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PII: S0376-7388(16)30465-3  
DOI: <http://dx.doi.org/10.1016/j.memsci.2016.05.042>  
Reference: MEMSCI14517

To appear in: *Journal of Membrane Science*

Received date: 1 April 2016  
Revised date: 21 May 2016  
Accepted date: 26 May 2016

Cite this article as: Tao Chen, Gaofeng Zeng, Zhiping Lai and Kuo-Wei Huang Environmentally benign synthesis of amides and ureas via catalytic dehydrogenation coupling of volatile alcohols and amines in a Pd-Ag membrane reactor, *Journal of Membrane Science* <http://dx.doi.org/10.1016/j.memsci.2016.05.042>

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# Environmentally benign synthesis of amides and ureas via catalytic dehydrogenation coupling of volatile alcohols and amines in a Pd-Ag membrane reactor

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## Abstract

In this study, we report the direct synthesis of amides and ureas via the catalytic dehydrogenation of volatile alcohols and amines using the Milstein catalyst in a Pd-Ag/ceramic membrane reactor. A series of amides and ureas, which could not be synthesized in an open system by catalytic dehydrogenation coupling, were obtained in moderate to high yields via catalytic dehydrogenation of volatile alcohols and amines. This process could be monitored by the hydrogen produced. Compared to the

traditional method of condensation, this catalytic system avoids the stoichiometric pre-activation or *in situ* activation of reagents, and is a much cleaner process with high atom economy. This methodology, only possible by employing the Pd-Ag/ceramic membrane reactor, not only provides a new environmentally benign synthetic approach of amides and ureas, but is also a potential method for hydrogen storage.

Keywords: Pd-Ag/ceramic membrane reactor, amide and urea synthesis; dehydrogenative acylation, hydrogen production

## Introduction

Supported Pd-based composite membranes possess many attractive properties such as high and exclusive hydrogen permeability, high thermal stability, moderate chemical resistance and mechanical strength, making them one of the most applicable candidates for the selective removal of hydrogen [1, 2]. This offers unique opportunities to achieve dehydrogenative (oxidative) organic transformations which are otherwise impossible under the conventional reaction conditions. For example, we have previously demonstrated an environmentally friendly method of producing ethyl acetate from ethanol in a quantitative conversion and yield using an ultrathin Pd-Ag/ceramic membrane reactor. Since such a reaction can only be carried out at a reaction temperature higher than the boiling point of the reactant (ethanol 78 °C) and therefore, the produced hydrogen needs to be removed from the reaction system to overcome chemical equilibrium and also to avoid pressure build-up. The selective

removal of hydrogen by an ultrathin Pd-Ag membrane reactor was demonstrated to be a viable solution.[3] From the previous studies we also noticed that the reaction rate of dehydrogenative reactions is typically slow, presumably because of the relatively low reaction temperature. Therefore, a relatively long reaction time (typically in several hours) is required in order to achieve high conversion rate, but this also imposes a high requirement in membrane selectivity since otherwise the material loss during the reaction will be substantial. A membrane selectivity over 2000 for H<sub>2</sub>/N<sub>2</sub> was used in our previous studies as a good indicator of membrane quality.[3] Such a high selectivity requirement can be easily achieved by Pd-Ag membranes fabricated through a silver concentration-controlled co-plating method, but it is very challenging for other hydrogen selective membranes, such as polymer, silica, zeolite or carbon molecular sieve membranes [4]. The main disadvantage of the Pd-Ag membrane is its high material cost, but this can be well justified by the high value-added products.

Herein, we report the efficient synthesis of amides via catalytic dehydrogenative coupling of volatile alcohols and amines, and ureas using methanol as a non-toxic carbonyl source in an ultrathin Pd-Ag ceramic membrane reactor. The amide linkage is a common and very important functional group which contributes to the special properties of peptides, proteins, beta-lactam antibiotics, and numerous synthetic polymers [5]. Traditional methods of preparing amides mainly involve the use of activated acid derivatives (including acid chlorides and anhydrides). These processes usually require a stoichiometric amount of activating reagents, produce large amounts

of chemical waste, and involve tedious procedures for separation [6]. The development of atom economic reactions is an important aspect of green chemistry, which aims in the elimination or minimization of pollution caused by unwanted side-products. The direct synthesis of amides from alcohols with amines by extrusion of hydrogen to construct amide bonds has recently been reported [7-17]. This environmentally friendly approach does not require the use of stoichiometric amounts of oxidants, and hydrogen is produced as an additional value-generating product. The Milstein catalyst, carbonylhydrido [6-(di-*t*-butylphosphinomethylene)-2-(*N,N*-diethylaminomethyl) 1,6-dihydropyridine] ruthenium (Fig. 1, complex II), via aromatization-dearomatization of the central pyridine ring, has shown significant catalytic activities towards the direct synthesis of amides from alcohols and amines [7]. In the presence of the Milstein catalyst, a wide range of amides have been obtained through the dehydrogenative acylation of amines with alcohols, with the extension of the application for the synthesis of bis-amides and polyamides. However, high reaction temperatures are normally required in order to achieve good chemical yields. The utilization of these reactions to alcohols and amines with lower boiling points, such as methanol, ethanol and 1-propanol, still remains a challenge.

Urea derivatives are important biologically active compounds, which are frequently used in a variety of areas such as pharmaceuticals, chemical dyes, and agricultural pesticides [18]. These compounds are commonly synthesized using highly toxic phosgene or phosgene derivatives, such as carbodiimidazole (CDI), tri-phosgene

or S, S-dimethyl dithiocarbonate (DMDTC) [19]. Amines can also be oxidatively carbonylated with carbon monoxide in the presence of transition metal catalysts [20-24]. However, aside from the toxicity of CO, there exists the risk of explosions due to the usage of high pressures of CO. An alternative route of synthesizing urea derivatives is the direct reaction of amines with carbon dioxide [25, 26], but in general this method requires harsh reaction conditions (around 200 °C,  $P_{\text{CO}_2} > 6$  MPa), or the presence of stoichiometric amounts of bases such as  $\text{NEt}_3$ , or DBU [27]. Therefore, it is desirable to develop an environmentally benign and mild reaction for the construction of ureas.

Methanol, the simplest alcohol with an annual output of more than 40 million tons, has found widespread applications [28, 29]. It processes a high hydrogen to carbon ratio and carries 12.5 wt% of hydrogen. The production of hydrogen from methanol has received attention due to several advantages as compared to other fuels. For example, methanol is biodegradable and is liquid at atmospheric conditions, which makes it easy to manipulate. In addition, the reforming temperatures is low (200-300 °C) [30], which is much lower than that of other common fuels such as methane (>500 °C) and ethanol (ca. 400 °C) [25, 31]. For the dehydrogenation of methanol, there is a parallel side-reaction of the decomposition of methanol to CO. At 200 °C the equilibrium constant for the formation of formaldehyde is  $3.4 \times 10^{-2}$ , while the equilibrium constant for the decomposition of methanol to CO is  $2.6 \times 10$  [32]. While the complete dehydrogenation of methanol is favoured at equilibrium, formaldehyde

may combine with one molecule of amine to form a formamide, with the liberation of one molecule of H<sub>2</sub>. The formyl carbonyl will provide another position for the combination of one more amine. This will allow the direct synthesis of ureas from methanol and amines with a suitable catalytic system, utilizing methanol as a carbonyl source.

## Experimental

### Materials

Silver nitrate (AgNO<sub>3</sub>), palladium chloride (PdCl<sub>2</sub>), palladium sulfate (PdSO<sub>4</sub>), and ethylene diamine tetra-acetic acid disodium salt dihydrate (Na<sub>2</sub>EDTA), ammonia (NH<sub>4</sub>OH, 28-30% NH<sub>3</sub>), [2-(Di-*tert*-butylphosphinomethyl)-6 (diethylaminomethyl)pyridine] carbonyl chlorohydrido ruthenium (II) (Milstein catalyst I, precursor of Milstein Catalyst II), potassium *tert*-butoxide (KO<sup>t</sup>Bu), methanol (MOH), 1-propylamine (CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>NH<sub>2</sub>), butylamine (CH<sub>3</sub>(CH<sub>2</sub>)<sub>3</sub>NH<sub>2</sub>), hexylamine (CH<sub>3</sub>(CH<sub>2</sub>)<sub>5</sub>NH<sub>2</sub>), benzylamine (C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>NH<sub>2</sub>), ethylenediamine (NH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>NH<sub>2</sub>), and hydrazine hydrate (N<sub>2</sub>H<sub>4</sub>·H<sub>2</sub>O) were all received from Sigma-Aldrich and used without further purification. The purity of N<sub>2</sub>, H<sub>2</sub> and NH<sub>3</sub> is 99.999%. The water used in all reactions was obtained by filtering through a Millipore system. Asymmetric porous alumina tubular supports were supplied by Inopor Co. The inner and outer diameters and the length of the tubes are 7, 10 and 35 mm, respectively, and the nominal pore size of the surface layer is ~100 nm.

### Preparation of Pd-Ag/ceramic membrane

The Pd-Ag/ceramic membranes were prepared by the Ag-controlled electroless co-plating of Pd and Ag [3, 33]. Before plating the supports were cleaned sequentially by ethanol, 4% aqueous KOH solution and deionized water and well Pd seeding activated [34]. In a typical process, 60 mL Pd bath was loaded into a glass container and 15 mL Ag bath in a syringe. The Pd bath contain 3.9 mmol/L PdCl<sub>2</sub>, 5.0 mol/L NH<sub>4</sub>OH and 0.12 mol/L Na<sub>2</sub>EDTA dissolved in deionized water, and the Ag bath contain 5.1 mmol/L AgNO<sub>3</sub>, 5.0 mol/L NH<sub>4</sub>OH, and 0.12 mol/L Na<sub>2</sub>EDTA mixed in deionized water. To achieve a defect-free membrane, the plating process was conducted twice. After the first plating, the membrane was washed, dried and then annealed 10 h at 500 °C in H<sub>2</sub>. Then the membrane was seeded again before the second co-plating. The final Pd-Ag membrane was heat-treated at 500 °C in H<sub>2</sub> for 36 h before used for reaction.

### Reactions in the membrane reactor

The design of the membrane reactor was previously described [3]. The tubular membrane was mounted in a custom-designed cylinder cell and sealed by graphite gasket O-rings at both ends. The space between the shell side of the membrane and the cylinder cell, which is about 2 ml, is used as the reaction chamber. The membrane surface area is approximately 6 cm<sup>2</sup>. The cylinder cell was placed inside a vertical furnace with programmable temperature controller. The reaction temperature was fixed on 140-180 °C for different reactions. In a typical reaction, methanol (1.25-5 mmol), amine (5 mmol), Milstein catalyst I (0.005 mmol), KO<sup>t</sup>Bu (0.005 mmol) and



solvent (1 mL, toluene/NMP/dioxane) mixture was loaded into the chamber of reactor under an argon atmosphere. The reaction was then monitored until completion. The actual feed side pressure was monitored and recorded every 20 seconds with a pressure sensor on real-time at the retentate exit of the reactor. The liberated hydrogen in the permeance side of membrane was swept by constant flow rate Argon and the gas mixture was sequenced analyzed by an on-line GC (Agilent 7890A with PLOT/Q column) per 4 min. The Pd-Ag membrane was washed with acetone and methanol several times and then dried at 100 °C after each reaction. The leakage of membrane with 8 bar N<sub>2</sub> was checked by soap bubble meter (range 0-10 ml) before each reaction. For comparison purpose, the above reaction was also conducted in a closed autoclave. The maximum pressure that might generate from the released hydrogen is about 35 bar.

### **Product Analysis**

NMR spectra were recorded using Bruker AVIII 400 or AVIII 500 spectrometer. Chemical shifts in <sup>1</sup>H NMR were reported in parts per million (ppm) downfield from tetramethylsilane. GC-MS spectra of final product were obtained on an Agilent 5975C with an HP-5 MS column.

### **Results and discussion**

#### **Pd-Ag Membrane properties and quality test**

The Pd-Ag membrane contains about 25 wt% silver uniformly distributed along the entire membrane. It is reported that the Pd-Ag membrane at this composition has the best chemical and mechanical stability [35]. The membrane thickness is about 5

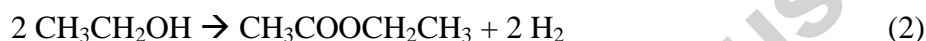
$\mu\text{m}$ . the  $\text{H}_2$  flux of the fresh membrane under  $\Delta P = 100 \text{ kPa}$  were 0.28 and 0.47  $\text{mol/m}^2 \text{ s}$  at 150 °C and 350 °C, respectively. Because the total amount of reaction solution loaded into the membrane reactor is about 2 ml and the reaction lasts typically for more than 5 h, so the membrane must be very compact to avoid notable material loss during the reaction. Nitrogen leakage test was used to monitor the membrane quality. The nitrogen leakage rate under 8 bar less than 1 ml/min measured by a soap bubble meter, which is equivalent to a  $\text{H}_2/\text{N}_2$  selectivity of 2000, was used as a guideline for a direct-free membrane. The membrane reactor can be easily changed to a gas permeation cell without taking the membrane out. So this leakage test can be performed conveniently before each batch of reaction.

#### **Acylation of amines with alcohols**

The  $\text{H}_2$  permeability of the membrane in our design ensures the capability of the Pd-Ag membrane in fully removing the produced hydrogen during the course of the reaction. Initial experiments were conducted using ethanol and 1-butylamine as the substrate under a variety of reaction conditions. The results of these experiments are summarized in Table 1. The reaction proceeds smoothly in the presence of a base. Toluene was found to be the best solvent compared to 1,4-dioxane and tetrahydrofuran, affording the N-butylacetamide in 61% yield at 160 °C in 5 h (Table 1, entry 3). Increasing the reaction temperature to 180 °C did not improve the yield, leading to a messy reaction, presumably due to the decomposition of the catalyst at high temperatures (Table 1, entry 4). Prolonging the reaction time to 24 hours led to

no observable improvement to the reaction outcome (Table 1, entry 5), while lowering the reaction temperature to 140 °C gave a cleaner reaction with a slightly higher yield of 70% (Table 1, entry 6). As a comparison, all the reactions in Table 1 have less than 10% yield when carried out in a closed autoclave under the same reaction conditions.

Fig. 2 shows the rate of H<sub>2</sub> release and the total pressure of the chamber at time intervals of 20 seconds, when the reaction was carried out at 160 °C (Table 1, entry 5). The possible reactions in the case of ethanol and 1-butylamine are listed in Eq. (1)-(3):



The maximum amount of H<sub>2</sub>, 244.5 mL, will be generated if all the ethanol is fully dehydrogenated. The total volume of H<sub>2</sub> was calculated to be 178.3 mL, as seen in Fig.2, indicating that the conversion of ethanol in the reaction was approx. 73%. The H<sub>2</sub> release rate approached to zero after 3.5 h of reaction time (Fig. 2). This is consistent with the negligible increase in chemical yield when the reaction time was extended to 24 h (Entry 5, Table 1). The inner pressure of the reaction chamber can be used to monitor whether non-permeable gases were generated and retained in the system. It was observed that there was a sharp increase in the inner pressure curve in the first 85 min of the reaction as the reaction chamber was heated to the target temperature (160 °C) during this period. Thereafter, the inner pressure synchronously

decreased with the H<sub>2</sub> release rate. The net inner pressure decreased to zero when the system was cooled down to room temperature, indicating that no non-permeable gases such as CO were residual and the Pd-Ag membrane can remove hydrogen from the system very efficiently.

With the optimized conditions in hand, we subsequently investigated the substrate scope of the direct synthesis of amides by catalytic dehydrogenative coupling of alcohols and amines in the Pd-Ag/ceramic membrane reactor. Several reactions either containing low boiling point alcohols (ethanol) or low boiling point amines (propylamine, *n*-butylamine) were tested, and moderate to good yields could be obtained (Table 2). Acylation of different amines with ethanol afforded the products in 65-72% yields, while higher yields were obtained with longer chain amines (Table 2, entry 1-3). This reaction also worked well with 1-butanol (60-74% yields) and 1-hexanol (61-68% yields).

#### **Ureas synthesis from methanol and amines**

Inspired by these results, we examined the dehydrogenation reactions of methanol in the Pd-Ag membrane reactor with the Milstein catalyst. Fig. 3 shows the H<sub>2</sub> release rate and inner pressure of reaction chamber for the dehydrogenation of 1 mL methanol with 0.5 mol% catalyst at 160 °C. After 18 h, the H<sub>2</sub> collected in the lumen side of the membrane was only 51 mL. This suggested that the conversion of methanol was between 4.2-8.5 % depending on whether it was dehydrogenated to CO, formate or carbonate. During the reaction, the inner pressure (ca. 23 bar) was much

higher than the saturated vapour pressure of methanol at 160 °C (17.1 bar) and the inner pressure remained 3.7 bar when the reactor was cooled down to room temperature. These observations showed that some impermeable gases were generated in this reaction. Further analysis of the gas phase proved that the impermeable gas was CO with trace amounts of methyl formate detected from the liquid mixture, indicating that methanol was catalytically dehydrogenated to form CO by the catalyst, consistent with its thermodynamic properties [32].

From the amide synthesis, we rationalized that the dehydrogenation of methanol may be facilitated in the presence of an amine. To investigate the possibility, initial experiments were conducted using methanol and 1-butylamine as the substrates in a variety of reaction conditions. When a toluene solution of Milstein catalyst (0.5 mol%) with methanol and butylamine (1:1 ratio) was heated in the Pd-Ag membrane reactor at 180 °C for 12 hours, 38% yield of 1, 3-dibutylurea was observed (Entry 1, Table 3). The yield of *N,N'*-dibutylurea was increased to 65% when the methanol to butylamine ratio was changed to 1:2 (Entry 2, Table 3). The effect of temperature on the yield of dibutylurea was tested and the yield slightly increased to 67% when the reaction temperature was lowered to 140 °C (Entry 5, Table 3).

The H<sub>2</sub> release rate on the lumen side of membrane and pressure inside the reaction chamber were monitored in real time. Fig. 4 shows the H<sub>2</sub> flux and inner pressure of reaction Entry 5 of Table 3. The total H<sub>2</sub> volume was 164 mL by the integration of H<sub>2</sub> release rate curve. For each of the urea molecule formed, three

hydrogen molecules are generated for one molecule of methanol and 2 molecules of amine. In the case of Table 3 Entry 5, the conversion of methanol was approx. 90%. The H<sub>2</sub> release rate was close to zero after a reaction time of 7.5 h. After the reaction, the net inner pressure decreased to zero when cooling the system to room temperature, again indicating that there was no impermeable gases in the residual. The observations show that the dehydrogenative coupling of the amine with methanol was more efficient than the dehydrogenative homocoupling of methanol.

The scope of the reaction was examined using various amines. Heating a toluene solution containing methanol (2.5 mmol), propylamine (5 mmol) and Milstein catalyst in the Pd-Ag membrane reactor at 140 °C for 12 h resulted in ca. 95% conversion of methanol as observed by on-line H<sub>2</sub> collection, with the exclusive formation of *N,N'*-dipropylurea in 70 and 78% isolated yield, respectively (Entry 7 & 8, Table 3). Similarly, heating a toluene solution containing methanol and hexylamine or benzylamine resulted in ca. 94% conversion of methanol, with the yield of the corresponding ureas 65% and 62%, respectively. The generated H<sub>2</sub> was *in-situ* removed by the Pd-Ag membrane from the reaction system.

### **Cyclic ureas synthesis from methanol and diamines**

To explore the synthetic utility of this reaction, various diamines instead of *n*-amines, and methanol were introduced to the reaction system to form cyclic ureas. When a NMP solution of Milstein catalyst (0.5 mol%) with methanol and propanediamine (1:1 ratio) was heated in the Pd-Ag membrane reactor at 140 °C for

12 hours, 46% yield of *N,N'*-trimethyleneurea was observed (Entry 1, Table 4). The yield of cyclic urea increased to 59% when the methanol to propanediamine ratio was changed to 3.7:5 (Entry 2, Table 4). The yield slightly decreased to 54% when the reaction was carried out with the same substrates and the temperature up to 180 °C (Entry 3, Table 4). Doubling the catalyst amount led to an increase in the yield to 67% after 12 h reaction at 140 °C (Entry 4, Table 4). The net inner pressure of the reactor decreased to zero when the system was cooled down to room temperature. Similar to the case of noncyclic urea synthesis, it indicated that no non-permeable gases were formed. Ethanediamine and butanediamine can be used to prepare 2-imidazolidone and *N,N'*-tetramethyleneurea in 46% and 40% yields (Entries 5 and 6, Table 4).

### Membrane stability

During the reactions the membrane exhibited exceptional mechanical/thermal stability. The membrane maintained defect-free over more than 600 h of the dehydrogenative acrylation reactions and more than 30 times heating/cooling processes between room temperature and the reaction temperature (140-180 °C), even the reaction solution contained corrosive amines, amides, ureas, alcohol and homogenous Ru catalysts. Fig. 6 shows the SEM image of the Pd-Ag membrane at fresh and after 600 h reaction. No apparent change was observed.

### Conclusions

In summary, we reported the highly efficient synthesis of amides directly from volatile alcohols and amines using an ultrathin Pd-Ag membrane reactor. This

environmentally benign reaction is homogeneously catalyzed by the Milstein catalyst, a dearomatized PNN-Ru complex. A series of amides and ureas could be obtained in moderate to good yields. Compared with conventional condensation methods, our catalytic system avoids the requirement of stoichiometric pre-activation or *in situ* activation reagents and provides a much cleaner process with high atomic economy. A defect-free Pd-Ag membrane is employed to remove the liberated hydrogen *in-situ*, which allows the reaction to operate at an elevated temperature and high pressure. Liberated H<sub>2</sub> fluxes and the inner pressure of reactor can be used to accurately monitor the reaction progress in real-time. The Pd-Ag membrane showed excellent mechanical/thermal stability during the reactions.

### Acknowledgements

We are grateful for the generous financial support from King Abdullah University of Science and Technology. T. C. thanks the Natural Science Foundation of China (21302170) and the Public Projects of Zhejiang Province (2016C33017). G. Z thanks the support of Natural Science Foundation of China (21506243), Shanghai Municipality Sci & Tech Commission (14DZ1203700) and Youth Innovation Promotion Association of CAS (Y624211401).

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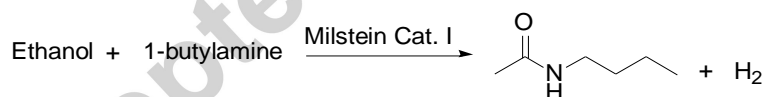
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**Table 1:** Direct dehydrogenative coupling of 1-butylamine with ethanol in a Pd-Ag membrane reactor.<sup>a</sup>

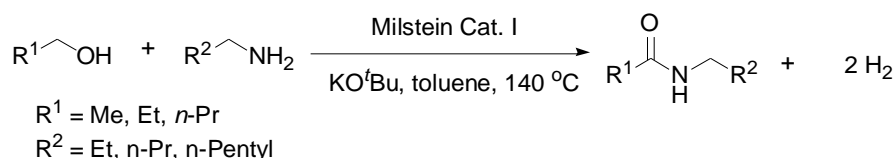


Entry	Solvent	T (°C)	Time (h)	Yield(%) <sup>b</sup>
1	1,4-dioxane	160	5	57
2	THF	160	5	52
3	Toluene	160	5	61
4	Toluene	180	5	55
5	Toluene	160	24	63
6	Toluene	140	5	70

<sup>a</sup> Reaction conditions: Milstein Catalyst II (0.025 mmol), alcohol (5 mmol), amine (5 mmol), and toluene (1 mL) were heated in a Pd-Ag/ceramic membrane reactor. <sup>b</sup>

Yields were determined by <sup>1</sup>H NMR.

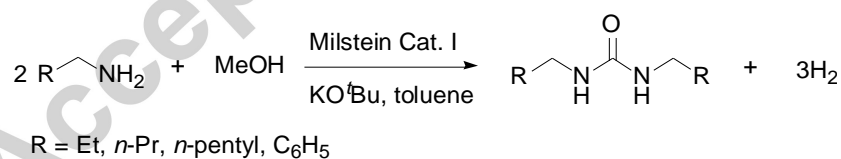
**Table 2:** Direct dehydrogenative coupling of amines with alcohols in a Pd-Ag membrane reactor.<sup>a</sup>



Entry	Alcohol	Amine	Amide	Yield(%) <sup>b</sup>
1	ethanol	1-butylamine	N-Butyl-acetamide	70
2	ethanol	1-hexylamine	N-Hexyl-acetamide	72
3	ethanol	1-propylamine	N-Propyl-acetamide	65
4	1-butanol	1-propylamine	N-Propyl-butyramide	60
5	1-butanol	1-butylamine	N-Butyl-butyramide	67
6	1-butanol	1-hexylamine	N-Hexyl-butyramide	74
7	1-hexanol	1-propylamine	Hexanoic acid propylamide	61
8	1-hexanol	1-butylamine	Hexanoic acid butylamide	63
9	1-hexanol	1-hexylamine	Hexanoic acid hexylamide	68

<sup>a</sup> Reaction conditions: Milstein Catalyst II (0.025 mmol), alcohol (5 mmol), amine (5 mmol), and toluene (1 mL) were heated at 140 °C in a Pd-Ag/ceramic membrane reactor. <sup>b</sup> Yields were determined by <sup>1</sup>H NMR.

**Table 3:** Direct synthesis of symmetrical ureas from methanol and amines in a Pd-Ag membrane reactor.<sup>a</sup>



Entry	T (°C)	Methanol (mmol)	Amine (mmol)	Yield(%) <sup>b</sup>
1	180	5	Butyl amine (5)	38
2	180	2.5	Butyl amine (5)	65
3	180	1.25	Butyl amine (5)	83
4 <sup>c</sup>	180	2.5	Butyl amine (5)	70
5	140	2.5	Butyl amine (5)	67
6 <sup>d</sup>	140	2.5	Butyl amine (5)	78
7	140	2.5	Propyl amine (5)	70
8 <sup>d</sup>	140	2.5	Propyl amine (5)	78
9	140	2.5	Hexyl amine (5)	65

10

140

2.5

Benzyl amine (5)

62

<sup>a</sup> Reaction conditions: Milstein Catalyst II (0.5 mol% based on amine), methanol, amine (5 mmol), and toluene (1 mL) were heated in a Pd-Ag/ceramic membrane reactor. <sup>b</sup> Yields were determined by GC-MS or <sup>1</sup>H NMR. <sup>c</sup> The reaction time is 24 h. <sup>d</sup> the catalyst loading is 1.0 mmol%.

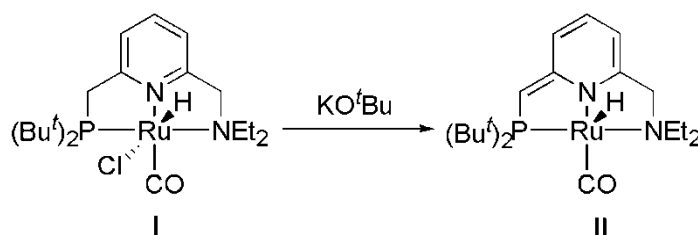
**Table 4:** Direct synthesis of lactams from methanol and diamines in a Pd-Ag membrane reactor.<sup>a</sup>

$$\text{H}_2\text{N}-(\text{CH}_2)_n\text{NH}_2 + \text{MeOH} \xrightarrow[\text{KO}^t\text{Bu, NMP}]{\text{Milstein Cat. I}} \text{HN}(\text{C}_n\text{H}_2)\text{NH} \begin{matrix} \text{O} \\ \parallel \end{matrix}$$

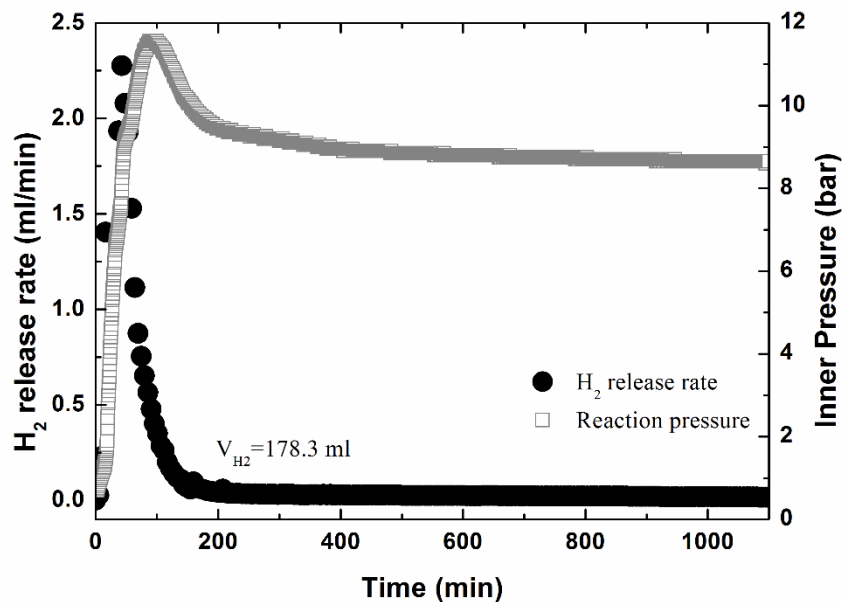
$n = 2, 3, 4$

Entry	T (°C)	Methanol (mmol)	Amine (mmol)	Yield <sup>b</sup> (%)
1	140	5	1,3-Diaminopropane	46
2	140	3.7	1,3-Diaminopropane	59
3	180	3.7	1,3-Diaminopropane	54
4 <sup>c</sup>	140	3.7	1,3-Diaminopropane	67
5	140	5	1,2-Diaminoethane	46
6	140	5	1,4-Diaminobutane	40

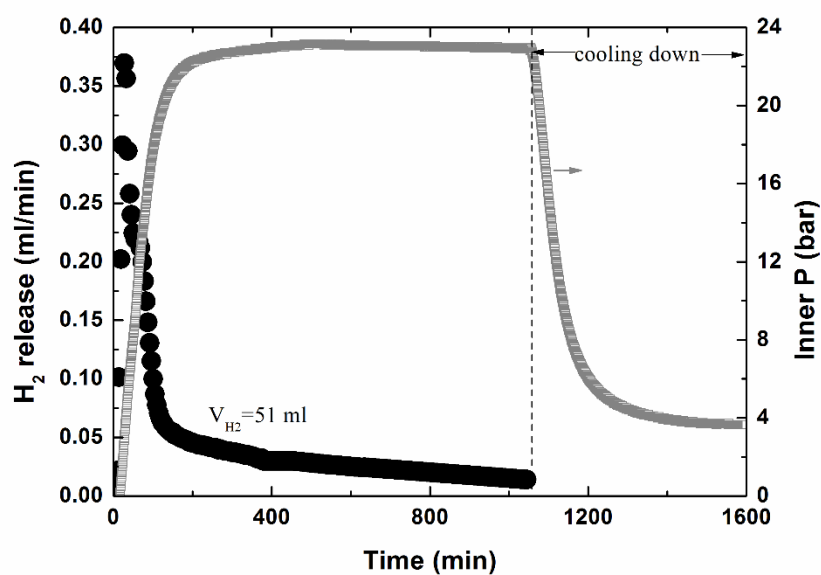
<sup>a</sup> Reaction conditions: Milstein Catalyst II (0.5 mol% based on amine), methanol, amine (5 mmol), and toluene (1 mL) were heated in a Pd-Ag/ceramic membrane reactor. <sup>b</sup> Yields were determined by GC-MS or <sup>1</sup>H NMR. <sup>c</sup> the catalyst loading is 1.0 mmol%.



**Figure 1.** The Milstein catalysts

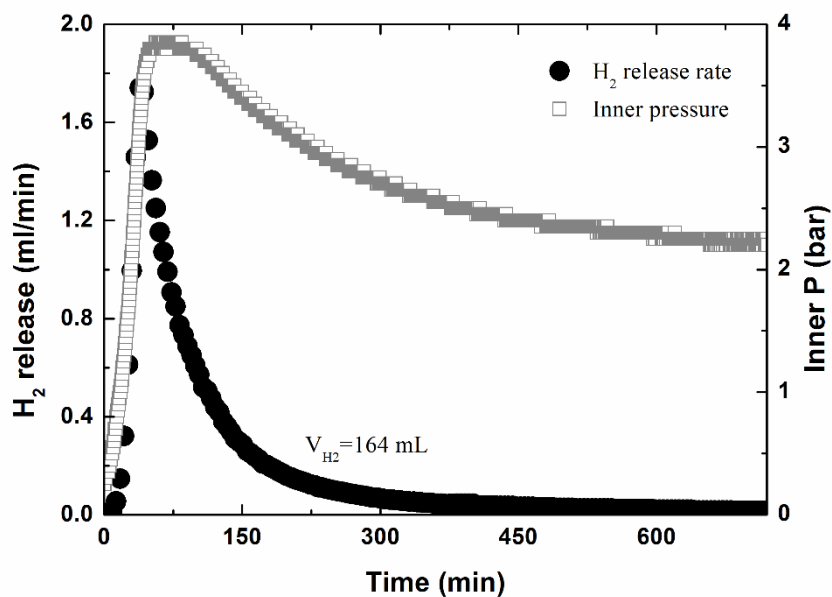


**Figure 2.** H<sub>2</sub> liberation rate and the total pressure of the reaction at different reaction time at 160 °C using ethanol and 1-butylamine as substrates.

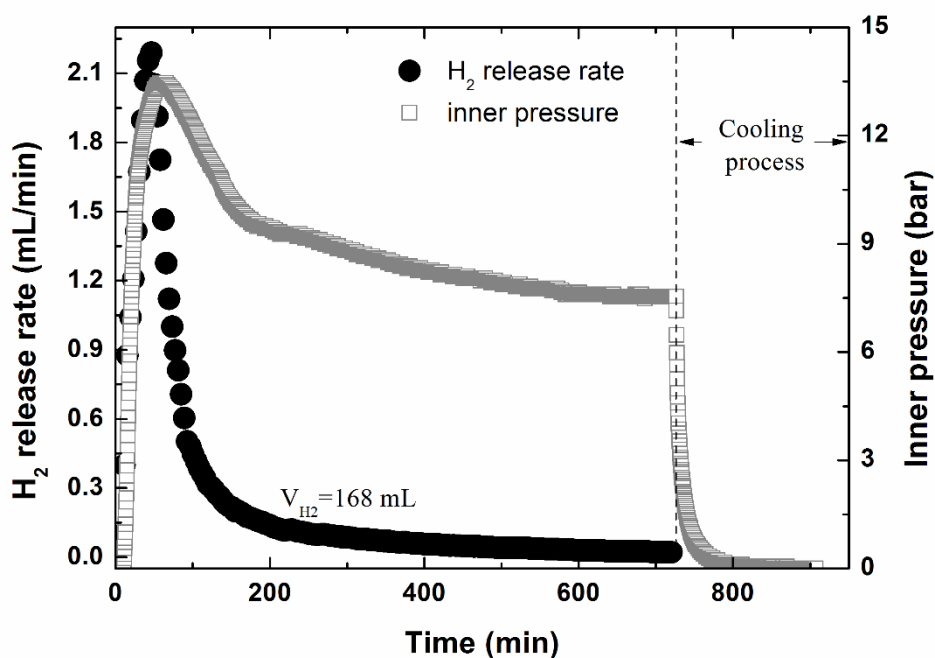


**Figure 3.** H<sub>2</sub> liberation rate and the total pressure of the methanol dehydrogenation at different reaction time at 160 °C.





**Figure 4.** H<sub>2</sub> liberation rate and the total pressure of the reaction at different reaction time at 140 °C using methanol and 1-butylamine as substrates.



**Figure 5.** H<sub>2</sub> liberation rate and the total pressure of the reaction at different reaction time at 140 °C using methanol and 1,3-diaminopropane as substrates.

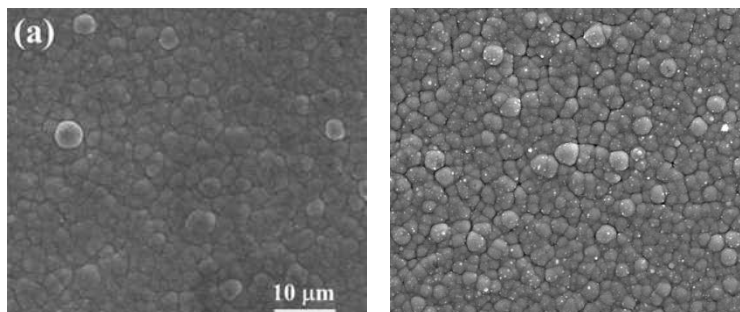
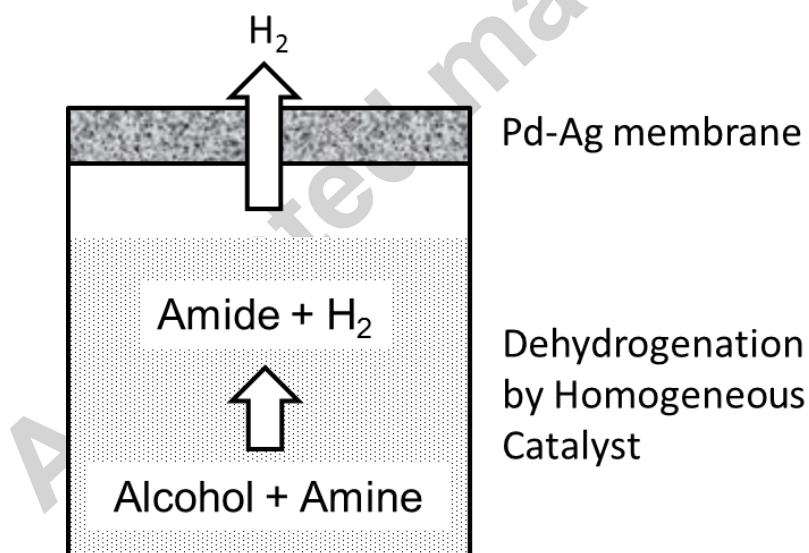


Figure 6: Top view SEM images of Pd-Ag membrane. (a) Fresh membrane and (b) after more than 600 h dehydrogenative reaction and over 30 times heating/cooling processes.

### Graphical Abstract



Using a Pd-Ag membrane reactor makes it possible to use homogeneous catalysts as a novel approach to prepare amides through direct dehydrogenation coupling of alcohols and amines at elevated temperature, and the removal of hydrogen during the reaction pushes the reaction to be completely almost quantitatively.

**Highlights**

- An environmentally benign synthetic approach for amides and ureas were developed
- Dehydrogenation coupling of volatile alcohols and amines were realized
- Pd-Ag/ceramic membrane reactor for hydrogen separation was adopted
- A potential method for hydrogen storage was provided

Accepted manuscript