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(54) Title: PROCESS FOR PERFORMING AN ISOLATED PD(0) CATALYZED REACTION ELECTROCHEMICALLY ON AN ELECTRODE ARRAY DEVICE

(57) Abstract: There is disclosed a process for performing an isolated Pd(0) catalyzed reaction electrochemically on an electrode array device. Preferably the Pd(0) catalyzed reaction is a Heck reaction. Specifically, there is disclosed a process for conducting an isolated Pd(0) catalyzed reaction on a plurality of electrodes, comprising providing an electrode array device having a matrix or coating material over metallic or conductive electrodes surfaces and a plurality of electrodes; providing a solution bathing the electrode array device, wherein the solution comprises a transition metal catalyst and a confining agent; and biasing one or a plurality of electrodes on the electrode array device with a voltage or current to regenerate the transition metal catalyst required for the isolated Pd(0) catalyzed reaction, whereby the confining agent limits diffusion of the transition metal catalyst to a volume surrounding each selected electrode surface.

PROCESS FOR PERFORMING AN ISOLATED Pd(0) CATALYZED REACTION ELECTROCHEMICALLY ON AN ELECTRODE ARRAY DEVICE

Technical Field of the Invention

The present invention provides a process for performing an isolated Pd(0) catalyzed reaction electrochemically on an electrode array device. Preferably the Pd(0) catalyzed reaction is a Heck reaction. Specifically, the inventive process provides a process for conducting an isolated Pd(0) catalyzed reaction on a plurality of electrodes, comprising providing an electrode array device having a matrix or coating material over metallic or conductive electrodes surfaces and a plurality of electrodes; providing a solution bathing the electrode array device, wherein the solution comprises a transition metal catalyst and a confining agent; and biasing one or a plurality of electrodes on the electrode array device with a voltage or current to regenerate the transition metal catalyst required for the isolated Pd(0) catalyzed reaction, whereby the confining agent limits diffusion of the transition metal catalyst to a volume surrounding each selected electrode surface.

Background of the Invention

Electronically addressable chip-based molecular libraries (Lipshutz et al., *Nature Genetics*, 21:20, 1999; Pirrung, *Chem. Rev.* 97:473, 1997; Webb et al., *J. Steroid Biochem. Mol. Biology*, 85:183, 2003; Shih et al., *J. Virological Methods*, 111:55, 2003) have long been desired but have not been created. CombiMatrix Corporation scientists have been utilizing active-semiconductor electrode arrays that incorporate individually addressable microelectrodes to synthesize oligonucleotide and polypeptide molecules (US Patent 6,093,302; WO/0053625; Oleinikov et al., *J. Proteome Res.*, 2:313, 2003; Sullivan et al., *Anal. Chem.*, 71:369, 1999; Zhang et al., *Anal. Chim. Acta*, 421:175, 2000; and Hintsche et al., *Electroanal.* 12:660, 2000).

In this way, each unique set of molecules in a library can be located proximal to a unique electrode or set of electrodes that can in turn be used to monitor their behavior (Dill et al., *Analytica Chimica Acta*, 444:69, 2001). This is accomplished by coating the electrode-containing devices with a porous polymer and then utilizing the electrodes to both attach monomers to the chips and then generate reagents capable of performing reactions on the monomers.

The Heck reaction is a powerful synthetic tool that allows for the efficient generation of new carbon – carbon bonds. The availability of a Heck reaction on an electrode array device would dramatically expand the types of molecules that could be constructed within a volume proximal to an electrode surface. Such a tool would allow for massively parallel electrochemical synthesis in small volumes on an electrode array device and create arrays containing highly diverse libraries of chemical compounds that are different from each other yet synthesized in parallel. Such combinatorial libraries could be synthesized rapidly, in small

volumes and highly diverse. Therefore, there is a need in the art to be able to rapidly create diverse chemical libraries on a single solid electrode array device for large scale screening of combinatorial libraries. The present invention was made to address this need in the art.

Moreover, the Heck reaction represents a unique challenge for a site-selective reaction on an electrode array device because it is catalytic with respect to Pd(0).

Summary of the Invention

The present invention provides a process for conducting an isolated Pd(0) catalyzed reaction on a plurality of electrodes, comprising:

(a) providing an electrode array device having a matrix or coating material over metallic or conductive electrodes surfaces and a plurality of electrodes;

(b) providing a solution bathing the electrode array device, wherein the solution comprises a transition metal catalyst, and a confining agent;

(c) biasing one or a plurality of electrodes on the electrode array device with a voltage or current to regenerate the transition metal catalyst consumed during the Pd(0) catalyzed reaction, whereby the confining agent limits diffusion of the transition metal catalyst to a volume surrounding each selected electrode surface.

Preferably, the isolated Pd(0) catalyzed reaction is selected from the group consisting of a Heck reaction, a Suzuki coupling reaction, displacement of an aryl halide with an RS-nucleophile of NH_2R nucleophile, coupling an aryl bromide to an aluminoacetylene Al (C≡C-R)$_4$ Na salt, displacement of an aryl halide with an esterenolate, alkyl group Suzuki coupling (aryl boron reagent with alkyl halide), Stille coupling R-X plus R'SnR"$_3$, alkyne-BF_3 salt coupling to aryl triflate halide, vinyl-BF_3 salt or alkyne-BF_3 salt coupling, reaction of an alcohol with alkyl/allyl carbonate to make alcohol allyl ether, conversion of an alpha aminoacetylene to a ketene, conversion of Ar-X plus acid chloride to acetylinic ketone, and combinations thereof.

Preferably, the transition metal catalyst for an isolated Pd(0) catalyzed reaction is a palladium (Pd) or a platinum (Pt) catalyst system. Most preferably, a Pd catalyst is stabilized with stabilizer selected from the group consisting of a phosphine ligand, a phosphite ligand, an arsenic derivative, a triphenylphosphine ligand, and combinations thereof. Most preferably, the Pd catalyst is stabilized by a triphenylphosphine ligand.

Preferably, the confining agent is an oxidant added to solution sufficient to convert Pd(0) back to Pd(II). Most preferably, the confining agent is an oxidant selected from the group consisting of substituted or unsubstituted allyl alkyl carbonates, allyl acetate, O2, peroxides, quinines, and combinations thereof. More preferably, the confining agent is a substituted or unsubstituted allyl alkyl carbonate wherein the alkyl moiety can be a C_{1-6} alkyl group. Preferably, the biasing step used a voltage no greater than 2.4 V. Preferably, the biasing step was performed for a time of from about 1 sec to 3 min.

Brief Description of the Drawings

Figure 1 shows a an electrode array surface under a fluorescent scanner device (Axon Instruments) wherein 1-pyrenemethylacrylate was deposited at selected electrode sites using electrodes as cathodes to reduce Pd(II) to Pd(0). The Pd(0) triggered a Heck reaction between the substrate and the aryl iodide on the surface of the selected electrodes (selected to form a square pattern with an electrode in the middle). The bright spots are the selected electrodes with 1-pyrenemethylacrylate as an indicator.

Figure 2 shows the design of the experiment performed in Example 1.

Figure 3 shows the synthetic scheme for the experiment. In the first step an aryl iodide is placed on the chips surface using the same methodology employed in earlier studies (Tesfu et al., *J. Am. Chem. Soc.* 126:6212, 2004). To this end, all of the electrodes on the electrode array device were utilized as cathodes in order to reduce vitamin B_{12}. This effectively generated a base. The base served to catalyze an esterification reaction between the hydroxyl groups of the polysaccharide polymer coating the electrode array device and the N-hydroxysuccinimide ester of 4-iodobenzoic acid. The effect of this process was to concentrate the aryl iodide substrate near the electrodes on the electrode array device. The second step in the sequence is the Heck reaction. The Heck reaction is performed by submerging the electrode array device in a 2:7:1 DMF/MeCN/H_2O solution containing $Pd(0Ac)_2$, triphenyl-phosphine, triethylamine, allyl methyl carbonate, and tetrabutyl-ammonium bromide electrolyte. Selected electrodes were turned on as cathodes at a voltage of -2.4 V (relative to a Pt auxiliary electrode as an anode) in order to generate a box pattern of electrodes on the array with a dot in the center. The electrodes (Pt surface) were cycled for 0.5 sec on and then 0.1 sec off for 3 min.

Detailed Description of the Invention

In the exemplified experiments Pd(II) was reduced to Pd(0) at selected electrodes on the electrode array device. Further, a confining agent was necessary to confine the reaction to the region surrounding a selected electrode. Allyl methyl carbonate was a preferred confining agent. This is because the reaction performed without the preferred confining agent, allyl methyl carbonate, led to significant spreading of fluorescent signal away from selected electrode sites.

The reagents generated at any given electrode were confined to the area surrounding the electrode by placing a substrate in the solution above the electrode that consumed the reagent. Briefly, this process was described in connection with the generation of acids and bases confined to a volume on electrode array devices (see, for example, Montgomery US Patent 6,093,302, the disclosure of which is incorporated by reference herein). In previous work, a Pd(II) reagent was generated electrochemically and confined to a region surrounding an electrode (Tesfu et al., *J. Am. Chem. Soc.* 126:6212, 2004). The Pd(II) reagent was generated by utilizing the electrodes on an electrode array device as anodes to oxidize a Pd(0) reagent added to the solution above the electrode array device. The Pd(II) reagent generated was confined to the electrode sites of its generation with the use of ethyl vinyl ether. The

feasibility of this process was demonstrated by performing a Wacker oxidation at selected electrodes on the electrode array.

The present invention was motivated by the desire to determine if the electrodes be used as cathodes in order to reduce a Pd(II) reagent to a Pd(0) reagent at pre-selected sites on a microarray device having a plurality of electrode sites (each separately addressable). The problem solved by the present invention was to find an efficient confinement strategy for the Pd(0) reagent generated so that it was confined to one electrode and did not catalyze a reaction at a neighboring electrode. This is necessary in order to be able to perform the Heck reaction (a Pd(0) catalyzed reaction) at selected electrode sites while avoiding the reaction at non-selected electrode sites.

In the case of the earlier Wacker oxidation, Pd(II) was used as a stoichiometric oxidant. Hence, most of the reagent generated at a selected electrode on an electrode array was consumed by the reaction. Ethyl vinyl ether added to the solution (bathing the electrode array device) effectively confined the Pd(II) generated by scavenging any excess reagent. Such is not the case for the proposed Heck reaction or other Pd(0) catalyzed reactions. In this case, the reaction did not consume the Pd(0) catalyst. A confining agent was needed to keep all of the reagent generated from migrating to areas of the electrode array device where it was not wanted. In other words, rather than use an electrolysis reaction to make a normally stoichiometric reaction catalytic as in a normal mediated electrolysis, for the Heck reaction the electrode array-based environment must be used to make a normally catalytic reaction stoichiometric thereby confining the catalyst to pre-selected sites on the selected electrode of the array.

The present invention provides a process for conducting a parallel Heck reaction on a plurality of electrodes, comprising

(a) providing an electrode array device having a matrix or coating material over metallic or conductive electrodes surfaces and a plurality of electrodes;

(b) providing a solution bathing the electrode array device, wherein the solution comprises a transition metal catalyst, and a confining agent;

(c) biasing one or a plurality of electrodes on the electrode array device with a voltage or current to regenerate the transition metal catalyst consumed during the Heck reaction, whereby the confining agent limits diffusion of the transition metal catalyst to a volume surrounding each selected electrode surface.

The present invention further provides a process for conducting an isolated Pd(0) catalyzed reaction on a plurality of electrodes, comprising:

(a) providing an electrode array device having a matrix or coating material over metallic or conductive electrodes surfaces and a plurality of electrodes;

(b) providing a solution bathing the electrode array device, wherein the solution comprises a transition metal catalyst, and a confining agent;

(c) biasing one or a plurality of electrodes on the electrode array device with a voltage or current to regenerate the transition metal catalyst consumed during the Pd(0) catalyzed reaction, whereby the confining agent limits diffusion of the transition metal catalyst to a volume surrounding each selected electrode surface.

Preferably, the isolated Pd(0) catalyzed reaction is selected from the group consisting of a Heck reaction, a Suzuki coupling reaction, displacement of an aryl halide with an RS-nucleophile of NH_2R nucleophile, coupling an aryl bromide to an aluminoacetylene Al (C≡C-R)$_4$ Na salt, displacement of an aryl halide with an esterenolate, alkyl group Suzuki coupling (aryl boron reagent with alkyl halide), Stille coupling R-X plus R'SnR"$_3$, alkyne-BF_3 salt coupling to aryl triflate halide, vinyl-BF_3 salt or alkyne-BF_3 salt coupling, reaction of an alcohol with alkyl/allyl carbonate to make alcohol allyl ether, conversion of an alpha aminoacetylene to a ketene, conversion of Ar-X plus acid chloride to acetylinic ketone, and combinations thereof. Preferably, a Pd catalyst is stabilized with stabilizer selected from the group consisting of a phosphine ligand, a phosphite ligand, an arsenic derivative, a triphenylphosphine ligand, and combinations thereof. Most preferably, the Pd catalyst is stabilized by a triphenylphosphine ligand.

Preferably, the confining agent is an oxidant added to solution sufficient to convert Pd(0) back to Pd(II). Most preferably, the confining agent is an oxidant selected from the group consisting of substituted or unsubstituted allyl alkyl carbonates, allyl acetate, O2, peroxides, quinines, and combinations thereof. More preferably, the confining agent is a substituted or unsubstituted allyl alkyl carbonate wherein the alkyl moiety can be a $C_{1\text{-}6}$ alkyl group. Preferably, the biasing step used a voltage no greater than 2.4 V. Preferably, the biasing step was performed for a time of from about 1 sec to 3 min.

Preferably, the transition metal catalyst for a Heck reaction is a palladium (Pd) or a platinum (Pt) catalyst system.

The term "substituted" or "substitution," in the context of a moiety of the confining agent, means a moiety independently selected from the group consisting of (1) the replacement of a hydrogen on at least one carbon by a monovalent radical, (2) the replacement of two hydrogens on at least one carbon by a divalent radical, (3) the replacement of three hydrogens on at least one terminal carbon (methyl group) by a trivalent radical, (4) the replacement of at least one carbon and the associated hydrogens (*e.g.*, methylene group) by a divalent, trivalent, or tetravalent radical, and (5) combinations thereof. Meeting valence requirements restricts substitution. Substitution occurs on alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, heterocyclic ring, and polycyclic groups, providing substituted alkyl, substituted alkenyl, substituted alkynyl, substituted cycloalkyl, substituted cycloalkenyl, substituted cycloalkynyl, substituted aryl group, substituted heterocyclic ring, and substituted polycyclic groups.

The groups that are substituted on an alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, heterocyclic ring, and polycyclic groups are independently selected from

the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, heterocyclic ring, polycyclic group, halo, heteroatom group, oxy, oxo, carbonyl, amide, alkoxy, acyl, acyloxy, oxycarbonyl, acyloxycarbonyl, alkoxycarbonyloxy, carboxy, imino, amino, secondary amino, tertiary amino, hydrazi, hydrazino, hydrazono, hydroxyimino, azido, azoxy, alkazoxy, cyano, isocyano, cyanato, isocyanato, thiocyanato, fulminato, isothiocyanato, isoselenocyanato, selenocyanato, carboxyamido, acylimino, nitroso, aminooxy, carboximidoyl, hydrazonoyl, oxime, acylhydrazino, amidino, sulfide, thiol, sulfoxide, thiosulfoxide, sulfone, thiosulfone, sulfate, thiosulfate, hydroxyl, formyl, hydroxyperoxy, hydroperoxy, peroxy acid, carbamoyl, trimethyl silyl, nitrilo, nitro, aci-nitro, nitroso, semicarbazono, oxamoyl, pentazolyl, seleno, thiooxi, sulfamoyl, sulfenamoyl, sulfeno, sulfinamoyl, sulfino, sulfinyl, sulfo, sulfoamino, sulfonato, sulfonyl, sulfonyldioxy, hydrothiol, tetrazolyl, thiocarbamoyl, thiocarbazono, thiocarbodiazono, thiocarbonohydrazido, thiocarbonyl, thiocarboxy, thiocyanato, thioformyl, thioacyl, thiosemicarbazido, thiosulfino, thiosulfo, thioureido, thioxo, triazano, triazeno, triazinyl, trithio, trithiosulfo, sulfinimidic acid, sulfonimidic acid, sulfinohydrazonic acid, sulfonohydrazonic acid, sulfinohydroximic acid, sulfonohydroximic acid, and phosphoric acid ester, and combinations thereof.

As an example of a substitution, replacement of one hydrogen or ethane by a hydroxyl provides ethanol, and replacement of two hydogens by an oxo on the middle carbon of propane provides acetone (dimethyl ketone.) As a further example, replacement the middle carbon (the methenyl group) of propane by the oxy radical (–O–) provides dimethyl ether (CH_3–O–CH_3.) As a futher example, replacement of one hydrogen on a benzene by a phenyl group provides biphenyl.

As provided above, heteroatom groups can be substituted inside an alkyl, alkenyl, or alkylnyl group for a methylene group (:CH_2) thus forming a linear or branched substituted structure rather than a ring or can be substituted for a methylene inside of a cycloalkyl, cycloalkenyl, or cycloalkynyl ring thus forming a heterocyclic ring. As a further example, nitrilo (—N=) can be substituted on benzene for one of the carbons and associated hydrogen to provide pyridine, or and oxy radical can be substituted to provide pyran.

The term "unsubstituted" means that no hydrogen or carbon has been replaced on an alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, or aryl group.

It was noted that the use of triphenylphosphine as a ligand for the palladium was important for keeping the Pd(0) generated at the cathode (electrode) from plating out on the electrode array device. Preferably, some DMF was added the reaction mixture to further allow a Heck reaction to proceed. However, the reaction could not be done using DMF/H_2O as solvent. Without being bound by theory, it is anticipated that the DMF caused cleavage occurs due to base generated from either the reaction of Pd(0) with the allyl methyl carbonate or the reduction of water at the cathode. Further still, the presence of a confining agent was necessary. A reaction without the allyl methyl carbonate led to significant spreading of the fluorescence away from the selected electrodes.

We found that voltages higher than -2.4V or reaction times longer than three minutes led to a decrease in the intensity of the product spots on the electrode array device. Apparently, the harsher conditions or longer reaction times led to cleavage of the newly formed pyrene product from the electrode array device. Without being bound by theory, this cleavage occured due to base generated from either the reaction of Pd(0) with allyl methyl carbonate (Tsuji and Minami, *Acc. Chem. Res.* 20:140, 1987) or reduction of water at the cathode.

The following example support the conclusion that a Heck reaction (that is a preferred Pd(0) catalyzed reaction) has been performed at pre-selected sites on an electrochemically-addressable electrode array device. The experiment highlights the utility of a Pd(0) reagent on the electrode array device, and for the first time demonstrates the potential for employing a transition metal catalyst to selectively construct molecules proximal to specific addressable electrodes.

Example 1

This example tested the feasibility of the inventive process. The experiment outlined in Figure 2 was performed. First, an aryl iodide was placed on the surface of an electrode array device (Combimatrix Corporation, Mukilteo, WA) coated with polysaccharide, and then the electrode array device was submerged in an electrolyte solution containing 1-pyrenemethyl acrylate, palladium acetate, triphenylphoshine ligand, and allyl methyl carbonate. Selected cathodes were used to reduce the palladium acetate to the desired Pd(0) catalyst. If there was successful reduction, the Pd(0) catalyst generate would trigger a Heck reaction between the surface-bound aryl iodide the 1-pyrenemethyl acrylate, but only at those electrode sites whose electrodes were activated as a cathode. A successful Heck reaction would place the fluorescent pyrene moiety onto the surface of the electrode array device, but only in the region surrounding an electrode. This creates the ability to monitor the success of the reaction.

Following the reaction, the active Pd(0) catalyst was scavenged by the allyl methyl carbonate in order to generate a Pd(II) π-allyl complex and stop the catalytic process. Reformation of the Pd(0) catalyst at either a selected electrode site or another selected electrode site would require either reduction of more of the $Pd(OAc)_2$ reagent or reduction of the π-allyl Pd(II) complex (Hayakawa et al., *Nucleosides Nucleotides*, 17:441, 1988). By balancing the rate at which the Pd(II) is reduced at the selected electrodes with the concentration of the allyl methyl carbonate in solution, the Heck reaction was confined to just the regions surrounding the selected electrodes (that is, the ones acting as cathodes).

Example 2

A series of solution phase Heck reactions were performed in order to determine reaction conditions that would allow for an electrochemically generated Heck reaction. Two key discoveries were made along these lines. First, a Heck reaction between methyl 4-iodobenzoate and 1-pyrenemethyl acrylate proceeded slowly (18h/ 82% yield) with $Pd(OAc)_2$ in a 9:1 DMF:H_2O solution containing triethylamine and tetrabutylammonium bromide while

the same reaction proceeded to completion in just 3h when a cathode was inserted and the $Pd(OAc)_2$ reduced electrochemically. Second, the Heck reaction did not proceed at all (0% after 18h) in the absence of the cathode when the DMF solvent was exchanged for acetonitrile. The corresponding electrochemical reaction proceeded to completion (76% yield) in 12 hours. Hence, using acetonitrile as the solvent for the reactions would assure that the Heck reaction would not spontaneously occur at sites on the electrode array device without a working cathode. Even if the more efficient DMF reaction conditions were eventually needed on the electrode array device, it appeared that the non-electrochemical background reaction was slow enough to be negligible, especially since on the electrode array device, a high concentration of the catalyst was generated at the electrodes directly next to the selected substrates.

Electrode array device-based experiments were initiated by depositing aryl iodide onto the electrode array device using the same methodology employed in the earlier Wacker oxidation experiment (Figure 3) (Tesfu et al., *J. Am. Chem. Soc.* 126:6212, 2004). To this end, all of the electrodes on the electrode array device were utilized as cathodes in order to reduce vitamin B_{12}. This effectively generated a base. The base served to catalyze an esterification reaction between the hydroxyl groups of the polysaccharide polymer coating the electrode array device and the N-hydroxysuccinimide ester of 4-iodobenzoic acid. The effect of this process was to concentrate the aryl iodide substrate near the electrodes on the electrode array device.

The Heck reaction was then performed by submerging the electrode array device in a 2:7:1 DMF/MeCN/H_2O solution containing $Pd(0Ac)_2$, triphenyl-phosphine, triethylamine, allyl methyl carbonate, and tetrabutyl-ammonium bromide electrolyte. Selected electrodes were turned on as cathodes at a voltage of -2.4 V (relative to a Pt auxiliary electrode as an anode) in order to generate a box pattern of electrodes on the array with a dot in the center. The electrodes (Pt surface) were cycled for 0.5 sec on and then 0.1 sec off for 3 min.

Following the reaction, the electrode array device was washed with hexane to remove any unreacted pyrene containing substrate and then the electrode array device imaged using a fluorescent microscope. The result is shown in Figure 1. Figure 1 shows an expanded view of 81 of the 1028 electrodes on the electrode array device. The bright spots in the figure are formed by pyrene on the electrode array device's surface and coincide perfectly with the selected or activated electrodes. The dark spots are electrodes that were not activated and block the background fluorescence of the electrode array device. Therefore, the confining or scavenging agent worked well and the Heck reaction was restricted to only the selected electrode regions.

We claim:

1. A process for conducting an isolated Pd(0) catalyzed reaction on a plurality of electrodes, comprising:

(a) providing an electrode array device having a matrix or coating material over metallic or conductive electrodes surfaces and a plurality of electrodes;

(b) providing a solution bathing the electrode array device, wherein the solution comprises a transition metal catalyst, and a confining agent;

(c) biasing one or a plurality of electrodes on the electrode array device with a voltage or current to regenerate the transition metal catalyst consumed during the Pd(0) catalyzed reaction, whereby the confining agent limits diffusion of the transition metal catalyst to a volume surrounding each selected electrode surface.

2. The process for conducting an isolated Pd(0) catalyzed reaction on a plurality of electrodes of claim 1 wherein the isolated Pd(0) catalyzed reaction is selected from the group consisting of a Heck reaction, a Suzuki coupling reaction, displacement of an aryl halide with an RS-nucleophile of NH_2R nucleophile, coupling an aryl bromide to an aluminoacetylene Al $(C{\equiv}C\text{-}R)_4$ Na salt, displacement of an aryl halide with an esterenolate, alkyl group Suzuki coupling (aryl boron reagent with alkyl halide), Stille coupling R-X plus R'SnR"$_3$, alkyne-BF_3 salt coupling to aryl triflate halide, vinyl-BF_3 salt or alkyne-BF_3 salt coupling, reaction of an alcohol with alkyl/allyl carbonate to make alcohol allyl ether, conversion of an alpha aminoacetylene to a ketene, conversion of Ar-X plus acid chloride to acetylinic ketone, and combinations thereof.

3. The process for conducting an isolated Pd(0) catalyzed reaction on a plurality of electrodes of claim 2 wherein the transition metal catalyst for an isolated Pd(0) catalyzed reaction is a palladium (Pd) or a platinum (Pt) catalyst system.

4. The process for conducting an isolated Pd(0) catalyzed reaction on a plurality of electrodes of claim 3 wherein a Pd catalyst is stabilized with stabilizer selected from the group consisting of a phosphine ligand, a phosphite ligand, an arsenic derivative, a triphenylphosphine ligand, and combinations thereof.

5. The process for conducting an isolated Pd(0) catalyzed reaction on a plurality of electrodes of claim 4 wherein the Pd catalyst is stabilized by a triphenylphosphine ligand.

6. The process for conducting an isolated Pd(0) catalyzed reaction on a plurality of electrodes of claim 1 wherein the confining agent is an oxidant added to solution sufficient to convert Pd(0) back to Pd(II).

7. The process for conducting an isolated Pd(0) catalyzed reaction on a plurality of electrodes of claim 6 wherein the confining agent is an oxidant selected from the group consisting of substituted or unsubstituted allyl alkyl carbonates, allyl acetate, O_2, peroxides, quinines, and combinations thereof.

8. The process for conducting an isolated Pd(0) catalyzed reaction on a plurality of electrodes of claim 6 wherein the confining agent is a substituted or unsubstituted allyl alkyl carbonate wherein the alkyl moiety can be a C_{1-6} alkyl group.

9. The process for conducting an isolated Pd(0) catalyzed reaction on a plurality of electrodes of claim 1 wherein the biasing step used a voltage no greater than 2.4 V.

10. The process for conducting an isolated Pd(0) catalyzed reaction on a plurality of electrodes of claim 1 wherein the biasing step was performed for a time of from about 1 sec to 3 min.

Figure 1

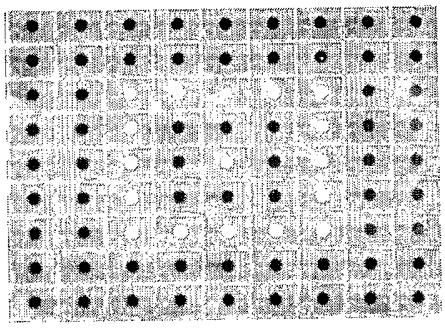


Figure 2

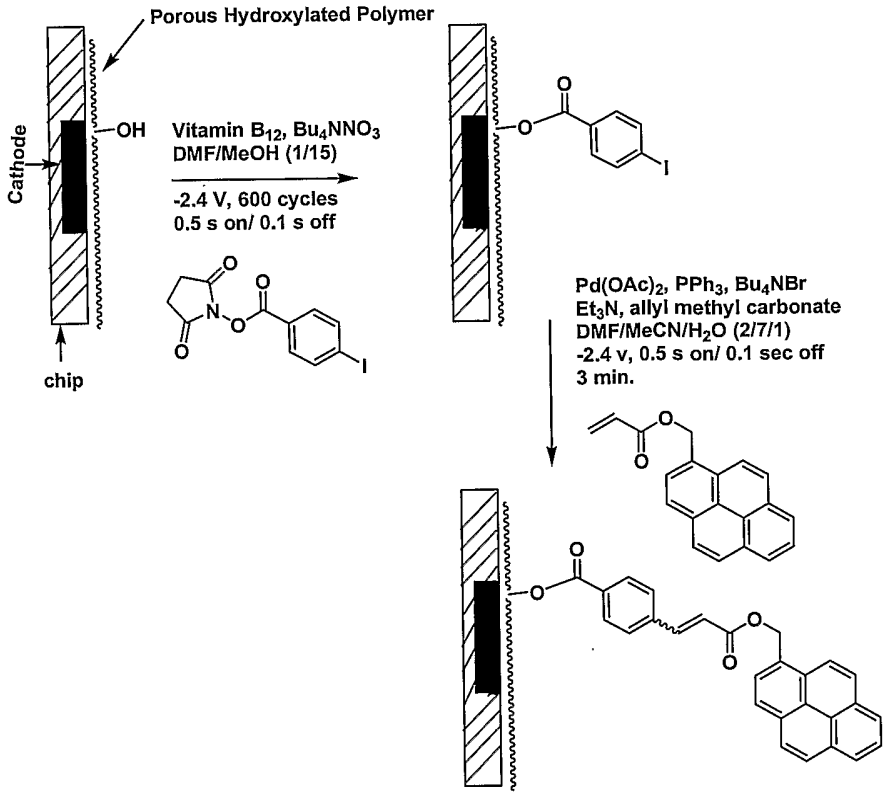
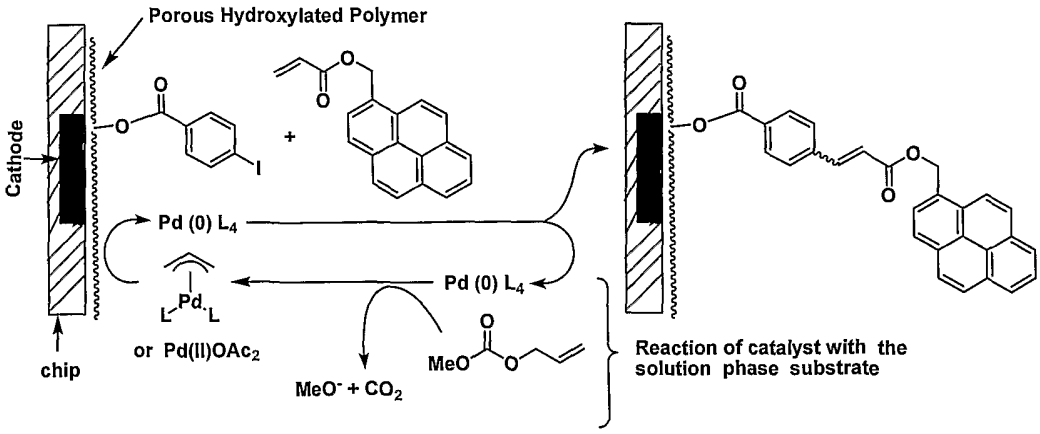

Porous Hydroxylated Polymer
Cathode
OH
chip
Vitamin B_{12}, Bu_4NNO_3
DMF/MeOH (1/15)
-2.4 V, 600 cycles
0.5 s on/ 0.1 s off
$Pd(OAc)_2$, PPh_3, Bu_4NBr
Et_3N, allyl methyl carbonate
DMF/MeCN/H_2O (2/7/1)
-2.4 v, 0.5 s on/ 0.1 sec off
3 min.

Figure 3


Porous Hydroxylated Polymer
Cathode
chip
Pd (0) L4
Pd (0) L4
or Pd(II)OAc2
MeO- + CO2
Reaction of catalyst with the solution phase substrate