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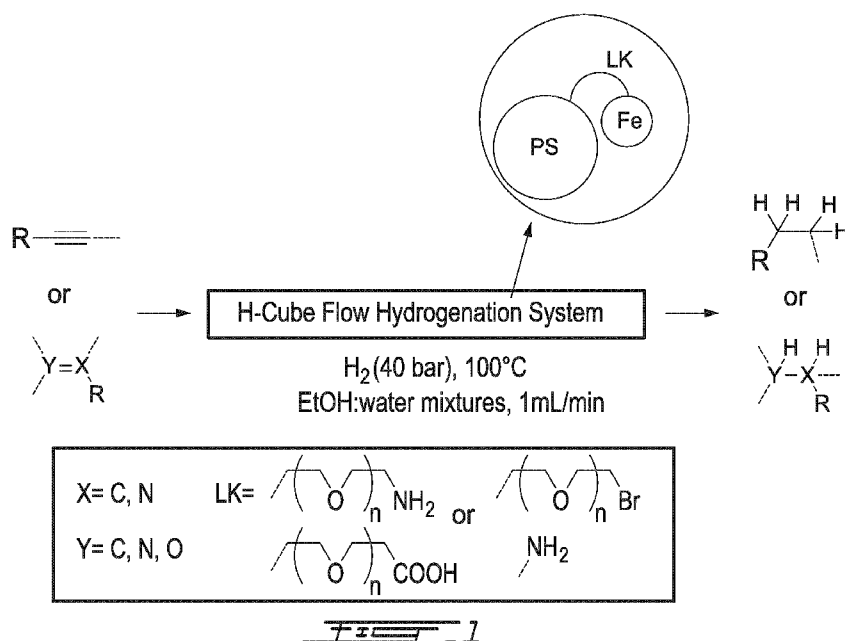
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[Continued on next page]

(54) Title: HYDROGENATION CATALYST



(57) Abstract: Described herein is a catalyst for hydrogenation of chemical compounds comprising an amphiphilic polymer resin with embedded iron nanoparticles and its use. Also described herein is a process for the manufacture of a chemical compound comprising hydrogenation of alkenes, alkynes, aromatic aldehydes and aromatic imines functionalities in the presence of a catalyst defined and a process for hydrogenation of chemical compounds using the catalyst comprising an amphiphilic polymer resin with embedded iron nanoparticles.

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HYDROGENATION CATALYST

FIELD OF INVENTION

[0001] The invention relates generally to a catalyst for selective hydrogenation of chemical compounds.

BACKGROUND OF THE INVENTION

[0002] Hydrogenation, known to chemists for decades, remains to this day among the most studied reactions. Its industrial applications span from petrochemical conversion to pharmaceuticals synthesis and there is a plethora of catalysts active for this transformation. However, hydrogenation reactions heavily rely on the chemistry of group 9 and 10 metals. These elements are very expensive and their price is highly volatile on the stock market. Additionally, regulations on their presence at ppm levels in drugs is highly regulated by organizations such as the FDA, because of their inherent toxicity. In response to both the economic and environmental concerns, research efforts have been made to improve recovery and limit leaching, or to seek group 9 and 10 metal-free solutions.

SUMMARY

[0003] The present invention describes a novel synthesis of a polymer supported Fe⁰ NPs (nano-particles) catalyst, which displays excellent reactivity for the selective hydrogenation of alkenes, alkynes, aromatic imines and aldehydes in a flow system. Further demonstrating the industrial applicability of the present catalyst, it is robust to water exposure, surpassing hydrogenation reaction yields for aqueous mixtures of known iron nanoparticle systems. This work represents for the first time the merger of three green chemistry themes: flow hydrogenation with H₂; water and ethanol as benign solvents, and the use of biologically benign heterogeneous iron as a catalyst. The present invention also reduces the aforesaid difficulties and disadvantages.

[0004] The present invention describes the embedding of the catalytically active Fe NPs into an amphiphilic polymer resin. Two beneficial effects on catalysis are observed from this functionalization. Firstly, the polymer increased the longevity or lifespan of the nanoparticles, which revealed catalytic activity in ethanol and water:ethanol mixtures, up to 9:1. Secondly, the Fe NPs polymer resin enabled use of the formed catalyst in a flow system. The chemical industry has widely accepted the use of flow systems to alleviate waste, work-up effort and scale-up problems, given the ease by which the pressurizing of flow systems can be performed.

[0005] We herein report for the first time the application to alkene and alkyne hydrogenation of three green chemistry themes—flow chemistry, water as a benign solvent, and the use of cheap, non-toxic and biologically-essential heterogeneous iron.

[0006] From one aspect, there is provided a catalyst comprising an amphiphilic polymer resin with embedded iron (Fe^0) nanoparticles for hydrogenation of chemical compounds.

[0007] Advantageously, the catalyst of the present invention increase longevity of the zero (0) oxidation state of the iron (Fe^0) nanoparticles in protic solvents.

[0008] In a further aspect, there is provided the use of a catalyst of the present invention for hydrogenation of chemical compounds.

[0009] In a further aspect, there is provided a process for the manufacture of a chemical compound comprising hydrogenation step in the presence of a catalyst of the present invention.

[0010] Alternatively, there is provided a process for hydrogenation of a chemical compound using a catalyst comprising an amphiphilic polymer resin that embedded iron (Fe^0) nanoparticles.

[0011] Advantageously, the process of the present invention enabled hydrogenation of chemical compounds using iron nanoparticles catalyst in a flow system using protic solvents. In one aspect of the present invention there is provided a hydrogenation catalyst comprising an amphiphilic polymer resin with a resin support; a linker attached to the support, wherein the linker comprises a functionalized group (FG) selected from COOH , NH_2 a halide or combinations thereof, and an embedded iron Fe^0 nanoparticles..

[0012] In accordance with a further aspect of the present invention, there is provided the catalyst herein described, wherein the iron is embedded in a lipophilic portion of the amphiphilic polymer.

[0013] In accordance with a yet further aspect of the present invention, there is provided the catalyst herein described, wherein the resin support is composed of polystyrene beads..

[0014] In accordance with a still further aspect of the present invention, there is provided the catalyst herein described, wherein the functional groups are attached to the polystyrene beads with a linker.

[0015] [0014] In accordance with a still further aspect of the present invention, there is provided the catalyst herein described, wherein the linker includes a spacer.

[0016] In accordance with another aspect of the present invention, there is provided the catalyst herein described, wherein the linker is polyethylene glycol derivative.

[0017] In accordance with a further aspect of the present invention, there is provided the catalyst herein described, wherein the spacer is polyethylene glycol.

[0018] In accordance with a further aspect of the present invention, there is provided the catalyst herein described, wherein the functional group is NH_2 .

[0019] In accordance with a further aspect of the present invention, there is provided the catalyst herein described, wherein the embedded Fe^0 nanoparticles are loaded at a concentration of from 1 to 15 mg Fe / g catalyst.

[0020] In accordance with a further aspect of the present invention, there is provided the catalyst herein described, wherein the concentration is 12 mg Fe / g catalyst.

[0021] In accordance with a further aspect of the present invention, there is provided the catalyst herein described, for hydrogenation of alkenes, alkynes, aromatic aldehydes and aromatic imines.

[0022] In another aspect of the present invention there is provided a process for the manufacture of a chemical compound comprising hydrogenation of alkenes, alkynes, aromatic aldehydes and aromatic imines functionalities in the presence of a catalyst defined herein

[0023] In a further aspect of the present invention there is provided a process for hydrogenation of chemical compounds using a catalyst comprising an amphiphilic polymer resin with embedded iron nanoparticles.

[0024] In accordance with another aspect of the present invention, there is provided the process for hydrogenation herein described, wherein the hydrogenation is carried out in a protic solvent.

[0025] In accordance with a further aspect of the present invention, there is provided the process for hydrogenation herein described, wherein the protic solvent is ethanol, water or a mixture thereof.

[0026] In accordance with a yet further aspect of the present invention, there is provided the process for hydrogenation herein described, wherein the hydrogenation is carried out under pressure between 10 to 60 bar.

[0027] In accordance with a still further aspect of the present invention, there is provided the process for hydrogenation herein described, wherein the hydrogenation is carried out in at a temperature between 60 to 100°C.

[0028] In accordance with a further aspect of the present invention, there is provided the process for hydrogenation herein described, wherein the catalyst is used in a flow system.

[0029] In accordance with another aspect of the present invention, there is provided the process for hydrogenation herein described, wherein the flow system is used with a flow rate between 0.5 ml/min to 2 ml/min.

BRIEF DESCRIPTION OF THE DRAWINGS

[0030] Further aspects and advantages of the present invention will become better understood with reference to the description in association with the following drawings in which:

[0031] Fig.1 represents a schematic view of flow hydrogenation with polymer supported iron (Fe^0) nano-particles according to one embodiment of the present invention;

[0032] Fig.2 represents a Catalyst prepared by thermal decomposition of $\text{Fe}(\text{CO})_5$ according to one embodiment of the present invention;

[0033] Fig.3 represents Catalyst prepared by black tea reduction of FeSO_4 according to one embodiment of the present invention;

[0034] Fig 4 A to F are TEM (transmission electron micrograph) images of various embodiments of the present invention: A) and B) FeNP@PS-PEG-NH_2 (thermal decomposition); C) FeNP@PS-PEG-NH_2 (tea reduction); D) FeNP@PS-PEG-Br (thermal decomposition); E) FeNP@PS-PEG-COOH (thermal decomposition); F) FeNP@PS-NH_2 (thermal decomposition);

[0035] Fig. 5 is a high resolution TEM image depicting lattice fringes of FeNP@PS-PEG-NH_2 according to one embodiment of the present invention; and

[0036] Fig. 6 is a five gram scale up of cinnamyl acetate demonstrating the ease of scale-up that the flow system provides, and also the robust nature of the catalyst in prolonged reactions according to one embodiment of the present invention.

DETAILED DESCRIPTION OF THE INVENTION

[0037] This invention is not limited in its application to the details of construction and the arrangement of components set forth in the following description or illustrated in the drawings. The invention is capable of other embodiments and of being practiced or of being carried out in various ways. Also, the phraseology and terminology used herein is for the purpose of description and should not be regarded as limiting. The use of “including”, “comprising”, or “having”, “containing”, “involving” and variations thereof herein, is meant to encompass the items listed thereafter as well as, optionally, additional items. In the following description, the same numerical references refer to similar elements. In the drawings, like reference characters designate like or similar parts.

[0038] In one embodiment, catalyst, use and process of the present invention comprise those wherein the following embodiments are present, either independently or in combination.

[0039] In one embodiment, there is provided a catalyst for hydrogenation of chemical compounds comprising an amphiphilic polymer resin supporting iron nanoparticles according to an embodiment of the invention is described herein with reference to hydrogenation of functional groups present on a chemical compound. In a further embodiment, there is provided a catalyst comprising an amphiphilic polymer resin that supports iron nanoparticles for hydrogenation of alkenes, alkynes, aromatic aldehyde and aromatic imine functionalities on a chemical compound.

[0040] The term “amphiphilic polymer” is defined herein as a polymer having at least one lipophilic portion and at least one hydrophilic portion.

[0041] The term “lipophilic” is defined herein as a material that has an affinity for and the ability to dissolve lipids. It is believed that Fe is found and protected in a lipophilic area of the amphiphilic polymer resin.

[0042] The term “embedded” is herein defined with regard to the iron NP as at least partially within the polymer resin.

[0043] In a further embodiment, there is provided an hydrogenation catalyst comprising an amphiphilic polymer resin with a resin support, a linker attached to the support, wherein the linker comprises a functionalized group selected from NH_2 ; COOH ; halogen such as Br, Cl, and I; SH; OH; OSO_3H ; $\text{OP}(\text{OH})_2$ and combinations thereof, and an embedded iron Fe^0 nanoparticles.

[0044] In a further embodiment, the amphiphilic polymer resin is composed of polystyrene beads having functional groups that coordinate iron. In another embodiment, the functional groups that coordinate iron are attached to the polystyrene beads by a linker. In a further embodiment, the linker coordinates iron. The present inventors have discovered that the embedded iron⁰ catalyst of the present invention is surprisingly stable even after numerous

hydrogenation reactions cycles. This stability is most likely due to the combination of elements of the catalyst but particularly the coordination of the iron⁰ with a functional group, and where in a preferred embodiment the functional group is with an amine.

[0045] In a further embodiment, the linker is polyethylene glycol derivative.

[0046] In a further embodiment, the functional groups that coordinate iron are NH₂ or CO₂H.

[0047] In a further embodiment, the functional group that coordinates iron is NH₂.

[0048] In a further embodiment, the functional group that coordinates iron is CO₂H.

[0049] In a further embodiment, the iron nanoparticles are loaded between 1.03 and 11.72 mg of iron nanoparticles for 1 g of polymer resin.

[0050] In another embodiment, there is provided a process for hydrogenation of chemical compounds using a catalyst comprising an amphiphilic polymer resin that supported iron nanoparticles. In a further embodiment, there is provided a process comprising an amphiphilic polymer resin that supported iron nanoparticles for hydrogenation of alkenes, alkynes, aromatic aldehyde and aromatic imine functionalities on a chemical compound.

[0051] In a further embodiment, the process is carried out in a protic solvent. In a further embodiment, the protic solvent is alcohol based solvent, water or a mixture thereof. In a further embodiment, the protic solvent is ethanol, water or a mixture thereof. In a further embodiment, the protic solvent is ethanol.

[0052] In a further embodiment, the process is carried out under pressure between 10 to 60 bar. In a further embodiment, the process is carried out under pressure between 20 to 50 bar. In a further embodiment, the process is carried out under pressure between 30 to 50 bar. In a further embodiment, the process is carried out under pressure between 35 to 45 bar.

[0053] In a further embodiment, the process is carried out at a temperature between 60 to 100°C.

[0054] In a further embodiment, the process is carried out in a flow system. In an alternate embodiment, the catalyst of the present invention is used in a flow system. In a further embodiment, the flow system is used with a flow rate between 0.5 ml/min to 2 ml/min. In a further embodiment, the flow system is used with a flow rate between 0.75 ml/min to 1.25 ml/min.

[0055] The amphiphilic polymer resin as a support for Fe NPs is illustrated in Figure 1. The resin is composed of a support resin such as polystyrene (PS) beads (average size 90 micron), functionalized with a variety of linkers (LK). These linkers are terminated with a functional

group (FG = NH₂; COOH; halogen such as: Br, Cl, I; SH; OH; OSO₃H; OP(OH)₂ and combinationals thereof) and may optionally contain a polyethylene glycol (PEG) spacer. It is the linker with the support that affords the amphiphilic polymer resin its duality of hydrophobicity and hydrophilicity. These polymer resins were purchased and used as is. Alternate support resins include polyalkylene polymers, halogenated polymers, polyesters, , polyamides, cellulose derived polymers sulfonated polymers and combinations thereof.

[0056] The linker spacers include: ethylene glycol, diethylene glycols; triethylene glycol; propylene glycol; 1,3-propanediol; 1,4-butanediol (examples of which include 2-methoxyethanol, 2-ethoxyethanol, 2-propoxyethanol and 2-butoxyethanol) and combinations thereof. The preferred spacer is a PEG with a molecular weight of between 1000 and 5000 Da, where in a preferred embodiment the molecular weight of the PEG is 3000 Da.

[0057] The Fe NPs were synthesized in situ, in the presence of the resin, either by thermal decomposition of Fe(CO)₅ (Figure 2) or through the greener black tea reduction of FeSO₄ (Figure 3).

[0058] The second synthesis (greener black tea reduction) was only performed with PS-PEG-NH₂ polymer resin. The resulting materials were characterized by transmission electron microscopy (TEM) of slices of the materials obtained through microtomy. This method allowed visualizing the Fe NPs inside the matrix (Figure 4). Once again, PS-(PEG)-NH₂ afforded good results. Well dispersed and monodispersed approximate 5 nm Fe NPs were observed in the case of thermal decomposition (Figure 4, A and B). At high resolution, regular lines evince the crystal lattice of FeNP@PS-PEG-NH₂ (Figure 5).

[0059] The lines are separated by 2.45 Å, which is in good agreement with the interatomic spacing calculated to be 2.49 Å, from either base-centered cubic (bcc) or face-centered cubic (fcc) iron. These are very different from spacing measured for iron oxides.

[0060] Figure 5 demonstrates the Fe(0) nature of the nanoparticles. Fewer particles were visible when using the tea reduction method, most of them having again a size of ~5nm (Figure 4 C).

[0061] With both PS-(PEG)-Br and PS-(PEG)-COOH, the thermal decomposition produced larger particles between 15 and 20 nm for Br and 5 and 20 nm for COOH. PS-NH₂ afforded localized clusters of particles between 5 and 10 nm. Large sections of the matrix did not contain Fe NPs. In no sample tested was there any iron oxide layer at the surface of the particles, as we had observed in past work for iron. This demonstrates a very high stability of this system toward oxidation.

[0062] In addition to TEM, the materials were characterized by ICP-MS (Table 1). The highest loading was obtained with FeNP@PS-PEG-NH₂ with 11.72 mg Fe/g catalyst (entry 1), confirming the observation made by TEM. Interestingly, thermal decomposition was a more efficient method than tea reduction as the latter produced material with about 5 times less iron content (entry 2). In fact, the reaction conditions of thermal decomposition, which occurs at 180°C, are more favorable to iron diffusion, than those of tea reduction (room temperature). A change in the terminal group, from NH₂ to COOH (entry 3) or Br (entry 4) affected loading, although all PEGylated systems could successfully immobilize Fe NPs. Amines are found to be the best Fe NPs stabilizers, where they used notably in the original synthesis of fFe NPs by thermal decomposition, and are better ligands than either -Br or -COOH functionalized polymers. Removal of the PEG spacer while keeping the amine functionality (entry 5) had a drastic effect on loading with a 10 fold drop in Fe content, perhaps because the extra oxygen atoms help to coordinate iron, helping seed the formation of nanoparticles.

[0063] These polymer supported-Fe NPs were then used in both flow and batch reactors for hydrogenation of styrene in ethanol (Table 1). Though all polymer systems provided quantitative yields in flow, only the FeNP@PS-PEG-NH₂ generated by thermal decomposition provided a moderate yield in batch conditions (entry 1).

Table 1 - Iron loading and styrene hydrogenation yield of polymer-immobilized Fe NPs

Entry	Composition	Fe Loading ^a	Flow Yield (%) ^b	Batch (%) ^c	Yield
1	FeNP@PS-PEG-NH ₂ ^d	11.72	100	44%	
2	FeNP@PS-PEG-NH ₂ ^e	2.55	100	13%	
3	FeNP@PS-PEG-COOH ^d	5.01	100	24%	
4	FeNP@PS-PEG-Br ^d	4.05	100	8%	
5	FeNP@PS-NH ₂ ^d	1.03	100	19%	

^a mg Fe/g catalyst measured by ICP

^b reaction conditions: 100°C, 40 bar, 1 mL/min through 300 mg catalyst, 0.05M Styrene in EtOH

^c reaction conditions: 100°C, 40 bar, 0.005M Styrene in EtOH (17 mL), 6 hours

^d Fe nanoparticles generated by thermal decomposition of Fe(CO)₅

^e Fe nanoparticles generated by reduction of black tea-extract reduction of FeSO₄

[0064] Selective hydrogenation of styrene's olefinic double bond served as a model reaction for the optimization of reaction conditions (Table 2). A pressure of 40 bar H₂, temperature of 100°C and flow rate of 2 mL/min constituted the benchmark conditions, achieving a 92% conversion of styrene to ethyl benzene (entry 1). Increasing the pressure to 60 bar pushed the yield to 95% (entry 2). Decreasing the flow rate to 1mL/min afforded a quantitative yield, by improving residence time on the catalyst (entry 4). From there, decreasing the pressure to 10 bar dropped the yield to 54% (entry 6). Decreasing the temperature (entries 7 and 8) slightly decreased the yield. Interestingly, the reaction still proceeded with a 95% yield in a 50:50 mixture of water and ethanol (entry 10), and an 88% yield in a 10:90 mixture of ethanol and water (entry 11).

[0065] This result contrasts with what is observed when using iron/iron oxide core-shell where the 50:50 mixture did affect drastically catalysis. It is believed that increased stability of the Fe NPs in an almost pure water environment is caused by the embedding of the particles inside lipophilic pockets of the polymers, preventing water oxidation of their surface of the iron NPs.

[0066] These optimized conditions of the one embodiment of the present invention also afforded quantitative yields for FeNP@PS-PEG-COOH, FeNP@PS-PEG-Br, FeNP@PS-NH₂ (Table 1), all generated by thermal decomposition of Fe(CO)₅ as well as FeNP@PS-PEG-NH₂ generated by black tea extract reduction of FeSO₄. At least for the nanoparticles generated by thermal decomposition of Fe(CO)₅, we assume all reduction to happen by iron because 1) the

purity of the reagent was 99.999% and 2) ICP-MS of the digested sample detected no nickel, a common contaminant of iron known to be active for hydrogenation. We also assume the mechanism to be heterogeneous because ICP-MS analysis of the product solution indicated only 0.007 ppm soluble iron.

Table 2 - Screening of hydrogenation conditions^a

Entry	Pressure (bar)	Temp (°C)	Flow (ml/min)	Yield (%)
1	40	100	2	92
2	60	100	2	95
3	20	100	2	85
4	40	100	1	100
5	40	100	0.5	94
6	10	100	1	54
7	40	80	1	95
8	40	60	1	94
9 ^b	40	100	1	100
10 ^c	40	100	1	95
11 ^d	40	100	1	88
12 ^e	40	100	1	0

^a Reaction Conditions: Styrene (0.05 M) in EtOH was passed through 250 mg of FeNP@PS-PEG-NH₂ resin (generated by thermal decomposition of Fe(CO)₅).

^b A mixture of EtOH and H₂O (1:99 v:v) was used as the solvent.

^c A mixture of EtOH and H₂O (50:50 v:v) was used as the solvent.

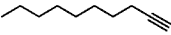
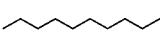
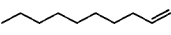
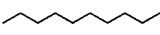
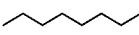
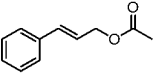
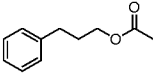
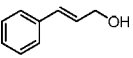
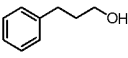
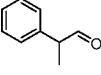
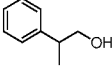
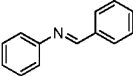
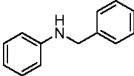
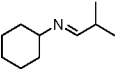
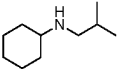
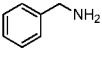
^d A mixture of EtOH and H₂O (10:90 v:v) was used as the solvent.

^e No catalyst was used

[0067] The functional group tolerance and selectivity are herein described (Table 3). The catalyst system is very active for aromatic alkene hydrogenation (entries 1, 5, 16 and 17). Aliphatic alkenes (entry 3) and alkynes, either internal (entry 4) or terminal (entry 2), are moderately active. With slightly harsher conditions, however, such substrates can be converted in higher yields (Table 4). The system demonstrates a selectivity for C-C double and triple bonds over ketones (entries 10 and 11), esters (entry 5), nitriles (entry 14), arenes (entries 1, 5, 6, 15, and 16). The system also selected against aliphatic aldehydes (entry 9) and imines (entry 13).

When activated by an aromatic ring, however, aldehydes (entries 7 and 8) and imines (entry 12) could be converted. With such mild conditions, we did not have to worry about reductive elimination of aryl halides (entry 15) or reduction of nitro groups (entry 16) opening the doors for selective synthesis. Given the sensitivity of aryl halides and aryl nitro groups to reducing conditions, these two examples of chemoselectivity make the presented system very interesting from a synthetic viewpoint.

Table 3 - Functional group tolerance and selectivity^a

Entry	Substrate	Product	Yield:Selectivity (%:%)
1			100:100
2			73:91
3			67:100
4			79:87
5			98:100
6			100:100
7			35:96
8 ^b			85:98
9			0:N/A
10			0:N/A
11			100:100
12			100:100
13			0:N/A
14			0:N/A

15			99:100
16			84:100
17			0:N/A

^a Reaction Conditions: 0.05M substrate in EtOH, 100°C, 40 bar H₂, 1 mL/min, 300 mg FeNP@PS-PEG-NH₂

^b Reaction Conditions: 0.05M substrate in EtOH, 100°C, 60 bar H₂, 1 mL/min 300 mg FeNP@PS-PEG-NH₂

Table 4 - Reactivity of variously substituted alkenes^a

Entry	Substitution	Substrate	Yield (%)
1			90
2			87
3			83
4			14
5			6
6			trace

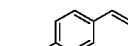
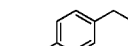
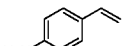
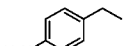
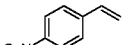
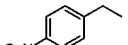
^a Reaction conditions: 40 bar H₂, 100°C, 0.5 ml/min, 0.05 M substrate in EtOH, (residence time 116 seconds)

[0068] In an effort to examine the reactivity of variously substituted, non-functionalized alkenes we used slightly harsher conditions (Table 4) because such alkenes, when not activated by an aromatic ring, do not react as quickly (Table 3). Mono-substituted alkenes (entry 1) proceeded in good yields. Cis alkenes (entry 2) reacted slightly faster than trans alkenes (entry 3). Geminal substitution is more problematic (entry 4). Considering this, it is not surprising that tri-substituted alkenes (entry 5) reacted exceptionally slowly and tetra-substituted alkenes provided only trace amounts of product (entry 6).

[0069] For the sake of comparing the reactivity of various styrene derivatives, we used milder reaction conditions in order to achieve greater separation of chemical yields (Table 5). This comparison suggests that sterics affect reactivity more than electronics. For example, the difference in yield between ortho (entry 6, 35%) and meta (entry 7, 58%) chloro substituted styrene overshadows the difference in yield between electron donating (NH₂, entry 9, 50%) and

electron withdrawing (NO₂, entry 10, 39%) para substituted styrene. The trend for methylstyrene further demonstrates this effect. Para methylstyrene (entry 2, 52%) and meta-methylstyrene (entry 3, 48%) both reacted faster than unsubstituted styrene (entry 1, 45%). However, ortho-methylstyrene reacts slower (entry 2, 42%). Once in the ortho position, the negative steric effect of the methyl group outweighs the positive electron-donating effect. The example with the largest ortho substituent (Br, entry 5) exhibits the lowest overall yield (18%).

Table 5 - Activity of styrene derivatives^a

Entry	Substrate	Product	Yield:Selectivity (%:%)
1			45:>99
2			52:>99
3			48:>99
4			42:>99
5			18:>99
6			35:>99
7			58:>99
8			54:>99
9			50:>99
10			39:>99

^a Reaction conditions: 0.05M substrate in EtOH, 80°C, 20 bar H₂, 3 mL/min, 300 mg FeNP@PS-PEG-NH₂

[0070] Ease of reaction scale-up represents one of the most attractive benefits of flow chemistry. We therefore preformed a five gram-scale up with cinnamyl acetate (Figure 6) to demonstrate this scale-up potential and robust nature of the catalyst in prolonged reactions. The hourly snapshots indicate that the yield never dipped below 94%, with an overall yield of 96%.

This equates to a turn over number (TON) of 434. In a 20.7 gram scale-up of styrene this TON increased to 1685.

EXPERIMENTAL SECTION

Chemicals

[0071] Styrene (99.0% w/ ~0.003% p-t-butylcatechol stabilizer) and p-methoxystyrene (99% w/ 200 ppm p-t-butylcatechol stabilizer) were purchased from Wako chemicals. Cinnmyl alcohol (98.0%), trans-2-heptene (99%), cis-2-heptene (97%), Fe(CO)₅ (99.999%) and 1-octadecene (90%) were purchased from Aldrich. 2-phenylpropionaldehyde (98%), cinnmyl acetate (99%), 4-methylstyrene (99%), benzylideneaniline (98%), and benzylcarbamate (97%) were purchased from TCI. Ethanol (99.5%) was purchased from Kanto Chemical Co. Tentagel™ S COOH, Tentagel™ S Br and Tentagel™ S NH₂ were purchased from RAPP polymere. Aminomethylated polystyrene was purchased from Nova biochem. High purity water was obtained by the use of a Milli-Q- Millipore™ with 0.22µm filter, Q-guard1 and ultrapure organex cartridge.

Instruments

[0072] The gas chromatograph fitted with a flame ionization detector (GC FID) was an Agilent Technologies 6850 series II Network GC system. The gas chromatography mass spectrometer (GC MS) was an Agilent 5973 Network Mass Selective Detector. High pressure hydrogenation flow reactor catalytic tests were performed on an H-Cube – Thales Nanotechnologies. The transmission electron microscope (TEM) used for imaging was a JEM-2010F (HR7). Microtome slices were performed with a Leica™ EMFCS. The inductively coupled plasma (ICP) measurements were recorded on a Leeman labs, inc. profile plus high dispersion ICP.

EXAMPLE 1 - Synthesis of FeNP@PS-LK by thermal decomposition:

[0073] Linker-terminated polystyrene/(polyethylene glycol) beads (Tentagel™ produced by RAPP Polymere or aminomethylated poly-styrene from Nova, 1 gram) and 1-octadecene (60 mL, 90% Aldrich) were combined with a magnetic stir bar in a 200 mL round bottom shlenk flask. The mixture was degassed with N₂ at 120°C for 30 minutes. The temperature was then raised to 180°C, at which point Fe(CO)₅ (2.1 mL, 99.99%, Aldrich) was quickly injected. The reaction was stirred for 30 minutes at 180°C under a blanket of N₂, then allowed to cool to room temperature. The resultant polymer-supported iron nanoparticles (FeNP@PS-(PEG)-FG) were then washed 3 times with hexanes (50 mL, 99% Aldrich) and dried under vacuum.

EXAMPLE 2 - Synthesis of FeNP@PS-(PEG)-NH₂ by black tea reduction:

[0074] The extract of black tea (20 g) was brewed with boiling water (1 L) and steeped until it reached room temperature. At room temperature, this extract was added to a solution of amine-terminated polystyrene/polyethylene glycol beads (1 gram), FeSO_4 (3.767 g) and water (2 L) with a magnetic stir bar in a 4L glass jug. After stirring for 24 hours, the polymer was filtered and collected.

EXAMPLE 3 - Characterization of PS-LK supported iron nanoparticles:

[0075] To visualize the $\text{FeNP}@PS\text{-(PEG)-FG}$ catalysts, the polymer was sliced with a Leica EMFCS microtome. The resultant slices were loaded onto carbon/formvar grids and subjected to TEM analysis on a JEM-2010F (HR7) operated at 120 kV. The interatomic spacing was measured on Figure 3 using the measuring tool of the GIMP software over 14 lines. The lattice parameter is 2.87 Å for (base-centered cubic) bcc iron and 3.515 Å for (face-centered cubic) fcc. Both of them provide an interatomic spacing of 2.49 Å using equation $d = a/\sqrt{3}$ for bcc and $d = a/\sqrt{2}$ for fcc, with "a" being the lattice parameter and "d" the interatomic spacing.

EXAMPLE 4 - PS-LK supported iron nanoparticles for Hydrogenation:

[0076] A cartridge was packed with 300 mg of PS-LK supported iron nanoparticles and connected to an H-CubeTM flow hydrogenation system. A solution of various substrates (0.05 M) in ethanol, water, or a mixture of the two was passed through the flow system at different rates, temperatures and hydrogen pressures. The resultant solution was characterized by GC-MS and quantified by GC-FID.

[0077] It should be appreciated that the invention is not limited to the particular examples and embodiments described and illustrated herein but includes all modifications and variations falling within the scope of the invention as defined in the appended claims.

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CLAIMS:

1. A hydrogenation catalyst comprising
an amphiphilic polymer resin with
a resin support;
a linker attached to the support,
wherein the linker comprises a functionalized group selected from COOH, NH₂ a halide or combinations thereof, and
an embedded iron Fe⁰ nanoparticles.
2. A catalyst according to claim 1, wherein the resin support is composed of polystyrene beads.
3. A catalyst according to claim 2, wherein the the linker includes a spacer.
4. The catalyst according to claim 3, wherein the spacer is polyethylene glycol (PEG).
5. A catalyst according to claim 1, wherein the functional group is NH₂.
6. A catalyst according to any one of claims 2 to 4, wherein the functional groups are attached to the polystyrene beads with a linker.
7. A catalyst according to claim 6, wherein the linker is polyethylene glycol derivative.
8. A catalyst according to any one of claims 1 to 7, wherein the embedded iron Fe⁰ nanoparticles are loaded at a concentration from 1 to 15 mg Fe / g catalyst.
9. A catalyst according to claim 8, wherein the concentration is 12 mg Fe / g catalyst.
10. The use of a catalyst comprising
an amphiphilic polymer resin with
a resin support;
a linker attached to the support,
wherein the linker comprises a functionalized group selected from COOH, NH₂ a halide or combinations thereof, and

an embedded iron Fe^0 nanoparticles.,

for hydrogenation of alkenes, alkynes, aromatic aldehydes and aromatic imines.

11. A process for the manufacture of a chemical compound comprising hydrogenation of alkenes, alkynes, aromatic aldehydes and aromatic imines functionalities in the presence of a catalyst comprising

an amphiphilic polymer resin with

a resin support;

a linker attached to the support,

wherein the linker comprises a functionalized group selected from COOH , NH_2 a halide or combinations thereof, and

an embedded iron Fe^0 nanoparticles.

12. A process for hydrogenation of chemical compounds using a catalyst comprising

an amphiphilic polymer resin with

a resin support;

a linker attached to the support,

wherein the linker comprises a functionalized group selected from COOH , NH_2 a halide or combinations thereof, and

an embedded iron Fe^0 nanoparticles.

13. A process according to claim 12, wherein the hydrogenation is carried out in a protic solvent.

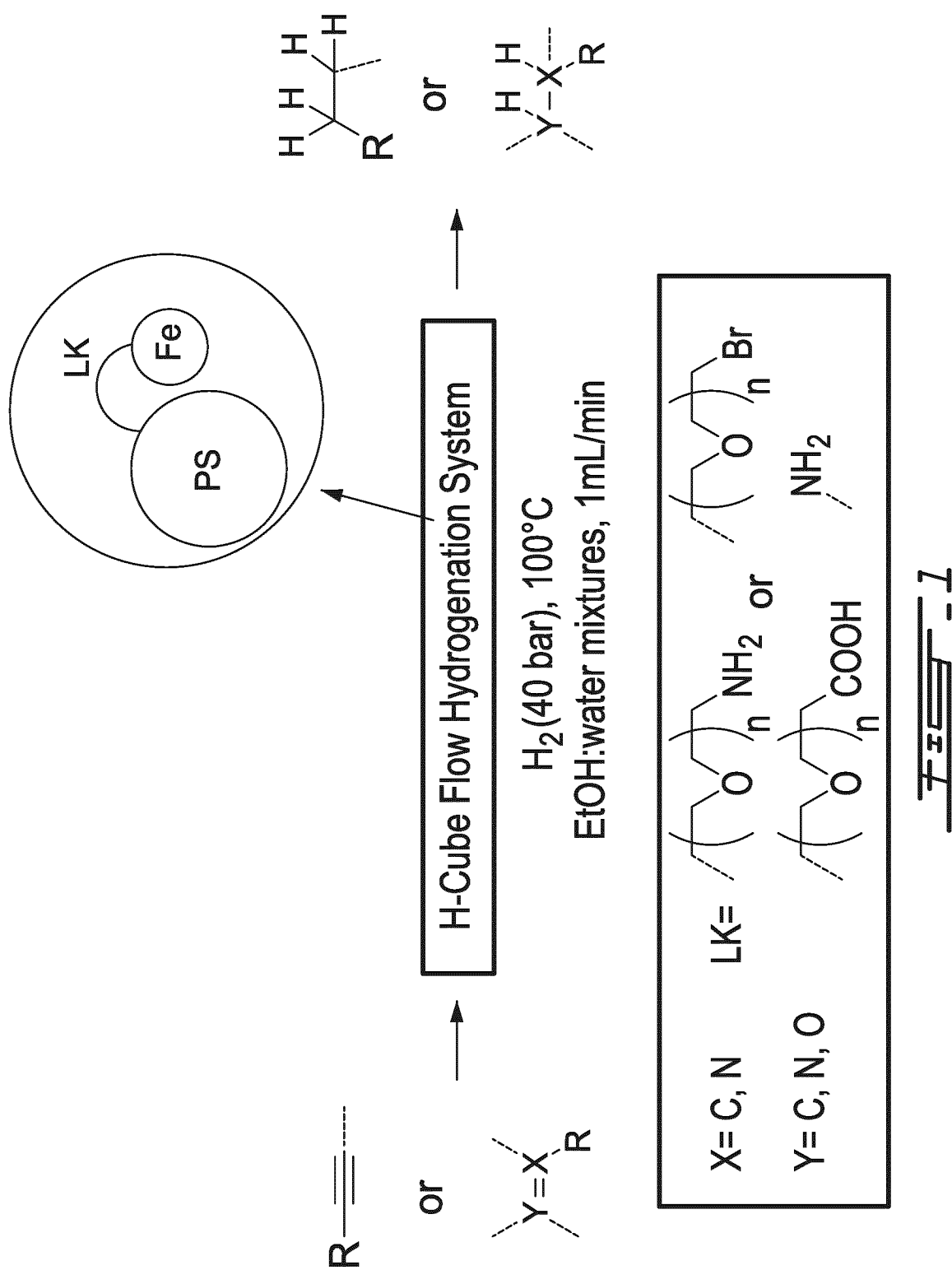
14. A process according to claim 13, wherein the protic solvent is ethanol, water or a mixture thereof.

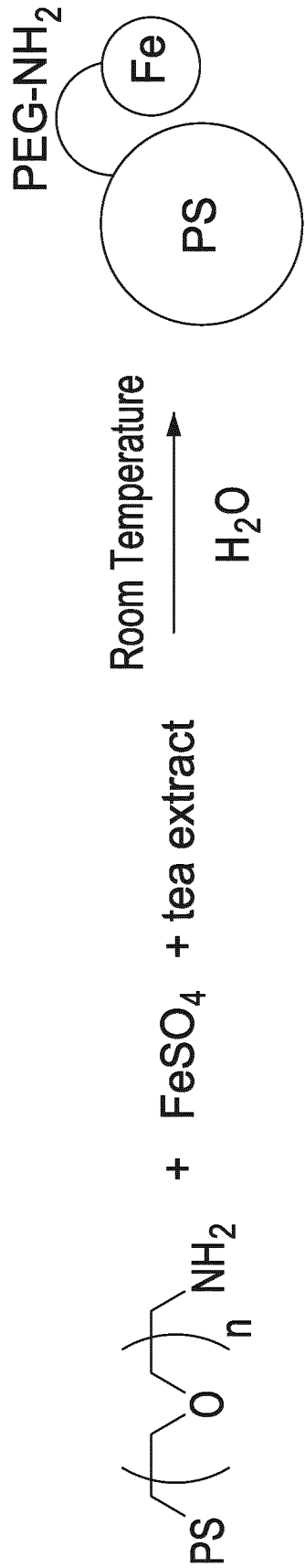
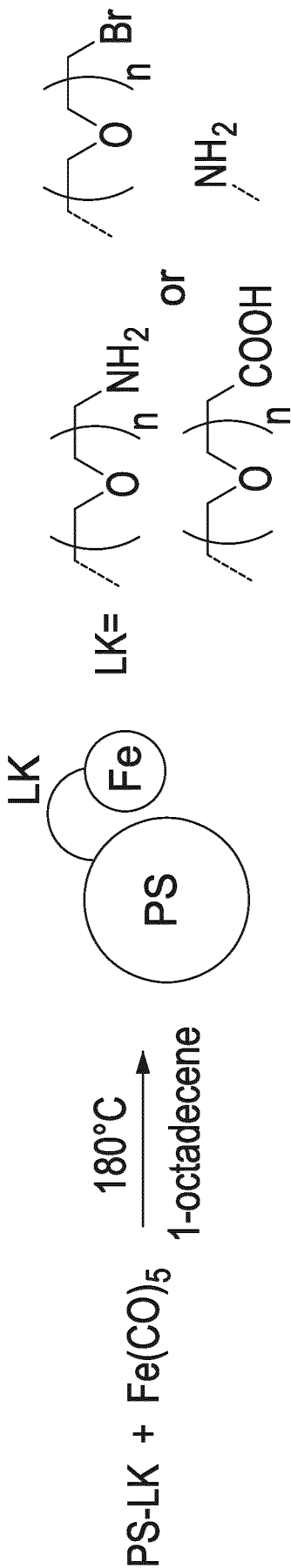
15. A process according to claim 12, wherein the hydrogenation is carried out under pressure between 10 to 60 bar.

16. A process according to claim 12, wherein the hydrogenation is carried out in at a temperature between 60 to 100°C .

17. A process according to claim 12, wherein the catalyst is used in a flow system.

18. A process according to claim 17, wherein the flow system is used with a flow rate between 0.5 ml/min to 2 ml/min.





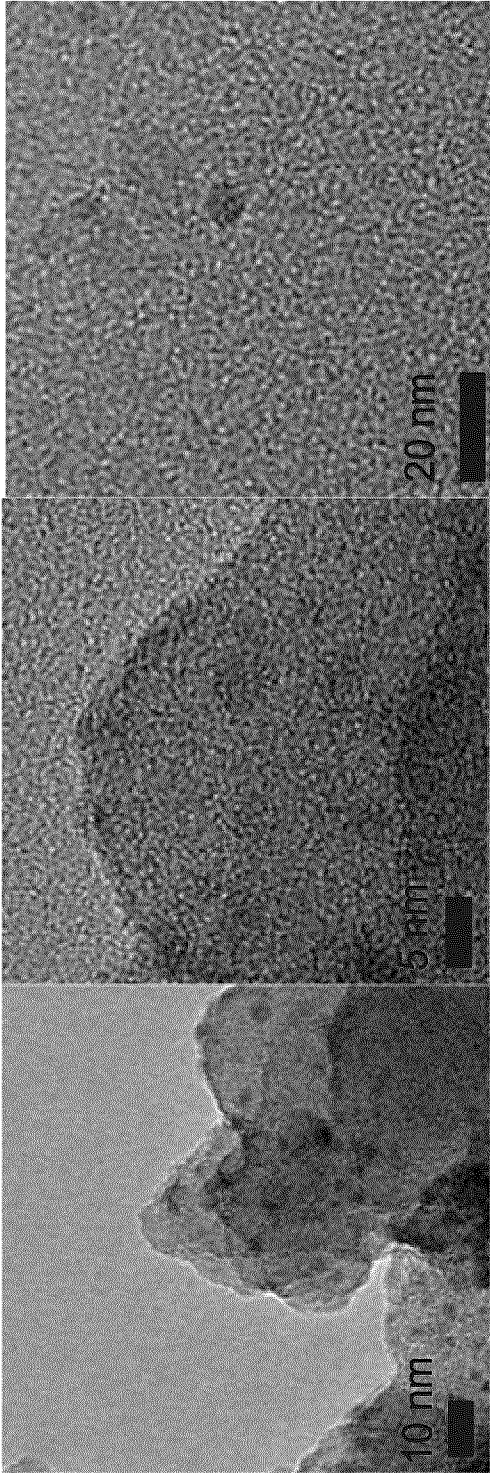


Fig. 4A Fig. 4B Fig. 4C

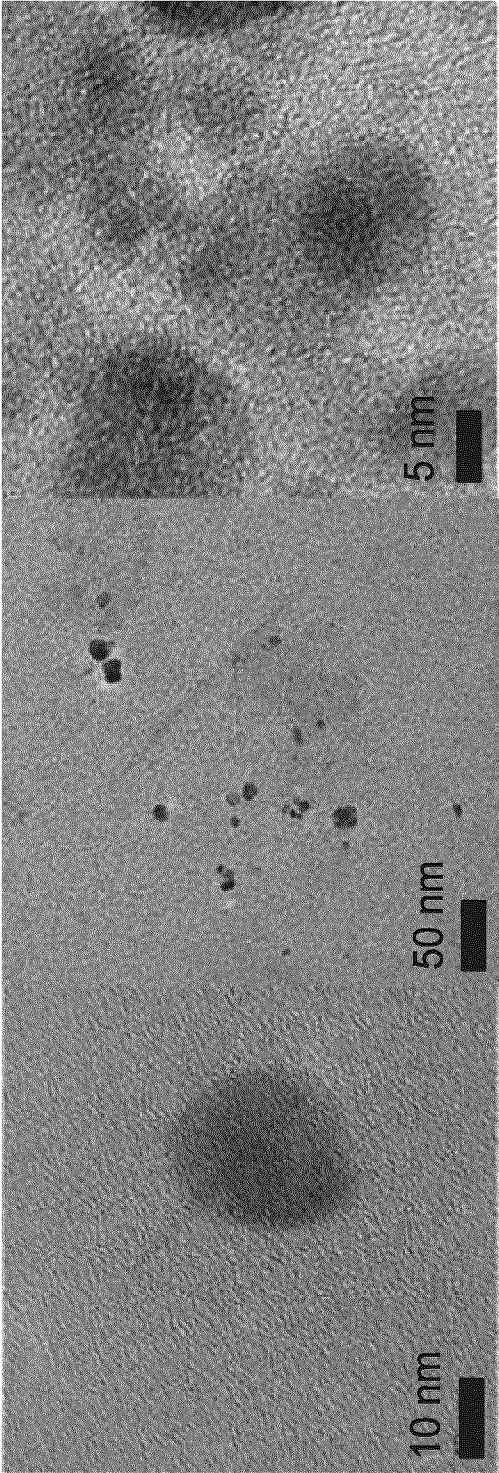


Fig. 4D Fig. 4E Fig. 4F

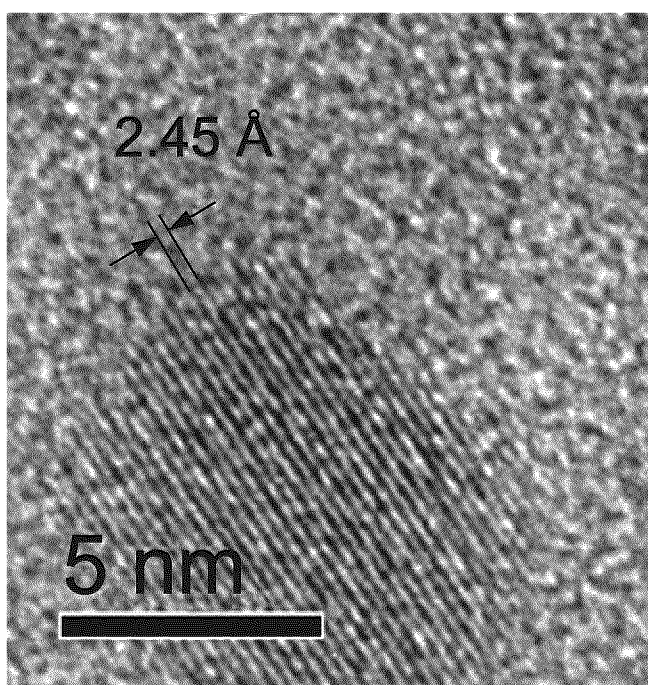
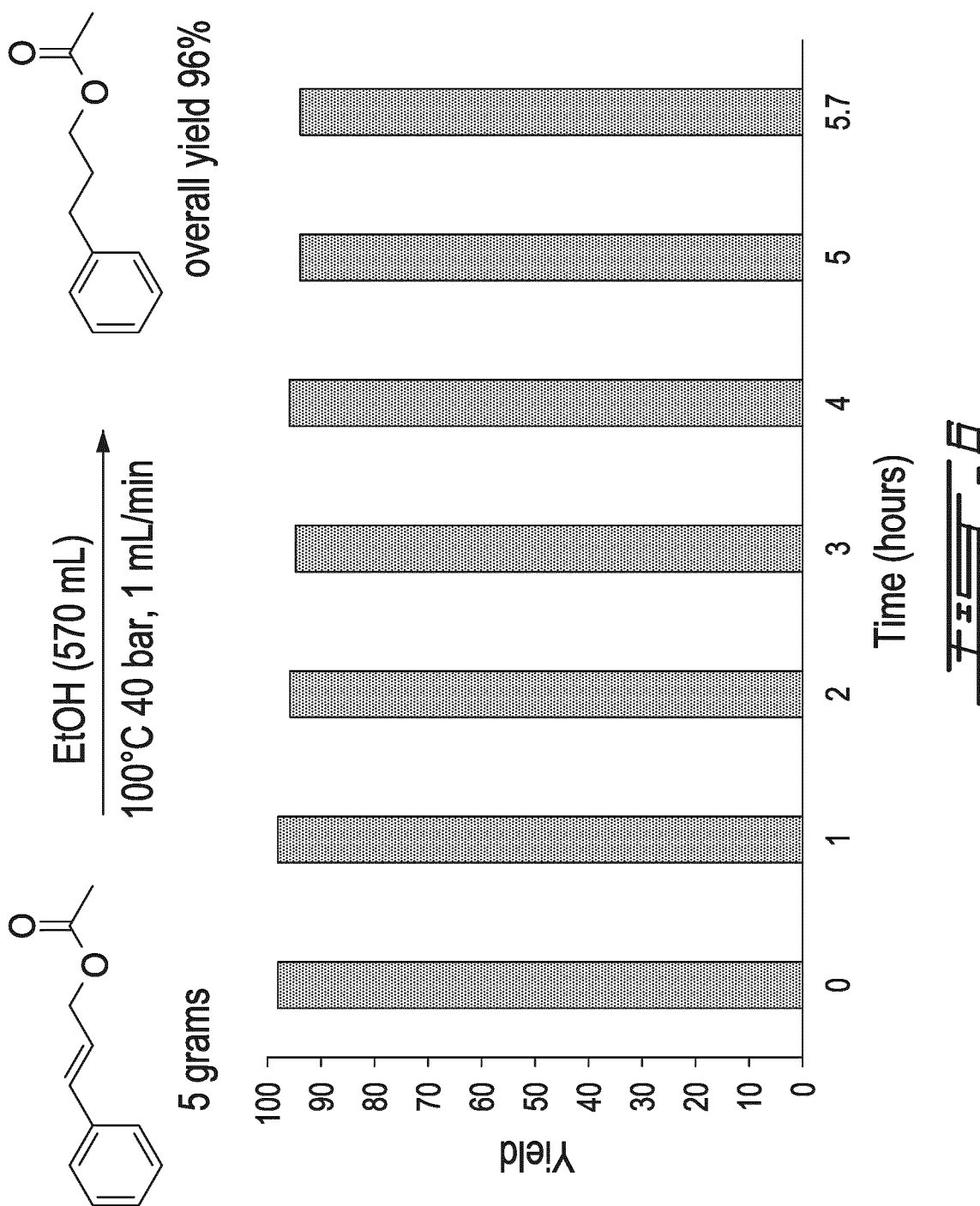


FIG. 5

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/CA2013/050995

A. CLASSIFICATION OF SUBJECT MATTER
IPC: **B01J 23/745** (2006.01)

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: B01J (2006.1)

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

Electronic database(s) consulted during the international search (name of database(s) and, where practicable, search terms used)
LexisNexis Total Patent, Canadian Patent Database, Google (amphiphilic, polymer, resin, iron, zero valent)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 1739104 A1 (KOBAYASHI et al.) 03 January 2007 (03-01-2007)	1, 12
Y	* abstract, [0010], [0019], [0039], examples, claims *	2-11, 13-18
Y	NAKAO et al. "Hydrogenation and Dehalogenation under Aqueous Conditions with an Amphiphilic-Polymer-Supported Nanopalladium Catalyst" Organic Letters, Vol 7, No. 1, 2005, Pages 163-165 * whole document *	1-18

 Further documents are listed in the continuation of Box C.

 See patent family annex.

* "A" "E" "L" "O" "P"	Special categories of cited documents: document defining the general state of the art which is not considered to be of particular relevance earlier application or patent but published on or after the international filing date 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) document referring to an oral disclosure, use, exhibition or other means document published prior to the international filing date but later than the priority date claimed	"T" "X" "Y" "&"	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 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 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
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Date of the actual completion of the international search
17 February 2014 (17-02-2014)

Date of mailing of the international search report
24 March 2014 (24-03-2014)

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INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/CA2013/050995

Patent Document Cited in Search Report	Publication Date	Patent Family Member(s)	Publication Date
EP1739104A1	03 January 2007 (03-01-2007)	CN1930197A CN100543050C EP1739104A4 JP5055525B2 US2008058200A1 US8110519B2 WO2005085307A1	14 March 2007 (14-03-2007) 23 September 2009 (23-09-2009) 07 January 2009 (07-01-2009) 24 October 2012 (24-10-2012) 06 March 2008 (06-03-2008) 07 February 2012 (07-02-2012) 15 September 2005 (15-09-2005)