst composition. The code for the first metal element is related to the type of salt used during the catalyst preparation:

FeNH4: Ammonium iron(III) citrate
FeNO3: $Fe(NO_3)_3.9H_2O$
IrCl4: $IrCl_4.H_2O$
IrNH4: NH_4IrCl_6
PtNH3: $(NH_3)_4Pt(NO_3)_2$
PtNO3: $Pt(NO_3)_2(H_2O)_2$
RhNH4: $(NH_4)_3RhCl_6$
RhNO3: $Rh(NO_3)_3$
RuCl3: $RuCl_3.H_2O$
RuNO: $Ru(NO)(NO_3)_x.(H_2O)_y$

Testing of physical mixtures

It is mentioned in the available literature, that the physical mixture Rh/C + Re/C constitutes one of the most active catalytic systems, capable to form 1-ethylpiperidine from 1-acetylpiperidine in 98% yield in a reaction carried out in 1,2-DME at 100 bar, 170°C, for 16 h and using 1 mol% of catalyst (Hirosawa, C.; Wakasa, N.;

Takamasa, F. *Tetrahedron Lett.* 1996, *37*, 6749-6752). The authors also claim that the performance of the physical mixture is equivalent to the pre-made Rh-Re/C catalyst. We decided to test these aspects under our reaction conditions (i.e. reduction of 1-acetylpiperidine for 16 h in batch mode at 10 bar, 130°C, 5 mol% of metal, and acetic acid as solvent). A similar test was carried out with catalyst 0.5:0.5 Pt(NO3)Re/Ti; we tested the performance of the physical mixture 0.5 Pt/Ti + 0.5 Re/C, and also the situation in which rhenium was not present. The results are shown in Figure 10.

As can be seen, unlike the case of 0.5:0.5 Pt(NO3) Re/Ti, the amine is formed in yields lower than 10%, showing the superiority of the catalyst system explored in the course of this work. Moreover, the described experiment points out the importance of having platinum and rhenium intimately mixed for the generation of a catalytic active system able to reduce the amide substrate under the applied mild reaction conditions.

CLAIMS

1. Method for the catalytic reduction of an amide for the preparation of an amine at a temperature of below 200°C and a pressure of below 50 bar, the catalyst being chosen from bimetallic and trimetallic catalysts of the group consisting of ABC, AB, AC and BC, wherein:
A is a metal, chosen from the group, consisting of Co, Fe, Ir, Pt, Rh and Ru,
B is a metal, chosen from the group, consisting of Cr, Mo, Re and V, and,
C is a metal, chosen from the group, consisting of Cu, In and Zn.

2. Method according to claim 1, wherein the catalyst is a heterogeneous catalyst on a support.

3. Method according to claim 2, wherein the support is chosen from carbon, silica, titania, silica-alumina or a combination thereof.

4. Method according to any of the preceding claims, wherein the pressure is 30 bar or less, preferably 15 bar or less.

5. Method according to claim 4, wherein the pressure is between 1-17 bar, preferably between 5-10 bar, most preferably between 6-10 bar.

6. Method according to any of the preceding claims, wherein the reduction is performed in continuous flow mode, preferably in a gaseous phase.

7. Method according to any of the preceding claims, wherein the temperature is 160° or less.

8. Method according to claim 7, wherein the temperature is 130°C or less.

9. Method according to claim 8, wherein the temperature is between 70°C-100°C, preferably around 80°C.

10. Method according to any of the claims 1-5, wherein the reduction is performed in batch mode, preferably in liquid phase.

11. Method according to claim 10, wherein the amide is dissolved in a Bronsted-acid.

12. Method according to claim 11, wherein the acid is an organic acid.

13. Method according to claim 12, wherein the organic acid is a carboxylic acid.

14. Method according to claim 13, wherein the carboxylic acid comprises acetic acid.

15. Method according to any of the claims 11-14, the acid having a pKa value of 5 or less, preferably between 3 and 5.

16. Method according to any of the preceding claims, the concentration of the acid being 1.0 M or less, preferably between 0.2 and 0.8 M, more preferably between 0.4 and 0.5 M.

17. Method according to any of the claims 10-16, the liquid phase comprising an additive comprising a Lewis acid.

18. Method according to claim 17, wherein the Lewis acid comprises a Boron compound.

19. Method according to claim 17 or 18, wherein the ratio amide:additive is 4 or less, preferably 2 or less, most preferably between 0.9 and 1.1.

20. Method according to any of the claims claim 10-19, wherein the temperature is between 90-140°C, preferably 100-130°C.

21. Method according to any of the preceding claims, wherein the catalyst is chosen from the group, consisting of:

CoCu
FeIn
FeRe
IrMo
IrRe
IrV
MoIn
PtMo
PtRe
PtrV
ReIn
RhCu
RhIn
RhM
RhRe
RhV
RuRe
CoMoZn
CoReCu
CoReIn
CoVIn
FeCrIn
FeReCu
FeReIn
FeReZn
IrMoCu
IrReCu
IrReZn
IrVZn
PtMoCu
PtMoIn
PtMoZn
PtReCu
PtReIn
PtReZn
PtVIn
PtVZn
RhMoCu
RhMoIn
RhMoZn
RhReCu
RhReIn
RhReZn
RhMoZn
RhVIn
RuReCu
RuReZn

22. Method according to claim 21, wherein the catalyst is chosen from the group, consisting of IrMo, IrRe, PtRe, PtV, RhRe, RhV, FeReIn, PtReCu, PtReIn, PtReZn, RhMoCu, RuReZn, PtMo, RhMo, RuRe, IrReZn and PtMoCu.

23. Method according to claim 22, wherein the catalyst is chosen from the group, consisting of IrReZn, PtReCu, PtReIn, FeReIn, PtMo, PtV, RhMo, PtMoCu, RhMoCu, PtRe, and RuRe.

24. Method according to claim 23, wherein the catalyst is chosen from the group, consisting of PtReCu, PtRe, PtMo IrReZn, PtMoCu and PtReIn.

25. Bi- or trimetallic catalysts for the reduction of amides to amines, chosen from the group, consisting of:

CoCu
FeIn
FeRe
IrMo
IrRe
IrV
MoIn
PtMo
PtRe
PtrV
ReIn
RhCu
RhIn
RhV
CoMoZn
CoReCu
CoReIn
CoVIn
FeCrIn
FeReCu
FeReIn
FeReZn
IrMoCu
IrReCu
IrReZn
IrVZn
PtMoCu
PtMoIn
PtMoZn
PtReCu
PtReIn
PtReZn
PtVIn
PtVZn
RhMoCu
RhMoIn
RhMoZn
RhReCu
RhReIn
RhReZn
RhMoZn
RhVIn
RuReCu
RuReZn

26. Bi- or trimetallic catalyst according to claim 25, the catalyst being chosen from the group, consisting of IrMo, IrRe, PtRe, PtV, RhV, FeReIn, PtReCu, PtReIn, PtReZn, RhMoCu, RuReZn, PtMo, IrReZn and PtMoCu.

27. Catalyst according to claim 26, chosen from the group, consisting of PtReCu, PtRe, PtMo IrReZn, PtMoCu and PtReIn.

28. Method for the selection of at least one bi- or trimetallic catalyst, active in the reduction of amides into amines, from a collection of bi- and/or trimetallic catalysts comprising the steps of:

A) preparing the catalysts on separate carriers,

B) loading the catalysts prepared in step A) in separate reactor vessels, the vessels having a parallel arrangement,

C) feeding and incubating the reactor vessels with an amide and hydrogen at identical conditions regarding at least one of the quantities, chosen from reaction time, temperature and pressure,

D) measuring the conversion of amides into amines in each reactor vessel,

E) selecting one or more of the catalysts, based on the measured conversion in step D).

29. Method according to claim 28, wherein in step C) the reaction time, temperature and pressure in the reactor vessel are similar for each reactor vessel.

30. Method according to any of the claims 28-29, wherein in step A) the catalysts are prepared on separate carriers in parallel.

31. Method according to any of the claims 28-30, wherein in step C) the reaction vessels are fed in parallel.

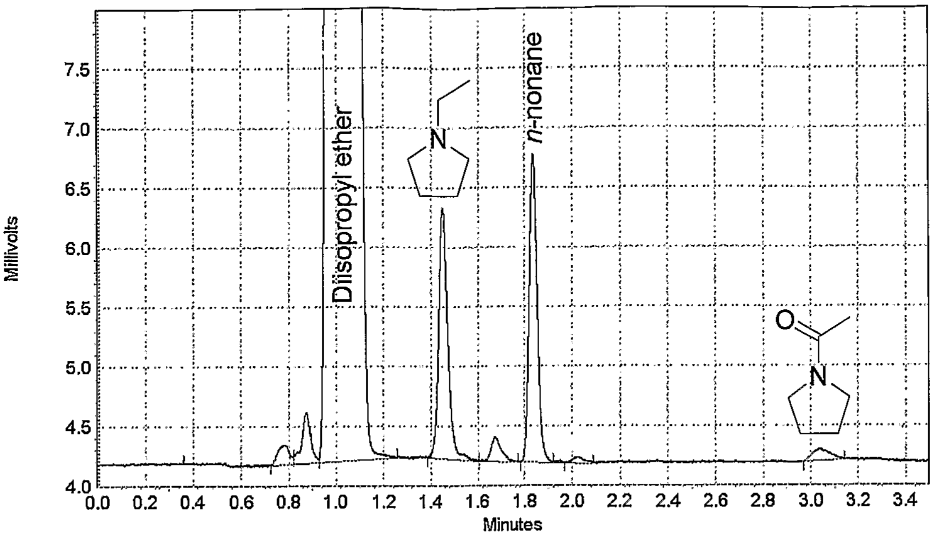

Millivolts
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
0.0
0.2
0.4
0.6
0.8
1.0
1.2
1.4
1.6
1.8
2.0
2.2
2.4
2.6
2.8
3.0
3.2
3.4
Minutes
Diisopropyl ether
N
n-nonane
O
N

Figure 1

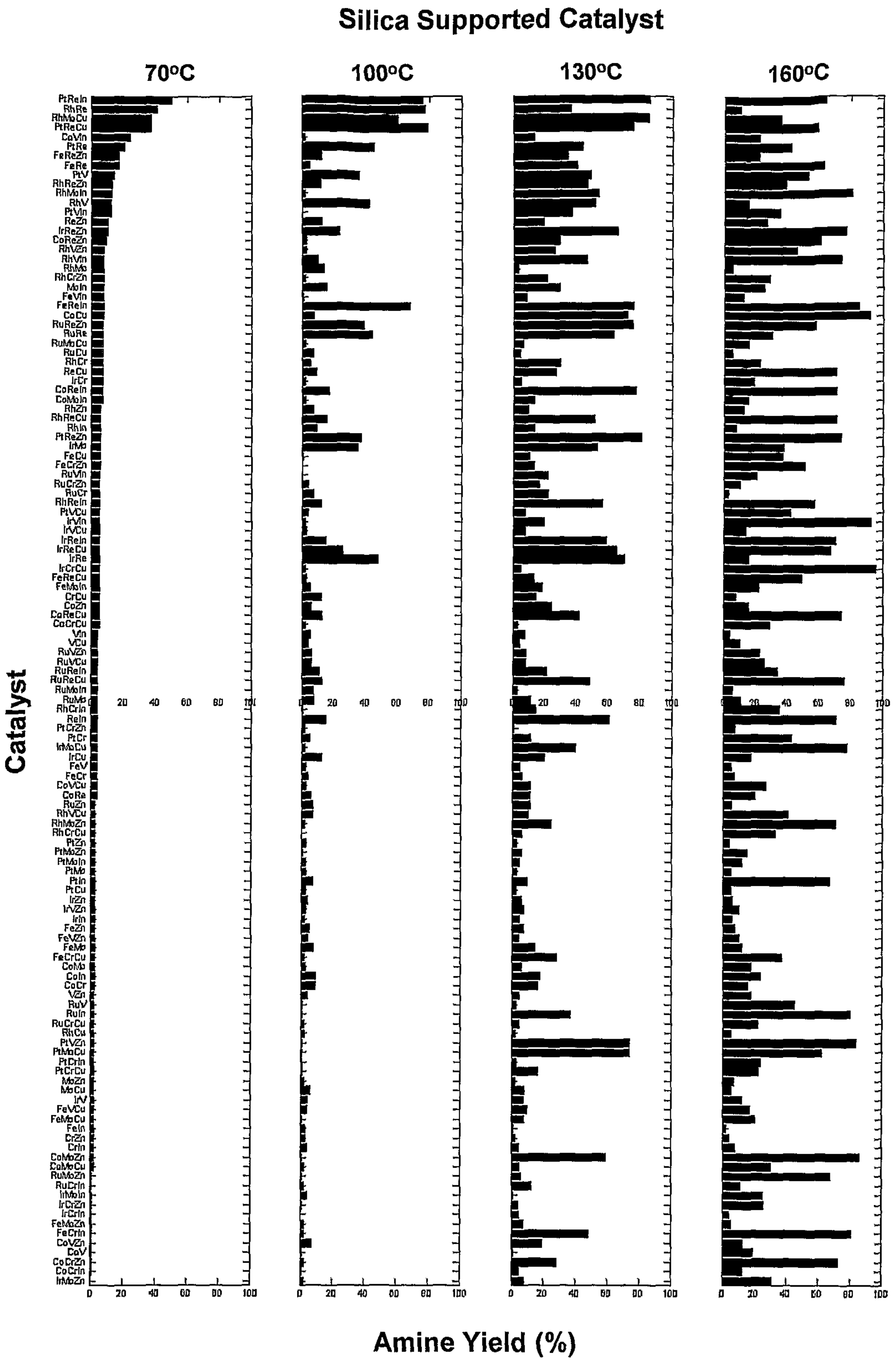
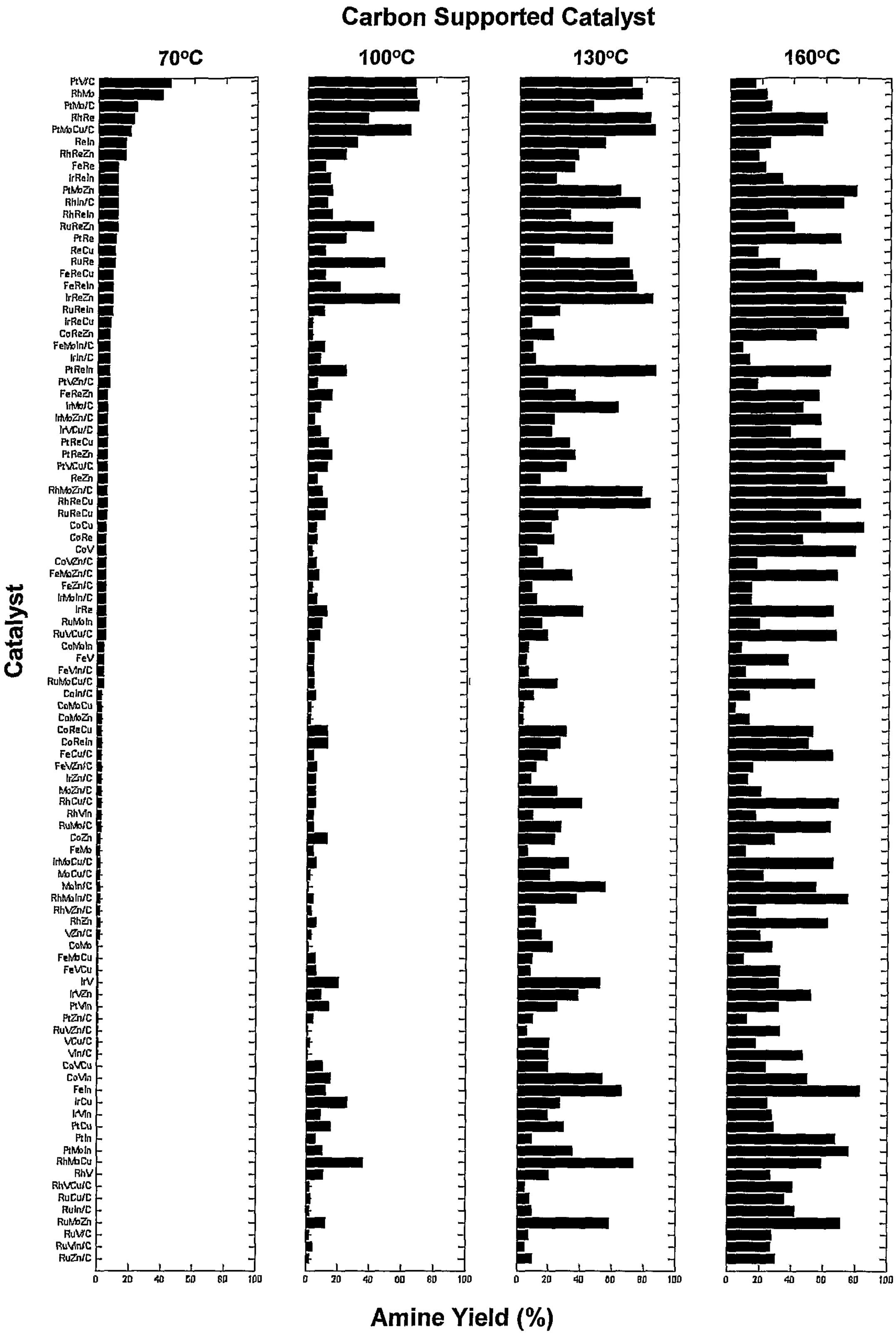

Silica Supported Catalyst
70°C
100°C
130°C
160°C
Catalyst
PtReIn
RhRe
RhMoCu
PtReCu
CoVIn
PtRe
FeReZn
FeRe
PtV
RhReZn
RhMoIn
RhV
PtVIn
ReZn
IrReZn
CoReZn
RhVZn
RhVIn
RhMo
RhCrZn
MoIn
FeVIn
FeReIn
CoCu
RuReZn
RuRe
RuMoCu
RuCu
RhCr
ReCu
IrCr
CoReIn
CoMoIn
RhZn
RhReCu
RhIn
PtReZn
IrMo
FeCu
FeCrZn
RuVIn
RuCrZn
RuCr
RhReIn
PtVCu
IrVIn
IrVCu
IrReIn
IrReCu
IrRe
IrCrCu
FeReCu
FeMoIn
CrCu
CoZn
CoReCu
CoCrCu
VIn
VCu
RuVZn
RuVCu
RuReIn
RuReCu
RuMoIn
RuMo
RhCrIn
ReIn
PtCrZn
PtCr
IrMoCu
IrCu
FeV
FeCr
CoVCu
CoRe
RuZn
RhVCu
RhMoZn
RhCrCu
PtZn
PtMoZn
PtMoIn
PtMo
PtIn
PtCu
IrZn
IrVZn
IrIn
FeZn
FeVZn
FeMo
FeCrCu
CoMo
CoIn
CoCr
VZn
RuV
RuIn
RuCrCu
RhCu
PtVZn
PtMoCu
PtCrIn
PtCrCu
MoZn
MoCu
IrV
FeVCu
FeMoCu
FeIn
CrZn
CrIn
CoMoZn
CoMoCu
RuMoZn
RuCrIn
IrMoIn
IrCrZn
IrCrIn
FeMoZn
FeCrIn
CoVZn
CoV
CoCrZn
CoCrIn
IrMoZn
0
20
40
60
80
100
Amine Yield (%)

Figure 2


Carbon Supported Catalyst
70°C
100°C
130°C
160°C
Catalyst
PtV/C
RhMo
PtMo/C
RhRe
PtMoCu/C
ReIn
RhReZn
FeRe
IrReIn
PtMoZn
RhIn/C
RhReIn
RuReZn
PtRe
ReCu
RuRe
FeReCu
FeReIn
IrReZn
RuReIn
IrReCu
CoReZn
FeMoIn/C
IrIn/C
PtReIn
PtVZn/C
FeReZn
IrMo/C
IrMoZn/C
IrVCu/C
PtReCu
PtReZn
PtVCu/C
ReZn
RhMoZn/C
RhReCu
RuReCu
CoCu
CoRe
CoV
CoVZn/C
FeMoZn/C
FeZn/C
IrMoIn/C
IrRe
RuMoIn
RuVCu/C
CoMoIn
FeV
FeVIn/C
RuMoCu/C
CoIn/C
CoMoCu
CoMoZn
CoReCu
CoReIn
FeCu/C
FeVZn/C
IrZn/C
MoZn/C
RhCu/C
RhVIn
RuMo/C
CoZn
FeMo
IrMoCu/C
MoCu/C
MoIn/C
RhMoIn/C
RhVZn/C
RhZn
VZn/C
CoMo
FeMoCu
FeVCu
IrV
IrVZn
PtVIn
PtZn/C
RuVZn/C
VCu/C
VIn/C
CoVCu
CoVIn
FeIn
IrCu
IrVIn
PtCu
PtIn
PtMoIn
RhMoCu
RhV
RhVCu/C
RuCu/C
RuIn/C
RuMoZn
RuV/C
RuVIn/C
RuZn/C
0
20
40
60
80
100
Amine Yield (%)

5 Figure 3

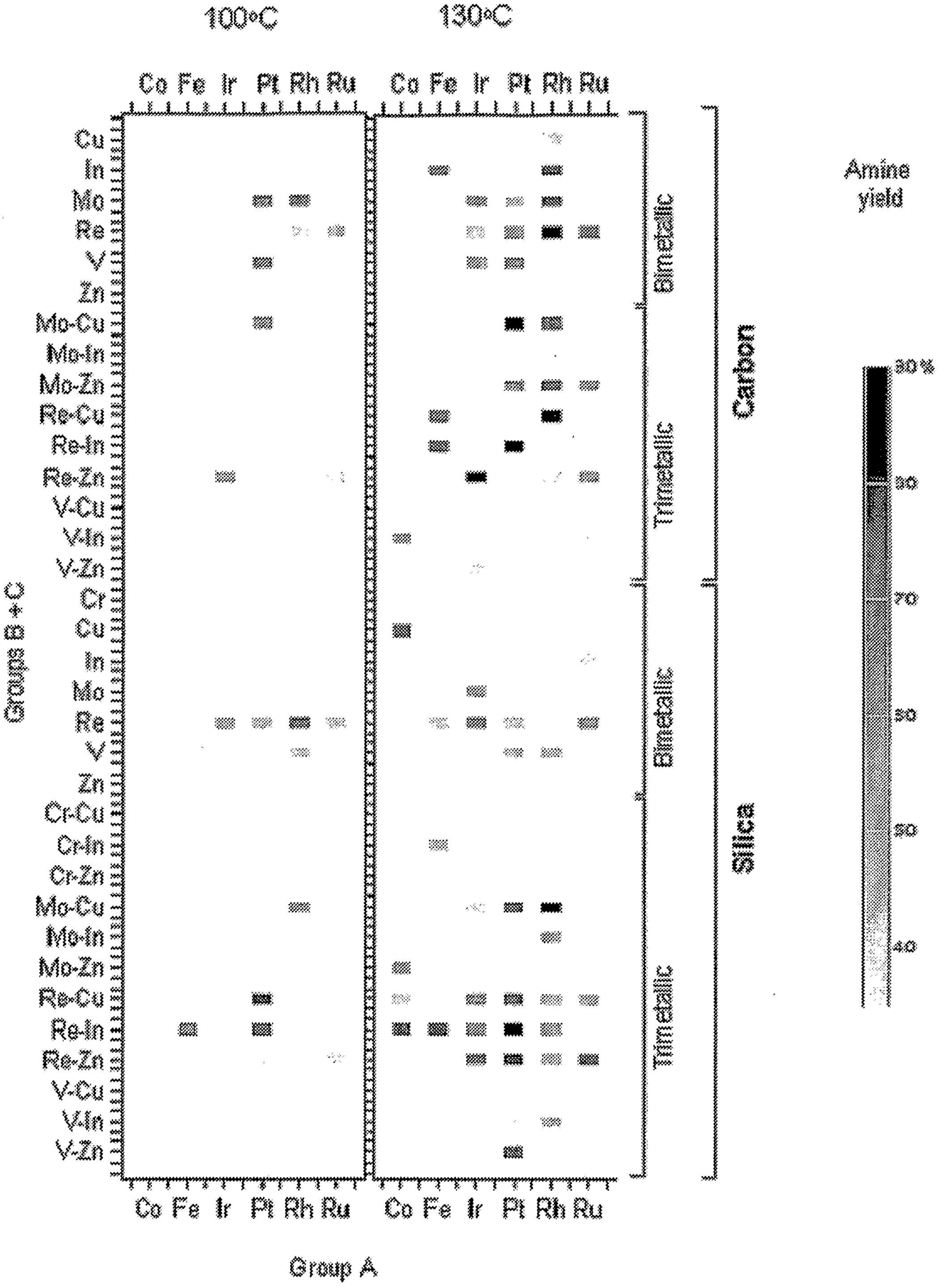

100°C
130°C
Co Fe Ir Pt Rh Ru
Co Fe Ir Pt Rh Ru
Cu
In
Mo
Re
V
Zn
Mo-Cu
Mo-In
Mo-Zn
Re-Cu
Re-In
Re-Zn
V-Cu
V-In
V-Zn
Cr
Cu
In
Mo
Re
V
Zn
Cr-Cu
Cr-In
Cr-Zn
Mo-Cu
Mo-In
Mo-Zn
Re-Cu
Re-In
Re-Zn
V-Cu
V-In
V-Zn
Groups B + C
Group A
Bimetallic
Trimetallic
Bimetallic
Trimetallic
Carbon
Silica
Amine yield
90 %
80
70
60
50
40

Figure 4

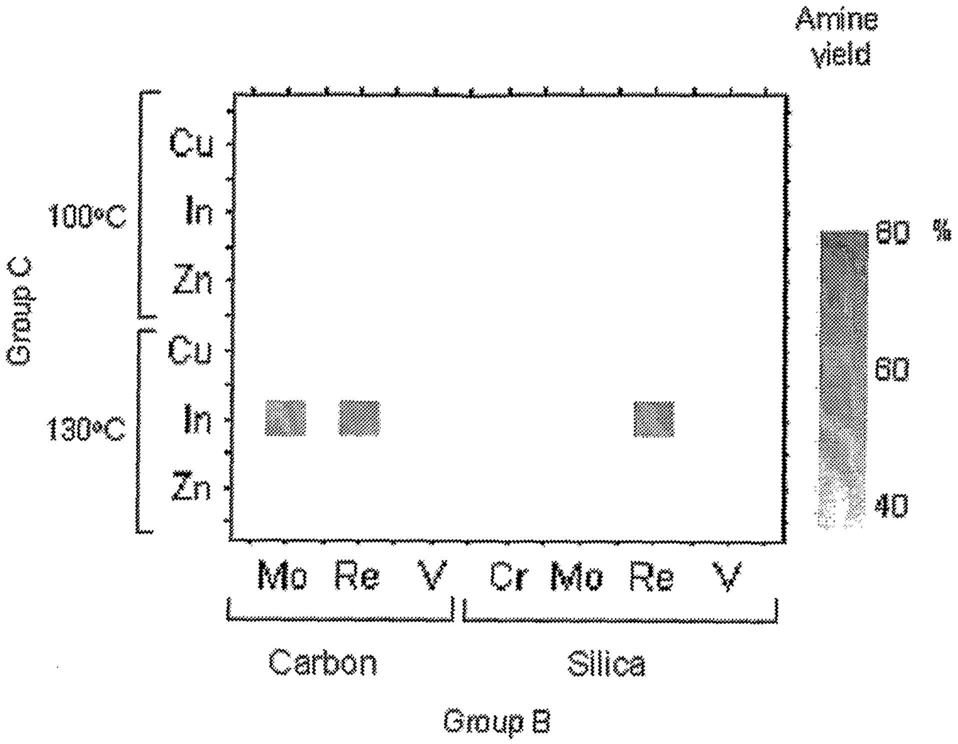

Amine yield
Group C
100°C
130°C
Cu
In
Zn
Cu
In
Zn
80 %
60
40
Mo
Re
V
Cr
Mo
Re
V
Carbon
Silica
Group B

Figure 5

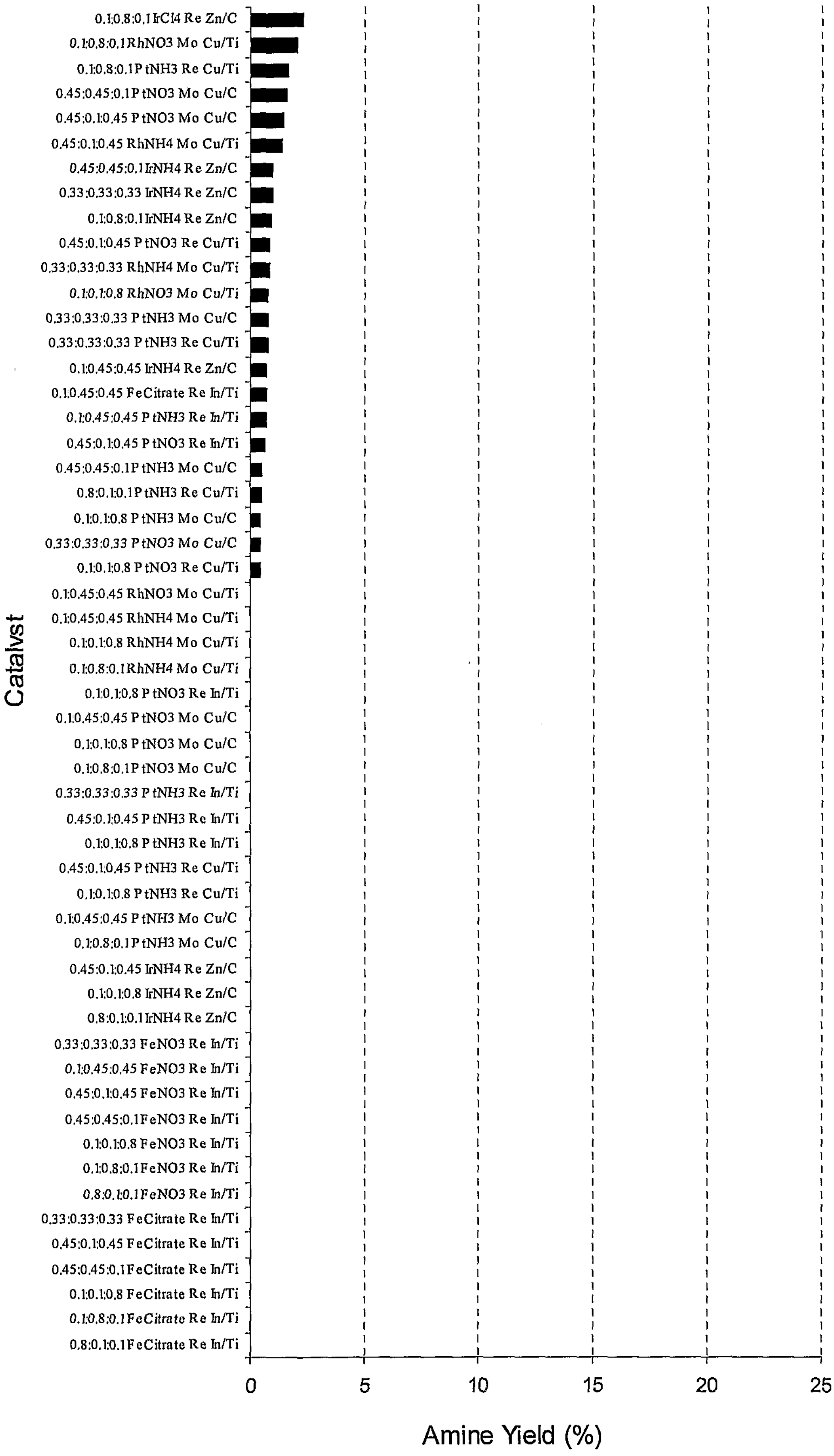

0.1:0.8:0.1IrCl4 Re Zn/C
0.1:0.8:0.1RhNO3 Mo Cu/Ti
0.1:0.8:0.1PtNH3 Re Cu/Ti
0.45:0.45:0.1PtNO3 Mo Cu/C
0.45:0.1:0.45 PtNO3 Mo Cu/C
0.45:0.1:0.45 RhNH4 Mo Cu/Ti
0.45:0.45:0.1IrNH4 Re Zn/C
0.33:0.33:0.33 IrNH4 Re Zn/C
0.1:0.8:0.1IrNH4 Re Zn/C
0.45:0.1:0.45 PtNO3 Re Cu/Ti
0.33:0.33:0.33 RhNH4 Mo Cu/Ti
0.1:0.1:0.8 RhNO3 Mo Cu/Ti
0.33:0.33:0.33 PtNH3 Mo Cu/C
0.33:0.33:0.33 PtNH3 Re Cu/Ti
0.1:0.45:0.45 IrNH4 Re Zn/C
0.1:0.45:0.45 FeCitrate Re In/Ti
0.1:0.45:0.45 PtNH3 Re In/Ti
0.45:0.1:0.45 PtNO3 Re In/Ti
0.45:0.45:0.1PtNH3 Mo Cu/C
0.8:0.1:0.1PtNH3 Re Cu/Ti
0.1:0.1:0.8 PtNH3 Mo Cu/C
0.33:0.33:0.33 PtNO3 Mo Cu/C
0.1:0.1:0.8 PtNO3 Re Cu/Ti
0.1:0.45:0.45 RhNO3 Mo Cu/Ti
0.1:0.45:0.45 RhNH4 Mo Cu/Ti
0.1:0.1:0.8 RhNH4 Mo Cu/Ti
0.1:0.8:0.1RhNH4 Mo Cu/Ti
0.1:0.1:0.8 PtNO3 Re In/Ti
0.1:0.45:0.45 PtNO3 Mo Cu/C
0.1:0.1:0.8 PtNO3 Mo Cu/C
0.1:0.8:0.1PtNO3 Mo Cu/C
0.33:0.33:0.33 PtNH3 Re In/Ti
0.45:0.1:0.45 PtNH3 Re In/Ti
0.1:0.1:0.8 PtNH3 Re In/Ti
0.45:0.1:0.45 PtNH3 Re Cu/Ti
0.1:0.1:0.8 PtNH3 Re Cu/Ti
0.1:0.45:0.45 PtNH3 Mo Cu/C
0.1:0.8:0.1PtNH3 Mo Cu/C
0.45:0.1:0.45 IrNH4 Re Zn/C
0.1:0.1:0.8 IrNH4 Re Zn/C
0.8:0.1:0.1IrNH4 Re Zn/C
0.33:0.33:0.33 FeNO3 Re In/Ti
0.1:0.45:0.45 FeNO3 Re In/Ti
0.45:0.1:0.45 FeNO3 Re In/Ti
0.45:0.45:0.1FeNO3 Re In/Ti
0.1:0.1:0.8 FeNO3 Re In/Ti
0.1:0.8:0.1FeNO3 Re In/Ti
0.8:0.1:0.1FeNO3 Re In/Ti
0.33:0.33:0.33 FeCitrate Re In/Ti
0.45:0.1:0.45 FeCitrate Re In/Ti
0.45:0.45:0.1FeCitrate Re In/Ti
0.1:0.1:0.8 FeCitrate Re In/Ti
0.1:0.8:0.1FeCitrate Re In/Ti
0.8:0.1:0.1FeCitrate Re In/Ti
Catalyst
0
5
10
15
20
25
Amine Yield (%)

Figure 6

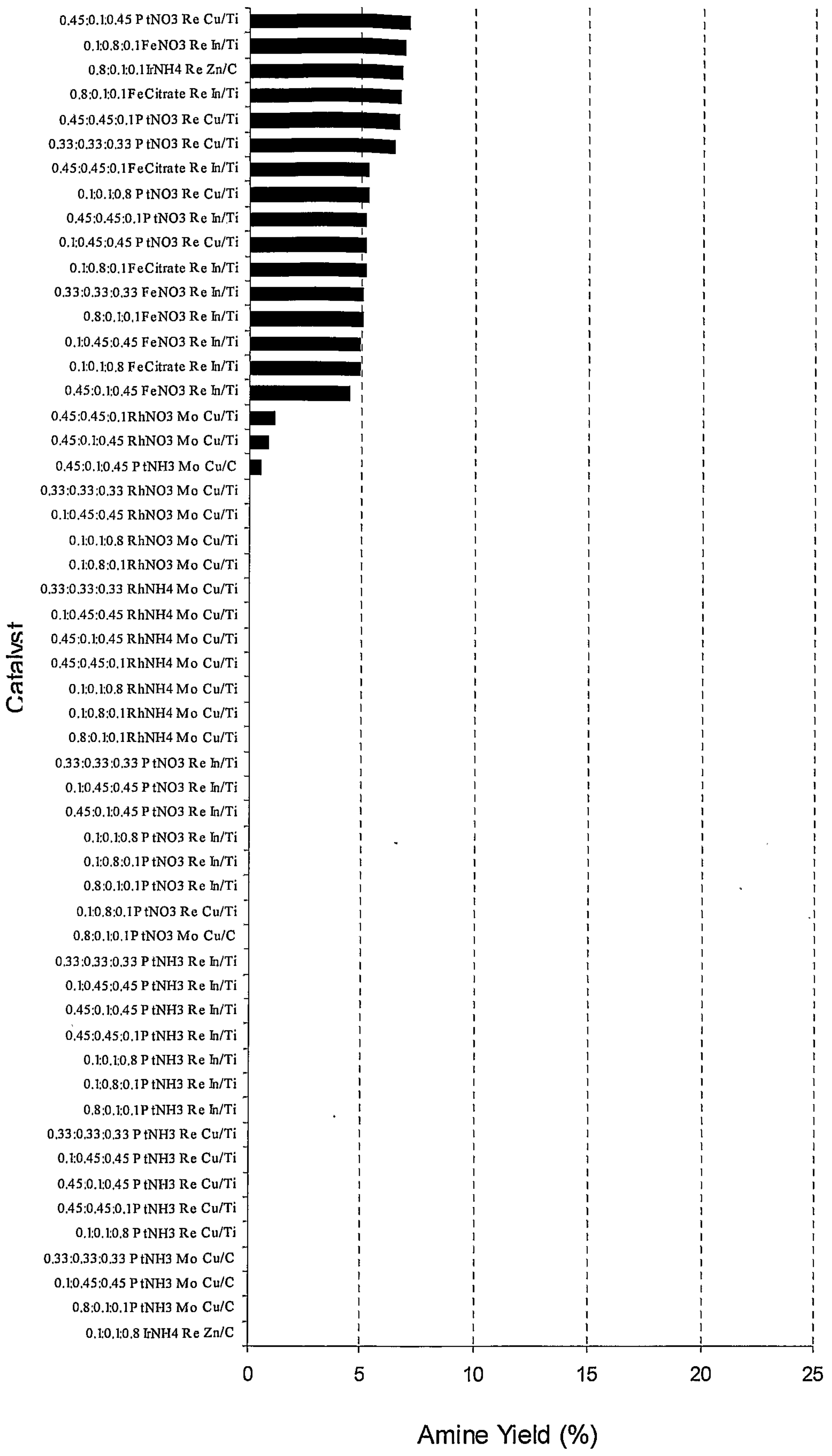
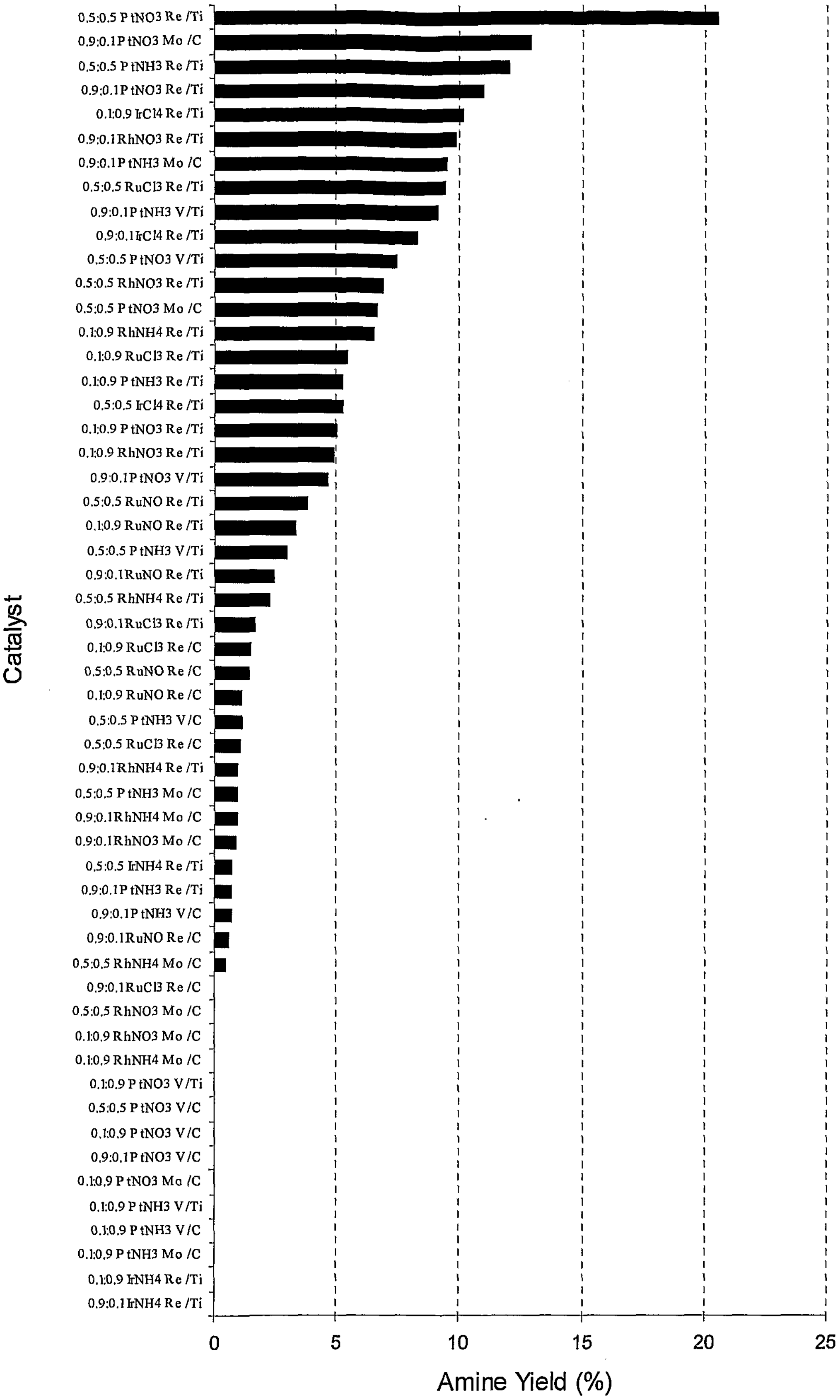

0.45:0.1:0.45 PtNO3 Re Cu/Ti
0.1:0.8:0.1FeNO3 Re In/Ti
0.8:0.1:0.1IrNH4 Re Zn/C
0.8:0.1:0.1FeCitrate Re In/Ti
0.45:0.45:0.1PtNO3 Re Cu/Ti
0.33:0.33:0.33 PtNO3 Re Cu/Ti
0.45:0.45:0.1FeCitrate Re In/Ti
0.1:0.1:0.8 PtNO3 Re Cu/Ti
0.45:0.45:0.1PtNO3 Re In/Ti
0.1:0.45:0.45 PtNO3 Re Cu/Ti
0.1:0.8:0.1FeCitrate Re In/Ti
0.33:0.33:0.33 FeNO3 Re In/Ti
0.8:0.1:0.1FeNO3 Re In/Ti
0.1:0.45:0.45 FeNO3 Re In/Ti
0.1:0.1:0.8 FeCitrate Re In/Ti
0.45:0.1:0.45 FeNO3 Re In/Ti
0.45:0.45:0.1RhNO3 Mo Cu/Ti
0.45:0.1:0.45 RhNO3 Mo Cu/Ti
0.45:0.1:0.45 PtNH3 Mo Cu/C
0.33:0.33:0.33 RhNO3 Mo Cu/Ti
0.1:0.45:0.45 RhNO3 Mo Cu/Ti
0.1:0.1:0.8 RhNO3 Mo Cu/Ti
0.1:0.8:0.1RhNO3 Mo Cu/Ti
0.33:0.33:0.33 RhNH4 Mo Cu/Ti
0.1:0.45:0.45 RhNH4 Mo Cu/Ti
0.45:0.1:0.45 RhNH4 Mo Cu/Ti
0.45:0.45:0.1RhNH4 Mo Cu/Ti
0.1:0.1:0.8 RhNH4 Mo Cu/Ti
0.1:0.8:0.1RhNH4 Mo Cu/Ti
0.8:0.1:0.1RhNH4 Mo Cu/Ti
0.33:0.33:0.33 PtNO3 Re In/Ti
0.1:0.45:0.45 PtNO3 Re In/Ti
0.45:0.1:0.45 PtNO3 Re In/Ti
0.1:0.1:0.8 PtNO3 Re In/Ti
0.1:0.8:0.1PtNO3 Re In/Ti
0.8:0.1:0.1PtNO3 Re In/Ti
0.1:0.8:0.1PtNO3 Re Cu/Ti
0.8:0.1:0.1PtNO3 Mo Cu/C
0.33:0.33:0.33 PtNH3 Re In/Ti
0.1:0.45:0.45 PtNH3 Re In/Ti
0.45:0.1:0.45 PtNH3 Re In/Ti
0.45:0.45:0.1PtNH3 Re In/Ti
0.1:0.1:0.8 PtNH3 Re In/Ti
0.1:0.8:0.1PtNH3 Re In/Ti
0.8:0.1:0.1PtNH3 Re In/Ti
0.33:0.33:0.33 PtNH3 Re Cu/Ti
0.1:0.45:0.45 PtNH3 Re Cu/Ti
0.45:0.1:0.45 PtNH3 Re Cu/Ti
0.45:0.45:0.1PtNH3 Re Cu/Ti
0.1:0.1:0.8 PtNH3 Re Cu/Ti
0.33:0.33:0.33 PtNH3 Mo Cu/C
0.1:0.45:0.45 PtNH3 Mo Cu/C
0.8:0.1:0.1PtNH3 Mo Cu/C
0.1:0.1:0.8 IrNH4 Re Zn/C
Catalyst
0
5
10
15
20
25
Amine Yield (%)

Figure 7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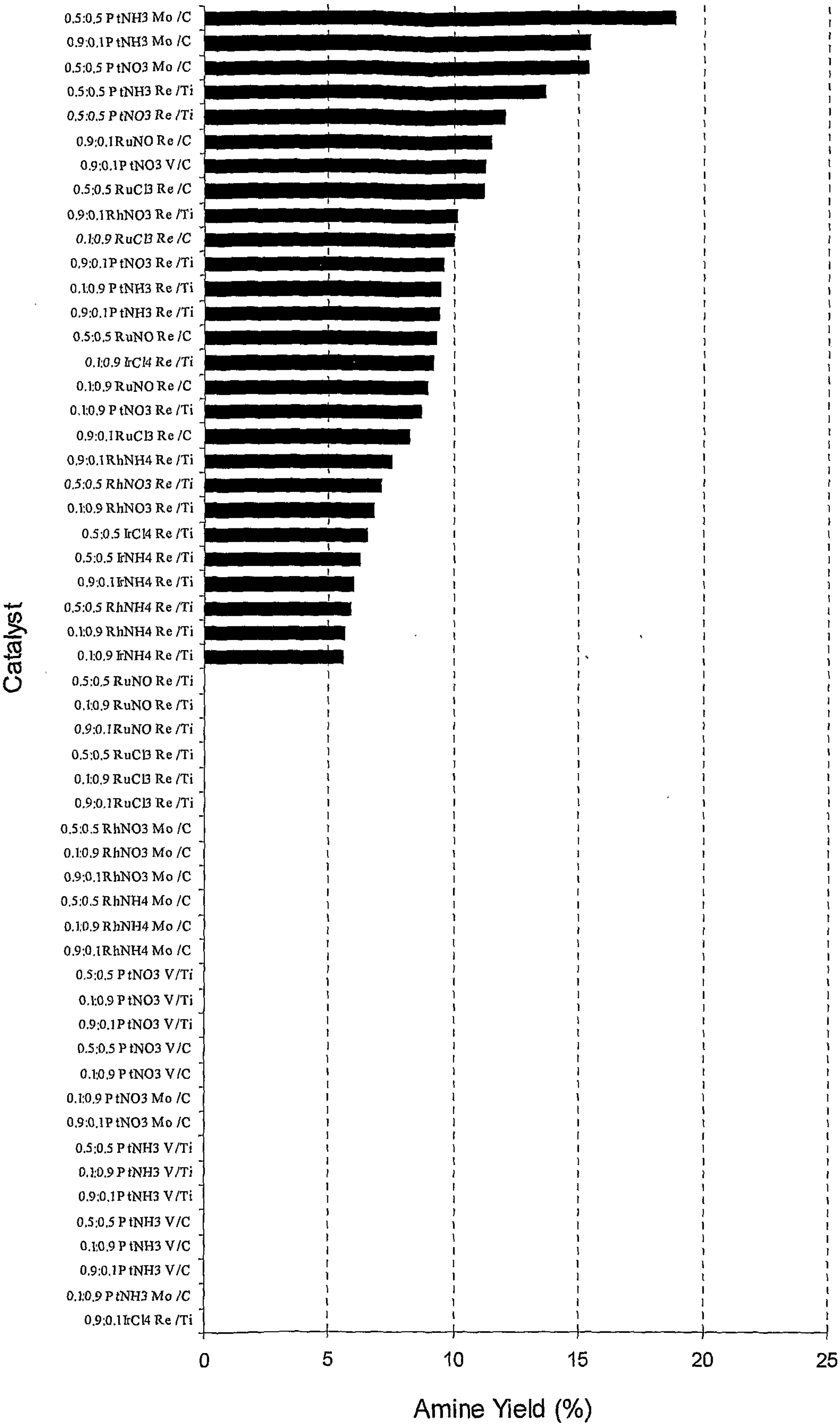
0.5:0.5 PtNH3 Re /Ti
0.9:0.1PtNO3 Re /Ti
0.1:0.9 IrCl4 Re /Ti
0.9:0.1RhNO3 Re /Ti
0.9:0.1PtNH3 Mo /C
0.5:0.5 RuCl3 Re /Ti
0.9:0.1PtNH3 V/Ti
0.9:0.1IrCl4 Re /Ti
0.5:0.5 PtNO3 V/Ti
0.5:0.5 RhNO3 Re /Ti
0.5:0.5 PtNO3 Mo /C
0.1:0.9 RhNH4 Re /Ti
0.1:0.9 RuCl3 Re /Ti
0.1:0.9 PtNH3 Re /Ti
0.5:0.5 IrCl4 Re /Ti
0.1:0.9 PtNO3 Re /Ti
0.1:0.9 RhNO3 Re /Ti
0.9:0.1PtNO3 V/Ti
0.5:0.5 RuNO Re /Ti
0.1:0.9 RuNO Re /Ti
0.5:0.5 PtNH3 V/Ti
0.9:0.1RuNO Re /Ti
0.5:0.5 RhNH4 Re /Ti
0.9:0.1RuCl3 Re /Ti
0.1:0.9 RuCl3 Re /C
0.5:0.5 RuNO Re /C
0.1:0.9 RuNO Re /C
0.5:0.5 PtNH3 V/C
0.5:0.5 RuCl3 Re /C
0.9:0.1RhNH4 Re /Ti
0.5:0.5 PtNH3 Mo /C
0.9:0.1RhNH4 Mo /C
0.9:0.1RhNO3 Mo /C
0.5:0.5 IrNH4 Re /Ti
0.9:0.1PtNH3 Re /Ti
0.9:0.1PtNH3 V/C
0.9:0.1RuNO Re /C
0.5:0.5 RhNH4 Mo /C
0.9:0.1RuCl3 Re /C
0.5:0.5 RhNO3 Mo /C
0.1:0.9 RhNO3 Mo /C
0.1:0.9 RhNH4 Mo /C
0.1:0.9 PtNO3 V/Ti
0.5:0.5 PtNO3 V/C
0.1:0.9 PtNO3 V/C
0.9:0.1PtNO3 V/C
0.1:0.9 PtNO3 Mo /C
0.1:0.9 PtNH3 V/Ti
0.1:0.9 PtNH3 V/C
0.1:0.9 PtNH3 Mo /C
0.1:0.9 IrNH4 Re /Ti
0.9:0.1IrNH4 Re /Ti
Catalyst
0
5
10
15
20
25
Amine Yield (%)

Figure 8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0.5:0.5 PtNO3 Mo /C
0.5:0.5 PtNH3 Re /Ti
0.5:0.5 PtNO3 Re /Ti
0.9:0.1RuNO Re /C
0.9:0.1PtNO3 V/C
0.5:0.5 RuCl3 Re /C
0.9:0.1RhNO3 Re /Ti
0.1:0.9 RuCl3 Re /C
0.9:0.1PtNO3 Re /Ti
0.1:0.9 PtNH3 Re /Ti
0.9:0.1PtNH3 Re /Ti
0.5:0.5 RuNO Re /C
0.1:0.9 IrCl4 Re /Ti
0.1:0.9 RuNO Re /C
0.1:0.9 PtNO3 Re /Ti
0.9:0.1RuCl3 Re /C
0.9:0.1RhNH4 Re /Ti
0.5:0.5 RhNO3 Re /Ti
0.1:0.9 RhNO3 Re /Ti
0.5:0.5 IrCl4 Re /Ti
0.5:0.5 IrNH4 Re /Ti
0.9:0.1IrNH4 Re /Ti
0.5:0.5 RhNH4 Re /Ti
0.1:0.9 RhNH4 Re /Ti
0.1:0.9 IrNH4 Re /Ti
0.5:0.5 RuNO Re /Ti
0.1:0.9 RuNO Re /Ti
0.9:0.1RuNO Re /Ti
0.5:0.5 RuCl3 Re /Ti
0.1:0.9 RuCl3 Re /Ti
0.9:0.1RuCl3 Re /Ti
0.5:0.5 RhNO3 Mo /C
0.1:0.9 RhNO3 Mo /C
0.9:0.1RhNO3 Mo /C
0.5:0.5 RhNH4 Mo /C
0.1:0.9 RhNH4 Mo /C
0.9:0.1RhNH4 Mo /C
0.5:0.5 PtNO3 V/Ti
0.1:0.9 PtNO3 V/Ti
0.9:0.1PtNO3 V/Ti
0.5:0.5 PtNO3 V/C
0.1:0.9 PtNO3 V/C
0.1:0.9 PtNO3 Mo /C
0.9:0.1PtNO3 Mo /C
0.5:0.5 PtNH3 V/Ti
0.1:0.9 PtNH3 V/Ti
0.9:0.1PtNH3 V/Ti
0.5:0.5 PtNH3 V/C
0.1:0.9 PtNH3 V/C
0.9:0.1PtNH3 V/C
0.1:0.9 PtNH3 Mo /C
0.9:0.1IrCl4 Re /Ti
Catalyst
0
5
10
15
20
25
Amine Yield (%)

Figure 9

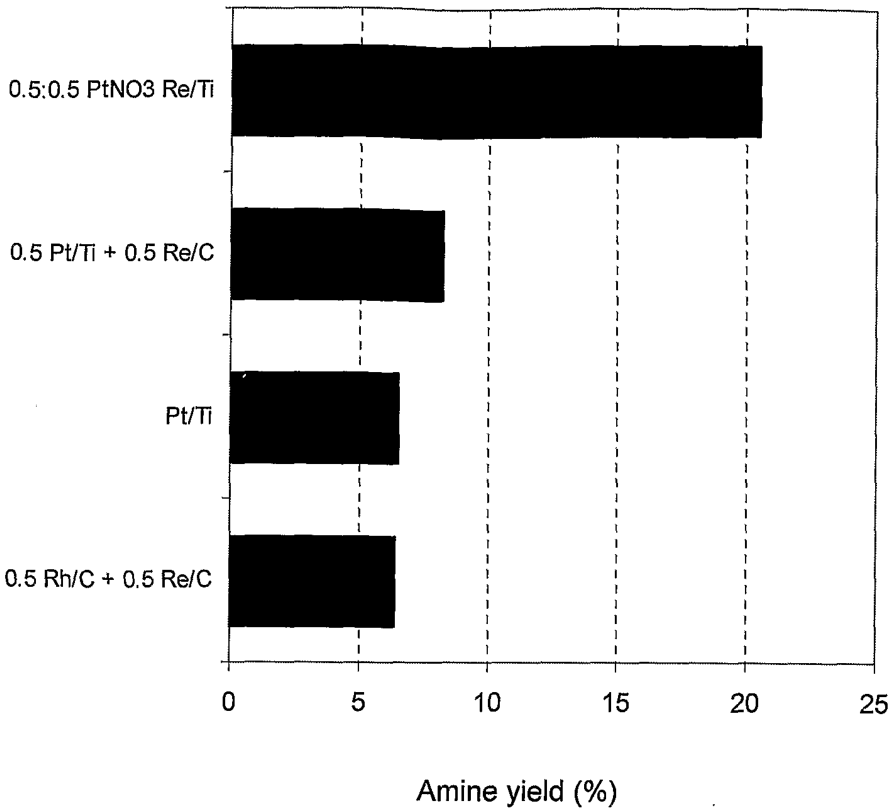
0.5:0.5 PtNO3 Re/Ti
0.5 Pt/Ti + 0.5 Re/C
Pt/Ti
0.5 Rh/C + 0.5 Re/C
0
5
10
15
20
25
Amine yield (%)

Figure 10

INTERNATIONAL SEARCH REPORT

International Application No
PCT/NL2004/000018

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07C209/50 C07D295/02 B01J23/26 B01J23/28 B01J23/36
B01J23/60 B01J23/62 B01J23/64 B01J23/80 B01J23/84
B01J23/86 B01J23/885 B01J23/89

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)
IPC 7 C07C C07D B01J

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

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

EPO-Internal, CHEM ABS Data, INSPEC, COMPENDEX

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 4 035 353 A (KANETAKA JUNICHI ET AL) 12 July 1977 (1977-07-12) claim 1 -----	1-25
X	HIROSAWA C ET AL: "Hydrogenation of Amides by the Use of Bimetallic Catalysts Consisting of Group 8 to 10, and Group 6 or 7 Metals" TETRAHEDRON LETTERS, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 37, no. 37, 9 September 1996 (1996-09-09), pages 6749-6752, XP004088084 ISSN: 0040-4039 cited in the application the whole document ----- -/--	1-27

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search 10 September 2004	Date of mailing of the international search report 01. 12. 2004
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 Veefkind, V

INTERNATIONAL SEARCH REPORT

International Application No
PCT/NL2004/000018

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 286 280 A (BP CHEM INT LTD) 12 October 1988 (1988-10-12) page 5, line 13 - line 18; claim 1 -----	1-27
A	US 4 772 750 A (HABERMANN CLARENCE E) 20 September 1988 (1988-09-20) claim 2 -----	1

INTERNATIONAL SEARCH REPORT

International application No.
PCT/NL2004/000018

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-27 (in part)

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

Invention 1: claims 1-27 (in part)

Claims 1-24 insofar the catalyst is chosen from A1B1C1, claims 25-27 if they comprise one or more catalysts A1B1C1. Claims 1-24 insofar the catalyst is chosen from A2B2, claims 25-27 if they comprise one or more catalysts A2B2. in which AxByCz are defined below

1.1. claims: 1-27 (in part)

Claims 1-24 insofar the catalyst is chosen from A1B1C1, claims 25-27 if they comprise one or more catalysts A1B1C1.

1.2. claims: 1-27 (in part)

Claims 1-24 insofar the catalyst is chosen from A2B2, claims 25-27 if they comprise one or more catalysts A2B2.

Inventions 2-38: claims 1-27 (in part)

Inventions 2-18: Claims 1-24 insofar the catalyst is chosen from A1B1C2, A1B1C3, A1B2C1, A1B2C2, A1B2C3, A1B3C1, A1B3C2, A1B3C3, A2B1C1, A2B1C2, A2B1C3, A2B2C1, A2B2C2, A2B2C3, A2B3C1, A2B3C2, A2B3C3, respectively.
claims 25-27 if they comprise one or more of these catalysts
.

Inventions 19-38: Claims 1-24 insofar the catalysts is chosen from A1B1, A1B2, A1B3, A2B1, A2B3, A1C1, A1C2, A1C3, A2C1, A2C2, A2C3, B1C1, B1C2, B1C3, B2C1, B2C2, B2C3, B3C1, B3C2, B3C3 respectively.
claims 25-27 if they comprise one or more of these catalysts
.

in which :
A1 = Co or Fe,
A2 = Ir, Pt, Rh or Ru,
B1 = Cr or Mo,
B2 = Re
B3 = V
C1 = Cu
C2 = In
C3 = Zn

Invention 39: claims 28-31

Method for the selection of at least one bi- or trimetallic catalyst

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/NL2004/000018

Patent document cited in search report		Publication date	Patent family member(s)			Publication date
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			JP	50089383	A	17-07-1975
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