[19] Patents Registry
The Hong Kong Special Administrative Region
香港特別行政區
專利註冊處

[11] 1188411 B
EP 2629889 B1

[12] **STANDARD PATENT (R) SPECIFICATION**
轉錄標準專利說明書

[21] Application no. 申請編號
13113739.4

[22] Date of filing 提交日期
10.12.2013

[51] Int. Cl.
C07D 487/14 (2006.01) C07C 29/136 (2006.01)
C07C 29/149 (2006.01) C07C 29/17 (2006.01)
C07C 67/00 (2006.01) C07C 67/03 (2006.01)
C07D 309/30 (2006.01) C07C 41/16 (2006.01)
C07C 45/00 (2006.01) C07F 15/00 (2006.01)
C07C 209/62 (2006.01) C07C 213/00 (2006.01)
C07D 241/08 (2006.01) C07D 241/12 (2006.01)
C07C 231/02 (2006.01) C07C 231/10 (2006.01)
C07D 207/08 (2006.01) C07D 295/023 (2006.01)
C07D 213/38 (2006.01) C07C 51/23 (2006.01)

[54] RUTHENIUM COMPLEXES AND THEIR USES IN PROCESSES FOR FORMATION AND/OR HYDROGENATION OF ESTERS, AMIDES AND DERIVATIVES THEREOF
釕複合物及其用在酯類、酰胺類及其衍生物的形成及/或氫化反應的方法的用途

[30] Priority 優先權
19.10.2010 US 61/394,387

[43] Date of publication of application 申請發表日期
02.05.2014

[45] Date of publication of grant of patent 批予專利的發表日期
17.04.2020

[86] International application no. 國際申請編號
PCT/IL2011/000817

[87] International publication no. and date 國際申請發表編號及日期
WO2012/052996 26.04.2012

EP Application no. & date 歐洲專利申請編號及日期
EP 11788587.1 11.10.2011

EP Publication no. & date 歐洲專利申請發表編號及日期
EP 2629889 28.08.2013

Date of grant in designated patent office 指定專利當局批予專利日期
03.04.2019

[73] Proprietor 專利所有人
Yeda Research and Development Co. Ltd.
At the Weizmann Institute of Science
P.O. Box 95, 76100 Rehovot
ISRAEL

[72] Inventor 發明人
MILSTEIN, David
BALARAMAN, Ekambaram
GUNANATHAN, Chidambaram
GNANAPRAKASAM, Boopathy
ZHANG, Jing

[74] Agent and / or address for service 代理人及/或送達地址
NTD PATENT & TRADE MARK AGENCY LIMITED
Units 1805-6, 18/F., Greenfield Tower, Concordia Plaza
No. 1 Science Museum Road, Tsimshatsui East, Kowloon
HONG KONG

(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) EP 2 629 889 B1

(12) **EUROPEAN PATENT SPECIFICATION**

(45) Date of publication and mention of the grant of the patent:
03.04.2019 Bulletin 2019/14

(21) Application number: **11788587.1**

(22) Date of filing: **11.10.2011**

(51) Int Cl.:
C07D 487/14 *(2006.01)*
C07C 29/149 *(2006.01)*
C07C 67/00 *(2006.01)*
C07D 309/30 *(2006.01)*
C07C 45/00 *(2006.01)*
C07C 209/62 *(2006.01)*
C07D 241/08 *(2006.01)*
C07C 231/02 *(2006.01)*
C07D 207/08 *(2006.01)*
C07D 213/38 *(2006.01)*
C07C 29/136 *(2006.01)*
C07C 29/17 *(2006.01)*
C07C 67/03 *(2006.01)*
C07C 41/16 *(2006.01)*
C07F 15/00 *(2006.01)*
C07C 213/00 *(2006.01)*
C07D 241/12 *(2006.01)*
C07C 231/10 *(2006.01)*
C07D 295/023 *(2006.01)*
C07C 51/23 *(2006.01)*

(86) International application number:
PCT/IL2011/000817

(87) International publication number:
WO 2012/052996 (26.04.2012 Gazette 2012/17)

(54) **RUTHENIUM COMPLEXES AND THEIR USES IN PROCESSES FOR FORMATION AND/OR HYDROGENATION OF ESTERS, AMIDES AND DERIVATIVES THEREOF**

RUTHENIUMKOMPLEXE UND IHRE VERWENDUNG BEI VERFAHREN ZUR BILDUNG UND/ODER HYDRIERUNG VON ESTERN, AMIDEN UND DERIVATEN DAVON

COMPLEXES DE RUTHÉNIUM ET LEURS UTILISATIONS DANS DES PROCÉDÉS DE PRÉPARATION ET/OU D'HYDROGÉNATION D'ESTERS, D'AMIDES ET DE LEURS DÉRIVÉS

(84) Designated Contracting States:
AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HR HU IE IS IT LI LT LU LV MC MK MT NL NO PL PT RO RS SE SI SK SM TR

(30) Priority: **19.10.2010 US 394387 P**

(43) Date of publication of application:
28.08.2013 Bulletin 2013/35

(73) Proprietor: **Yeda Research and Development Co. Ltd.**
76100 Rehovot (IL)

(72) Inventors:
- **MILSTEIN, David**
  76100 Rehovot (IL)
- **BALARAMAN, Ekambaram**
  76100 Rehovot (IL)
- **GUNANATHAN, Chidambaram**
  76100 Rehovot (IL)
- **GNANAPRAKASAM, Boopathy**
  76100 Rehovot (IL)
- **ZHANG, Jing**
  76100 Rehovot (IL)

(74) Representative: **Pearl Cohen Zedek Latzer Baratz UK LLP**
16 Upper Woburn Place
London WC1H 0BS (GB)

(56) References cited:
EP-A1- 2 161 251 US-A1- 2009 112 005

- **FOGLER E ET AL: "New CNN-Type Ruthenium Pincer NHC Complexes. Mild, Efficient Catalytic Hydrogenation of Esters", ORGANOMETALLICS, vol. 30, no. 14, 25 July 2011 (2011-07-25) , pages 3826-3833, XP55023109, ISSN: 0276-7333, DOI: 10.1021/om200367j**
- **BALARAMAN E ET AL: "Efficient hydrogenation of organic carbonates, carbamates and formates indicates alternative routes to methanol based on CO2 and CO", NATURE CHEMISTRY, vol. 3, no. 8, August 2011 (2011-08), pages 609-614, XP009150768, ISSN: 1755-4330, DOI: 10.1038/nchem.1109**

Note: Within nine months of the publication of the mention of the grant of the European patent in the European Patent Bulletin, any person may give notice to the European Patent Office of opposition to that patent, in accordance with the Implementing Regulations. Notice of opposition shall not be deemed to have been filed until the opposition fee has been paid. (Art. 99(1) European Patent Convention).

Printed by Jouve, 75001 PARIS (FR)

(Cont. next page)

- CANTILLO D: "Mechanistic Insights on the Ruthenium-Catalyzed Hydrogenation of Amides - C-N vs. C-O Cleavage", EUROPEAN JOURNAL OF INORGANIC CHEMISTRY, vol. 2011, no. 19, July 2011 (2011-07), pages 3008-3013, XP55023120, ISSN: 1434-1948, DOI: 10.1002/ejic.201100443
- BALARAMAN E ET AL: "Direct Hydrogenation of Amides to Alcohols and Amines under Mild Conditions", JOURNAL OF THE AMERICAN CHEMICAL SOCIETY, vol. 132, no. 47, 1 December 2010 (2010-12-01), pages 16756-16758, XP55016966, ISSN: 0002-7863, DOI: 10.1021/ja1080019
- ZIESSEL R ET AL: "Co-ordinative properties of a hybrid phosphine-bipyridine ligand", JOURNAL OF THE CHEMICAL SOCIETY, DALTON TRANSACTIONS, no. 20, 1997, pages 3777-3784, XP55023123, ISSN: 0300-9246, DOI: 10.1039/a702463k
- ZHANG J ET AL: "Electron-Rich PNP- and PNN-Type Ruthenium(II) Hydrido Borohydride Pincer Complexes. Synthesis, Structure, and Catalytic Dehydrogenation of Alcohols and Hydrogenation of Esters", ORGANOMETALLICS, vol. 30, no. 21, 18 October 2011 (2011-10-18), pages 5716-5724, XP55030403, ISSN: 0276-7333, DOI: 10.1021/om200595m
- ZHANG J ET AL: "Electron-rich, bulky PNN-type ruthenium complexes: synthesis, characterization and catalysis of alcohol dehydrogenation", DALTON TRANSACTIONS, no. 1, 2007, pages 107-113, XP55023397, ISSN: 1477-9226, DOI: 10.1039/b613438f
- NÚÑEZ MAGRO A A ET AL: "The synthesis of amines by the homogeneous hydrogenation of secondary and primary amides", CHEMICAL COMMUNICATIONS, vol. 30, 6 July 2007 (2007-07-06), pages 3154-3156, XP002471049, ISSN: 1359-7345, DOI: 10.1039/B706635J
- ZHANG J ET AL: "Efficient Homogeneous Catalytic Hydrogenation of Esters to Alcohols", ANGEWANDTE CHEMIE, INTERNATIONAL EDITION, vol. 45, no. 7, 6 February 2006 (2006-02-06), pages 1113-1115, XP55016953, ISSN: 1433-7851, DOI: 10.1002/anie.200503771

Description

FIELD OF THE INVENTION

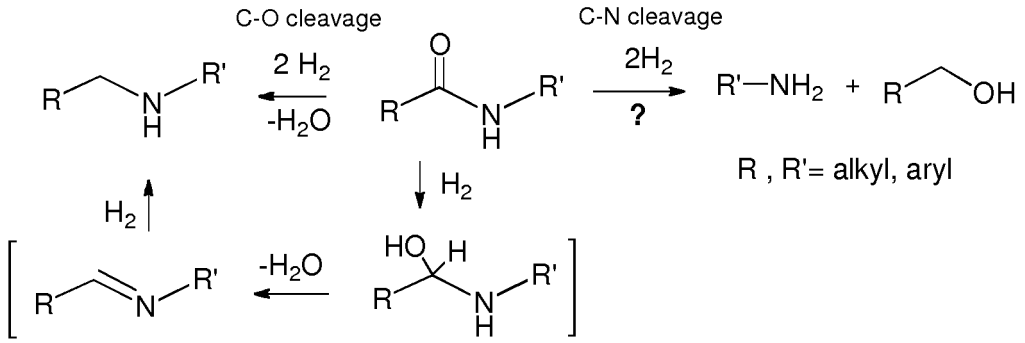
[0001] The present invention relates to novel Ruthenium complexes and related borohydride complexes, and their use, *inter alia,* for (1) hydrogenation of amides (including polyamides) to alcohols and amines; (2) preparing amides from alcohols with amines (including the preparation of polyamides (e.g., polypeptides) by reacting dialcohols and diamines and/or by polymerization of amino alcohols); (3) hydrogenation of esters to alcohols (including hydrogenation of cyclic esters (lactones) or cyclic di-esters (di-lactones), or polyesters); (4) hydrogenation of organic carbonates (including polycarbonates) to alcohols and hydrogenation of carbamates (including polycarbamates) or urea derivatives to alcohols and amines; (5) dehydrogenative coupling of alcohols to esters; (6) dehydrogenation of secondary alcohols to ketones; (7) amidation of esters (i.e., synthesis of amides from esters and amines); (8) acylation of alcohols using esters; (9) coupling of alcohols with water and a base to form carboxylic acids; and (10) dehydrogenation of beta-amino alcohols to form pyrazines. The present invention further relates to the novel uses of certain pyridine Ruthenium complexes.

BACKGROUND OF THE INVENTION

[0002] Reduction of carboxylic acids and their derivatives plays an important role in organic synthesis, both in laboratory and industrial processes. Traditionally, the reduction is performed using stochiometric amounts of hydride reagents, generating stochiometric amounts of waste (Seyden-Penne). A much more attractive, atom-economical approach is a catalytic reaction using H_2; however, hydrogenation of carboxylic acid derivatives under mild conditions is a very challenging task (Rylander; Hartwig), with amides presenting the one of the highest challenges among all classes of carbonyl compounds. A few examples of the important hydrogenation of amides to amines, in which the C-O bond is cleaved with the liberation of water (Scheme 1), were reported (Hirosawa et al., Núñez Magro et al., Beamson et al.). This reaction can also be affected with silanes as reducing agents (Fernandes et al., Das et al.). In addition, the interesting hydrogenation of cyclic N-acylcarbamates and N-acylsolfonamides, which involves cleavage of the C-N bond, but does not form amines, was recently reported (Ito et al., 2009).

[0003] On the other hand, selective, direct hydrogenation of amides to form amines and alcohols has not been reported. Hydrogenation of amides to amines (*via* C-O cleavage, generating water) can have C-N cleavage as a side reaction, requiring the presence of water, and resulting from catalytic hydrolysis of the amides to acids and amines, followed by hydrogenation of the acids to alcohols: see Núñez Magro et al. and Beamson et al) However, no amide C-N hydrogenolysis to form alcohols and amines was reported in absence of water.

[0004] Amines and alcohols are used extensively in the chemical, pharmaceutical and agrichemical industries (Lawrence; Ricci; Kumara et al.). Design of such a reaction is conceptually challenging, since the first mechanistic step in amide hydrogenation is expected to be H_2 addition to the carbonyl group to form a very unstable hemiaminal which, in the case of primary or secondary amides, spontaneously liberates water to form an imine; further hydrogenation of the imine then leads to amine formation (Scheme 1). For amine and alcohol formation, cleavage of the C-N bond in preference to the C-O bond is required.



Scheme 1. General scheme for hydrogenation of amides.

[0005] The reverse reaction, i.e., amide formation from alcohols and amines with liberation of H_2, was previously reported by inventors of the present invention, and later, by others (Nordstrom; Ghosh; Shimizu) Formation of amides from alcohols and amines by use of hydrogen acceptors was also reported recently (Zweifel; Watson). The importance of amides in chemistry and biology is well recognized and has been studied extensively (Sewald et al.; Greenberg et

al.; Smith and March; Bray). Although several methods are known for the synthesis of amides, preparation under neutral conditions and without generation of waste is a challenging goal (Larock; Smith). Synthesis of amides is mostly based on activated acid derivatives (acid chlorides, anhydrides) or rearrangement reactions induced by acid or base which often involve toxic chemical waste and tedious work-up (Smith). Transition-metal catalyzed conversion of nitriles into amides was reported (Cobley et al.; Murahashi et al. 1986 and 1992). Catalytic acylation of amines by aldehydes in the presence of a stoichiometric amount of oxidant and a base is known (Tamaru et al., Tillack et al.). Recently, oxidative amide synthesis was achieved from terminal alkynes (Chan et al.). Cu(I) catalyzed reaction of sulfonyl azides with terminal alkynes is a facile method for the synthesis of sulfonyl amides (Cho et al.; Cassidy et al.).

[0006] Polyamides are one of the most important polymer classes, extensively used in fiber products, plastics and their derivatives, with many applications, including in biomedical studies. Recently, the synthesis of functional polyamides has received considerable attention. Generally, polyamides are synthesized by condensation of diamines and activated dicarboxylic acid derivatives and/or in the presence of coupling reagents. In some cases, ring opening of small-ring lactams at high temperatures leads to polyamides. To avoid the use of activators, waste generation, or harsh conditions, the development of economical, efficient and environmentally benign protocols are desirable.

[0007] Transition metal borohydride complexes display extensive reactivity with organic substrates and are useful starting materials for the preparation of transition metal hydrides and borides (Dick et al; White et al). They have found uses in catalytic hydroboration (Burgess et al., Isagawa et al., Lee et al); polymerization of olefins (Barbier-Baudry et al., Bonnet et al, and Marks et al.) and cyclic esters (Palard et al.). Ruthenium hydrido borohydride complexes based on bidentate phosphorus ligands and diamines, reported by Ohkuma et al, Sandoval et al. and Guo et al. are effective catalysts in asymmetric transfer hydrogenation of ketones (Ohkuma et al., Sandoval et al., Guo et al) and enantioselective Michael addition (Guo et al.). In addition, borohydride complexes may represent plausible models for CH_4 coordination in the transition state for C-H activation (Jensen et al. 1986 and 1988).

[0008] Transition metal complexes of bulky, electron-rich tridentate ligands have found useful applications in synthesis, bond activation, and catalysis (see recent reviews: Van der Boom et al., Albrecht et al., Vigalok et al., Jensen 1999 and Rybtchinski et al.). The highly electron-donating ^{t}Bu-PNP (2,6-bis(di-tert-butylphosphinomethyl)pyridine) and its group 8 metal complexes have been explored by several groups (Kawatsura et al., Stambuli et al., Gibson et al., and Kloek et al) as well as by some of the inventors of the present invention (Hermann et al., Ben-Ari et al. 2003 and 2006, Zhang et al. 2004, 2005 and 2006, and Feller et al).

[0009] Dehydrogenation of alcohols to carbonyl compounds without a hydrogen acceptor or oxidant, with the evolution of molecular hydrogen, is attractive economically and environmentally (Scheme 2), but homogeneous systems capable of thermally catalyzing dehydrogenation of alcohols are relatively rare (Zhang et al. 2004 and 2005, Murahashi et al. 1987, Charman et al., Morton et al., Dobson et al., Jung et al., Ligthart et al., Shinoda et al., Matsubara et al., Adair et al., Lin et al. 1997 and 1992, Blum et al., and Zhao et al.).

$$\mathrm{RCH(OH)R'} \xrightarrow{\text{Catalyst}} \mathrm{R\overset{O}{\overset{\|}{C}}R'} + \mathrm{H_2}$$

$$\mathrm{2\ RCH_2OH} \xrightarrow{\text{Catalyst}} \mathrm{RCOOCH_2R} + \mathrm{2H_2}$$

(R = alkyl, aryl; R' = alkyl, H)

Scheme 2

[0010] Catalytic hydrogenation of polar carbonyl bonds is a simple, convenient, and sustainable method which plays a pivotal role in both industrial processes and academic research. The hydrogenation of esters to alcohols is an important transformation and remains a challenging task in the perspective of "green and sustainable chemistry (GSC)" where the transformation is atom-economic without generating any large amount of metal waste. Despite well-documented homogeneously catalyzed reductions of ketones and aldehydes, the catalytic hydrogenation of esters to alcohols under mild and homogeneous conditions is relatively underdeveloped, owing to the poor hydridophilicity (electrophilicity) of the ester carbonyl functionality. The common trend in the reactivity of carbonyl groups towards hydrogenation reactions is RC(O)H > RC(O)R' >> RC(O)OR' > RC(O)NR'.

[0011] Simple 1,2-diols, e.g., propylene glycol (PG) and ethylene glycol (EG), are utilized as high value-added specialty chemical intermediates, in the manufacture of biodegradable polyester fibers, unsaturated polyester resins, antifreeze, pharmaceuticals and other important products. Currently, these two vicinal diols are industrially produced from petroleum-derived propylene and ethylene via hydration of their corresponding epoxy alkanes. However, as crude oil resources

become limited, substitutes for petroleum feedstocks are increasingly sought after, and as such the synthesis 1,2-diols, indirectly from biomass derived resources is of great interest. Alternative methods which proceed under mild reaction conditions with stable and easy-to-handle homogeneous catalysts and environmentally benign are desirable.

[0012] Glycolide and lactide are important classes of cyclic di-esters (di-lactones) utilized as starting materials for Lewis-acid catalyzed polymerization reactions to synthesize biodegradable polymers. Since these compounds are produced from biomass derived resources such as glycolic acid (derived from sugar cane) and lactic acid (from fermentation of glucose) respectively via self-esterification, their efficient hydrogenation can provide alternative, mild approaches to the indirect transformation of biomass to important synthetic building blocks. Although few catalytic hydrogenations of (mono lactones) to diols are known in the literature, the complete hydrogenation of cyclic di-esters to the corresponding 1,2-diols (e.g. ethylene glycol and propylene glycol) is extremely difficult due to presence of two ester moieties and the chelating ability of the final product, 1,2-diol, which may retard the catalytic activity of the catalyst. Indeed, to the applicant's best knowledge, catalytic hydrogenation of these important families of cyclic di-esters has never been reported, be it under heterogeneous or homogeneous catalysis.

[0013] The applicants of the present invention have recently reported on new catalytic reactions of alcohols, such as dehydrogenative coupling of primary alcohols to esters and dehydrogenation of secondary alcohols to ketones using pyridine-based pincer complexes (Zhang et al. 2004, 2005, 2006 and 2007; Gunanathan 2007; Gnanaprakasam and Milstein) and acridine (Gunanathan 2008 and 2009). The catalytic efficiency of the reaction of the conversion of primary alcohols to ester was enhanced with Ru(II) complexes of an analogous ligand having a potentially "hemilabile" amine "arm", PNN (2-(di-*tert*-butylphosphinomethyl)-6-(diethylaminomethyl)pyridine). (PNN)Ru(II) complexes effectively catalyze the acceptorless dehydrogenation of primary alcohols to the corresponding esters and molecular hydrogen in high yields and turnover numbers, in the presence of a catalytic amount of base. Mechanistic studies of this reaction have led to the discovery of a PNN Ru hydrido carbonyl complex, which does not require the presence of base, the catalytic reaction proceeding very effectively under neutral, mild conditions (Zhang et al. 2005).

[0014] The pyridine-based PNN Ru complex 1 (Figure 1A) efficiently catalyzes the dehydrogenative coupling of alcohols to form esters (Zhang 2005, Zhang 2007 and Milstein), the hydrogenation of esters to alcohols under mild conditions (Zhang 2006 and Milstein) and the coupling of alcohols and amines to form amides and H_2 (Gunanathan 2007 and Milstein). The PNP complex 2 (Figure 1A) is an efficient catalyst for the dehydrogenative coupling of alcohols and amines to form imines (Gnanaprakasam 2010 and Milstein). Complex 1 is also effective in N-H activation (Khaskin et al.) and in the unique light induced splitting of water to H_2 and O_2 (Kohl et al.).

[0015] US patent publication no. US 2009/0112005, to some of the inventors of the present invention, describes methods for preparing amides, by reacting a primary amine and a primary alcohol in the presence of Ruthenium complexes, to generate the amide compound and molecular hydrogen.

[0016] PCT patent publication no. WO 2010/018570, to some of the inventors of the present invention, describes methods for preparing primary amines from alcohols and ammonia in the presence of Ruthenium complexes, to generate the amine and water.

[0017] Zeng et al., published after the priority date of the present application, describes a process for preparation of polyamides via catalytic dehydrogenation of diols and diamines using PNN pincer ruthenium complexes.

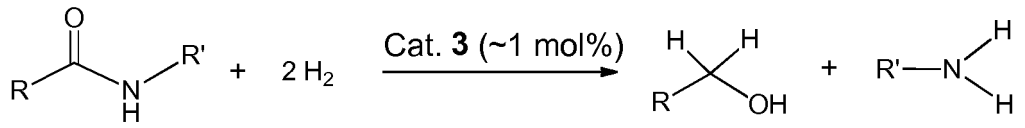
[0018] Given the widespread importance of amines, alcohols, amides and esters in biochemical and chemical systems, efficient syntheses that avoid the shortcomings of prior art processes are highly desirable.

SUMMARY OF THE INVENTION

[0019] The present invention relates to novel Ruthenium complexes and related borohydride complexes, and the use of such complexes (e.g., catalysts), *inter alia,* for (1) hydrogenation of amides (including polyamides) to alcohols and amines; (2) preparing amides from alcohols with amines (including the preparation of polyamides (e.g., polypeptides) by reacting dialcohols and diamines and/or by polymerization of amino alcohols); (3) hydrogenation of esters to alcohols (including hydrogenation of cyclic esters (lactones) or cyclic di-esters (di-lactones) or polyesters); (4) hydrogenation of organic carbonates (including polycarbonates) to alcohols and hydrogenation of carbamates (including polycarbamates) or urea derivatives to alcohols and amines; (5) dehydrogenative coupling of alcohols to esters; (6) dehydrogenation of secondary alcohols to ketones; (7) amidation of esters (i.e., synthesis of amides from esters and amines); (8) acylation of alcohols using esters; (9) coupling of alcohols with water to form carboxylic acids; and (10) dehydrogenation of beta-amino alcohols to form pyrazines. The present invention further relates to the novel uses of certain pyridine Ruthenium complexes.

[0020] The inventors have unexpectedly discovered new, bipyridine-based pincer complexes of general formulae A1, A2 and A3 as described herein. Examples of such complexes include, but are not limited to, compounds of general formulae B1, C1, B2 and C2, and compounds represented by the structures 3, 4, 7 and 9. Also unexpectedly discovered are borohydride complexes of said bipyridine-based pincer complexes, represented by the structure of general formulae D and E, as well as pyridine-based borohydride complexes of general formulae F, G or H and some borohydride complexes

such as 2', 4', 6' and 8'. These compounds efficiently catalyze various processes as described and exemplified herein. In one embodiment, the complex is a pincer complex represented by the structure of formula 3 (Figure 1B). It has unexpectedly been discovered that complex 3 efficiently catalyzes the unprecedented selective hydrogenation of amides to form amines and alcohols (Scheme 3). The reaction proceeds under mild pressure and neutral conditions, with no additives being required. Since the reaction proceeds well under anhydrous conditions, hydrolysis of the amide is not involved in this process.

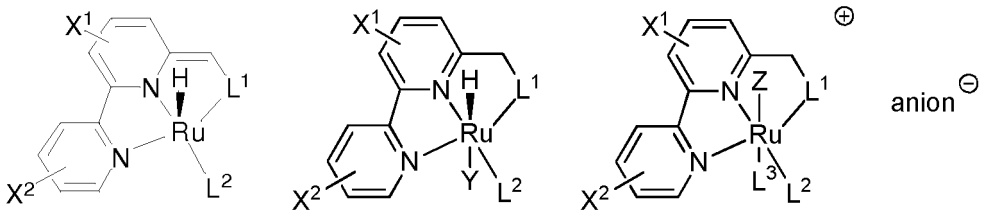


R, R' = H, aryl, alkyl, alkylaryl, et.

Scheme 3

[0021] Other reactions catalyzed by pincer complex 3 and the other pincer complexes described herein, and their borohydride derivatives, are described in more detail hereinbelow. The simplicity, generality and excellent atom-economy of these processes make them attractive for use both in small and large scale applications.

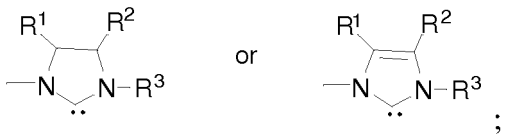
[0022] The present invention thus provides a Ruthenium complex represented by the structure of any of formulae B1, B2 or A3:



B1 **B2** **A3**

wherein

L^1 is selected from the group consisting of phosphine (PR^aR^b), and a N-heterocyclic carbene represented by the structures:



;

L^2 is a mono-dentate two-electron donor selected from the group consisting of CO, $P(OR^a)(OR^b)(OR^c)$, NO^+, isonitrile (RNC), PF_3, and CS;

L^3 is absent or is **L^2;**

Y and **Z** are each independently H or an anionic ligand selected from the group consisting of halogen, OCOR, $OCOCF_3$, OSO_2R, and OSO_2CF_3;

R^a, **R^b** and **R^c** are each independently C_1 to C_{12} linear or branched substituted or unsubstituted alkyl, C_3 to C_8 saturated or unsaturated substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl system containing 6-14 ring carbon atoms, 5-8 membered saturated or unsaturated heterocyclyl that have 1 to 4 heteroatoms selected from O, S and N, heteroaryl containing 5 or more ring atoms, wherein at least one ring atom is selected from N, S and O, or combinations thereof selected from: alkylcycloalkyl, alkylaryl, alkylheterocyclyl or alkylheteroaryl; wherein substitutions are one or more selected from the group consisting of halogen, hydroxy, alkoxy, aryloxy, alkylaryloxy, heteroaryloxy, oxo, cycloalkyl, phenyl, heteroaryls, heterocyclyl, naphthyl, amino, alkylamino, arylamino, heteroarylamino, dialkylamino, diarylamino, alkylarylamino, alkylheteroarylamino, arylheteroarylamino, acyl, acyloxy, nitro,

carboxy, carbamoyl, carboxamide, cyano, sulfonyl, sulfonylamino, sulfinyl, sulfinylamino, thiol, alkylthio, arylthio, or alkylsulfonyl groups;

R, **R^1**, **R^2** and **R^3** are each independently H, C_1 to C_{12} linear or branched substituted or unsubstituted alkyl, C_3 to C_8 saturated or unsaturated substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl system containing 6-14 ring carbon atoms, 5-8 membered saturated or unsaturated heterocyclyl that have 1 to 4 heteroatoms selected from O, S and N, heteroaryl containing 5 or more ring atoms, wherein at least one ring atom is selected from N, S and O, or combinations thereof selected from: alkylcycloalkyl, alkylaryl, alkylheterocyclyl or alkylheteroaryl; wherein substitutions are one or more selected from the group consisting of halogen, hydroxy, alkoxy, aryloxy, alkylaryloxy, heteroaryloxy, oxo, cycloalkyl, phenyl, heteroaryls, heterocyclyl, naphthyl, amino, alkylamino, arylamino, heteroarylamino, dialkylamino, diarylamino, alkylarylamino, alkylheteroarylamino, arylheteroarylamino, acyl, acyloxy, nitro, carboxy, carbamoyl, carboxamide, cyano, sulfonyl, sulfonylamino, sulfinyl, sulfinylamino, thiol, alkylthio, arylthio, or alkylsulfonyl groups;

X^1 represents zero, one, two or three substituents and **X^2** represents zero, one, two, three or four substituents, wherein each such substituent is independently selected from the group consisting of C_1 to C_{12} linear or branched substituted or unsubstituted alkyl, C_3 to C_8 saturated or unsaturated substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl system containing 6-14 ring carbon atoms, 5-8 membered saturated or unsaturated heterocyclyl that have 1 to 4 heteroatoms selected from O, S and N, heteroaryl containing 5 or more ring atoms, wherein at least one ring atom is selected from N, S and O, or combinations thereof selected from: alkylcycloalkyl, alkylaryl, alkylheterocyclyl or alkylheteroaryl; wherein substitutions are one or more selected from the group consisting of halogen, hydroxy, alkoxy, aryloxy, alkylaryloxy, heteroaryloxy, oxo, cycloalkyl, phenyl, heteroaryls, heterocyclyl, naphthyl, amino, alkylamino, arylamino, heteroarylamino, dialkylamino, diarylamino, alkylarylamino, alkylheteroarylamino, arylheteroarylamino, acyl, acyloxy, nitro, carboxy, carbamoyl, carboxamide, cyano, sulfonyl, sulfonylamino, sulfinyl, sulfinylamino, thiol, alkylthio, arylthio, or alkylsulfonyl groups,, halogen, nitro, amide, ester, cyano, alkoxy, alkylamino, arylamino, an inorganic support and a polymeric moiety; and

anion represents a group bearing a single negative charge; or

a borane derivative of said complex.

[0023] Embodiments of the invention provide the complex of formulae B1, B2 or A3,

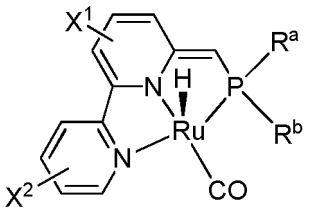
wherein X^1 and X^2 are each absent, and the bipyridine moiety is unsubstituted; or

wherein L^1 is phosphine (PR^aR^b); or

wherein L^2 is CO; or

wherein Z and Y are H or halogen; or

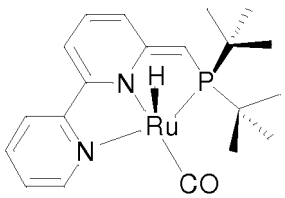
wherein the complex is represented by formula **C1**:



C1

wherein each of X^1, X^2 R^a and R^b are as defined above,

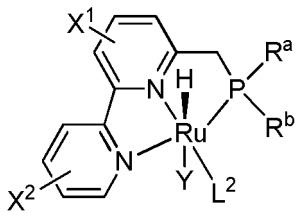
preferably wherein the Ruthenium complex is represented by the structure of formula 3:



3

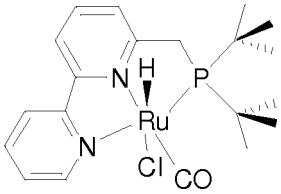
;

or
wherein the complex is represented by formula **C2**:

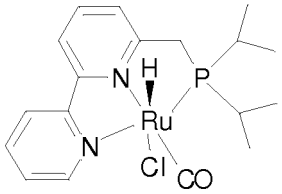


C2

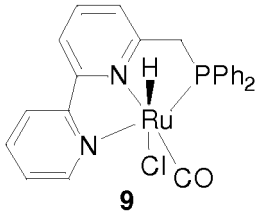
wherein each of L^2, X^1, X^2, Y, R^a and R^b are as defined in claim 1,
preferably wherein Y is halogen or wherein L^2 is CO, more preferably wherein the Ruthenium complex is represented by the structure of formulae 4, 7 or 9:



4



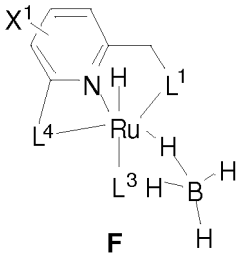
7



9

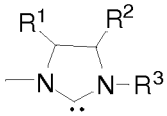
.

[0024] The present invention also provides a borane derivative of a Ruthenium complex, wherein said borane derivative is represented by the structure of formula F:

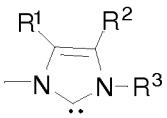


F

wherein
each $\mathbf{L^1}$ is independently selected from the group consisting of phosphine (PR^aR^b), and a N-heterocyclic carbene represented by the structures:

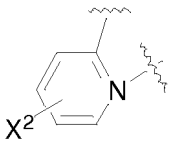


or



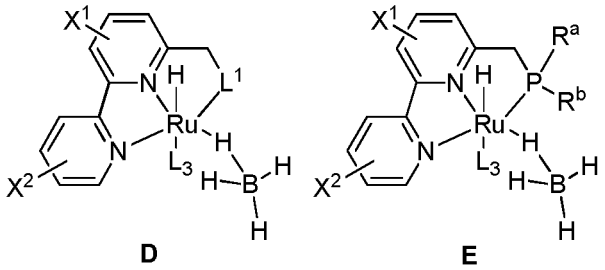
;

$\mathbf{L^3}$ is absent or is a mono-dentate two-electron donor selected from the group consisting of CO, $P(OR^a)(OR^b)(OR^c)$, NO^+, isonitrile (RNC), PF_3, and CS;
$\mathbf{L^4}$ is a group of the formula:



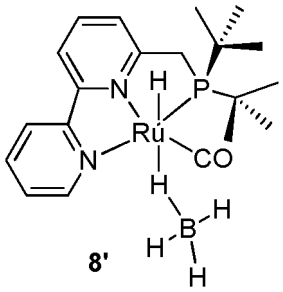
R^a, **R^b** and **R^c** are each independently alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkylcycloalkyl, alkylaryl, alkylheterocyclyl or alkylheteroaryl;
R, **R^1**, **R^2** and **R^3** are each independently H, alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkylcycloalkyl, alkylaryl, alkylheterocyclyl or alkylheteroaryl;
X^1 represents zero, one, two or three substituents and **X^2** represents zero, one, two, three or four substituents, wherein each such substituent is independently selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkylcycloalkyl, alkylaryl, alkylheterocyclyl, alkylheteroaryl, halogen, nitro, amide, ester, cyano, alkoxy, alkylamino, arylamino, an inorganic support and a polymeric moiety,

preferably wherein the Ruthenium complex is represented by the structure of any of formula:



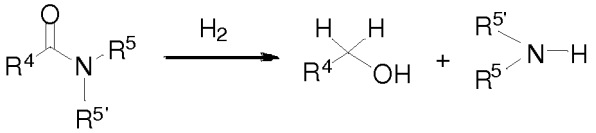
D **E**

wherein each of L^1, L^3, X^1, X^2, R^a and R^b is as defined above, more preferably wherein the Ruthenium complex is represented by the structure of formula 8':



8'

[0025] The present invention also provides a process for hydrogenating an amide to an alcohol and an amine, comprising the step of reacting the amide represented by the formula $R^4C(=O)\text{-}N\text{-}R^5R^{5'}$ with molecular hydrogen (H2), to generate an alcohol of formula R^4CH_2OH and amine of formula $R^5R^{5'}NH$:

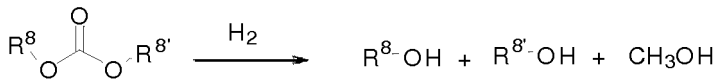


wherein R^4, R^5 and $R^{5'}$ are each independently selected from the group consisting of H, an unsubstituted or substituted alkyl, alkoxyalkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl;
wherein the process is conducted in the presence of the Ruthenium complex of the invention, preferably wherein the amide is selected from the group consisting of N-benzyl-2-methoxyacetamide, N-hexyl-2-methoxyacetamide, N-hexyl- 3-methyloxetane-3-carboxamide, N-hexyl-2-furanylcarboxamide, N-benzylbenzamide, N- ethylacetamide, N-methylpropionamide, N-cyclohexyl-2-methoxyacetamide, N- phenylacetamide, N-phenylhexylamide, 2-methoxy-N-phenylacetamide, N-phenylbenzamide, Ethylenediamine-N,N'-(2-methoxyacetamide), N-hexanoylmorpholine, N-butanoylmorpholine, N-2-metoxyacetylpyrrolidine, N-formylmorpholine, N,N-dimethylformamide, N,N-diethylbenzamide, benzamide, 4-methylbenzamide, cyclohexanecarboxamide, hexanamide, acetamide, acrylamide and pivalamide; and
optionally wherein the amide is a cyclic amide (lactam) and the process results in an amino alcohol, or optionally wherein the amide is a polyamide, or wherein the amide is a polypeptide.

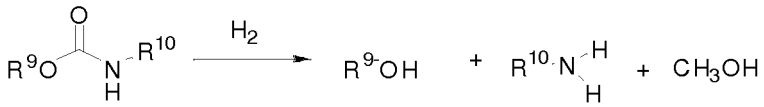
[0026] The present invention also provides process for hydrogenating an ester, organic carbonate, carbamate or urea derivative, comprising the step of reacting the ester, organic carbonate, carbamate or urea derivative with molecular hydrogen (H_2) in the presence of the Ruthenium complex of the invention, thereby hydrogenating the ester, organic carbonate, carbamate or urea derivative and generating at least one alcohol, amine or combination thereof;

(I) preferably wherein the process is selected from the group consisting of:

a. a process comprising the step of hydrogenating a carbonate represented by the formula $R^8O\text{-}C(=O)\text{-}OR^{8'}$ to the corresponding alcohols(s) and methanol:

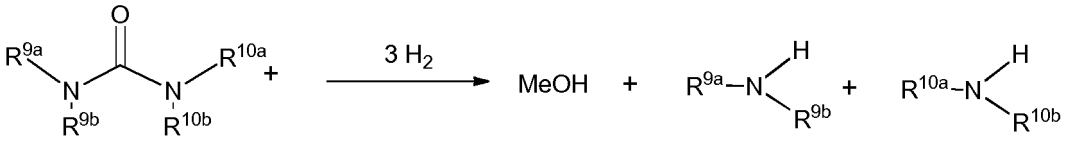


wherein R^8 and R^8 are the same or different and are selected from the group consisting of an unsubstituted or substituted alkyl, alkoxyalkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl, wherein the carbonate is preferably dimethyl carbonate, diethyl carbonate, dipropyl carbonate or dibutyl carbonate;
b. a process comprising the step of hydrogenating a carbamate represented by the formula $R^9O\text{-}C(=O)\text{-}NHR^{10}$ to the corresponding amine, alcohol and methanol:



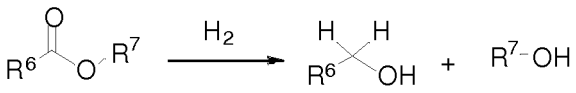
wherein R^9 is selected from the group consisting of an unsubstituted or substituted alkyl, alkoxyalkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl; and
R^{10} is selected from the group consisting of H or an unsubstituted or substituted alkyl, alkoxyalkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl,

wherein the carbamate is preferably methyl benzylcarbamate or methyl 4-methoxybenzylcarbamate; and
c. a process comprising the step of hydrogenating a urea derivative to the corresponding amine and methanol:



or;

(II) preferably wherein said process comprising the step of hydrogenating an ester represented by the formula $R^6C(=O)\text{-}OR^7$ to the corresponding alcohol or alcohols:



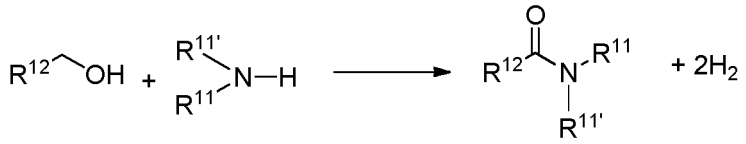
wherein

R^6 is selected from the group consisting of H, an unsubstituted or substituted alkyl, alkoxyalkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl; and
R^7 is selected from the group consisting of an unsubstituted or substituted alkyl, alkoxyalkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl;

preferably wherein R^6 is H and the process comprises hydrogenating a formate ester of formula H- $C(=O)\text{-}OR^7$ to methanol and an alcohol of formula $R^7\text{-}OH$;
more preferably wherein the ester is selected from the group consisting of hexyl hexanoate, butyl butyrate, methyl

formate, ethyl formate, propyl formate and butyl formate; or wherein the ester is a polyester, or whererin the ester is cyclic ester (lactone), or wherein the ester is a cyclic di-ester (di- lactone), and the process results in the formation of a diol; preferably wherein the cyclic di-ester is biomass-derived, preferably wherein the cyclic di-ester is glycolide or lactide.

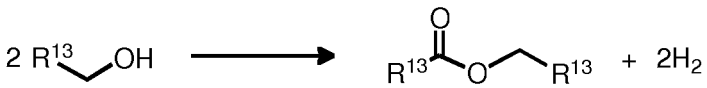
[0027] The present invention also provides a process for preparing an amide, comprising the step of reacting a primary or secondary amine with a primary alcohol in the presence of the Ruthenium complex of the invention, thereby generating the amide and molecular hydrogen,
wherein the process comprises the step of reacting an amine represented by formula $R^{11}R^{11'}NH$ with an alcohol represented by the formula $R^{12}CH_2OH$ to generate an amide represented by the structure R^{12}-C(=O)-$NR^{11}R^{11'}$:



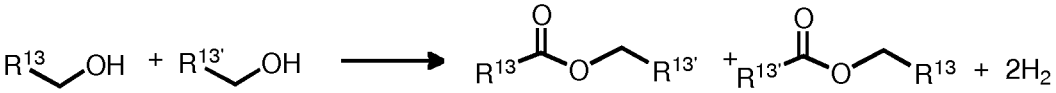
wherein R^{10}, R^{11} and R^{12} are each independently selected from the group consisting of H an unsubstituted or substituted alkyl, alkoxyalkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl;
preferably wherein the alcohol is selected from the group consisting of methanol, ethanol, propanol, butanol, pentanol, hexanol, 2-methoxyethanol, and 2-methyl-1-butanol; or wherein the amine is selected from the group consisting of benzylamine, 1-hexylamine, 1-pentylamine, 1-(2-furyl)methylamine, aniline, morpholine, pyrrolidine, 2-methylhexylamine, cyclohexylamine, ethylenediamine, diethylenetriamine and 1,6-diaminohexane; and
optionally, wherein (a) the amine is a diamine or the alcohol is a dialcohol, and the process results in a diamide; or (b) the amine is a diamine and the alcohol is a dialcohol, and the process results in a polyamide; or (c) the amine and alcohol are present in the same molecule, and the process is an intra-molecular process which results in a lactam; or (d) the amine and the alcohol are present in the same molecule, and the process is an inter-molecular process which results in a polyamide; or (e) the amine and alcohol together represent a beta-amino alcohol, and the process results in a polypeptide; or (f) the amine and alcohol together represent a beta-amino alcohol, and the process results in a cyclic dipeptide.

[0028] The present invention further provides a process for preparing an ester by dehydrogenative coupling of primary alcohols, or by dehydrogenative coupling of a primary alcohol and a secondary alcohol, comprising the step of reacting the alcohols in the presence of the Ruthenium complex of the invention, thereby generating the ester and molecular hydrogen, wherein the process is selected from the group consisting of:

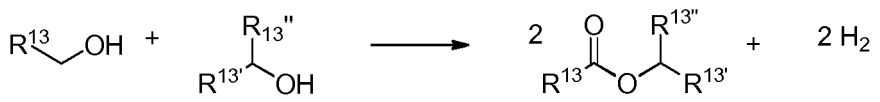
(a) a process comprising the step of converting a primary alcohol represented by formula $R^{13}CH_2OH$ to an ester by the structure R^{13}-C(=O)-OCH_2R^{13}:



wherein R^{13} is selected from the group consisting of H, an unsubstituted or substituted alkyl, alkoxyalkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl;
(b) a process comprising the step of reacting a first primary alcohol represented by formula $R^{13}CH_2OH$ with a second alcohol represented by formula $R^{13'}CH_2OH$ so as to generate an ester by the structure R^{13}-C(=O)-$OCH_2R^{13'}$ or an ester of formula $R^{13'}$-C(=O)-OCH_2R^{13}

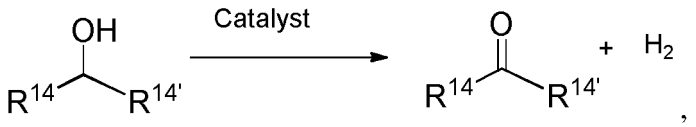


wherein R^{13} and $R^{13'}$ are the same or different from each other and are each independently selected is from the group consisting of H, an unsubstituted or substituted alkyl, alkoxyalkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl; and
(c) a process comprising the step of reacting a primary alcohol represented by formula $R^{13}CH_2OH$ with a secondary alcohol of formula $R^{13'}R^{13''}CHOH$ so as to generate an ester by the structure R^{13}-C(=O)-$OCHR^{13'}R^{13''}$:



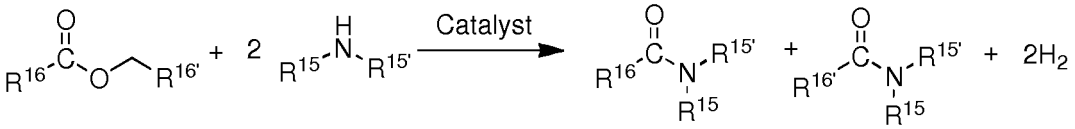
wherein R^{13}, $R^{13'}$ and $R^{13''}$ are each independently selected from the group consisting of H, an unsubstituted or substituted alkyl, alkoxyalkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl;
preferably wherein the alcohol is selected from the group consisting of methanol, ethanol, propanol, butanol, pentanol, hexanol, 2-methoxyethanol, 2-methyl-1-butanol, benzyl alcohol, 1-phenylethanol and cyclohexane methanol; or wherein the alcohol is a dialcohol, and the process results in a polyester or a lactone.

[0029] The present invention also provides a process for preparing a ketone by dehydrogenation of a secondary alcohol, comprising the step of reacting the secondary alcohol in the presence of the Ruthenium complex of the invention, thereby generating the ester and molecular hydrogen; wherein the process comprises the step of converting a secondary alcohol represented by formula $R^{14}CH(OH)R^{14'}$ to a ketone represented by the structure R^{14}-C(=O)-$R^{14'}$:



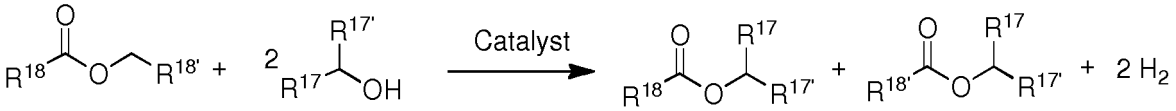
preferably
wherein the secondary alcohol is selected from the group consisting of 1-phenyl-1-ethanol, 2-hexanol, cyclohexanol and 2-propanol.

[0030] The present invention also provides a process for preparing an amide, comprising the step of reacting a primary or secondary amine with an ester in the presence of the Ruthenium complex of the invention, thereby generating the amide and molecular hydrogen,
wherein the process comprises the step of reacting an amine represented by formula $R^{15}R^{15'}NH$ with an ester represented by the formula R^{16}-C(=O)-$OCH_2R^{16'}$ to generate an amide represented by the structure R^{16}-C(=O)-$NR^{15}R^{15'}$:



wherein R^{15}, $R^{15'}$, R^{16} and $R^{16'}$ are each independently selected from the group consisting of H an unsubstituted or substituted alkyl, alkoxyalkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl;
preferably wherein the ester is selected from the group consisting of ethyl acetate, butyl butyrate, pentyl pentanoate and hexyl hexanoate.; orwherein the amine is selected from the group consisting of pyrrolidine, morpholine, 1-methyl piperazine, piperidine, piperazine, 1-hexylamine and p-tolylmethanamine.

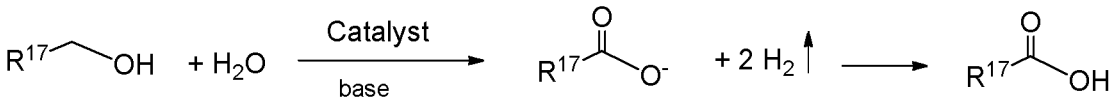
[0031] The present invention still further provides a process for preparing an ester by reacting a primary or secondary alcohol with an ester in the presence of the Ruthenium complex of the invention, thereby generating the ester and molecular hydrogen, wherein the process comprises the step of reacting a primary or secondary alcohol represented by formula $R^{17}R^{17'}CHOH$ with an ester by the structure R^{18}-C(=O)-$OCH_2R^{18'}$:



wherein R^{17}, $R^{17'}$, R^{18} and $R^{18'}$ are each independently selected from the group consisting of H, an unsubstituted or substituted alkyl, alkoxyalkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl;
preferably wherein the alcohol is selected from the group consisting of cyclohexanol, cyclopentanol, 1-phenylethanol, isopropanol and 3-pentanol; or wherein the ester is selected from the group consisting of ethyl acetate, hexyl hexanoate, pentyl pentanoate, butyl butyrate, ethyl butyrate and methyl hexanoate.

[0032] The present invention yet further provides a process for preparing a carboxylic acid comprising the step of

reacting a primary alcohol with water and a base in the presence of the Ruthenium complex of the invention, thereby generating the carboxylic acid and molecular hydrogen,
wherein the process comprises the step of reacting a primary alcohol represented by formula $R^{17}CH_2OH$ with water in the presence of a base so as to generate a carboxylic acid salt represented by the structure R^{17}-C(=O)O^- and, optionally, if desired, converting the carboxylic acid salt to the corresponding carboxylic acid of formula R^{17}-C(=O)OH.



wherein R^{17} is selected from the group consisting of H, an unsubstituted or substituted alkyl, alkoxyalkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl;
preferably wherein the alcohol is selected from the group consisting of butanol, pentanol, decanol, 2-methoxyethanol, 2-phenylethanol, cyclohexylmethanol, 3-phenylbutan-1-ol, but-3-en-1-ol, (4-methoxyphenyl)methanol, and (2,4-dimethoxyphenyl)methanol.

BRIEF DESCRIPTION OF THE DRAWINGS

[0033] The present invention will be understood and appreciated more fully from the following detailed description taken in conjunction with the appended figures:

FIGURE 1: shows the structure of dearomatized PNN pincer complexes 1 and 2 (Fig 1A) and complex 3 (Fig 1B).

FIGURE 2: shows the X-ray structure of Ruthenium complex 4 with the thermal ellipsoids at 50% probability level. All C-H hydrogen atoms are omitted for clarity.

FIGURE 3: shows the X-ray structure of Ruthenium borohyride complex 2' with the thermal ellipsoids at 50% probability level. All C-H hydrogen atoms are omitted for clarity.

FIGURE 4: shows the variable-temperature (213K-373K) 1H NMR of Ruthenium borohydride complex 4' in the region of Ru-H and BH_4^- ligands (toluene-d_8 as solvent).

FIGURE 5: shows MALDI-TOF mass spectra of polyamides synthesized by the processes of the present invention. **Fig. 5A:** polyamide **3a** in TFA using HBA matrix. **Fig 5B:** polyamide **3c** in TFA using HBA matrix. **Fig 5C:** polyamide **3d** in 50%TFA/DCM using HBA-NaI. **Fig 5D:** polyamide **3e** in TFA using HBA matrix. **Fig 5E:** polyamide **3h** in TFA using HBA matrix.

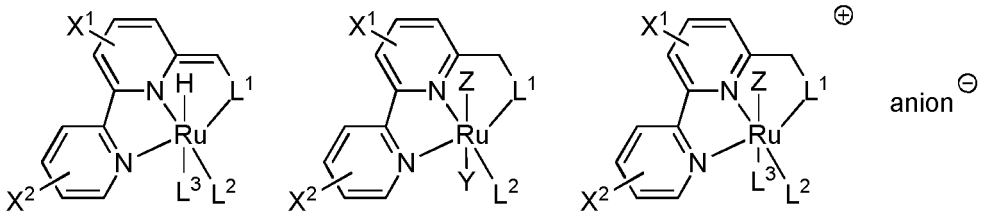
FIGURE 6: TGA of polyamides **3.**

DETAILED DESCRIPTION OF THE PRESENT INVENTION

[0034] The present invention provides novel Ruthenium based complexes and catalysts and borohydride complexes thereof, and the use of such complexes for, *inter alia,* (1) hydrogenation of amides (including polyamides) to alcohols and amines; (2) preparing amides from alcohols with amines (including the preparation of polyamides (e.g., polypeptides) by reacting dialcohols and diamines and/or by polymerization of amino alcohols); (3) hydrogenation of esters to alcohols(including hydrogenation of cyclic esters (lactones) or cyclic di-esters (lactones) or polyesters); (4) hydrogenation of organic carbonates (including polycarbonates) to alcohols and hydrogenation of carbamates (including polycarbamates) or urea derivatives to alcohols and amines; (5) dehydrogenative coupling of alcohols to esters; (6) dehydrogenation of secondary alcohols to ketones; (7) amidation of esters (i.e., synthesis of amides from esters and amines); (8) acylation of alcohols using esters; (9) coupling of alcohols with water to form carboxylic acids; and (10) dehydrogenation of beta-amino alcohols to form pyrazines. The present invention further relates to the novel uses of certain pyridine Ruthenium complexes.

Ruthenium complexes

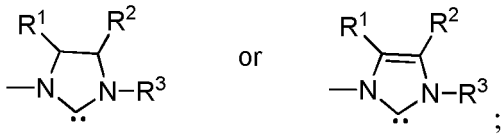
[0035] Disclosed herein are Ruthenium complexes represented by any one of formulae A1, A2 or A3:



A1 **A2** **A3**

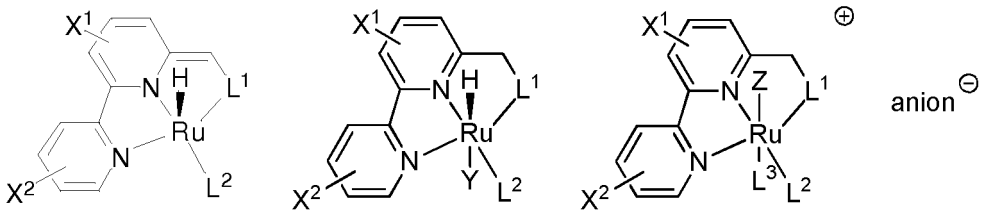
wherein

L^1 is selected from the group consisting of phosphine (PR^aR^b), phosphite $P(OR^a)(OR^b)$, phosphinite $P(OR^a)(R^b)$, amine (NR^aR^b), imine, oxazoline, sulfide (SR^a), sulfoxide ($S(=O)R^a$), heteroaryl containing at least one heteroatom selected from nitrogen and sulfur; arsine (AsR^aR^b), stibine (SbR^aR^b) and a N-heterocyclic carbene represented by the structures:



L^2 is a mono-dentate two-electron donor selected from the group consisting of CO, $PR^aR^bR^c$, $P(OR^a)(OR^b)(OR^c)$, NO^+, $AsR^aR^bR^c$, $SbR^aR^bR^c$, SR^aR^b, nitrile (RCN), isonitrile (RNC), N_2, PF_3, CS, heteroaryl, tetrahydrothiophene, alkene and alkyne;
L^3 is absent or is **L^2;**
Y and **Z** are each independently H or an anionic ligand selected from the group consisting of H, halogen, OCOR, $OCOCF_3$, OSO_2R, OSO_2CF_3, CN, OR, $N(R)_2$ and RS;
R^a, **R^b** and **R^c** are each independently alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkylcycloalkyl, alkylaryl, alkylheterocyclyl or alkylheteroaryl;
R, R^1, **R^2** and **R^3** are each independently H, alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkylcycloalkyl, alkylaryl, alkylheterocyclyl or alkylheteroaryl;
X^1 represents zero, one, two or three substituents and **X^2** represents zero, one, two, three or four substituents, wherein each such substituent is independently selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkylcycloalkyl, alkylaryl, alkylheterocyclyl, alkylheteroaryl, halogen, nitro, amide, ester, cyano, alkoxy, alkylamino, arylamino, an inorganic support and a polymeric moiety; and anion represents a group bearing a single negative charge; or a borane derivative of said complex.

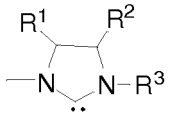
[0036] The present invention thus provides a Ruthenium complex represented by the structure of any of formulae B1, B2 or A3:



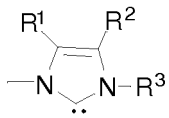
B1 **B2** **A3**

wherein

L^1 is selected from the group consisting of phosphine (PR^aR^b), and a N-heterocyclic carbene represented by the structures:



or



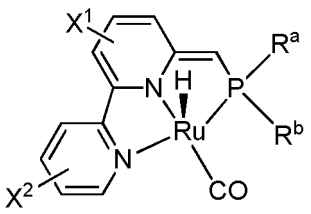
;

L^2 is a mono-dentate two-electron donor selected from the group consisting of CO, $P(OR^a)(OR^b)(OR^c)$, NO^+, isonitrile (RNC), PF_3, and CS;
L^3 is absent or is **L^2;**
Y and **Z** are each independently H or an anionic ligand selected from the group consisting of halogen, OCOR, $OCOCF_3$, OSO_2R, and OSO_2CF_3;
R^a, **R^b** and **R^c** are each independently C_1 to C_{12} linear or branched substituted or unsubstituted alkyl, C_3 to C_8 saturated or unsaturated substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl system containing 6-14 ring carbon atoms, 5-8 membered saturated or unsaturated heterocyclyl that have 1 to 4 heteroatoms selected from O, S and N, heteroaryl containing 5 or more ring atoms, wherein at least one ring atom is selected from N, S and O, or combinations thereof selected from: alkylcycloalkyl, alkylaryl, alkylheterocyclyl or alkylheteroaryl; wherein substitutions are one or more selected from the group consisting of halogen, hydroxy, alkoxy, aryloxy, alkylaryloxy, heteroaryloxy, oxo, cycloalkyl, phenyl, heteroaryls, heterocyclyl, naphthyl, amino, alkylamino, arylamino, heteroarylamino, dialkylamino, diarylamino, alkylarylamino, alkylheteroarylamino, arylheteroarylamino, acyl, acyloxy, nitro, carboxy, carbamoyl, carboxamide, cyano, sulfonyl, sulfonylamino, sulfinyl, sulfinylamino, thiol, alkylthio, arylthio, or alkylsulfonyl groups;
R, **R^1**, **R^2** and **R^3** are each independently H, C_1 to C_{12} linear or branched substituted or unsubstituted alkyl, C_3 to C_8 saturated or unsaturated substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl system containing 6-14 ring carbon atoms, 5-8 membered saturated or unsaturated heterocyclyl that have 1 to 4 heteroatoms selected from O, S and N, heteroaryl containing 5 or more ring atoms, wherein at least one ring atom is selected from N, S and O, or combinations thereof selected from: alkylcycloalkyl, alkylaryl, alkylheterocyclyl or alkylheteroaryl; wherein substitutions are one or more selected from the group consisting of halogen, hydroxy, alkoxy, aryloxy, alkylaryloxy, heteroaryloxy, oxo, cycloalkyl, phenyl, heteroaryls, heterocyclyl, naphthyl, amino, alkylamino, arylamino, heteroarylamino, dialkylamino, diarylamino, alkylarylamino, alkylheteroarylamino, arylheteroarylamino, acyl, acyloxy, nitro, carboxy, carbamoyl, carboxamide, cyano, sulfonyl, sulfonylamino, sulfinyl, sulfinylamino, thiol, alkylthio, arylthio, or alkylsulfonyl groups;
X^1 represents zero, one, two or three substituents and **X^2** represents zero, one, two, three or four substituents, wherein each such substituent is independently selected from the group consisting of C_1 to C_{12} linear or branched substituted or unsubstituted alkyl, C_3 to C_8 saturated or unsaturated substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl system containing 6-14 ring carbon atoms, 5-8 membered saturated or unsaturated heterocyclyl that have 1 to 4 heteroatoms selected from O, S and N, heteroaryl containing 5 or more ring atoms, wherein at least one ring atom is selected from N, S and O, or combinations thereof selected from: alkylcycloalkyl, alkylaryl, alkylheterocyclyl or alkylheteroaryl; wherein substitutions are one or more selected from the group consisting of halogen, hydroxy, alkoxy, aryloxy, alkylaryloxy, heteroaryloxy, oxo, cycloalkyl, phenyl, heteroaryls, heterocyclyl, naphthyl, amino, alkylamino, arylamino, heteroarylamino, dialkylamino, diarylamino, alkylarylamino, alkylheteroarylamino, arylheteroarylamino, acyl, acyloxy, nitro, carboxy, carbamoyl, carboxamide, cyano, sulfonyl, sulfonylamino, sulfinyl, sulfinylamino, thiol, alkylthio, arylthio, or alkylsulfonyl groups,, halogen, nitro, amide, ester, cyano, alkoxy, alkylamino, arylamino, an inorganic support and a polymeric moiety; and

anion represents a group bearing a single negative charge; or
a borane derivative of said complex.

[0037] In one embodiment, X^1 and X^2 are absent (i.e, the bipyridine moiety is unsubstituted). In another embodiment, L^1 is phosphine (PR^aR^b). In another embodiment, L^2 is CO. In another embodiment, Z and Y are H or halogen.

[0038] In a particular embodiment the Ruthenium complex is represented by the structure of formula C1.

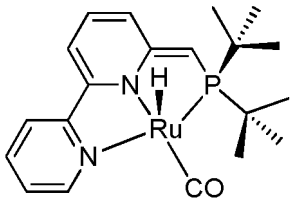


C1

wherein each of X^1, X^2, R^a and R^b is as defined above.

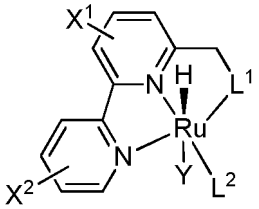
[0039] In one embodiment, each of R^a and R^b is tert-butyl. In another currently, each of R^c and R^d are isopropyl.

[0040] In one embodiment, the Ruthenium complex is represented by the structure of formula 3 (also shown in Fig 1B).



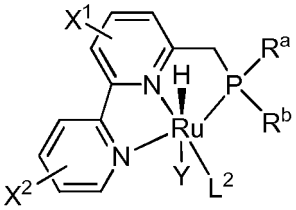
3

[0041] In one embodiment, the Ruthenium complex is represented by the structure of formula B2:



B2

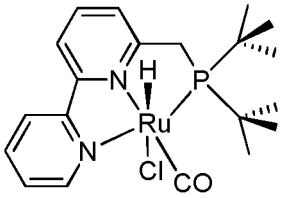
[0042] In another particular embodiment, the Ruthenium complex is represented by the following structure of formula C2:



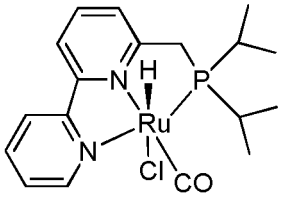
C2

wherein each of L^2, X^1, X^2, Y, R^a and R^b is as defined above.

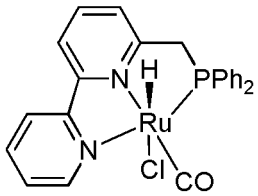
[0043] In one embodiment, Y is halogen, such as chloro, or L^2 is CO. For example, the Ruthenium complex may be represented by the structure of any of formulae 4, 7 or 9:



4

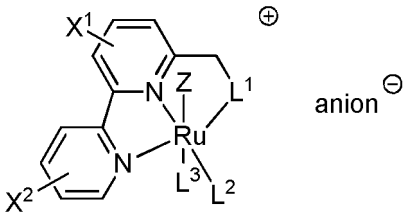


7



9

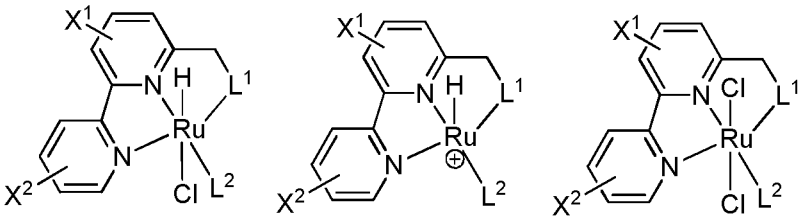
[0044] In another embodiment of the present invention, the Ruthenium complex is represented by the structure of formula A3:



A3

[0045] In one particular embodiment, Z is H in formula A3. When such a complex is used, the processes of the invention as described hereinbelow are typically conducted in the presence of at least one equivalent of a base relative to the Ruthenium complex. In another particular embodiment, Z is other than H in formula A3. When such a complex is used, the processes of the invention as described hereinbelow are typically conducted in the presence of at least two equivalents of a base relative to the Ruthenium complex.

[0046] It is disclosed herein that compounds of formula A2 and formula A3 are precursors of compounds of formula A1. Additionally some precursors of the complexes of formula A1 include, but are not limited to, compounds of general formulae (i), (ii) and (iii):

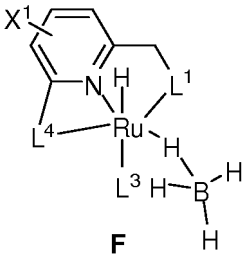


(i) (ii) (iii)

Borohydride Complexes:

[0047] It has been unexpectedly discovered that certain reactions such conversion of primary alcohols to esters, as well as the dehydrogenation of secondary alcohols to ketones, as well as other reactions contemplated herein, can be effectively accomplished with stable, readily synthesized PNN- and PNP Ru borohydride complexes, in the absence of a base, under mild and neutral conditions, optionally in the absence of hydrogen acceptor.

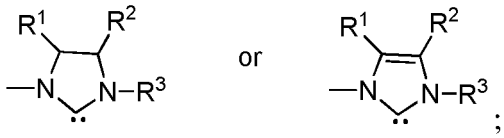
[0048] Thus, in one embodiment, the present invention provides a borane derivative of a Ruthenium complex, the borane derivative represented by the structure of formula F:



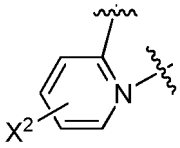
F

wherein

each $\mathbf{L^1}$ is independently selected from the group consisting of phosphine (PR^aR^b), and a N-heterocyclic carbene represented by the structures:

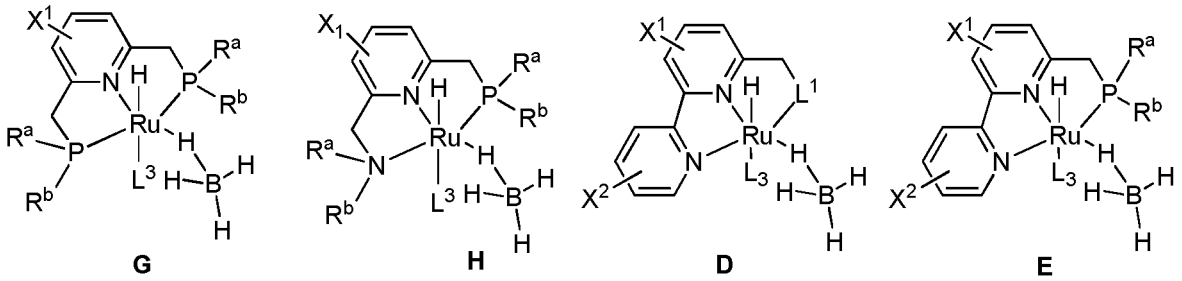


$\mathbf{L^3}$ is absent or is a mono-dentate two-electron donor selected from the group consisting of CO, $P(OR^a)(OR^b)(OR^c)$, NO^+, isonitrile (RNC), PF_3, and CS;
$\mathbf{L^4}$ is a group of the formula:



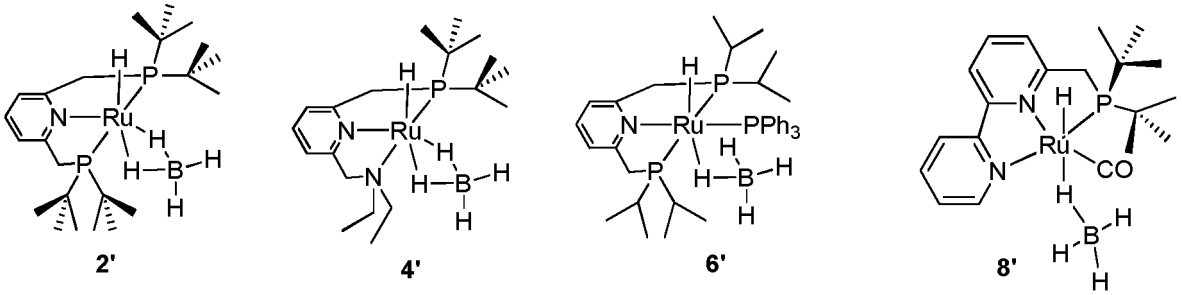
$\mathbf{R^a}$, $\mathbf{R^b}$ and $\mathbf{R^c}$ are each independently alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkylcycloalkyl, alkylaryl, alkylheterocyclyl or alkylheteroaryl;
R, $\mathbf{R^1}$, $\mathbf{R^2}$ and $\mathbf{R^3}$ are each independently H, alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkylcycloalkyl, alkylaryl, alkylheterocyclyl or alkylheteroaryl;
$\mathbf{X^1}$ represents zero, one, two or three substituents and $\mathbf{X^2}$ represents zero, one, two, three or four substituents, wherein each such substituent is independently selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkylcycloalkyl, alkylaryl, alkylheterocyclyl, alkylheteroaryl, halogen, nitro, amide, ester, cyano, alkoxy, alkylamino, arylamino, an inorganic support and a polymeric moiety.

[0049] In some embodiments, the borane derivative is represented by the structure of formulae D or E. Also disclosed are borane derivative G and H. It is noted that compounds D and E are borane derivatives of the Ruthenium complex of formula A1 as described hereinabove.



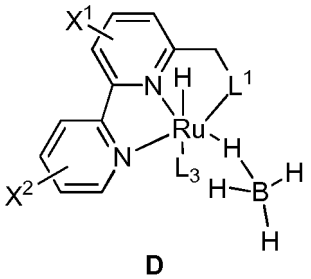
G **H** **D** **E**

[0050] In another embodiment, the borane derivative is represented by the structure of 8'.Other disclosed borane derivatives are represented by the structure of2', 4' and 6'.



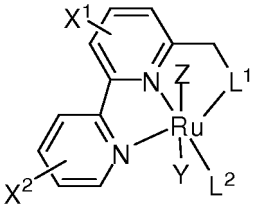
2' **4'** **6'** **8'**

[0051] The present disclosure further describes processes for preparing the novel boronated derivatives of Ruthenium based catalytic complexes. Thus, disclosed herein is a process for preparing a Ruthenium complex represented by the structure of formula D



D

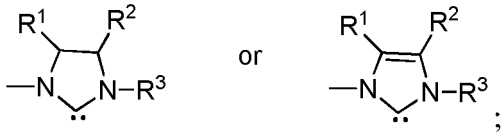
by reacting sodium borohydride (NaBH4) with a precursor of formula A2



A2

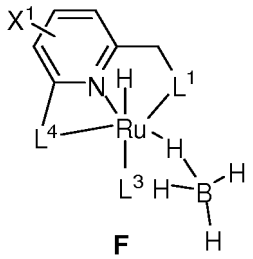
wherein

L1 is selected from the group consisting of phosphine (PR^aR^b), phosphite $P(OR^a)(OR^b)$, phosphinite $P(OR^a)(R^b)$, amine (NR^aR^b), imine, oxazoline, sulfide (SR^a), sulfoxide ($S(=O)R^a$), heteroaryl containing at least one heteroatom selected from nitrogen and sulfur; arsine (AsR^aR^b), stibine (SbR^aR^b) and a N-heterocyclic carbene represented by the structures:



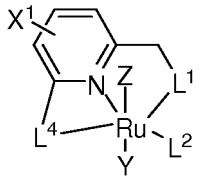
L2 is a mono-dentate two-electron donor selected from the group consisting of CO, $PR^aR^bR^c$, $P(OR^a)(OR^b)(OR^c)$, NO^+, $AsR^aR^bR^c$, $SbR^aR^bR^c$, SR^aR^b, nitrile (RCN), isonitrile (RNC), N_2, PF_3, CS, heteroaryl, tetrahydrothiophene, alkene and alkyne;
L^3 is absent or is **L2;**
Y and **Z** are each independently halogen, $OCOCF_3$, OSO_2R or OSO_2CF_3,
R^a, R^b and R^c are each independently alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkylcycloalkyl, alkylaryl, alkylheterocyclyl or alkylheteroaryl;
R, R^1, R^2 and R^3 are each independently H, alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkylcycloalkyl, alkylaryl, alkylheterocyclyl or alkylheteroaryl;
X^1 represents zero, one, two or three substituents and X^2 represents zero, one, two, three or four substituents, wherein each such substituent is independently selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkylcycloalkyl, alkylaryl, alkylheterocyclyl, alkylheteroaryl, halogen, nitro, amide, ester, cyano, alkoxy, alkylamino, arylamino, an inorganic support and a polymeric moiety.

[0052] In another embodiment, the present disclosure describes a process for preparing a borane derivative of a Ruthenium complex represented by the structure of formula F



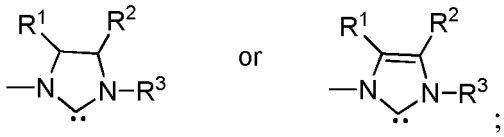
F

the process comprising the step of reacting sodium borohydride (NaBH4) with a precursor of formula

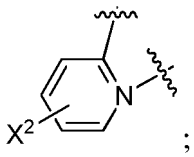


wherein

L¹ is selected from the group consisting of phosphine (PR^aR^b), phosphite $P(OR^a)(OR^b)$, phosphinite $P(OR^a)(R^b)$, amine (NR^aR^b), imine, oxazoline, sulfide (SR^a), sulfoxide ($S(=O)R^a$), heteroaryl containing at least one heteroatom selected from nitrogen and sulfur; arsine (AsR^aR^b), stibine (SbR^aR^b) and a N-heterocyclic carbene represented by the structures:



L² is a mono-dentate two-electron donor selected from the group consisting of CO, $PR^aR^bR^c$, $P(OR^a)(OR^b)(OR^c)$, NO^+, $AsR^aR^bR^c$, $SbR^aR^bR^c$, SR^aR^b, nitrile (RCN), isonitrile (RNC), N_2, PF_3, CS, heteroaryl, tetrahydrothiophene, alkene and alkyne;
L³ is absent or is **L²;**
L⁴ is $-CH_2-L^1-$ or a group of the formula:



Y and **Z** are each independently halogen, $OCOCF_3$, OSO_2R or OSO_2CF_3, $\mathbf{R^a}$, $\mathbf{R^b}$ and $\mathbf{R^c}$ are each independently alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkylcycloalkyl, alkylaryl, alkylheterocyclyl or alkylheteroaryl;
R, $\mathbf{R^1}$, $\mathbf{R^2}$ and $\mathbf{R^3}$ are each independently H, alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkylcycloalkyl, alkylaryl, alkylheterocyclyl or alkylheteroaryl;
$\mathbf{X^1}$ represents zero, one, two or three substituents and $\mathbf{X^2}$ represents zero, one, two, three or four substituents, wherein each such substituent is independently selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkylcycloalkyl, alkylaryl, alkylheterocyclyl, alkylheteroaryl, halogen, nitro, amide, ester, cyano, alkoxy, alkylamino, arylamino, an inorganic support and a polymeric moiety.

Chemical Definitions

[0053] As used herein, the term alkyl, used alone or as part of another group, refers, in one embodiment, to a "C_1 to C_{12} alkyl" and denotes linear and branched, saturated or unsaturated (e.g., alkenyl, alkynyl) groups, the latter only when

the number of carbon atoms in the alkyl chain is greater than or equal to two, and can contain mixed structures. Non-limiting examples are alkyl groups containing from 1 to 6 carbon atoms (C_1 to C_6 alkyls), or alkyl groups containing from 1 to 4 carbon atoms (C_1 to C_4 alkyls). Examples of saturated alkyl groups include, but are not limited to, methyl, ethyl, n-propyl, isopropyl, n-butyl, iso-butyl, sec-butyl, tert-butyl, amyl, tert-amyl, hexyl, Examples of alkenyl groups include, but are not limited to, vinyl, allyl, butenyl and the like. Examples of alkynyl groups include, but are not limited to, ethynyl, propynyl and the like. Similarly, the term "C_1 to C_{12} alkylene" denotes a bivalent radical of 1 to 12 carbons.

[0054] The alkyl group can be unsubstituted, or substituted with one or more substituents selected from the group consisting of halogen, hydroxy, alkoxy, aryloxy, alkylaryloxy, heteroaryloxy, oxo, cycloalkyl, phenyl, heteroaryls, heterocyclyl, naphthyl, amino, alkylamino, arylamino, heteroarylamino, dialkylamino, diarylamino, alkylarylamino, alkylheteroarylamino, arylheteroarylamino, acyl, acyloxy, nitro, carboxy, carbamoyl, carboxamide, cyano, sulfonyl, sulfonylamino, sulfinyl, sulfinylamino, thiol, alkylthio, arylthio, or alkylsulfonyl groups. Any substituents can be unsubstituted or further substituted with any one of these aforementioned substituents. By way of illustration, an "alkoxyalkyl" is an alkyl that is substituted with an alkoxy group.

[0055] The term "cycloalkyl" used herein alone or as part of another group, refers to a "C_3 to C_8 cycloalkyl" and denotes any unsaturated or unsaturated (e.g., cycloalkenyl, cycloalkynyl) monocyclic or polycyclic group. Nonlimiting examples of cycloalkyl groups are cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl or cycloheptyl. Examples or cycloalkenyl groups include cyclopentenyl, cyclohexenyl and the like. The cycloalkyl group can be unsubstituted or substituted with any one or more of the substituents defined above for alkyl. Similarly, the term "cycloalkylene" means a bivalent cycloalkyl, as defined above, where the cycloalkyl radical is bonded at two positions connecting together two separate additional groups.

[0056] The term "aryl" used herein alone or as part of another group denotes an aromatic ring system containing from 6-14 ring carbon atoms. The aryl ring can be a monocyclic, bicyclic, tricyclic and the like. Non-limiting examples of aryl groups are phenyl, naphthyl including 1-naphthyl and 2-naphthyl, and the like. The aryl group can be unsubtituted or substituted through available carbon atoms with one or more groups defined hereinabove for alkyl. An alkylaryl group denotes an alkyl group bonded to an aryl group (e.g., benzyl).

[0057] The term "heteroaryl" used herein alone or as part of another group denotes a heteroaromatic system containing at least one heteroatom ring atom selected from nitrogen, sulfur and oxygen. The heteroaryl contains 5 or more ring atoms. The heteroaryl group can be monocyclic, bicyclic, tricyclic and the like. Also included in this expression are the benzoheterocyclic rings. If nitrogen is a ring atom, the present invention also contemplates the N-oxides of the nitrogen containing heteroaryls. Nonlimiting examples of heteroaryls include thienyl, benzothienyl, 1-naphthothienyl, thianthrenyl, furyl, benzofuryl, pyrrolyl, imidazolyl, pyrazolyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, indolyl, isoindolyl, indazolyl, purinyl, isoquinolyl, quinolyl, naphthyridinyl, quinoxalinyl, quinazolinyl, cinnolinyl, pteridinyl, carbolinyl, thiazolyl, oxazolyl, isothiazolyl, isoxazolyl and the like. The heteroaryl group can be unsubtituted or substituted through available atoms with one or more groups defined hereinabove for alkyl.

[0058] The term "heterocyclic ring" or "heterocyclyl" used herein alone or as part of another group denotes a five-membered to eight-membered rings that have 1 to 4 heteroatoms, such as oxygen, sulfur and/or nitrogen. These five-membered to eight-membered rings can be saturated, fully unsaturated or partially unsaturated. Non-limiting examples of heterocyclic rings include piperidinyl, piperidinyl, pyrrolidinyl pyrrolinyl, pyrazolinyl, pyrazolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, pyranyl, thiopyranyl, piperazinyl, indolinyl, dihydrofuranyl, tetrahydrofuranyl, dihydrothiophenyl, tetrahydrothiophenyl, dihydropyranyl, tetrahydropyranyl, and the like. The heterocyclyl group can be unsubtituted or substituted through available atoms with one or more groups defined hereinabove for alkyl.

[0059] The inorganic support which is attached to the bipyridine ring can be, for example, silica, silica gel, glass, glass fibers, titania, zirconia, alumina and nickel oxide.

[0060] The polymer which is attached to the bipyridine pyridine ring can be, for example, selected from polyolefins, polyamides, polyethylene terephthalate, polyvinylchloride, polyvinylidenechloride, polystyrene, polymethracrylate, natural rubber, polyisoprene, butadiene-styrene random copolymers, butadiene acrylonitrile copolymers, polycarbonate, polyacetal, polyphenylenesulfide, cyclo-olefin copolymers, styrene-acrylonitrile copolymers, ABS, styrene-maleic anhydride copolymers, chloroprene polymers, isobutylene copolymers, polystyrene, polyethylene, polypropylene, and the like.

[0061] The term "anion" as used herein refers to any moiety or group bearing a negative charge. Examples of anionic moieties include, but are not limited to halogen (e.g., F, Cl, Br, I), OCOR', $OCOCF_3$, OSO_2R', OSO_2CF_3, BF_4, PF_6, SbF_6, BR_4, ClO_4, $AlCl_4$, CN, OH, OR' or NR'_2 wherein R' is selected from alkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl, wherein each of the alkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl is as defined above.

Novel Processes

[0062] The present invention further provides various processes which utilize the Ruthenium complexes of the present invention as catalysts.

[0063] In general, the processes of the present invention can be conducted in the absence or in the presence of a solvent. When a solvent is present, it can be an organic solvent, including but not limited to benzene, toluene, o-, m- or

p-xylene mesitylene (1,3,5-trimethyl benzene), dioxane, THF, DME, anisole and cyclohexane.

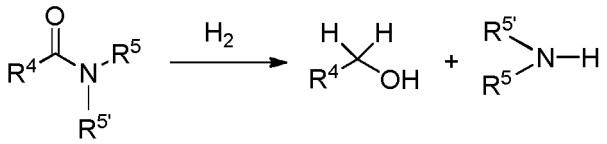
[0064] The stoichiometric ratios of reagents can vary, and depend on the particular alcohol, amine, amide, ester etc., being used, as well as solvent used for the reaction. The reactions of the present invention can be performed for as long as needed so as to effect desired transformation, for example 1 hr to 24 hr or longer than 24 hr. The temperature range can vary from room temperature to heated conditions, for example up to 200 °C.

1. Hydrogenation of Amides to Alcohols and Amines

[0065] The present invention provides a process for hydrogenating amides (including polyamides and polypeptides) by reacting the amide with molecular hydrogen (H_2) in the presence of the Ruthenium complexes of the present invention to generate the corresponding alcohol and amine. As contemplated herein, the inventors have discovered a novel process for converting amides to alcohols and amines in high yields and high turnover numbers. It is disclosed herein that this reaction is catalyzed by a Ruthenium complex, which is represented by anyone of formulae A1, A2, A3, B1, B2, C1, C2, 3, 4, 7 and 9 or any other Ruthenium complex covered by such formulae. In addition, it is disclosed that this reaction is catalyzed by any of the Ruthenium complexes described in US Patent publication US 2009/0112005. One embodiment of such compounds is a pincer complex represented by the structure of formula 1 (Figure 1A).

[0066] Depending on the complex being used, the reaction permits the optional use of one or more equivalents of a base.

[0067] The process of the present invention, i.e., the direct catalytic conversion of amides to alcohols and amides is illustrated in Scheme 4. This novel, environmentally benign reaction can be used to prepare alcohols and amines from any type of amide, with high atom economy and in some embodiments no stoichiometric activating agents, thus generating no waste. Thus, in one embodiment, the present invention provides a process for hydrogenating an amide represented by the formula $R^4C(=O)\text{-}N\text{-}R^5R^{5'}$ to an alcohol of formula R^4CH_2OH and amine of formula $R^5R^{5'}NH$:



Scheme 4

wherein R^4, R^5 and $R^{5'}$ are each independently selected from the group consisting of H, an unsubstituted or substituted alkyl, alkoxyalkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl; wherein the process is conducted in the presence of a Ruthenium complex of the present invention.

[0068] A variety of amides can be used in the process of the invention. In some embodiments, the amide is selected from the group consisting of N-benzyl-2-methoxyacetamide, N-hexyl-2-methoxyacetamide, N-hexyl-3-methyloxetane-3-carboxamide, N-hexyl-2-furanylcarboxamide, N-benzylbenzamide, N-ethylacetamide, N-methylpropionamide, N-cyclohexyl-2-methoxyacetamide, N-phenylacetamide, N-phenylhexylamide, 2-methoxy-N-phenylacetamide, N-phenylbenzamide, Ethylenediamine-N,N'-(2-methoxyacetamide), N-hexanoylmorpholine, N-butanoylmorpholine, N-2-metoxyacetylpyrrolidine, N-formylmorpholine, N,N-dimethylformamide, N,N-diethylbenzamide, benzamide, 4-methylbenzamide, cyclohexanecarboxamide, hexanamide, acetamide, acrylamide and pivalamide.

[0069] In a similar manner, cyclic amides (lactams) can be hydrogenated to the corresponding amino alcohols. In one embodiment, the lactam is a cyclic peptide, which can be hydrogenated with the Ruthenium complex of the present invention to the respective amino alcohol. In a similar manner, polyamides can be hydrogenated to amines and alcohols, and polypeptides can be hydrogenated to amino alcohols.

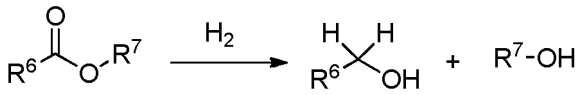
2. Hydrogenation of Esters, Organic Carbonates, Carbamates and Urea Derivatives

[0070] Similar to the hydrogenation of amides, the novel Ruthenium complexes of the present invention can also catalyze the hydrogenation of esters, hydrogenation of organic carbonates, hydrogenation of carbamates, or hydrogenation of urea derivatives to the corresponding amines and/or alcohols. Thus, in some embodiments, the present invention further provides a process for hydrogenating an ester, organic carbonate, carbamate or urea derivative with molecular hydrogen (H2) in the presence of the Ruthenium complex of the present invention. As contemplated herein, the inventors have discovered a novel process for converting esters (e.g., formate esters), organic carbonates, carbamates and/or urea derivatives to alcohols and/or amines in high yields and high turnover numbers. This reaction is catalyzed by a Ruthenium complex or borohydride complex of the present invention. Again, depending on the complex being used, the reaction permits the optional use of one or more equivalents of a base.

[0071] It is also disclosed that the hydrogenation of organic carbonates, carbamates and urea derivatives can be

catalyzed by any of the Ruthenium complexes described in US Patent publication US 2009/0112005. Examples of such compounds are compounds of formula A1', A2' and A3' wherein $\mathbf{L_1}$ is $N(R)_2$, as described above with respect to processes for hydrogenation of amides to amines and alcohols. One embodiment of such compounds is a pincer complex represented by the structure of formula 1 (Figure 1A).

[0072] One embodiment of the process of the invention, i.e., the direct catalytic conversion of esters to alcohols, is illustrated in Scheme 5A, whereby an ester represented by the formula $R^6C(=O)\text{-}OR^7$ is hydrogenated to the corresponding alcohol or alcohols:



Scheme 5A

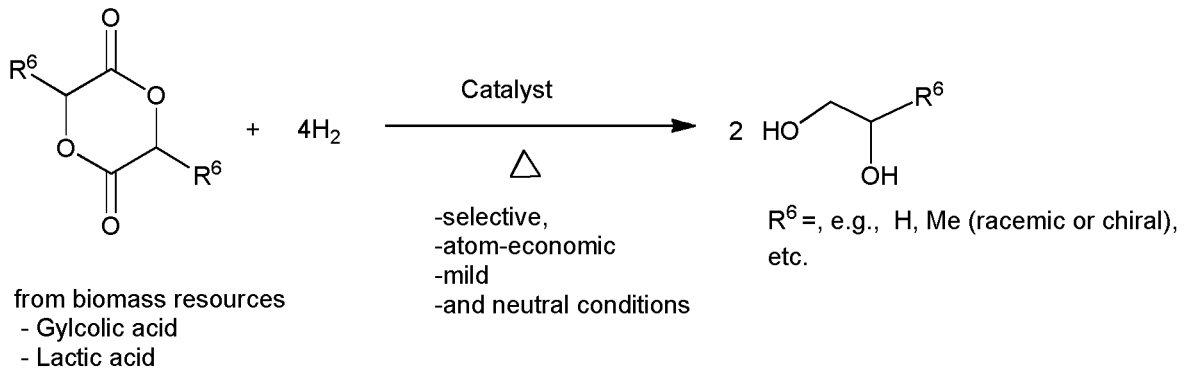
wherein R^6 is selected from the group consisting of H, an unsubstituted or substituted alkyl, alkoxyalkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl; and R^7 is selected from the group consisting of an unsubstituted or substituted alkyl, alkoxyalkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl.

[0073] It is apparent to a person of skill in the art that when the ester is symmetric (i.e., $R^6=R^7$), the reaction yields two equivalents of the same alcohol. However, when the ester is asymmetric (i.e., R^6 is different from R^7), the reaction yields a mixture of two alcohols.

[0074] In one embodiment, R^6 is H and the process comprises hydrogenating a formate ester of formula $H\text{-}C(=O)\text{-}OR^7$ to methanol and an alcohol of formula R^7-OH.

[0075] A variety of esters can be used in the process of the invention. In some embodiments, the ester is selected from the group consisting of hexyl hexanoate, butyl butyrate, methyl formate, ethyl formate, propyl formate and butyl formate. In other embodiments, the ester is a cyclic ester (a lactone). In yet other embodiments, the ester is a cyclic di-ester (di-lactone). In yet other embodiments, the ester is a biomass-derived cyclic di-ester (di-lactone) such as, but not limited to glycolide or lactide. In yet another embodiment, the ester is polyester. Catalytic homogeneous hydrogenation of cyclic di-esters (di-lactone), specifically glycolide and lactide to the corresponding 1,2-diols (*vicinal* diols) is of significant interest conceptually and practically, since these compounds are produced from biomass sources such as glycolic acid and lactic acid respectively via self-esterification, and their efficient hydrogenation can provide an alternative, mild approach to the indirect transformation of biomass resources to important synthetic building blocks. As contemplated herein, the unprecedented, environmentally benign, atom-economical route for the synthesis of propylene glycol and ethylene glycol are efficiently catalyzed by bipyridine based PNN-Ru(II) dearomatized pincer complex of formula (1), as well as other Ruthenium complexes as described herein. These catalytic reactions proceed under neutral, homogeneous conditions, at mild temperatures and mild hydrogen pressures. The optical purity of a chiral diol is unaffected during the hydrogenation reactions.

[0076] The process of lactone or di-lactone hydrogenation can be catalyzed by the same complexes described above with respect to hydrogenation of esters to alcohols.



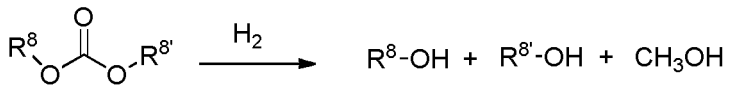
Scheme 5B

wherein R^6 is as described above.

[0077] A variety of cyclic di-esters (di-lactones) can be used in the process of the invention. In some embodiments, the ester is a biomass-derived cyclic di-ester (di-lactone) such as, but not limited to glycolide or lactide.

[0078] Another embodiment of the process of the invention, i.e., the direct catalytic hydrogenation of organic carbon-

ates, is illustrated in Scheme 6, whereby a carbonate represented by the formula $R^8O\text{-}C(=O)\text{-}OR^{8'}$ is hydrogenated to the corresponding alcohols(s) and methanol:



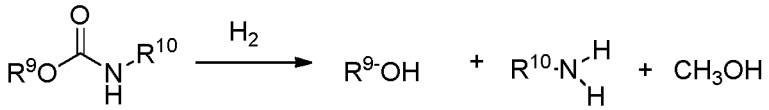
Scheme 6

wherein R^8 and $R^{8'}$ are the same or different and are selected from the group consisting of an unsubstituted or substituted alkyl, alkoxyalkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl.

[0079] It is apparent to a person of skill in the art that when the organic carbonate is symmetric (i.e., $R^8=R^{8'}$) the reaction yields two equivalents of the same alcohol, and one equivalent of methanol. However, when the organic carbonate is asymmetric (i.e., R^8 is different from $R^{8'}$), the reaction yields a mixture of two alcohols, and methanol.

[0080] A variety of organic carbonates can be used in the process of the invention. In some embodiments, the carbonate is dimethyl carbonate, diethyl carbonate, dipropyl carbonate or dibutyl carbonate. In another embodiment, the carbonate is a polycarbonate, such as polyethylene carbonate or polypropylene carbonate.

[0081] Another embodiment of the process of the present invention, i.e., the direct catalytic hydrogenation of carbamates, is illustrated in Scheme 7A, whereby a carbamate represented by the formula $R^9O\text{-}C(=O)\text{-}NHR^{10}$ is hydrogenated to the corresponding amine, alcohol and methanol:

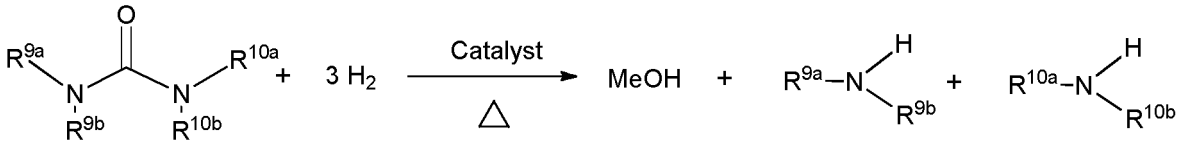


Scheme 7A

wherein R^9 is selected from the group consisting of an unsubstituted or substituted alkyl, alkoxyalkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl; and R^{10} is selected from the group consisting of H or an unsubstituted or substituted alkyl, alkoxyalkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl.

[0082] A variety of organic carbamates can be used in the process of the invention. In some embodiments, the carbamate is methyl benzylcarbamate or methyl 4-methoxybenzylcarbamate. In another embodiment, the carbamate is a polycarbamate.

[0083] Another embodiment of the process of the present invention, i.e., the direct catalytic hydrogenation of urea derivatives, is illustrated in Scheme 7B, whereby a urea derivative is hydrogenated to the corresponding amine(s) and methanol:



Scheme 7B

wherein each of R^{9a} and R^{10a}, which may be the same or different, is selected from the group consisting of an unsubstituted or substituted alkyl, alkoxyalkyl, cycloalkyl, aryl, alkylaryl, and heterocyclyl, and each of R^{9b} and R^{10b}, which may be the same or different, is selected from the group consisting of H, an unsubstituted or substituted alkyl, alkoxyalkyl, cycloalkyl, aryl, alkylaryl, and heterocyclyl. Alternatively, at least one of R^{9a} and R^{10a}, and/or R^{9b} and R^{10b} together with the nitrogen to which they are attached form a heterocyclic ring.

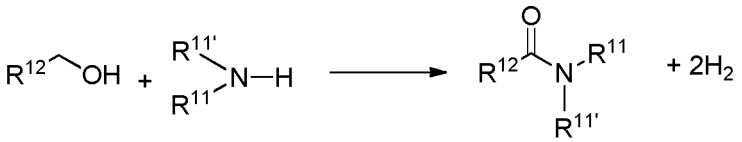
[0084] A variety of symmetrical ($R^{9a}=R^{10a}$, $R^{9b}=R^{10b}$) and asymmetrical ($R^{9a}\neq R10^a$, $R^{9b}\neq R10^b$) urea derivatives can be used in the process of the invention. In some embodiments, the urea derivative is 1,3-dimethylurea, and the product of the reaction is methanol and two molecules of methylamine. In another embodiment, the urea derivative is selected from the group consisting of 1,3-dipropylurea, 1,3-dihexylurea, 1,3-bis(2-methoxyethyl)urea, 1,3-dicyclohexylurea, 1,3-dibenzylurea, 1,3-bis(4-methylbenzyl)urea, 1,3-bis(4-methylbenzyl)urea, 1,3-diphenylurea, 1,3-bis(4-(tert-butyl)phenyl)urea, 1,1,3,3-tetramethylurea, and di(piperidin-1-yl)methanone. Polyurea derivatives can also be hydrogenated in a similar manner.

3. Dehydrogenative coupling of alcohols and amines with liberation of H_2 to form amides or of beta-amino alcohols to form pyrazines:

[0085] The present invention further provides a process for preparing amides, by reacting an amine and an alcohol in the presence of a Ruthenium complex, to generate the amide compound and molecular hydrogen (H_2). As contemplated herein, the inventors have further discovered a novel process for preparing amides in which primary and secondary amines are directly acylated by equimolar amounts of alcohols to produce amides and molecular hydrogen in high yields and high turnover numbers. It is disclosed herein that this reaction is catalyzed by a Ruthenium complex or a boronated complex thereof, which is represented by anyone of formulae A1, A2, A3, B1, C1, B2, C2, D, E, F (when complex F is used and L^4 is - CH_2-L^1, L^1 is preferably NR^aR^b), H, 3, 4, 7, 9, 4' and 8', or any other Ruthenium complex or their boronated complexes covered by such formulae. Depending on the complex being used, the reaction permits the optional use of one or more equivalents of a base.

[0086] Use of diamines or dialcohols in the reaction leads to diamides, whereas when diamines and dialcohols are used together, the process results in a polyamide. Furthermore, reactions of amino-alcohols results in cyclic amides (lactams). For example, reaction of $H_2N(CR^1R^2)_nCH_2OH$ results in lactams for n=4, 5 or 6, such as caprolactam for n=6 and R^1=R^2=H. For n>6, the reaction typically results in polymers. In another embodiment, when amino alcohols such as R-CH(NH_2)CH_2OH are used, peptides or polypeptides are formed (e.g., dehydrogenation of alaninol with the Ruthenium complexes of the present invention results in polyalanine).

[0087] The process of the present invention, i.e., the direct catalytic conversion of alcohols and amines into amides and dihydrogen is illustrated in Scheme 8A. In accordance with this process, an amine represented by formula $R^{11}R^{11'}NH$ is reacted with an alcohol represented by the formula $R^{12}CH_2OH$ in the presence of a Ruthenium complex of the present invention to generate an amide represented by the structure R^{12}-C(=O)-$NR^{11}R^{11'}$. This novel, environmentally benign reaction can be used to produce various amides from very simple substrates, with high atom economy and in some embodiments no stoichiometric activating agents, thus generating no waste.



Scheme 8A

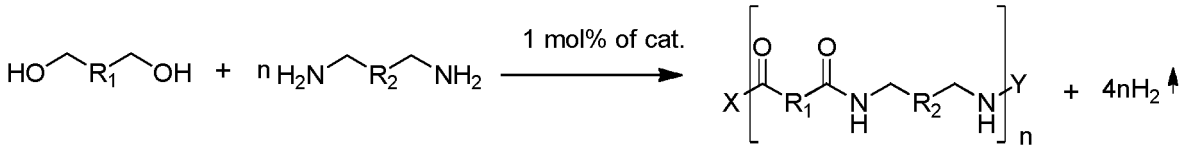
wherein R^{10}, R^{11} and R^{12} are each independently selected from the group consisting of H an unsubstituted or substituted alkyl, alkoxyalkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl, wherein R^{10}, R^{11} and R^{12} can be the same or different from each other.

[0088] A variety of alcohols can be used in the process of the invention. In some embodiments, the alcohol is selected from the group consisting of methanol, ethanol, propanol, butanol, pentanol, hexanol, 2-methoxyethanol, and 2-methyl-1-butanol.

[0089] A variety of primary and secondary amines (as well as ammonia) may be used in the process of the invention. In some embodiments, the amine is selected from the group consisting of benzylamine, 1-hexylamine, 1-pentylamine, 1-(2-furyl)methylamine, aniline, morpholine, pyrrolidine, 2-methylhexylamine, and cyclohexylamine.

[0090] In another embodiment, the process of the invention can also be applied to bis-acylation reactions with diamines. Upon reacting alcohols and diamines, the corresponding bis-amides are produced in high yields. In some embodiments, the diamine is ethylenediamine, diethylenetriamine or 1,6-diaminohexane.

[0091] Similarly, when diamines and dialcohols are used, polyamides or peptides are obtained. The applicants have surprisingly discovered that Ruthenium complexes catalyze the synthesis of polyamides directly from diols and diamines. This polyamidation reaction is general, environmentally benign and atom economical. It proceeds under neutral reaction conditions without the use of activators, condensing agents or other additives. A preferable solvent for use in this reaction is 1,4-dioxane, however other solvents can be used as apparent to a person of skill in the art. Moreover, these methods produce H_2 as the only byproduct (Scheme 8B):



Scheme 8B

[0092] A variety of dialcohols can be used for this reaction, non-limiting examples of which include hexane-1,2-diol, octane-1,8-diol, 1,3-phenylenedimethanol, (5-methoxy-1,3-phenylene)dimethanol, 1,4-phenylenedimethanol, pyridine-2,6-diyldimethanol, pentane-1,5-diol, cyclohexane-1,4-diyldimethanol, and (5-(hexyloxy)-1,3-phenylene)dimethanol.

[0093] A variety of diamines can be used for this reaction, non-limiting examples of which include hexane-1,6-diamine, ethane-1,2-diamine, 1,3-phenylenedimethanamine, and 1,4-phenylenedimethanamine. The reaction between the amine and alcohol can be inter-molecular (i.e., the amine and the alcohol are present in separate molecules). Alternatively, the reaction between the amine and alcohol can be intra-molecular, i.e., the amine and alcohol functionalities can be present in the same molecule, resulting in intra-molecular cyclization to generate a lactam.

[0094] It is also disclosed that the aforementioned amidation and polyamidation reactions are also catalyzed by the Ruthenium complexes described in US Patent publication US 2009/0112005, in particular Ruthenium complexes in which L_1 is $N(R)_2$, as described above for the reciprocal hydrogenation reactions of amides to alcohols and amines. One embodiment of such compounds is a pincer complex represented by the structure of formula 1 (Figure 1A).

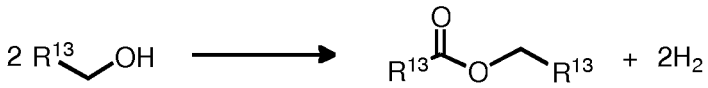
[0095] In some embodiments, beta-amino alcohols can be dehydrogenated in the presence of Ruthenium complexes to form cyclic dipeptides. Such reactions are catalyzed by a Ruthenium complex of the invention or a boronated complex thereof. It is also disclosed that such reactions can also be catalyzed by the Ruthenium complexes described in US Patent publication US 2009/0112005, in particular Ruthenium complexes in which L_1 is $N(R)_2$, as described above for the reciprocal hydrogenation reactions of amides to alcohols and amines.

[0096] Preparation of polypeptides or cyclic peptides by dehydrogenation of beta-amino alcohols, catalyzed by the Ruthenium complexes described in US Patent publication US 2009/0112005, namely compounds A1', A2' or A3' in which L_1 is $N(R)_2$, has not previously been described.

4. Dehydrogenative Coupling of Alcohols:

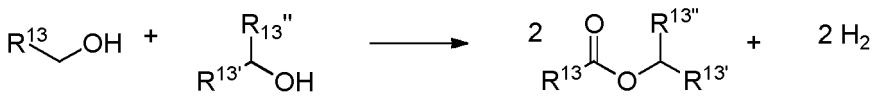
[0097] The present invention further provides a process for preparing esters by coupling of alcohols in the presence of a Ruthenium complex, to generate the ester compound and molecular hydrogen. In one embodiment, the process involves coupling of primary alcohols. In another embodiment, the process involves coupling of a primary and secondary alcohol. It is disclosed that these reactions are catalyzed by a Ruthenium complex or a boronated complex thereof, which is represented by anyone of formulae A1, A2, A3, B1, C1, B2, C2, D, E, F, G, H, 3, 4, 7, 9, 2', 4', 6' and 8' or any other Ruthenium complex or their boronated complexes covered by such formulae. Depending on the complex being used, the reaction permits the optional use of one or more equivalents of a base. Use of dialcohols in the reaction leads to polyesters or to lactones.

[0098] The process of the present invention, i.e., the direct catalytic coupling of primary alcohols into esters and dihydrogen in the presence of a Ruthenium complex of the present invention is illustrated in Scheme 9A. In accordance with this process, two equivalents of a primary alcohol represented by formula $R^{13}CH_2OH$ are converted to an ester by the structure R^{13}-C(=O)-OCH_2R^{13}. This novel, environmentally benign reaction, can be used to produce various esters from very simple substrates, with high atom economy and in some embodiments no stoichiometric activating agents, thus generating no waste.



Scheme 9A

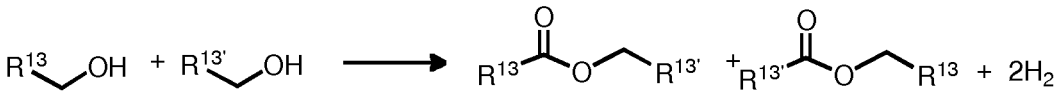
[0099] In another embodiment, the process of the invention involves the catalytic coupling of a primary alcohol and a secondary alcohol in the presence of a Ruthenium complex of the present invention, as illustrated in Scheme 9B.



Scheme 9B

wherein R^{13}, R^{13} and $R^{13''}$ are each independently selected from the group consisting of H, an unsubstituted or substituted alkyl, alkoxyalkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl.

[0100] When primary alcohols are used, the process of the invention contemplates symmetric coupling of alcohols to yield symmetric esters (i.e., 2 equivalents of the same alcohol are coupled). However, the present invention further contemplates the generation of asymmetric esters by coupling of different alcohols. In accordance with this embodiment, a first primary alcohol represented by formula $R^{13}CH_2OH$ is reacted with a second alcohol represented by formula $R^{13'}CH_2OH$ so as to generate an ester by the structure R^{13}-C(=O)-$OCH_2R^{13'}$ or an ester of formula $R^{13'}$-C(=O)-OCH_2R^{13}, as illustrated in Scheme 10:



Scheme 10

wherein R^{13} and $R^{13'}$ are the same or different from each other and are each independently selected is from the group consisting of H, an unsubstituted or substituted alkyl, alkoxyalkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl.

[0101] A variety of alcohols can be used in the process of the invention. In some embodiments, the alcohol is selected from the group consisting of methanol, ethanol, propanol, butanol, pentanol, hexanol, 2-methoxyethanol, 2-methyl-1-butanol, benzyl alcohol, 1-phenylethanol and cyclohexane methanol.

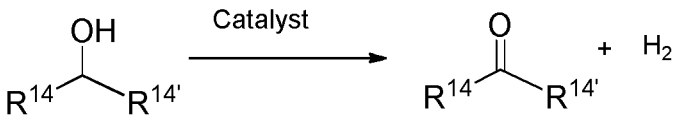
[0102] In another embodiment, the process of the invention can also be applied to bis-acylation reactions with dialcohols to yield polyesters.

[0103] The reaction between the alcohols can be inter-molecular (i.e., the two alcohols are separate molecules). Alternatively, the reaction between the alcohols can be intra-molecular, i.e., the alcohol functionalities can be present in the same molecule, resulting in intra-molecular cyclization to generate a lactone. In some embodiments, the intra-molecular dehydrogenation of diols to generate a lactone is catalyzed by borohydride Ruthenium complexes of the present invention as described herein

5. Dehydrogenation of Secondary Alcohols:

[0104] The present invention further relates to a process for preparing a ketone by dehydrogenation of a secondary alcohol, comprising the step of reacting the secondary alcohol in the presence of the Ruthenium complex of the present invention, thereby generating the ketone and molecular hydrogen.

[0105] The process of the present invention, i.e., the direct catalytic conversion of secondary alcohols into ketones and dihydrogen in the presence of a Ruthenium complex of the present invention is illustrated in Scheme 11A. In accordance with this process, a secondary alcohol represented by formula $R^{14}CH(OH)R^{14'}$ is converted to a ketone represented by the structure R^{14}-C(=O)-$R^{14'}$:



Scheme 11A

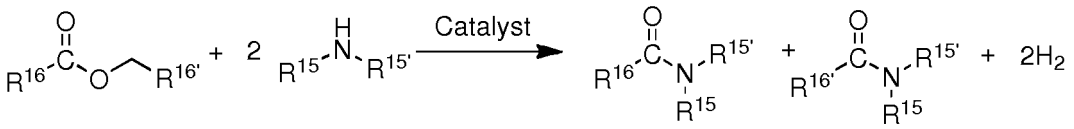
[0106] A variety of alcohols can be used in the process of the invention. In some embodiments, the alcohol is selected from the group consisting of 1-phenyl-1-ethanol, 2-hexanol, cyclohexanol and 2-propanol.

6. Synthesis of Amides from Esters and Alcohols

[0107] The present invention further provides a process for preparing amides, by reacting an amine and an ester in the presence of a Ruthenium complex, to generate the amide compound and molecular hydrogen (H2). As contemplated

herein, the inventors have further discovered a novel process for preparing amides in which primary and secondary amines are directly reacted with esters to produce amides and molecular hydrogen in high yields and high turnover numbers. As disclosed herein this reaction is catalyzed by a Ruthenium complex or a boronated complex thereof, which is represented by anyone of formulae A1, A2, A3, B1, C1, B2, C2, D, E, F (when complex F is used and L^4 is $-CH_2-L^1$, L^1 is preferably NR^aR^b), H, 3, 4, 7, 9, 4' and 8', or any other Ruthenium complex or their boronated complexes covered by such formulae. Depending on the complex being used, the reaction permits the optional use of one or more equivalents of a base. Reactions of esters with diamines leads to diamides.

[0108] The process of the present invention, i.e., the direct catalytic reaction of esters and amines into amides and dihydrogen is illustrated in Scheme 11B. In accordance with this process, an amine represented by formula $R^{15}R^{15'}NH$ is reacted with an ester represented by the formula R^{16}-C(=O)-$OCH_2R^{16'}$ in the presence of a Ruthenium complex of the present invention to generate an amide represented by the structure R^{16}-C(=O)-$NR^{15}R^{15'}$. This novel, environmentally benign reaction can be used to produce various amides from very simple substrates, with high atom economy and in some embodiments no stoichiometric activating agents, thus generating no waste.



Scheme 11B

wherein R^{15}, R^{15}, R^{16} and $R^{16'}$ are each independently selected from the group consisting of H, an unsubstituted or substituted alkyl, alkoxyalkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl, wherein R^{15}, $R^{15'}$ and R^{16} can be the same or different from each other.

[0109] A variety of esters can be used in the process of the invention. In some embodiments, the ester is selected from the group consisting of ethyl acetate, butyl butyrate, pentyl pentanoate and hexyl hexanoate.

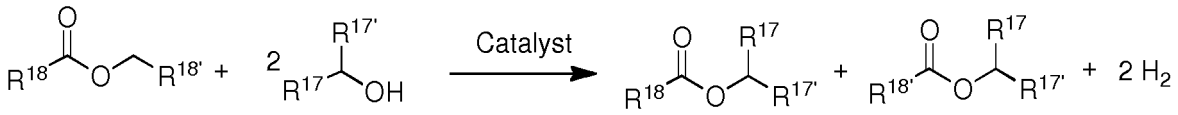
[0110] A variety of primary and secondary amines (as well as ammonia) may be used in the process of the invention. In some embodiments, the amine is selected from the group consisting of pyrrolidine, morpholine, 1-methyl piperazine, piperidine, piperazine, 1-hexylamine and p-tolylmethanamine.

[0111] In another embodiment, the process of the invention can also be applied to bis-acylation reactions with diamines. Upon reacting alcohols and diamines, the corresponding bis-amides are produced in high yields.

7. Acylation of Alcohols Using Esters with Liberation of H_2

[0112] The present invention further provides a process for preparing esters by acylation of alcohols using esters in the presence of a Ruthenium complex, to generate the ester compound and molecular hydrogen. In one embodiment, the process involves reaction of primary alcohols and esters. In another embodiment, the process involves reaction of a secondary alcohols and esters. It is disclosed herein that these reactions are catalyzed by a Ruthenium complex or a boronated complex thereof, which is represented by anyone of formulae A1, A2, A3, B1, C1, B2, C2, D, E, F, G, H, 3, 4, 7, 9, 2', 4', 6' and 8' or any other Ruthenium complex or their boronated complexes covered by such formulae. Depending on the complex being used, the reaction permits the optional use of one or more equivalents of a base.

[0113] The process of the present invention, i.e., the direct catalytic acylation of alcohols using esters to yield an ester and dihydrogen is illustrated in Scheme 12A. In accordance with this process, two equivalents of a primary or secondary alcohol represented by formula $R^{17}R^{17'}CHOH$ reacts with one equivalent of an ester by the structure R^{18}-C(=O)-$OCH_2R^{18'}$ in the presence of a Ruthenium complex of the present invention as shown in Scheme 12A. This novel, environmentally benign reaction, can be used to produce various esters from very simple substrates, with high atom economy and in some embodiments no stoichiometric activating agents, thus generating no waste.



Scheme 12A

wherein R^{17}, $R^{17'}$, R^{18} and $R^{18'}$ are each independently selected from the group consisting of H, an unsubstituted or

substituted alkyl, alkoxyalkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl.

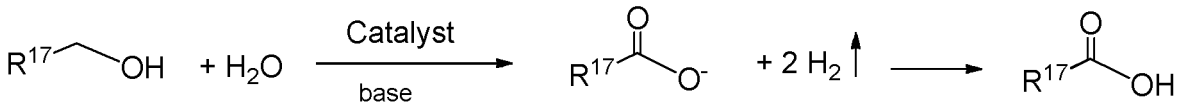
[0114] A variety of alcohols can be used in the process of the invention. In some embodiments, the alcohol is selected from the group consisting of cyclohexanol, cyclopentanol, 1-phenylethanol, isopropanol and 3-pentanol.

[0115] A variety of esters can be used as the starting materials. In some embodiments, the ester is selected from the group consisting of ethyl acetate, hexyl hexanoate, pentyl pentanoate, butyl butyrate, ethyl butyrate and methyl hexanoate.

8. Coupling of Alcohols with Water to Form Carboxylic Acid with Liberation of H_2

[0116] The present invention further provides a process for preparing carboxylic acids by contacting primary alcohols with water in the presence of a Ruthenium complex and a base, to generate the carboxylic acid salt and molecular hydrogen and, if desired, followed by conversion of the carboxylic acid salt to the corresponding carboxylic acid. It is disclosed that these reactions are catalyzed by a Ruthenium complex or a boronated complex thereof, which is represented by anyone of formulae A1, A2, A3, B1, C1, B2, C2, D, E, F, G, H, 3, 4, 7, 9, 2', 4', 6' and 8' or any other Ruthenium complex or their boronated complexes covered by such formulae. Depending on the complex being used, the reaction permits the optional use of one or more equivalents of a base. It is also disclosed that this reaction can also be catalyzed by the Ruthenium complexes described in US Patent publication US 2009/0112005. Some complexes for this reaction are Pincer complexes represented by the structure of Formula 1.

[0117] The process of the invention, i.e., the direct catalytic conversion of primary alcohols to carboxylic acids and dihydrogen in the presence of a Ruthenium complex of the present invention is illustrated in Scheme 12B. In accordance with this process, a primary alcohol represented by formula $R^{17}CH_2OH$ is contacted with water and a base (e.g., NaOH) as shown in Scheme 12B. This novel, environmentally benign reaction, can be used to produce various carboxylic acids and their salts from very simple substrates, with high atom economy and in some embodiments no stoichiometric activating agents, thus generating no waste. If desired, the salt is neutralized with the appropriate acid to provide the corresponding carboxylic acid.



Scheme 12B

wherein R^{17} is selected from the group consisting of H, an unsubstituted or substituted alkyl, alkoxyalkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl.

[0118] A variety of bases can be used for this reaction, non-limiting examples of which include an inorganic or organic base selected from sodium carbonate, potassium carbonate, sodium hydroxide, potassium hydroxide, sodium ethoxide, potassium tert-butoxide, sodium methoxide. The acid used to neutralize the salt can be, e.g. a mineral acid such as hydrochloric acid, hydrobromic acid, and the like.

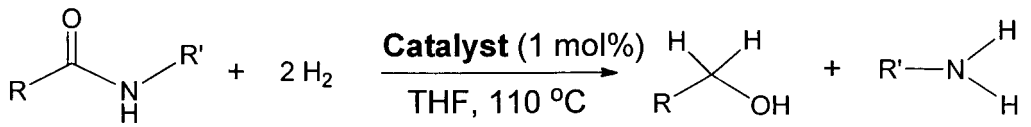
[0119] A variety of alcohols can be used in the process of the invention. In some embodiments, the alcohol is selected from the group consisting of butanol, pentanol, decanol, 2-methoxyethanol, 2-phenylethanol, cyclohexylmethanol, 3-phenylbutan-1-ol, but-3-en-1-ol, (4-methoxyphenyl)methanol, and (2,4-dimethoxyphenyl)methanol.

[0120] The principles of the present invention are demonstrated by means of the following non-limiting processes.

EXAMPLES

Example 1: Hydrogenation of Amides to the Corresponding Alcohols and Amines

[0121] Examples of processes involving the hydrogenation of amides to alcohol and amines are shown in Scheme 13:



R, R' = H, Aryl, alkyl, Aryalkyl, etc.

Scheme 13

(a) **Using catalyst 3:** A 100 mL Fischer-Porter tube was charged under nitrogen with the catalyst **3** (0.01 mmol), an amide (1.0 mmol), and THF (2 mL). The nitrogen present in the Fischer-Porter (100 mL) was replaced by H_2 (twice with 30 psi) at room temperature, then it was filled with H_2 (10 atm). The solution was heated at 110 °C (bath temperature) with stirring for 48 hrs. After cooling to room temperature, the H_2 was vented carefully and the products were determined by GC with m-xylene as internal standard, using a Carboxen 1000 column on a HP 690 series GC system.

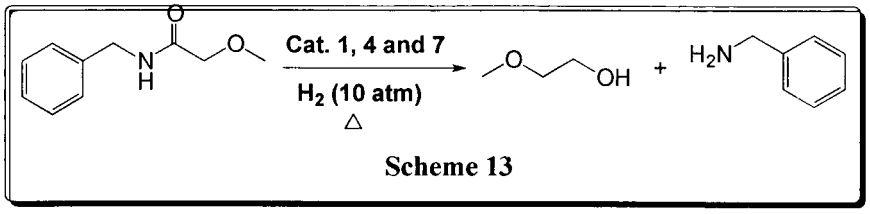
(b) **Using complex 4 + Base (generation of catalyst 3 *in situ*)**: In an open air, a solution of amide (1.0 mmol) in THF (1.0 mL) was transferred *via* syringe into a Fischer-Porter tube (100 mL) contains 0.01 mmol of catalyst **4.** Then, KO^{t}Bu (0.01 mmol) in THF (1.0 mL) was added and the air present in the Fischer-Porter tube was flushed with hydrogen (thrice with 30 psi) and filled with H_2 (10 atm). The solution was heated at 110 °C (bath temperature) with stirring for 48 hrs. After cooling to room temperature, the H_2 was vented carefully and the products were determined by GC with *m*-xylene as internal standard, using a Carboxen 1000 column on a HP 690 series GC system.

Results of some typical processes are shown in Tables 1A, 1B and 2.

A. Selective Hydrogenation of Amides to Alcohols and Amines Using H_2 catalyzed by BPy-PNN-Ru(II) pincer complexes 1, 4 and 7

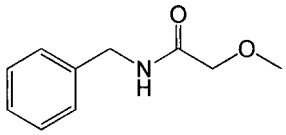
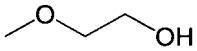
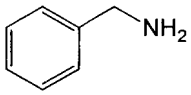
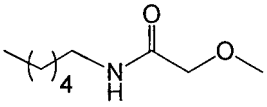
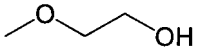
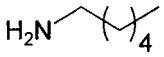
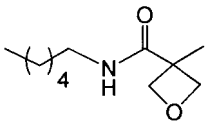
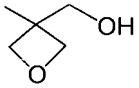
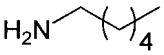
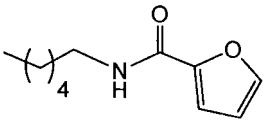
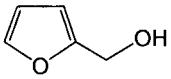
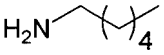
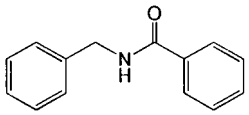
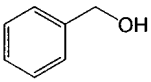
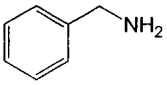
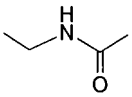
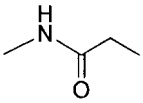
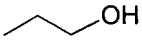
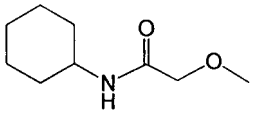
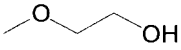
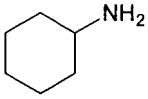
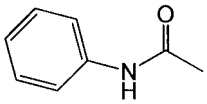
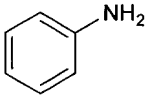
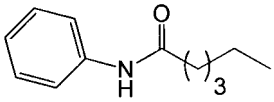
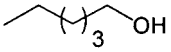
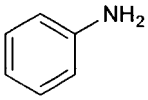
[0122]

Table 1A. Hydrogenation of amides catalyzed by complex **1, 4** and **7**

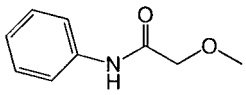
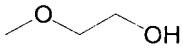
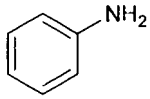
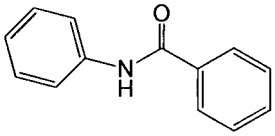
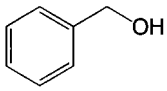
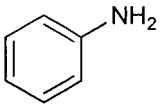
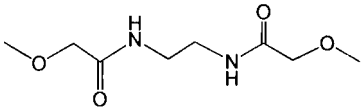
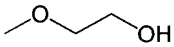
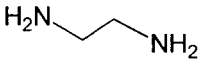
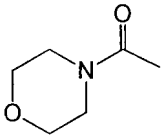
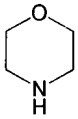
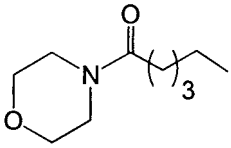
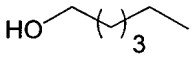
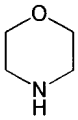
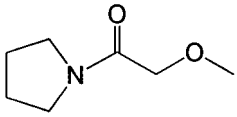
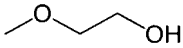
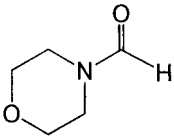
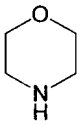
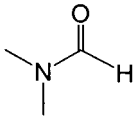
Entry	Catalyst	Reaction condition[a]	
			
		Yield (%)[b]	
		Alcohol	Amine
1	**1**	62.7	62.0
2	**1**	66.3	66.8[c]
3	**4**	--	--
4	**4** + KO^{t}Bu	80.2	81.8[d]
5	7 + KO^{t}Bu	76.8	78.0[d]

[a]Complex **1, 4** and **7** (0.01 mol), amide (1 mmol), H_2 (10 atm), and dry THF (2 ml) were heated in a Fischer-Porter tube at 110 °C (bath temperature) for 48 h. [b]Yields of products were analyzed by GC (m-xylene as internal standard). [c]1,4-dioxane (2 mL) at 140 °C after 48 h. [d]one equivalent (relative to Ru) of base was used.

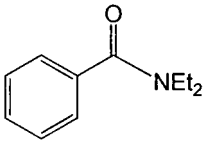
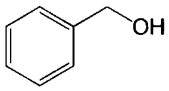
Table 1B. Hydrogenation of amides to alcohols and amines selectively catalyzed by pincer complex **3**[a]

Entry	Amide	Products (yield [%])[b]	
		Alcohol	Amine
1		 (89.2)	 (89.6)
2		 (90.7)	 (90.3)
3		 (73.6)	 (73.9)
4		 (68.8)	 (68.1)
5		 (56.8)	 (57.3)
6		EtOH (71.0)	$EtNH_2$[c]
7		 (68.4)	$MeNH_2$[c]
8		 (88.0)	 (87.3)
9		EtOH (94.1)	 (94.9)[d]
10		 (92.1)	 (92.0)

(continued)

Entry	Amide	Products (yield [%])[b]	
		Alcohol	Amine
11		 (95.3)	 (94.6)
12		 (91.6)	 (91.0)
13		 (78.0)	 (76.9)[e]
14		EtOH (97.1)	 (98.0)
15		 (95.8)	 (95.7)
16		 (97.0)	(97.4)
17		MeOH (97.1)	 (98.3)[f]
18		MeOH (96.3) (32.1)[g]	Me_2NH

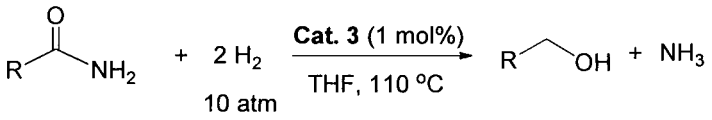
(continued)

Entry	Amide	Products (yield [%])[b]	
		Alcohol	Amine
19			$EtNH_2$[c]

[a]Complex **3** (0.01 mol), amide (1 mmol), H_2 (10 atm), and dry THF (2 ml) were heated in a Fischer-Porter tube at 110 °C (bath temperature) for 48 h. [b]Yields of products were analyzed by GC (m-xylene as internal standard). [c]The amines ($EtNH_2$ (entry 6 and 18) and $MeNH_2$ (entry 7)) were analyzed in the gas phase by GC-MS. [d]In the reactions involving anilide derivatives (entries 9-12), trace amounts of the corresponding secondary amines were detected by GC-MS. [e]0.5 mmol of bis-amide was used. [f]Yield after 32 h. [g]Complex **1** was used.

B. Selective Hydrogenation of Primary Amides to Alcohols and Ammonia Using H_2 Catalyzed by Ruthenium Pincer Complex **3**

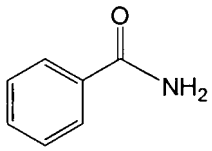
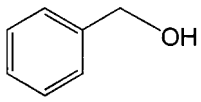
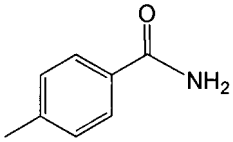
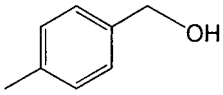
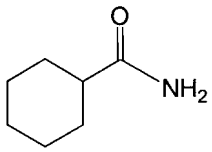
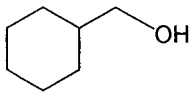
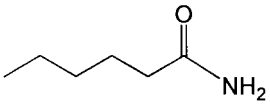
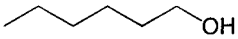
[0123]



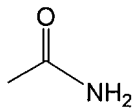
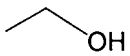
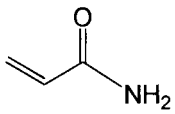
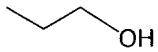
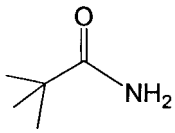
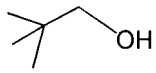
R = Aryl, alkyl, and vinyl

Scheme 14

Table 2. Hydrogenation of primary amides to alcohols and ammonia selectively catalyzed by complex **3**

Entry	Amides	Alcohols	Yield (%)[b]
1			86.8 (63.7)[c,d]
2			88.1[d]
3			90.7[d]
4			89.1 (91.7)[d,e]

(continued)

Entry	Amides	Alcohols	Yield (%)[b]
5			92.5[d]
6			95.7
7			42.4

[a]Complex **3** (0.01 mol), amide (1 mmol), H_2 (10 atm), and dry THF (2 ml) were heated in a Fischer-Porter tube at 110 °C (bath temperature) for 72 h. [b]Yields of products were analyzed by GC (m-xylene as internal standard) and ammonia was analyzed in the gas phase by GC-MS. [c]Yield in the parenthesis after 48 h. [d]Traces of corresponding esters were also observed in GC. [e]1,4-dioxane (2 mL) at 140 °C after 60 h.

Discussion:

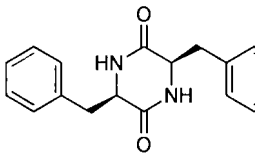
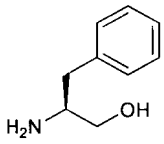
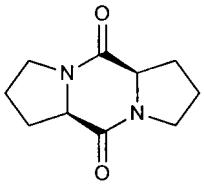
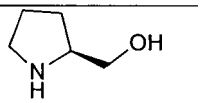
[0124] The applicants have previously reported the dehydrogenative coupling of alcohols with amines to form amides, catalyzed by complex **1,** with liberation of hydrogen gas (Gunanathan 2007). To explore whether it might be possible to reverse this reaction by the application of hydrogen pressure, complexes **1-4** were tested as catalysts for the hydrogenation of amides. Thus, upon treatment of *N*-benzyl-2-methoxyacetamide with dihydrogen (10 atm) at 110 °C (bath temperature) in dry THF for 48 h with a catalytic amount of **1** (1 mol%), 62.7% of 2-methoxyethanol and 62.0% of benzyl amine were obtained. Performing the reaction at 140 °C using 1,4-dioxane as solvent did not significantly improve the yield (alcohol yield 66.3%). It was significant that the reaction was selective and the corresponding secondary amine was not observed. Under the same conditions complex **2** was inactive. Remarkably, employing complex **3** (1 mol%) as catalyst, hydrogenation of *N*-benzyl-2-methoxyacetamide under identical conditions (THF, 110 °C) resulted in the selective formation of 89.2% 2-methoxyethanol and 89.6% benzyl amine (Table 1B, entry 1). Thus, the normally observed C-O hydrogenolysis did not take place at all. Of practical significance, the air-stable complex **4** (which is stable in air for at least two days in solution) in the presence of one equivalent (relative to Ru) of base also efficiently catalyzes the hydrogenation of amides to alcohols and amines, by generation of the catalyst **3** *in situ.* Thus, upon heating a THF solution of **4** (1 mol%) with KO^{t}Bu (1 mol%) and *N*-benzyl-2-methoxyacetamide (1 mmol) at 110 °C under H_2 (10 atm) for 48 h, 80.2% of alcohol and 81.8% of amine were formed. No reaction took place in the absence of base. Hydrogenation of *N*-hexyl-2-methoxyacetamide catalyzed by **3** yielded 2-methoxy ethanol and hexyl amine in 90.7% and 90.3% yields, respectively (Table 1B, entry 2). N-hexyl-3-methyloxetane-3-carboxamide undergoes hydrogenation to the alcohol and amine without hydrogenolysis of the strained oxetane ring (Table 1B, entry 3). The heterocyclic amide, *N*-hexylfuran-2-carboxamide was hydrogenated to yield 68.8% of furfuryl alcohol and 68.1% of hexylamine (Table 1B, entry 4). The aromatic non-activated amide, *N*-benzylbenzamide is also hydrogenated to benzyl alcohol and benzyl amine (Table 1B, entry 5), but the yield is lower, probably because of steric reasons. Significantly, the aliphatic non-activated amides, *N*-ethylacetamide and *N*-methylpropionamide also underwent hydrogenation to yield the corresponding alcohols and amines (71% of ethanol and ethylamine for entry 6 and 68.4% of *n*-propanol and methylamine for entry 7). The product gaseous amines were analyzed by GC-MS spectrometry of the gas phase and not quantified. As expected, the activated amides, anilide derivatives, were converted into their corresponding alcohols and aniline in excellent yields (91-95%; Table 1B, entries 9-12) along with trace amounts of the secondary amines (detected by GC-MS) under similar conditions. The reaction is also effective for bis-amides. Thus, *N,N'*-(ethane-1,2-diyl)bis(2-methoxyacetamide) (0.5 mmol) was also hydrogenated using catalyst **3** under mild conditions (Table 1B, entry 13). Noteworthy, *tert*-amides also underwent hydrogenation almost quantitatively to yield alcohols and secondary amines in equivalent amounts (Table 1B, entries 14-16). Gratifyingly, heating a solution of *N*-formymorpholine (1 mmol) and complex **3** in THF at 110 °C yielded after 32 h 97.1% of methanol and 98.3% of morpholine; no decarbonylation of the formyl group took place (Table 1B, entry 17). These results highlight the substantial scope of the unprecedented, selective hydrogenation of amides catalyzed by **3,** or by the air-stable **4** with an equivalent of base (which generates **3** *in situ*).

[0125] In conclusion, amides can be selectively hydrogenated to alcohols and amines for the first time. The reaction proceeds under mild pressure, neutral, homogeneous conditions using Ruthenium complexes as catalysts according to the invention and dihydrogen by metal-ligand cooperation. This new catalytic protocol exhibits a broad substrate scope providing a variety of amines and alcohols in good to excellent yield.

C. Hydrogenation of cyclic di-peptides

[0126] The process of the present invention can also be used for catalytic hydrogenation of di-peptides. For example, cyclic di-peptides can be hydrogenated to amino alcohols. In a general procedure, a 100 mL Fischer-Porter tube was charged with the catalyst 1 (0.02 mmol), the cyclic di-peptides (1.0 mmol) and THF (2 mL) under an atmosphere of purified nitrogen in a Vacuum Atmospheres glove box. The pressure tube was taken out of the glove box, and subjected to three successive cycles of pressurization/venting with H_2 (3 atm), then pressurized with H_2 (12 atm) and closed. The tube was placed behind a protective shield and the reaction mixture was heated in an oil bath at 110 °C with constant stirring for 60 h. After cooling to room temperature, excess H_2 was vented off carefully and the product was determined by GC and GC-MS. Some representative results are presented in Table 3 hereinbelow.

Table 3. Hydrogenation of cyclic di-peptides to amino alcohols selectively catalyzed by complex **1**

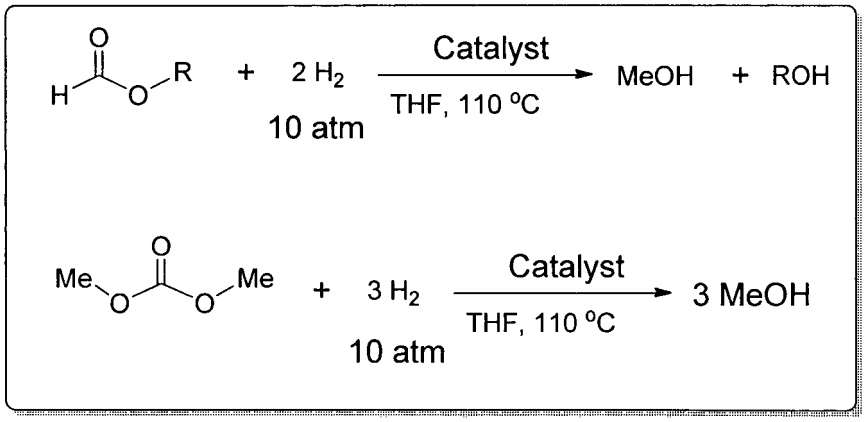
Entry	Cyclic di-peptides	Conditions	Amino alcohols (Yield (%))
1		Solvent = THF (2 mL) PH_2 = 10 atm Temperature = 110 °C (bath) Time = 60 h	 **(58%)**
2			 **(67%)**

Example 2: Hydrogenation of Formate Esters to methanol and alcohols; Dimethyl Carbonate to Methanol; Esters and Lactones to Alcohols, and Hydrogenation of Polycarbonates

A. Hydrogenation of Formates/Carbonate:

[0127] A 100 mL Fischer-Porter tube was charged under nitrogen with catalyst **3** (0.01 mmol), formate ester (15.0 mmol) or dimethyl carbonate (10.0 mmol) and THF (2 mL). After the nitrogen present in the Fischer-Porter tube was replaced by H_2 (twice with 30 psi) at room temperature, the tube was filled with H_2 (10 atm). The solution was heated at 110 °C (bath temperature) with stirring for 36 hrs. After cooling to room temperature, excess H_2 was vented carefully and the products were analyzed by GC with *m*-xylene as internal standard, using a Carboxen 1000 column on a HP 690 series GC system.

[0128] B. Hydrogenation of Methyl Formate and Dimethyl Carbonate under 50 atmospheres and very low catalyst loading (entries 6 and 10, respectively, Table 4): A 30 mL Teflon coated Iron-Fischer-Porter (Autoclave) was charged under nitrogen with catalyst 3 (0.005 mmol), Methyl Formate (25.0 mmol) and THF (5 mL). After the nitrogen present in the autoclave was replaced by H_2 (twice with 50 psi) at room temperature, it was filled with H_2 (40 atm). The solution was heated at 110 °C (bath temperature) with stirring for 14 hrs. After cooling to room temperature, the H_2 was vented carefully at 0 °C and the products were determined by GC with m-xylene as internal standard, using a Carboxen 1000 column on a HP 690 series GC system. The same procedure was used for hydrogenation of dimethyl carbonate.



Scheme 15

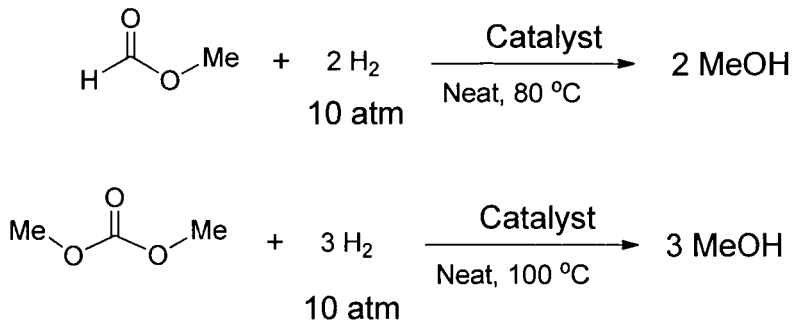
Table 4. Hydrogenation of Formates[a] and Dimethyl Carbonate[b]

Entry	Catalyst	Substrate	Conv. (%)	Products (%)[c]	TON
1	**1**	HCOOMe (MF)	71.7	71.0[d]	710
2	**1**	HCOOMe	>99	~99[e]	990
3	**1**	HCOOMe	78.3	2 MeOH (77.0)[a]	1155
4	**3**	HCOOMe	96.0	2 MeOH (95.8)	1440
5	**7** + KO^{t}Bu	HCOOMe	92.8	2 MeOH (91.2)[f]	1370
6	**3**	HCOOMe	94.0	2 MeOH (93.7)[g]	4685
7	**3**	HCOOEt	92.0	MeOH (92.0) and EtOH (91.7)	1380
8	**3**	HCOO^{n}Bu	86.3	MeOH (86.3) and *n*-BuOH (86.0)	1295
9	**3**	DMC	96.2	3 MeOH (96.2)	962
10	**3**	DMC	89.0	3 MeOH (87.6)[g]	4380

[a]Complex **1** or **3** (0.01 mmol), formate (15 mmol), H_2 (10 atm), and dry THF (2 ml) were heated in a Fischer-Porter tube at 110 °C (bath temperature) for 48 h. [b]10 mmol of DMC was used. [c]Yields of products and conversion of starting material were analyzed by GC (m-xylene as internal standard). [d]100 psi H_2, 1,4-dioxane (2 mL) at 145 °C after 30 h. [e]130 psi H_2, 1,4-dioxane (2 mL) at 145 °C after 36 h. [f]one equivalent (relative to Ru) of base was used. [g]Complex **3** (0.005 mmol), MF/DMC (25 mmol), H_2 (50 atm), and dry THF (5 ml) were heated in a autoclave at 110 °C (bath temperature) for 14 h.

C. Hydrogenation of Methyl Formate and Dimethyl Carbonate under Neat Conditions

[0129] A 100 mL Fischer-Porter tube was charged under nitrogen with catalyst 3 (0.01 mmol), and methyl formate or dimethyl carbonate (10.0 mmol). After the nitrogen in the Fischer-Porter tube was replaced by H_2 (twice with 30 psi) at 0 °C, the tube was filled with H_2 (10 atm). The solution was heated at 80 °C (for MF) and 100 °C (for DMC) (bath temperature) with stirring for 8 hrs. After cooling to room temperature, excess H_2 was vented carefully and the products were analyzed by GC with *m*-xylene as internal standard, using a Carboxen 1000 column on a HP 690 series GC system.



Scheme 16

Table 5. Hydrogenation of methyl formate and dimethyl carbonate

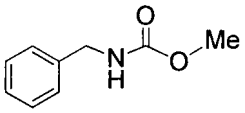
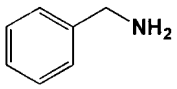
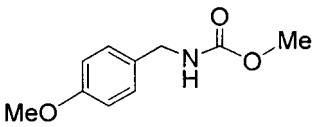
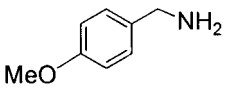
Entry	Catalyst	Substrate	Conv. (%)	Products (%)[a]
1	**1**	HCOOMe	15.6	2 MeOH (15.2)[b]
2	**3**	HCOOMe	>99	2 MeOH (>99)[c]
3	**3**	DMC	>99	3 MeOH (>99)[d] (89.1)[e]

[a] Yields of product and conversion of starting material were analyzed by GC (m-xylene as internal standard). Complex **3** or **1** (0.01 mol), formate (10 mmol), and H_2 (10 atm) were heated in a Fischer-Porter tube at 80 °C (bath temperature) for 18 h. [c] 10 mmol of DMC was used. [c] Yields after 8 h. [d] at 100 °C after 8 h. [e] at 100 °C after 2 h.

D. Hydrogenation of Carbamates:[a]

[0130]

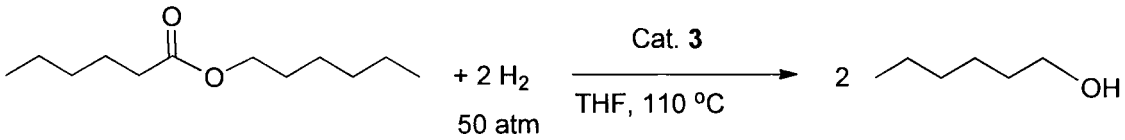
Table 6. hydrogenation of carbamates to amines and alcohols

Entry	Carbamate	Alcohol	Amine	Yield[b]
1		2 MeOH		97.8
2		2 MeOH		98.0

[a] Complex 3 (0.01 mol), carbamate (1 mmol), and H_2 (10 atm) were heated in a Fischer-Porter tube at 110 °C (bath temperature) for 48 h. [b] Yields of product (based on MeOH) were analyzed by GC (m-xylene as internal standard).

E. Hydrogenation of unactivated Esters (hexyl hexanoate):

[0131] A 30 mL Teflon coated Iron-Fischer-Porter (Autoclave) was charged under nitrogen with catalyst 3 (0.01 mmol for entry 1 and 0.005 mmol for entry 2 respectively), hexyl hexanoate (20.0 mmol) and THF (5 mL). After the nitrogen present in the autoclave was replaced by H_2 (twice with 50 psi) at room temperature, it was filled with H_2 (50 atm). The solution was heated at 110 °C (bath temperature) with stirring for 16 hrs. After cooling to room temperature, the H_2 was vented carefully and the yields of product and conversion of starting material were analyzed by GC (m-xylene as internal standard, using a Carboxen 1000 column on a HP 690 series GC system. Very high turnover numbers (TON) were obtained.



Scheme 17

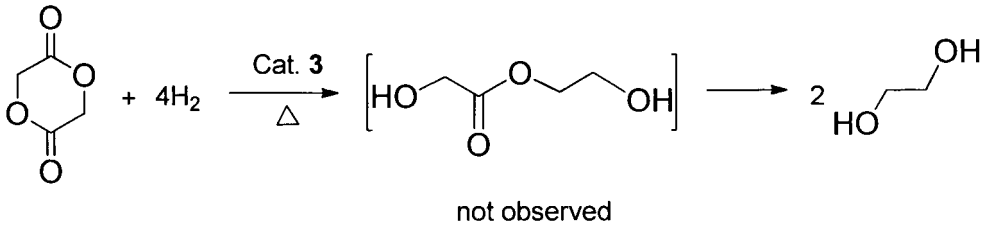
Table 7. Hydrogenation of esters to alcohols

Entry	Cat.	Ester	Alcohol (20 mmol)	Yield (%)	TON
1	**3** (0.01 mmol)	Hexyl hexanoate	1-Hexanol	>99	2000
2	**3** (0.005 mmol)	Hexyl hexanoate	1-Hexanol	82.1	3284

F. Hydrogenation of Biomass-Derived Cyclic Di-esters to 1,2-Diols

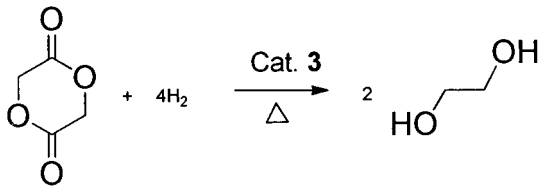
[0132] The cyclic di-ester of glycolic acid (derived from sugar cane), glycolide was chosen as a model substrate for catalytic hydrogenation by Ruthenium complex 3. A 1,4-dioxane solution containing glycolide (1 mmol) and 1 mol% of complex 3 was heated under hydrogen pressure (6 atm) at 135 °C for 36 h using a pressure vessel. The reaction mixture was cooled and excess H_2 was vented carefully and the products were determined by GC and GC-MS showing formation of ethylene glycol (EG) as the only product in 61% yield (Table 8, entry 1) with 67% conversion of the glycolide. After removal of the solvent, the obtained crude viscous liquid was further analyzed by ESI, illustrating that there was no formation of polymeric material.

[0133] Performing the same reaction under similar conditions using 10 atm of H_2 resulted in 88% of ethylene glycol after 36 h (Table 8, entry 2). Optimization studies revealed that the reaction could be performed at lower temperature using THF as solvent. Thus, heating complex **3** (0.01 mmol) with glycolide (1 mmol) and dihydrogen (10 atm) at 110 °C in 3 mL of dry THF for 48 h using a Fisher-Porter tube, yielded 93% of ethylene glycol (Table 8, entry 3). A high turnover number (425) was achieved at higher pressure. Thus, heating a THF solution of glycolide (10 mmol) and a catalytic amount of complex **3** (0.02 mmol) at 110 °C under H_2 (50 atm) using a high pressure reactor resulted in 85% yield of ethylene glycol selectively after 12 h (Table 8, entry 4).



Scheme 18

Table 8. Catalytic hydrogenation of glycolide to ethylene glycol



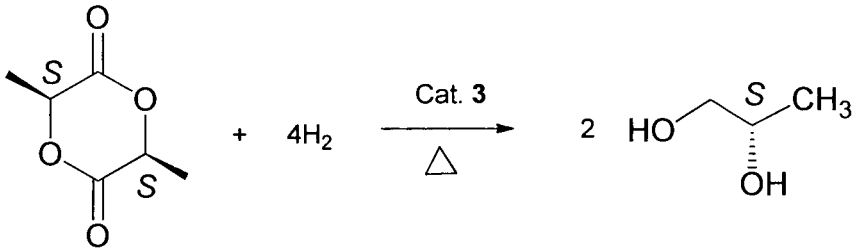
entry	solvent	temp. (°C)	$P(H_2)$ (atm)	time (h)	yield (%)[b]
1	1,4-dioxane	135	6	36	61
2	1,4-dioxane	135	10	36	88
3	THF	110	10	48	93

(continued)

entry	solvent	temp. (°C)	$P(H_2)$ (atm)	time (h)	yield (%)[b]
4[c]	THF	110	50	12	85

[a] Complex 3 (0.01 mmol), glycolide (1 mmol), H_2, and dry solvent (3 mL) were heated in a Fischer-Porter tube at the specified (oil bath) temperature. [b] Yields of ethylene glycol were analyzed by GC using m-xylene as an internal standard. [c] Complex **3** (0.02 mmol), glycolide (10 mmol), and THF (5 mL) were heated under H_2 pressure in a high-pressure reactor.

[0134] To expand the scope of this efficient hydrogenation reaction, optimized catalytic conditions were further tested with lactide, which is derived from the glucose fermentation product lactic acid. Thus, meso-lactide was heated with H_2 (10 atm) at 110 °C in THF for 48 h with a catalytic amount of **3** (1 mol%), 87% of 1,2-propanediol was obtained selectively (Table 9, entry 1). Remarkably, the hydrogenation of chiral lactide, L-lactide catalyzed by complex **3** under the optimized conditions yielded optically pure (S)-(+)-1,2-propanediol as sole product without racemization even under high pressure. Hence, upon treatment of L-lactide (10 mmol) with dihydrogen (50 atm) at 135 °C for 12 h with a catalytic amount of **3** (0.02 mmol) using 5 mL of THF as a solvent, selectively yielded 91% to propylene glycol (Table 9, entry 3). After careful removal of the solvent under reduced pressure, the reaction mixture was passed through short silica gel bed and the diol was eluted with CH_2Cl_2: MeOH (10:1) and concentrated under vacuum to yield 73% of the optically pure 1,2-propanediol. The optical rotation of the pure product was essentially the same as reported in the literature. Thus, under these experimental condition, no racemization took place.



Scheme 19

Table 9. Catalytic hydrogenation of lactide to propylene glycol

Entry	di-ester (lactide)	solvent	temp (°C)	$P(H_2)$ (atm)	time (h)	yield (%)[b]
1	meso	THF	110	10	48	87
2	chiral (S,S)	THF	110	10	48	82
3[c]	chiral (S,S)	THF	110	50	12	91(73)[d]

[a] Complex **3** (0.01 mmol), meso or chiral lactide (1 mmol), H_2, and dry THF (3 mL) were heated in a Fischer-Porter tube at 110 °C (oil bath) temperature. [b] Yields of propylene glycol were analyzed by GC using m-xylene as an internal standard. [c] Complex 3 (0.02 mmol), L-lactide (10 mmol), and THF (5 mL) were heated under H_2 pressure in a high-pressure reactor. [d] Isolated yield.

[0135] In conclusion, cyclic di-esters such as glycolide and lactide are selectively hydrogenated to the corresponding 1,2-diols for the first time. This offers an environmentally benign, atom economic and an alternative approach to the indirect transformation of biomass to important synthetic building blocks, propylene and ethylene glycol. The reactions proceed under mild, neutral and homogeneous conditions with minimal pressure of molecular hydrogen. Importantly, the chirality is unaffected during the hydrogenation.

General Experimental:

[0136] All experiments with metal complexes and phosphine ligands were carried out under an atmosphere of purified nitrogen in a Vacuum Atmospheres glove box equipped with a MO 40-2 inert gas purifier or using standard Schlenk techniques. All solvents were reagent grade or better. All non-deuterated solvents were refluxed over sodium/ benzophenone ketyl and distilled under argon atmosphere. Deuterated solvents were used as received. All solvents were

degassed with argon and kept in the glove box over 4Å molecular sieves. Most of the chemicals used in the catalytic reactions (cyclic di-esters) are commercially available and were used as received.

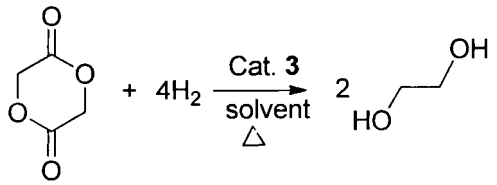
[0137] Thin layer chromatography (TLC) was performed using Merck 1.05554 aluminum sheets precoated with silica gel 60 F254 and the spots were visualized with UV light at 254 nm or under iodine vapor. Column chromatography purifications were performed by flash chromatography using Merck silica gel 60 (0.063-0.200 mm).

[0138] 1H, 13C and 31P NMR spectra were recorded using a Bruker AMX-300 NMR spectrometer. NMR chemical shifts are reported in ppm downfield from tetramethylsilane (for CDC13). 1H NMR chemical shift is referenced to the residual hydrogen signal of the deuterated solvent (7.15 ppm for benzene). 31P NMR chemical shift is reported in ppm downfield from H_3PO_4 and referenced to an external 85% solution of phosphoric acid in D2O. Abbreviations used in the NMR follow-up experiments: br, broad; s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. IR spectra were recorded on a Nicolet FT-IR spectrophotometer. Mass spectra were recorded on Micromass Platform LCZ 4000, using Electro Spray Ionization (ESI) mode. GC-MS was carried out on HP 6890 (flame ionization detector and thermal conductivity detector) and HP 5973 (MS detector) instruments equipped with a 30 m column (Restek 5MS, 0.32 mm internal diameter) with a 5% phenylmethylsilicone coating (0.25 mm) and helium as carrier gas. GC analysis were carried out using a Carboxen 1000 column on a HP 690 series GC system or HP-5 cross linked 5% phenylmethylsilicone column (30m × 0.32mm × 0.25 μm film thickness, FID) on a HP 6890 series GC system using m-xylene (1 mmol) as an internal standard.

General procedure for catalytic hydrogenation:

(a) Catalytic hydrogenation of glycolide to ethylene glycol:

[0139]



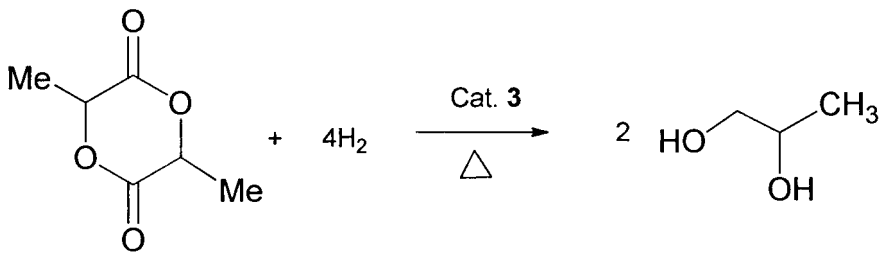
(i) Substrate/catalyst 100/1: A solution of catalyst **3** (4.5 mg, 0.01 mmol) in THF or 1,4-dioxane (1.0 mL) was transferred into a 100 mL Fischer-Porter tube followed by addition of the glycolide (116 mg, 1.0 mmol) in THF or 1,4-dioxane (2.0 mL) under an atmosphere of purified nitrogen in a Vacuum Atmospheres glove box. The pressure tube was taken out of the glove box, followed by three successive cycles of pressurization/ venting with H_2 (2 atm), then pressurized with H_2 (10 atm) and well-closed. The tube was covered by a protective shield and the reaction mixture was heated in an oil bath at 110 °C with constant stirring for 48 h. After cooling to room temperature, excess H_2 gas was vented carefully and the products were determined by GC with m-xylene (1.0 mmol) as an internal standard, using a HP-5 cross linked 5% phenylmethylsilicone column (30m × 0.32mm × 0.25 μm film thickness) on a HP 6890 series GC system.

(ii) Substrate/catalyst 500/1: in a nitrogen glove box, a solution of catalyst **3** (9 mg, 0.02 mmol) in THF (5 mL) was added to a stainless-steel high pressure reactor (30 mL) equipped with a magnetic stirring bar containing 10.0 mmol (1.16 g) of the solid glycolide. The high pressure reactor was taken out of the glove box and the nitrogen present in the pressure reactor was flushed with hydrogen by two successive cycles of pressurization/ venting with H_2 (5 atm), then pressurized with H_2 (50 atm) and well-closed. The tube was covered by a protective shield and the reaction mixture was heated in an oil bath at 110 °C with constant stirring for 12 h. After cooling to room temperature, excess H_2 gas was vented carefully and the products were determined by GC with m-xylene (1.0 mmol) as an internal standard. (After 3 hrs, the conversion of the glycolide was only 39%).

[0140] (Note: Complex 3 also catalyzed the dehydrogenation of ethylene glycol to glycolide and other polymeric material (poly glycolide) with liberation of H_2 after 24 hrs in 1,4-dioxane (conversion of ethylene glycol 16%) or under solvent free (neat) condition with less conversion (21%)).

(b) Catalytic hydrogenation of meso-lactide to propylene glycol:

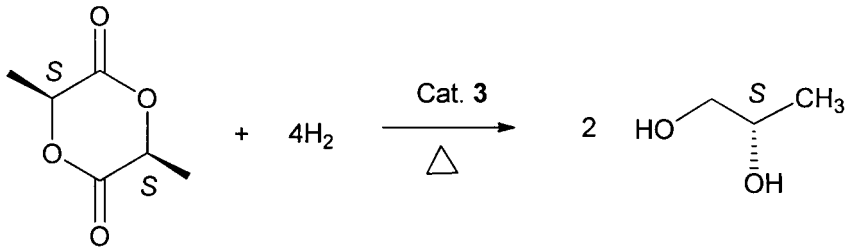
[0141]



[0142] A solution of catalyst **3** (4.5 mg, 0.01 mmol) in THF (1.0 mL) was transferred into a 100 mL Fischer-Porter tube followed by addition of the meso-lactide (144 mg, 1.0 mmol) in THF (2.0 mL) under an atmosphere of purified nitrogen in a Vacuum Atmospheres glove box. The pressure tube was taken out of the glove box, followed by three successive cycles of pressurization/ venting with H_2 (2 atm), then pressurized with H_2 (10 atm) and well-closed. The tube was covered by a protective shield and the reaction mixture was heated in an oil bath at 110 °C with constant stirring for 48 h. After cooling to room temperature, excess H_2 gas was vented carefully and the products were determined by GC with m-xylene (1.0 mmol) as an internal standard.

(c) Catalytic hydrogenation of L-lactide to S-(+)-1,2-propanediol:

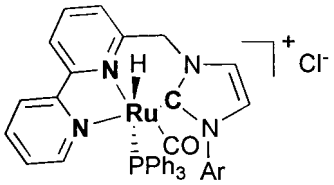
[0143]



(i) Substrate/catalyst 100/1: A solution of catalyst **3** (4.5 mg, 0.01 mmol) in TIIF (1.0 mL) was transferred into a 100 mL Fischer-Porter tube followed by addition of L-lactide (144 mg, 1.0 mmol) in THF (2.0 mL) under an atmosphere of purified nitrogen in a glove box. The pressure tube was taken out of the glove box, followed by three successive cycles of pressurization/venting with H_2 (2 atm), then pressurized with H_2 (10 atm) and closed. The tube was covered by a protective shield and the reaction mixture was heated in an oil bath at 110 °C with constant stirring for 48 h. After cooling to ~5 °C (with a cold water bath), excess H_2 gas was vented carefully and the products were determined by GC with m-xylene (1.0 mmol) as an internal standard. After careful removal of the solvent under reduced pressure, the reaction mixture was passed through short silica gel bed and the diol was eluted with CH_2Cl_2: MeOH (10:1) and concentrated under vacuum to yield 67% of the optically pure 1,2-propanediol. The optical rotation of the pure product was essentially the same as reported in the literature.
(ii) Substrate/catalyst 500/1: in a nitrogen glove box, a solution of catalyst **3** (9 mg, 0.02 mmol) in THF (5 mL) was added to a stainless-steel high pressure reactor (30 mL) equipped with a magnetic stirring bar containing 10.0 mmol (1.44 g) of the L-lactide. The high pressure reactor was taken out of the glove box and the nitrogen present in the pressure reactor was flushed with hydrogen by two successive cycles of pressurization/ venting with H_2 (5 atm), then pressurized with H_2 (50 atm) and well-closed. The tube was covered by a protective shield and the reaction mixture was heated in an oil bath at 110 °C with constant stirring for 12 h. After cooling to ~5 °C (with a cold water bath), excess H_2 gas was vented carefully and the products were determined by GC with m-xylene as an internal standard. After careful removal of the solvent under reduced pressure, the reaction mixture was passed through short silica gel bed and the diol was eluted with CH_2Cl_2: MeOH (10:1) and concentrated under vacuum to yield 67% of the optically pure 1,2-propanediol. The optical rotation of the pure product was essentially the same as reported in the literature.

Hydrogenation of L-lactide to *S*-(+)-1,2-propanediol catalyzed by NHC-Ru(II) catalyst

[0144]

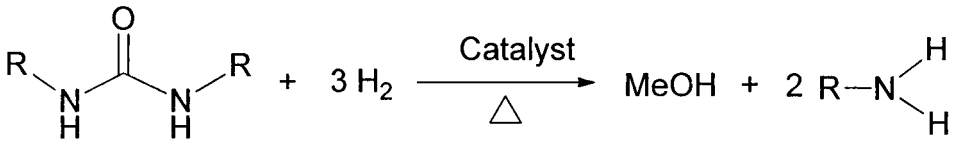


catalyst

[0145] The NHC Ru(II) pincer catalyst was prepared according to: E. Fogler, E. Balaraman, Y. Ben-David, G. Leitus, L. J. W. Shimon and D. Milstein, Organometallics, 2011, 30, 3826 A 100 mL Fischer-Porter tube was charged under nitrogen with the catalyst (4.5 mg, 0.01 mmol), L-lactide (144 mg, 1.0 mmol) and THF (3 mL). The Fischer-Porter tube was purged by three successive cycles of pressurization/venting with H_2 (2 atm), then pressurized with H_2 (10 atm). The solution was heated at 110 °C (bath temperature) with stirring for 48 h. After cooling to ~5 °C excess H_2 gas was vented and the products were determined by GC. The solvent was removed under reduced pressure and the reaction mixture was passed through short silica gel bed. The 1,2-diol was eluted with CH_2Cl_2:MeOH (10:1) and concentrated under vacuum to yield 57% of the optically pure (*S*)-(+)-1,2-propanediol ($[\alpha]_D^{22}$ = +27 ° (c = 1, $CHCl_3$)

G. Hydrogenation of Urea Derivatives to Amines and Methanol

[0146]

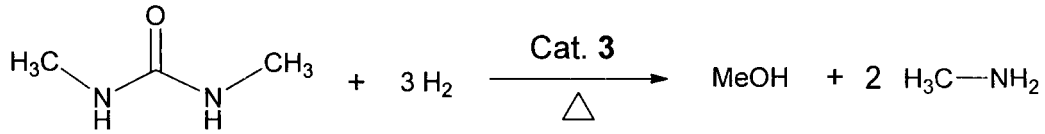


R = Aryl, alkyl, Aryalkyl, etc.

Scheme 20

[0147] 1,3-Dimethylurea was selected as a benchmark substrate for the unprecedented hydrogenation of urea derivatives catalyzed by complex **3.** Upon treatment of 1,3-dimethylurea (1 mmol) and a catalytic amount of complex **3** (1 mol%) with H_2 (10 atm) at 110 °C (bath temperature) in dry THF resulted in 41% conversion of dimethylurea to methanol and methylamine after 48 h (Table 10, entry 1). The formed methanol was quantified as 35% by GC and the gaseous amine was characterized by GC-MS of the gas phase of the reaction mixture and not quantified. The yield of methanol increased at longer reaction time (Table 10, entry 2). Performing the same reaction under using 13.6 atm of H_2 and 2 mol% of catalyst resulted in 93% of methanol after 72 h (Table 10, entry 3).

Table 10. Novel hydrogenation of 1,3-dimethylurea to methanol and methylamine catalyzed by **3**

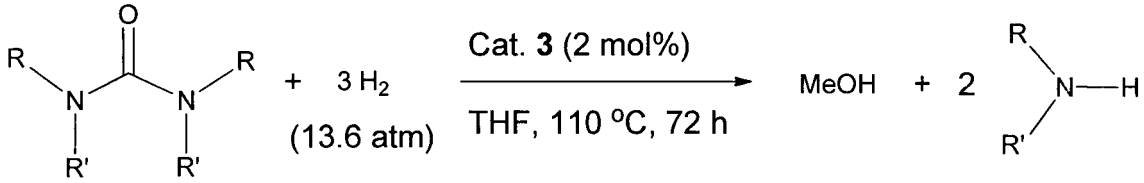


Entry	Cat. **3** (mol%)	Reaction conditions[a]			
		PH_2 (atm)	hrs (atm)	Conv. (%)[b]	Yield of MeOH (%)[b],[c]
1	1	10	48	41	35
2	1	10	60	53	52
3	2	13.6	72	96	93

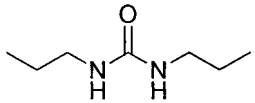
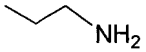
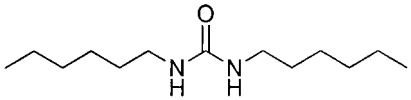
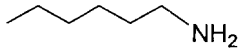
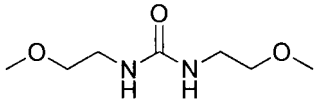
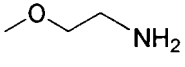
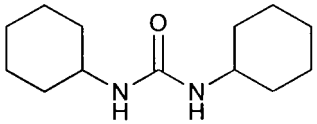
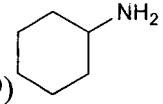
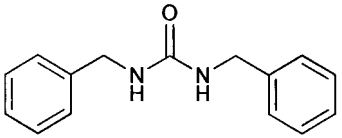
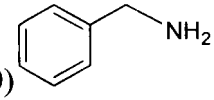
[a] Complex 3, 1,3-dimethylurea (1 mmol), H_2, and dry THF (2 mL) were heated in a Fischer-Porter tube (100 mL) at 110 °C (bath temperature) for specified time. [b] Conversion of dimethylurea and yields of methanol were analyzed by GC using m-xylene as an internal standard. [c] The $MeNH_2$ was analyzed in the gas phase (as well as in liquid phase) by GC-MS and not quantified.

[0148] Various urea derivatives were subjected to hydrogenation (Table 11). Hydrogenation of 1,3-dihexylurea under the same conditions (cat/urea derivative = 2:100 (mmol), 13.6 atm of H_2, 2 mL of dry THF, at 110 °C) yielded methanol and 1-hexylamine in 83% and 87% respectively after 72 h (Table 11, entry 2). As expected, the activated urea derivative, 1,3-bis(2-methoxyethyl)urea gave almost quantitative conversion to methanol and 2-methoxyethylamine upon hydrogenation (Table 11, entry 3). Aromatic and substituted aromatic urea derivatives also underwent hydrogenation very efficiently in moderate yields (Table 11, entries 5-7) along with trace amounts of the corresponding formamides (detected by GC-MS). The hydrogenation of diphenylurea derivatives proceeds very smoothly to yield methanol and anilines. Thus, upon heating a THF solution of **3** (0.02 mmol) and 1,3-diphenylurea (1 mmol) at 110 °C under H_2 (12 atm), complete conversion to selectively form 90% of methanol and 95% of aniline took place (Table 11, entry 8). Remarkably, tetra-substituted urea derivatives were also selectively hydrogenated to yield methanol and the corresponding amines, with cleavage of the C-N bond. Thus, heating a THF solution containing 1,1',3,3'-tetramethylurea (1 mmol) and a catalytic amount of the complex **3** (2 mol%) under hydrogen pressure (13.6 atm) using pressure vessel at 110 °C for 72 h resulted in 53% conversion of tetramethylurea (TMU) to methanol (51%) and N,N'-dimethylamine (Table 11, entry 11).

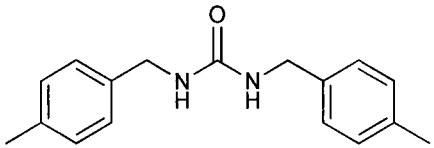
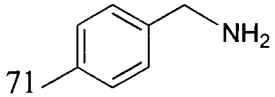
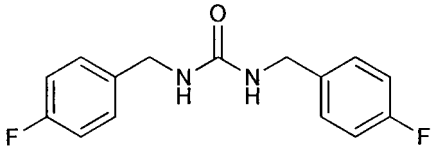
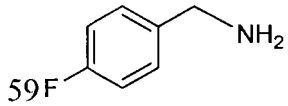
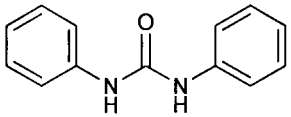
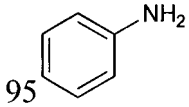
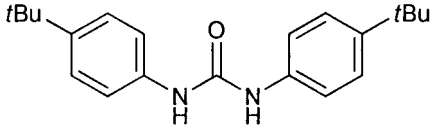
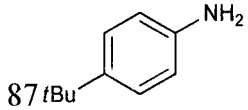
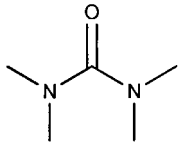
Table 11. Hydrogenation of urea derivatives to amines and methanol catalyzed by BP-PNN-RuII pincer complex 3.[a]



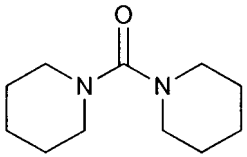
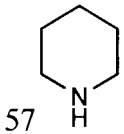
R = H; R = Aryl, alkyl, and Aryalkyl
R = R' =Me and -($CH_2(CH_2)_3CH_2$)—

Entry	Amide	Products (yield {%})[b]	
		MeOH	Amine
1[c]		89	
2		83	 (87)
3		94	(97) 
4		73	 (79)
5[c]		61	 (60)

(continued)

Entry	Amide	Products (yield {%})[b]	
		MeOH	Amine
6[c]		67	 71
7		58	 59
8		90	 95
9		93	 87
10[c],[d]		51	$(CH_3)_2NH$

(continued)

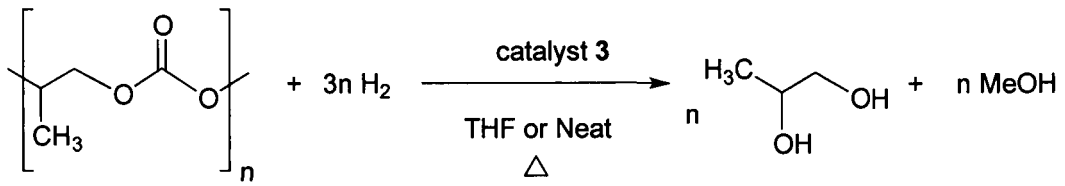
Entry	Amide	Products (yield {%})[b]	
		MeOH	Amine
11[c]		63	 57

[a] Complex 3 (0.02 mmol), urea derivative (1 mmol), H_2 (13.6 atm), and dry THF (2 mL) were heated in a Fischer-Porter tube (100 mL) at 110 °C (bath temperature) for 72 hrs (most of the reactions were repeated twice). [b] Yields of products were analyzed by GC (1 mmol of m-xylene as an internal standard). [c] The amines n-propylamine and Me_2NH for (entries 1 and 10 respectively) were analyzed in the gas phase (as well as in liquid phase) by GC-MS and not quantified. [d] The corresponding formamides (entries 5-6 and 10-11) were observed on GC-MS and not quantified.

[0149] General procedure for the catalytic hydrogenation of urea derivatives: A 100 mL Fischer-Porter tube was charged with catalyst **3** (0.02 mmol), urea derivative (1.0 mmol) and THF (2 mL) under an atmosphere of purified nitrogen in a Vacuum Atmospheres glove box. The pressure tube was taken out of the glove box, followed by three successive cycles of pressurization/ venting with H_2 (3 atm), then pressurized with H_2 (10 atm) and well-closed. The tube was covered by a protective shield and the reaction mixture was heated in an oil bath at 110 °C with constant stirring for 48 h. After cooling to room temperature, excess H_2 gas was vented carefully and the products were determined by gas chromatography (GC).

G. Hydrogenation of Polypropylene Carbonate

[0150]



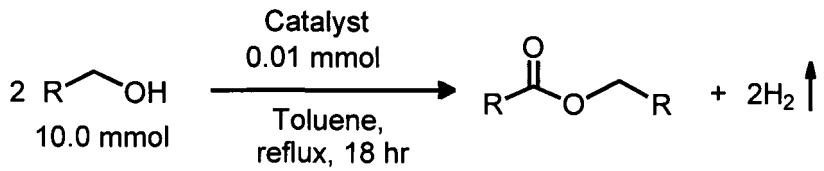
(1) A 100 mL Fischer-Porter tube was charged under nitrogen with catalyst **3** (9 mg, 0.02 mmol), polypropylene carbonate (M_n = 50,000 by GPC; 0.255 g) and THF (2 mL). The Fischer-Porter tube was purged by three successive cycles of pressurizing/ venting with H_2 (3 atm) and pressurized with 10 atm of H_2. The solution was heated at 110 °C (bath temperature) with stirring for 8 h. After cooling (~5 °C; ice/water), excess H_2 was vented carefully and the products were analyzed by GC-MS. The solvent was removed under vacuum to give pure 1,2-propanediol (isolated yield = 0.180 g corresponds to 94.8%) and methanol (97% yield).

(2) Hydrogenation under solvent-free (neat) conditions:

[0151] A 100 mL Fischer-Porter tube was charged with catalyst **3** (0.01 mmol) and polypropylene carbonate (M_n = 50,000 by GPC; 0.510 g) under an atmosphere of purified nitrogen in a glovebox. The pressure tube was taken out of the glove box and purged by three successive cycles of pressurization/ venting with H_2 (2 atm), then pressurized with H_2 (12.2 atm). The tube was placed behind a protective shield and heated in an oil bath at 130 °C with constant stirring for 14 h. After cooling to ~ 5 °C, excess H_2 gas was vented carefully and the products (methanol and 1,2-propanediol) were analyzed by gas chromatography (GC and GC-MS) and quantified by ^{1}H NMR using toluene as internal standard. Quantitative conversion of the polymer took place, to yield 4.96 mmol of 1,2-propanediol and methanol. Isolated yield of 1,2-propanediol was 0.368 g (4.83 mmol).

Example 3: Dehydrogenative Coupling of Primary Alcohols to Esters

[0152] Some processes involving the coupling of alcohols to esters are shown in Scheme 21:



Scheme 21

A. Typical procedures for the catalytic dehydrogenative coupling of primary alcohols *(Table 12)*

(a) Complex **3** (0.01 mmol), an alcohol (10 mmol), and toluene (2 mL) were taken in a Schlenk flask under an atmosphere of purified nitrogen in a glove box. The flask was equipped with a condenser and the solution was refluxed with stirring in an open system under argon for 24 hrs. After cooling to room temperature, the consumption of starting material and the formation of ester were determined by GC with m-xylene as an internal standard using a Carboxen 1000 column on a HP 690 series GC system.

(b) Complex **4** (0.01 mmol), an alcohol (10 mmol), KO^{t}Bu (0.01 mmol) and toluene (2 mL) were taken in a Schlenk

flask under an atmosphere of purified nitrogen in a glove box. The flask was equipped with a condenser and the solution was refluxed with stirring in an open system under argon for 18 hrs. After cooling to room temperature, the consumption of starting material and the formation of ester were determined by GC with m-xylene as an internal standard using a Carboxen 1000 column on a HP 690 series GC system.

Table 12. Coupling of primary alcohols to form esters

Entry	Cat.	Alcohol	Ester	Conv. (%)	Yield (%)
1	**4**	1-Hexanol	Hexyl hexanoate	---	---
2	**4** + *t*-BuOK	1-Hexanol	Hexyl hexanoate	95.3	95.0 + traces of aldehyde
3	**7** + *t*-BuOK	1-Hexanol	Hexyl hexanoate	90.0	89.3 + traces of aldehyde
4	**3**	1-Hexanol	Hexyl hexanoate	98.6	98.2
5	**3**	1-Pentanol	Pentyl pentanoate	98.3	98.0
6	**3**	Benzyl alcohol	Benzyl benzoate	94.1	92.9 + 0.9% aldehyde
7	**3**	1-Butanol	Butyl butyrate	90.1	89.7 + 0.3% aldehyde
8	**3**	Cyclohexane methanol	Cyclohexylmethyl cyclohexane carboxylate	98	96.2 + 1.6% aldehyde

B. Catalytic dehydrogenation of primary alcohols under neat condition (absence of solvent) *(Table 13):* Complex **3** (0.01 mmol) was heated under an argon flow in different alcohols (10 mmol) at the specified temperatures and times (Table 13). After cooling to room temperature, the consumption of starting material and the formation of ester were determined by GC with m-xylene as an internal standard using a Carboxen 1000 column on a HP 690 series GC.

Table 13. Coupling of primary alcohols to form esters under neat conditions

Entry	Cat.	Alcohol	Temp. (°C)	Time (hrs)	Ester	Conv. (%)	Yield (%)
1	**3**	1-Pentanol	138	12	Pentyl pentanoate	97.7	97.5 + traces of aldehyde
2	**3**	1-Butanol	117	12	Butyl butyrate	89.0	87.7 + 1.2% aldehyde
3	**3**	Ethanol (20 mmol)	79	72	Ethyl acetate	52.0	51.7

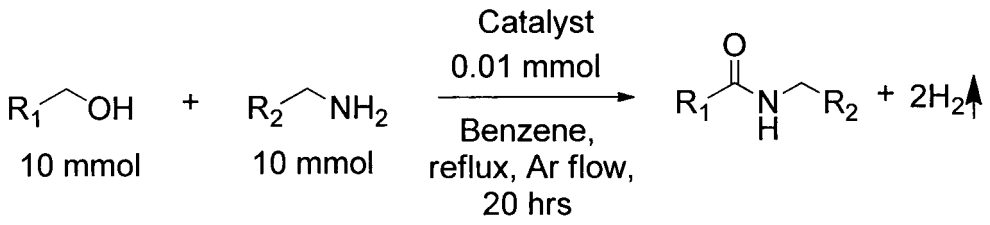
C. Catalytic dehydrogenative coupling of alcohols under open air (Table 14): To an oven dried Schlenk flask cooled to room temperature under open air were added complex **4** (0.01 mmol), an alcohol (5 mmol) in toluene (2 mL), followed by KO^{t}Bu (0.01 mmol) in toluene (1 mL) and the flask was equipped with a condenser and the solution was refluxed with stirring in an open system under air for 18 hrs. After cooling to room temperature, the consumption of starting materials was determined by GC with m-xylene as an internal standard, using a Carboxen 1000 column on a HP 690 series GC system.

Table 14: Coupling of primary alcohols to form esters under open air

Entry	Alcohol	Ester	Conv. (%)	Yield (%)
1	1-Hexanol	Hexyl hexanoate	89.8	86.3 + 2.8 % aldehyde
2	Benzyl alcohol	Benzyl benzoate	90.4	84.8 + 5.3% aldehyde

Example 4: Dehydrogenative Coupling of Alcohols and Amines With Liberation of H_2 to Form Amides

[0153] Some processes involving the coupling of alcohols and amines to generate amides are shown in Scheme 22:

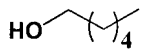
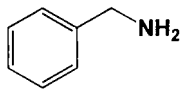
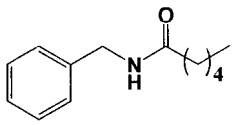
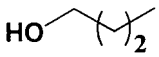
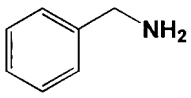
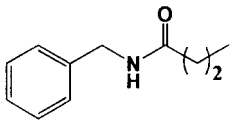
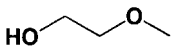
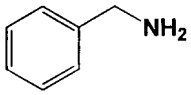
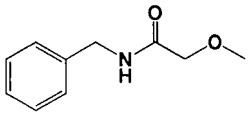
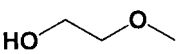
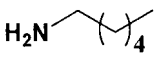
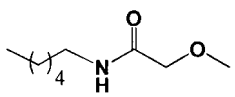
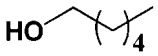
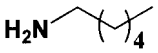
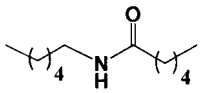
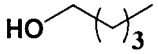
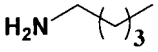
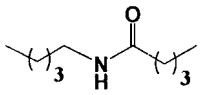


Scheme 22

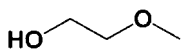
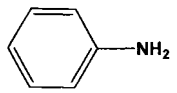
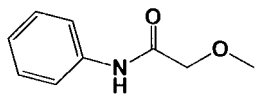
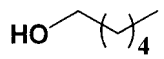
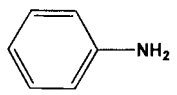
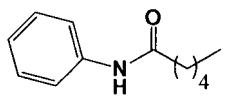
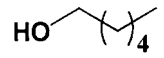
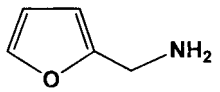
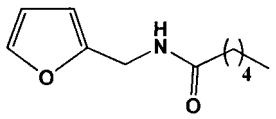
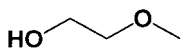
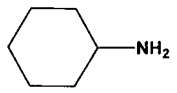
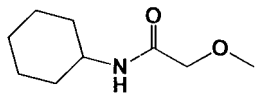
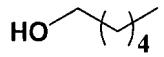
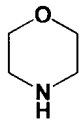
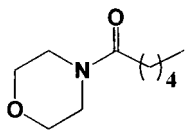
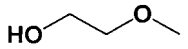
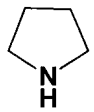
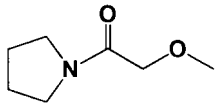
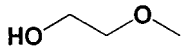
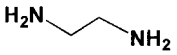
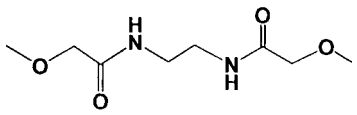
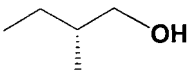
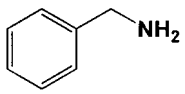
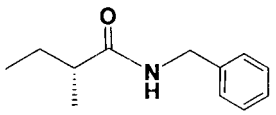
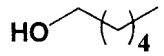
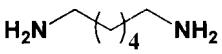
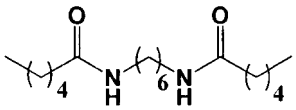
A. Typical procedure for the catalytic dehydrogenative mono-acylation of amines with alcohols *(Table 15):*

(a) Complex **3** (0.01 mmol), an alcohol (10 mmol), an amine (10 mmol), and benzene (3 mL) were taken in a Schlenk flask under an atmosphere of purified nitrogen in a Vacuum Atmospheres glove box. The flask was equipped with a condenser and the solution was refluxed with stirring in an open system under argon for 20 hrs. After cooling to room temperature, the consumption of starting materials was checked by GC using a Carboxen 1000 column on a HP 690 series GC system. (b) Complex **4** (0.01 mmol), an alcohol (10 mmol), an amine (10 mmol), KO^{t}Bu (0.01 mmol), and benzene (3 mL) were taken in a Schlenk flask under an atmosphere of purified nitrogen in a Vacuum Atmospheres glove box. The flask was equipped with a condenser and the solution was refluxed with stirring in an open system under argon for 20 hrs. After cooling to room temperature, the consumption of starting materials was checked by GC using a Carboxen 1000 column on a HP 690 series GC system.

Table 15. Coupling of amines and alcohols to generate amides

Entry	Alcohol	Amine	Amide	Yield (isolated)
1				95.0
2				96.3
3				97.8 (94.0)[a]
4				93.0
5				85.8
6				86.7

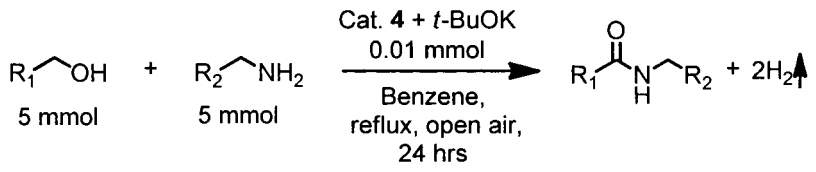
(continued)

Entry	Alcohol	Amine	Amide	Yield (isolated)
7				62.0
8				56.0
9				72.2
10				96.1
11				84.3
12				87.0
13				90.0
14				68[b]
15				88.4

[a] Complex **3** (0.0033 mmol), an alcohol (5.0 mmol), an amine (5.0 mmol), and benzene (3 mL) were refluxed for about 38 hrs (maximum turnover number = 1500). [b] No racemisation was observed.

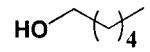
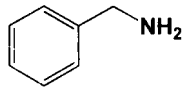
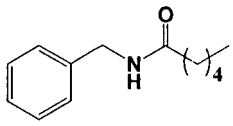
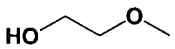
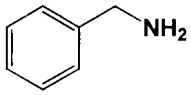
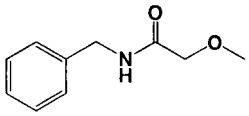
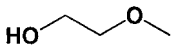
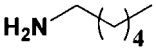
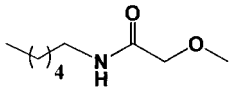
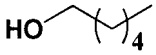
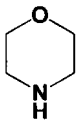
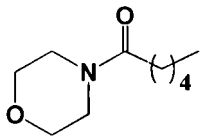
B. Catalytic dehydrogenative bis-acylation of diamines with alcohols *(Table 15; entries 13 and 15):* Complex **3** (0.01 mmol), an alcohol (10.5 mmol), a diamine (5 mmol), and benzene (5 mL) were placed in a Schlenk flask under an atmosphere of purified nitrogen in a Vacuum Atmospheres glove box. The flask was equipped with a condenser and the solution was refluxed with stirring in an open system under argon flow. The reaction mixture was cooled to room temperature and the consumption of starting materials was checked by GC using a Carboxen 1000 column on a HP 690 series GC system.

C. Amidation reaction under open air *(Table 16):* To an oven dried Schlenk flask cooled to room temperature under open air were added complex **4** (0.01 mmol), an alcohol (5 mmol), an amine (5 mmol) in benzene (2 mL), followed by KO^{t}Bu (0.01 mmol) in benzene (1 mL) and the flask was equipped with a condenser and the solution was refluxed with stirring in an open system under air for 24 hrs. After cooling to room temperature, the consumption of starting materials was determined by GC with *m*-xylene as an internal standard, using a Carboxen 1000 column on a HP 690 series GC system.

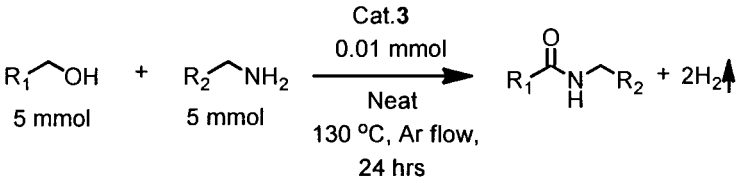


Scheme 23

Table 16. Coupling of amines and alcohols to generate amides under open air

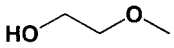
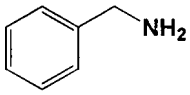
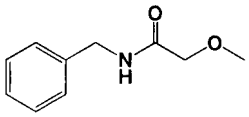
Entry	Alcohol	Amine	Amide	Conv. of alcohol (%)	Yield (isolated)
1				77	71
2				88	80
3				81	74
4				66	61

D. Amidation reaction under neat condition *(Table* 17): Complex **3** (0.01 mmol), an alcohol (5 mmol), an amine (5 mmol) were taken in a Schlenk flask under an atmosphere of purified nitrogen in a Vacuum Atmospheres glove box. The flask was equipped with a condenser and the solution was heated at 130° C (bath temperature) with stirring in an open system under argon for 24 hrs. After cooling to room temperature, the consumption of starting materials was determined by GC with *m*-xylene as an internal standard, using a Carboxen 1000 column on a HP 690 series GC system.

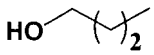
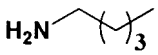
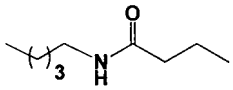
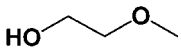
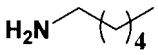
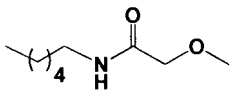
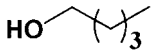
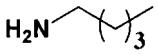
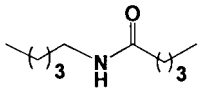
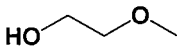
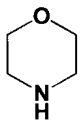
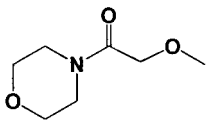


Scheme 24

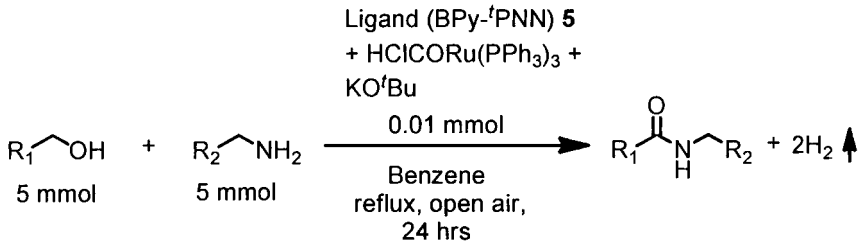
Table 17. Coupling of amines and alcohols to generate amides under neat conditions

Entry	Alcohol	Amine	Amide	Conv. of alcohol (%)	Yield (isolated)
1				97	87.6

(continued)

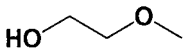
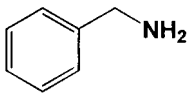
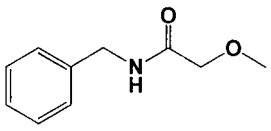
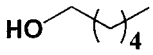
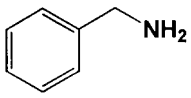
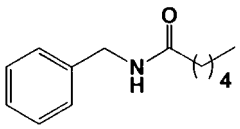
Entry	Alcohol	Amine	Amide	Conv. of alcohol (%)	Yield (isolated)
2				85.2	76.0
3				92.3	82.0
4				87.0	79.6
5				82.7	73.0

E. Amidation reaction by *in-situ* generation of the catalyst from the precursor ligand *(Table 18):* To a Schlenk flask cooled under argon were added ligand, BPy-^{t}PNN (5) (0.01 mmol) and Ru-Precursor $RuHCl(CO)(PPh_3)_3$ (0.01 mmol), followed by benzene (1 mL) and the solution was heated (~ 80° C) with stirring for about 1 hr. After cooling to room temperature, were added an alcohol (5 mmol), an amine (5 mmol), and *t*-BuOK (0.01 mmol) in benzene (2 mL) and the solution was refluxed with stirring in an open system under air for 24 hrs. After cooling to room temperature, the consumption of starting materials was determined by GC with *m*-xylene as an internal standard, using a Carboxen 1000 column on a HP 690 series GC system.



Scheme 25

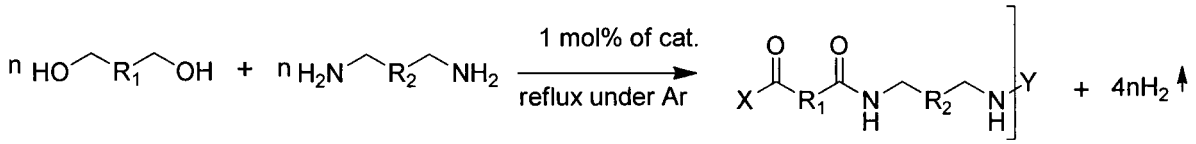
Table 18. Coupling of amines and alcohols to generate amides with in-situ generation of catalyst

Entry	Alcohol	Amine	Amide	Yield (isolated)
1				72.0
2				67.6

Purification of amides: After completion of the reaction, the solvent was removed (*Table 15-16, and 18*) under vacuum and the resulting residue was purified by the column chromatography on silica gel using EtOAc/*n*-hexane.

Example 5: Polyamides synthesis from diols and diamines:

[0154] The applicants have unexpectedly discovered that the catalysts of the present invention also catalyze the synthesis of polyamides directly from diols and diamines. In some preferred embodiments, 1,4-dioxane is used as a solvent. This polyamidation reaction is general, environmentally benign and atom economical. It proceeds under neutral reaction conditions without the use of activators, condensing agents or other additives. Moreover, these methods produce H_2 as the only byproduct (Scheme 26).

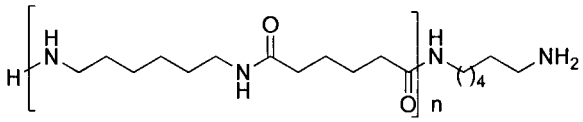


Scheme 26

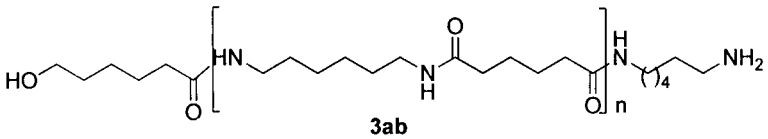
[0155] Upon refluxing a 1,4-dioxane solution containing equimolar amounts of 1,6-hexanediol and 1,6-hexanediamine in the presence of 1 mol% of complex 1 under an argon atmosphere for 3 days, a white solid separated out in the reaction mixture. The solid was filtered off and successively washed with THF:EtOAc (1:1), dichloromethane and 20% methanol in water. The resultant white solid was dried under high vacuum at 80 °C for 12 hrs to afford polymer **3a** in 82% yield (Table 19, entry 1). The solid was insoluble in MeOH, THF, 1,4-dioxane and chlorinated solvents, partially soluble in dimethylsulfoxide and dimethylformamide upon warming. The polyamide obtained was dissolved in deuterated trifluoroacetic acid (TFA) or trifluoroethanol (TFE) and characterized by NMR. The presence of CH_2 attached to the carbonyl group was confirmed by ^{1}H NMR, showing a broad singlet at 2.39 ppm for the four hydrogen atoms. A peak at 180.4 ppm in the $^{13}C\{^1H\}$ NMR spectrum and an IR band at 1633 cm^{-1} confirm the presence of the amide C=O group. The average molecular weight M_n of the polyamide **3a** was 16.6 kDa as measured by ^{1}H NMR using trifluoroethanol (TFE) as a solvent. The obtained solid was dissolved in TFA:CH_3CN (1:1) and MALDI-TOF mass spectrum was recorded using DHB (2,5-dihydroxybenzoic acid) as the matrix (Fig 5A). The polyamide has three possible types of end groups (amine-amine, amine-alcohol or alcohol-alcohol, compounds 3aa, 3ab and 3ac, respectively) and it also might result in a cyclic form. The spectrum revealed the highest molecular weight of 4195 Da, which corresponds to a polyamide having 18 monomers with OH/OH end groups. Due to insolubility of the polymer in DMF, GPC (gel permeation chromatography) was not performed.

Different types of end groups in polyamide **3a:**

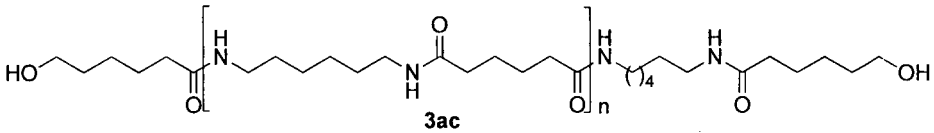
[0156]



3aa



3ab



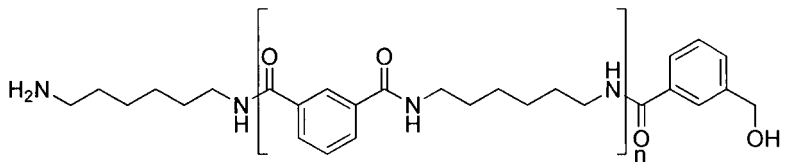
3ac

[0157] The same reaction was performed using the bipyridine based complex **3** as catalyst. After 3 days in refluxing dioxane polymer **3a** was formed as a white solid and isolated after work-up in 78% yield. Analysis of the obtained solid exhibited a similar MALDI-TOF pattern and ^{1}HNMR spectrum as observed with catalyst **1.** Thus, under these conditions

complexes **1** and **3** exhibit similar catalytic activity in the polyamidation reaction. However, using complex **3** it is possible to perform the polyamidation reaction in the absence of solvent, and using a lower catalyst loading. Thus, heating equivalent amounts of 1,6-hexanediol and 1,6-hexanediamine with the thermally stable complex **3** (0.2 mol%) in the absence of solvent at 130 °C for 14 hrs, followed by heating to 190 °C for an hour under Argon flow and cooling to room temperature resulted in a solid (Table 19, entry 16). The solid was washed with THF, water, ethanol and hexane and dried under vacuum for 12 hrs and isolated in 84% yield. The MALDI-TOF mass spectrum of this solid exhibited a highest molecular weight of 4951 Da. The higher molecular weight obtained under these conditions is likely due to the higher temperatures employed and absence of solvent, allowing polymerization in the melt.

[0158] Refluxing of 1,10-decanediol and 1,6-hexanediamine in 1,4-dioxane in the presence of 1 mol% of complex **1** resulted in 88% yield of the polyamide **3b** (Table 19, entry 2). The presence of the amide functional group of **3b** was confirmed by IR, showing an absorption frequency at 1637 cm^{-1} and a signal at 181.6 ppm in the $^{13}C\{^1H\}$ NMR spectrum. The number average molecular weight of **3b** was found to be 10.3 kDa based on ^1H NMR spectra using trifluoroethanol (TFE) as a solvent. A MALDI-TOF mass spectrum indicated a molecular weight up to 4965 Da, which corresponds to a polyamide comprised of 18 monomers. Due to insolubility in DMF, GPC was not performed.

[0159] To further investigate the polyamidation reaction, various combinations of diols and diamines were studied. Thus, polyamidation reaction of 1,3-phenylenedimethanol and 1,6-hexanediamine with 1 mol% of complex **1** under argon atmosphere for 3 days resulted in a solid which was isolated by filtration. The solid was washed successively with THF: EtOAC (1:1), dichloromethane and 20% MeOH in water, and finally dried under high vacuum at 80 °C to afford 82% of compound **3c** (Table 19, entry 3). The IR spectrum of the polyamide **3c** showed the presence of the NH group as broad peak at 3297 cm^{-1} and the amide C=O peak at 1631 cm^{-1}. The $^{13}C\{^1H\}$ NMR spectrum exhibited the C=O carbon at 165.8 ppm. Polyamide **3c** was further analyzed by MALDI-TOF by dissolving it in 80% TFA in acetonitrile using DHB as matrix (Fig. 5B). It gave a series of peaks in the range of 700-5932 Da. In an attempt to get a higher molecular weight, polyamide **3c** was refluxed with- or without 1,3-phenylenedimethanol in the presence of the complex **1.** However, a higher molecular weight was not observed. This might be due to the insolubility of **3c** in 1,4-dioxane. Due to insolubility in DMF, GPC analysis was not performed.)



3c

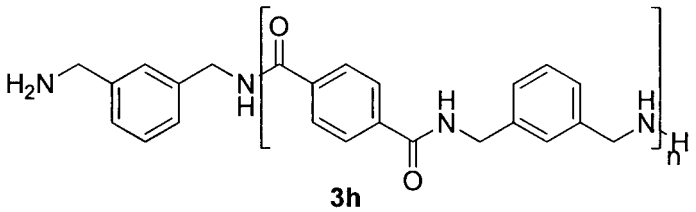
[0160] In order to increase the solubility of the polyamides, ether substituted aromatic diols were employed for the polymerization reactions. Thus, the reaction of (5-methoxy-1,3-phenylene)dimethanol and 1,6-hexanediamine gave 86% of compound **3d** (Table 19, entry 4) as a gummy solid and exhibited a mass peak at 7199 Da in the MALDI-TOF spectrum using HBA+NaI as a matrix and a solution of the polyamide **3d** in TFA : dichloromethane 1:1 (Fig. 5C). The polyamide **3d** was dissolved completely in warm DMF and the molecular weight was measured using gel-permeation chromatography (GPC) using DMF with 0.1% LiBr (wt/v) as the eluent at a flow rate of 1.0 mL/min with column temperature at 50 oC, yielding Mn = 18.7 kDa with PDI of 2.08. The significantly lower molecular weight in MALDI-TOF when compared with GPC is likely to be a result of the high PDI. As previously reported, in case of polydispersities higher than PDI=1.2, MALDI-TOF leads to under-represented high-mass components with respect to the lower mass components, resulting in significantly lower average molecular weight values.

[0161] Exploring the scope of the polyamidation reaction, equivalent amounts of 1,4-phenylenedimethanol and 1,6-hexanediamine were refluxed with 1 mol% of complex **1** for 3 days, leading to 88% yield of the crude compound **3e** (Table 19, entry 6). Successive washings with THF:EtOAC (1:1), dichloromethane, and 20% MeOH in water resulted in 80% yield of the solid after drying under vacuum. IR (peak at 1626 cm^{-1}) and NMR spectra confirm the presence of amide functionality. MALDI-TOF spectrum of the compound **3e** in TFA:CH_3CN (1:1) revealed only oligomeric mixtures in the range of 700-2500 Da (Fig. 5D). The mass unit of 2322 Da corresponds to only 9 monomer units. Reaction of the shorter diamine 1,2-ethylenediamine with 1,4-phenylenedimethanol did not result in significant progress of the polyamidation reaction, giving the polyamide **3f** in 63% yield (Table 19, entry 6), comprised of low molecular weight oligomeric mixtures in the range of 600-1900.

[0162] Next, the polyamidation reaction was examined using heteroaromatic diols. Thus, reaction of equivalent amounts of pyridine-2,6-diyldimethanol and 1,6-hexanediamine catalyzed by 1 mol% **1,** furnished after 3 days of reflux in 1,4-dioxane the polyamide **3g** (Table 19, entry 7) as a gummy insoluble solid which separated out from the reaction mixture and after work up gave a yield of 74%. The NMR and IR spectra confirm the presence of the amide carbonyl group. GPC analysis was performed for polyamide **3g** using DMF as a solvent upon heating at 80 °C. The Mn calculated

from the GPC was 26.9 kDa with PDI of 1.98. The polyamide **3g** was also analyzed by MALDI-TOF. The MALDI-TOF mass spectrum shows a series of peaks in the range of 600-4700 Da and the highest mass peak at 4583 appeared with low intensity and corresponds to 18 monomer units.

[0163] Next, aromatic diamines were studied for polyamidation reactions. Upon refluxing 1,4-phenylenedimethanol and 1,3-phenylenedimethanamine, a white solid was obtained after 3 days and was filtered off and dried under vacuum to provide 86% of polyamide **3h** (Table 19, entry 8). The NMR and MALDI-TOF of **3h** (Fig. 5E) reveal high molecular weight oligomeric mixtures. The highest mass unit obtained for the polyamide **3h** was 3861 Da, having amine end groups and corresponding to 14 monomer units in the chain. The other oligomer peaks appear at 3594, 3328, 3062, 2796, 2530, 2264, 1732, 1466, 1200, 668 mass units. Further, heating the compound **3h** in refluxing 1,4-dioxane in the presence of 1 mol% of the catalyst **1** did not result in progress of the polymer chain (due to insolubility in DMF, GPC analysis was not performed).



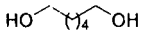
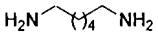
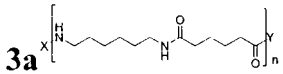
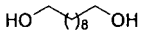
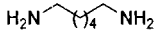
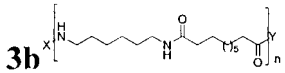
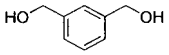
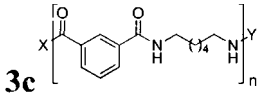
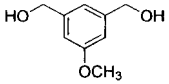
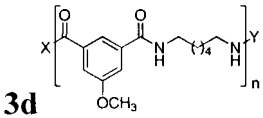
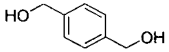
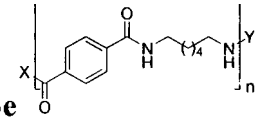
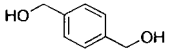
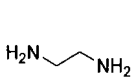
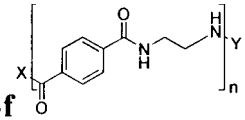
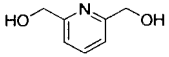
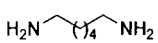
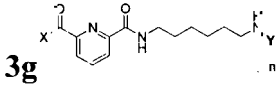
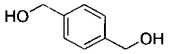
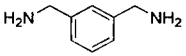
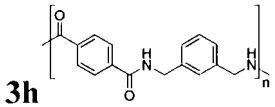
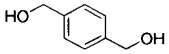
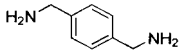
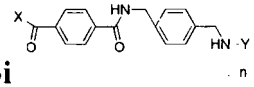
3h

[0164] The polyamidation reaction of 1,4-phenylenedimethanol and 1,4-phenylenedimethanamine afforded a mixture of oligomers **3i** in 84% isolated yield (Table 19, entry 9). The MALDI-TOF spectrum showed the highest mass unit of 3747 Da, indicating the presence of 14 monomer units. The reaction of 1,3-phenylenedimethanol and 1,3-phenylenedimethanamine led to **3j** (Table 19, entry 10) in 78% yield after workup, with a maximum mass unit of 1467, corresponding to 5.5 monomer units. The reaction of 1,5-pentanediol and 1,4-phenylenedimethanamine gave 80% of compound **3k** (Table 19, entry 11). Interestingly, **3k** showed a series of mass peaks in the range of 500-5200 Da corresponding to 22 monomer units. Reaction of cyclohexane-1,4-diyldimethanol and 1,4-phenylenedimethanamine gave 66% of compound **3l** (Table 15, entry 12), with peaks at 1912 Da corresponding to only 7 monomeric units in MALDI-TOF spectrum. (Due to insolubility in DMF, GPC analysis was not performed.)

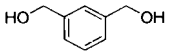
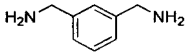
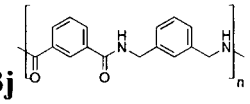
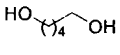
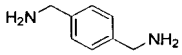
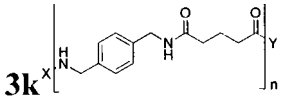
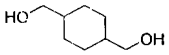
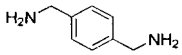
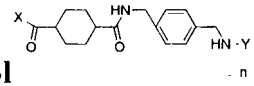
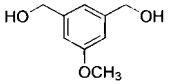
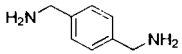
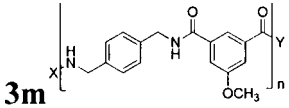
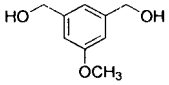
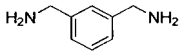
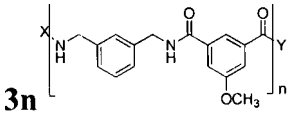
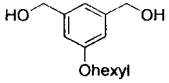
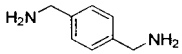
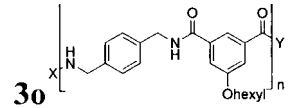
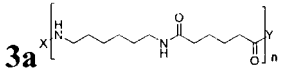
[0165] Polyamidation of (5-methoxy-1,3-phenylene)dimethanol, 1,4-phenylenedimethanamine using 1 mol% catalyst **1** afforded compound **3m** (Table 19, entry 13) in 76% yield, with the mass obtained at 4450 Da by MALDI-TOF, corresponding to 15 monomer units. The GPC analysis of **3m** showed a molecular weight Mn = 5.3 kDa. Similarly, the reaction of (5-(hexyloxy)-1,3-phenylene)dimethanol and 1,3-phenylenedimethanamine gave 88% of the polyamide **3n** (Table 19, entry 14). The number average molecular weight *M*n of **3n** was 11.3 kDa based on GPC analysis. Reaction of (5-(hexyloxy)-1,3-phenylene)dimethanol and 1,4-phenylenedimethanamine gave 77% of the polyamide **3o** (Table 15, entry 15) with a mass of 3052 Da corresponding to 8 monomers based on the MALDI-TOF spectrum.

[0166] Thus, a variety of polyamides have been synthesized having different spacers in good yield. The synthesis of polyamides using non-activated/non-ether linked substrates was demonstrated. The synthesized polyamides were characterized by spectroscopic techniques. The molecular weight was determined by ^{1}H NMR and GPC analysis. The heteroaromatic polyamide **3g** gave the highest number average molecular weight compared to the corresponding aliphatic and aromatic derived polyamides (**3a** and **3d** respectively). MALDI-TOF spectra of insoluble polyamides was also obtained. The results are summarized in Table 19.

Table 19. Catalytic polyamidation using diols and diamines.[a]

Entry	Diols	Diamines	Polyamides	Isolated Yield (%)	Highest molecular weight by MALDI-TOF (Da)	Mn (10^3)	PDI
1			**3a** 	82	4195	16.6[b]	-
2			**3b** 	88	5000	10.3[b]	-
3			**3c** 	82	5932	-	-
4			**3d** 	86	7199	18.7[c]	2.08
5			**3e** 	80	2322	-	-
6			**3f** 	63	1849	-	-
7			**3g** 	74	4583	26.9[c]	1.98
8			**3h** 	86	3861	-	-
9			**3i** 	84	3734	-	-

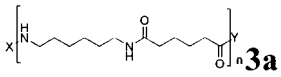
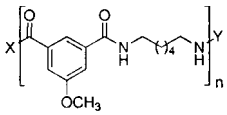
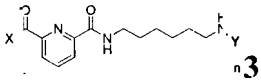
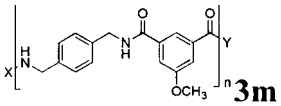
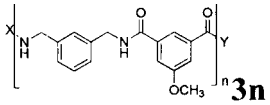
(continued)

Entry	Diols	Diamines	Polyamides	Isolated Yield (%)	Highest molecular weight by MALDI-TOF (Da)	Mn (10^3)	PDI
10			**3j** 	78	1467	-	-
11			**3k** 	80	5200	-	-
12			**3l** 	66	1912	-	-
13			**3m** 	76	4450	5.3[c]	3.20
14			**3n** 	88	-	11.3[c]	2.18
15			**3o** 	77	3052	5.4[c]	2.51
16[d]			**3a** 	84	4951	-	-

[a] Complex **1** (0.01 mmol), diol (1 mmol), diamine (1 mmol) and 1,4-dioxane (2 mL) were refluxed at an oil bath temperature of 135 °C in a Schlenk tube under Argon for 3 days.
[b] *M*n was calculated from ^{1}H NMR
[c] *M*n was obtained from GPC analysis
[d] No solvent was used. Catalyzed by complex **3.**

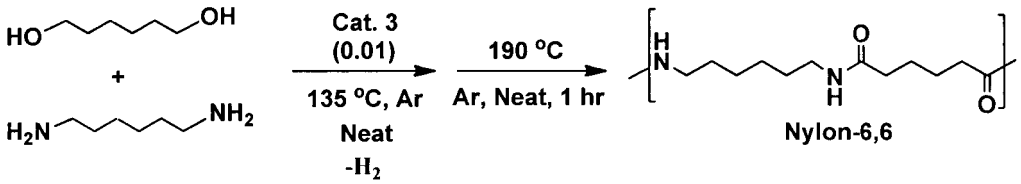
[0167] Thermogravimetric analyses (TGA) of the synthesized polyamides were performed. Weight losses of 30% and 50% occured at similar temperatures and were not significantly dependent on polymer structure (Fig. 6, Table 20). However, the aliphatic polyamide **3a** was less thermally stable and exhibited 83% weight loss at 495 °C, while the arene-based polyamides **3d,m,n** (except **3g**) exhibited 62-70% weight loss at 680 °C (Table 20). The pyridine-based polyamide **3g** was less stable, and exhibited 92% weight loss at 520 °C.

Table 20. Thermal studies of polyamides **3** at various temperatures by TGA.

Polyamides	*M*n (10^3)	T (°C at 5% weight loss)	T (°C at 10% weight loss)	T (°C at 30 % weight loss)	T (°C at 50 % weight loss)	T (°C at 70% weight loss)
 **3a**	16.6	360	395	425	437	451 (70%) 495 (83%)
 **3d**	18.7	120	170	430	458	680 (62%)
 **3g**	26.9	100	380	458	470	478 (70%) 520 (92%)
 **3m**	5.3	180	350	402	430	680 (64%)
 **3n**	11.3	140	170	400	420	680 (64%)

Polymerization with Catalyst **3**:

[0168] Synthesis of Nylon-6,6 by catalytic method under neat condition: Complex **3** (0.01 mmol), 1,6-hexanediol (5 mmol), and 1,6-hexanediamine (5 mmol) were taken in a Schlenk flask under an atmosphere of purified nitrogen in a glove box. The flask was equipped with a condenser and gradually heated up to 135 °C (bath temperature) and continued the heating at the same temperature with stirring in an open system under argon for 14 hrs. During the heating effervescence was observed and the viscous liquid became solid. After cooling to room temperature, the solid thus obtained (low molecular weight oligomer; m.p = 215.9 °C (by TGA)) was again heated up to 190 °C using sand bath for about an hour in an open system under argon. The resulting solid was washed with THF, water, ethanol and finally with hexane (in order to remove other impurities) and dried under vacuum for overnight.



Scheme 27

DSC:

Temperature (°C)	Weight loss (in %)
100	2.70
200	3.5

(continued)

Temperature (°C)	Weight loss (in %)
300	5.7
350	8.47
400	22.2
450	62.2
500	64.7
550	65.5
600	66.0

TGA: m.p 251.9 °C (regenerated with the same melting point after 4 cycles with freezing point of 216.1 °C).
MOLDI-TOF: (matrix= DHB (2,5-dihydroxybenzoicacid), solvent = trifluroethanol:CH_2Cl_2) up to 4800 Da.

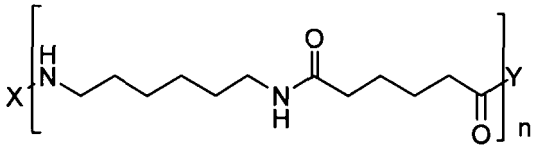
[0169] In conclusion, polyamidation based on coupling of non-activated diols and diamines, with extrusion of H_2, catalyzed by complexes 1 and 3 was developed. Guan et al have also reported the utilization of the amidation reaction catalyzed by complex 1 for the preparation of other polyamides, bearing ether-functionalized spacers. The polyamidation reaction proceeds under neutral conditions, with liberation of molecular hydrogen and with no preactivation of the substrate being required. The reaction can be applied to a variety of diols and diamines for the synthesis of functional polyamides. The number average molecular weight of the polymers obtained in our work was measured by ^{1}H NMR, MALDI-TOF and, in case of the DMF-soluble polymers, by GPC analysis. Mean molecular weights up to 26.9 kDa were obtained, with polydispersities in the range of PDI=1.98 - 3.2. The variation in chain lenghts for different substrate combinations is probably influenced by the different solubilities of the polymers. The insoluble polyamides were characterised spectroscpoically and by MALDI-TOF. It was observed that molecular weights determined by GPC were significantly higher than those obtained by MALDI-TOF. This is another example of the MALDI-TOF method favoring lower molecular weights in case of PDI >1.2 The thermal properties of the polyamides with different spacers were studied and it was found that aliphatic/pyridinic spacer-based polyamides are less stable at high temperature as compared with aromatic derived polyamides. Polyamidation in absence of solvent was also demonstrated. This simple, environmentally benign and general polymerization reaction provides a new approach to the important area of polyamide synthesis.

[0170] General procedure for the catalytic direct polyamidation of diols with diamines catalyzed by complex 1: Complex 1 (0.01 mmol), diol (1 mmol), amine (1 mmol), and 1,4-dioxane (2 mL) were added to schlenk flask under an atmosphere of purified nitrogen in a glove box. The flask was equipped with a condenser and the solution was refluxed with stirring in an open system under argon flow for 3 days. During the course of the reaction, a white colored solid separated out for 24 hrs. The reflux was continued for 3 days. After cooling to room temperature, the solid obtained was filtered and washed successively with methanol and dichloromethane, or with THF:ethylacetate (1:1), dichloromethane and 20% methanol in water to give the product polyamide. T. The solid obtained was dried under vacuum at 80°C for 8-12 hrs. The products were analyzed by NMR, IR and MALDI TOF.

Spectral Data for Polyamides:

Polyamide 3a:

[0171]



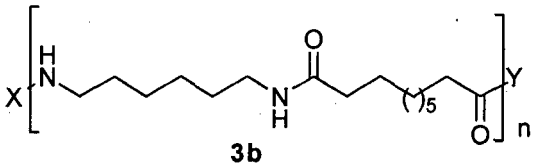
3a

[0172] IR (KBr pellet): 3304, 2935, 2859, 1633, 1536, 1474, 1276 cm^{-1}; ^{1}H NMR (TFA-d): 1.08 (broad s, 4H), 1.34 (broad s, 4H), 1.52 (broad s, 4H), 2.39 (broad s, 4H), 3.17 (broad s, 4H); ^{13}C{^{1}H}NMR (TFA-d): 26.8, 27.8, 29.5, 35.0, 44.5, 180.4.

MALDI-TOF (matrix: HBA (2,5-dihydroxybenzoic acid), solvent acetonitrile: TFA): m/z = 569 to 4195 Da. The spectrum of polyamide **3a** shows a series of peaks at 569 (**3aa+H⁺**(n=2)), 795 (**3aa+H⁺**(n=3)), 909 (**3ab+H⁺**(n=3)), 1022 (**3c**(n=4)), 1135 (**3ab+H⁺**(n=4)), 1247 (**3aa+H⁺**(n=5)), 1361 (**3ab+H⁺**(n=5)), 1474 (**3ac**(n=6)), 1588 (**3ab+2H⁺**(n=6)), 1700 (**3ac** (n=7)), 1814 (**3ab+2H⁺**(n=7)), 1926 (**3ac** (n=8)), 2041 (**3ab+3H⁺**(n=8)), 2153 (**3ac+H⁺**(n=9)), 2266 (**3ab+2H⁺**(n=9)), 2379 (**3ac+H⁺**(n=10)), 2494 (**3ab+4H⁺**(n=10)), 2606 (**3ac+2H⁺**(n=11)), 2720 (**3ab+4H⁺**(n=11)), 2832 (**3ac+2H⁺**(n=12)), 2947 (**3ab+5H⁺**(n=12)), 3058 (**3ac+2H⁺**(n=13)), 3170 (**3ab+H⁺**(n=13)), 3288 (**3ac+6H⁺**(n=14)), 3402 (**3ab+8H⁺**(n=14)), 3515 (**3ac+7H⁺**(n=15)), 3625, 3739 (**3ac+5H⁺**(n=16)), 3840, 3853, 3966 (**3ac+5H⁺**(n=17)), 4079 (**3ab+6H⁺**(n=13)), 4195 (**3ac+9H⁺**(n=18)).

Polyamide 3b:

[0173]

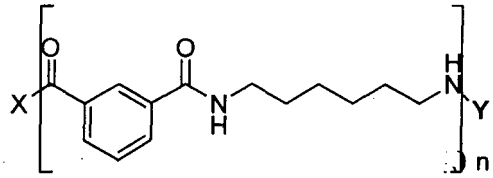


3b

[0174] IR (KBr pellet): 3306, 2933, 2854, 1637, 1540, 1437, 1383, 1239 cm^{-1}; ^{1}H NMR (TFA-d): 1.28 (broad s, 12H), 1.63 (broad s, 8H), 2.61 (broad s, 4H), 3.46 (broad s, 4H); $^{13}C\{^{1}H\}$NMR (TFA-d): 27.6, 29.3, 30.4, 35.5,44.7, 181.6. MALDI-TOF (matrix: HBA (2,5-dihydroxybenzoic acid)+NaI, solvent dichloromethane: TFA): m/z = 1258 to 4965 Da.

Polyamide 3c:

[0175]

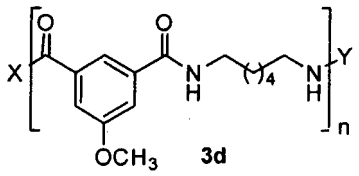


3c

[0176] IR (KBr pellet): 3297, 2935, 2857, 1631, 1532, 1274 cm^{-1}; ^{1}H NMR (DMSO-d_6): 1.32 (broad s, 4H, CH_2), 1.51 (broad s, 4H, CH_2), 3.23-3.32 (m, 4H, NCH_2), 7.50 (t, 1H, =C*H*), 7.91 (d, 2H, =C*H*), 8.26 (s, 1H, =C*H*), 8.54 (broad s, 2H, N*H*). $^{13}C\{^{1}H\}$NMR (DMSO-d_6): 26.2, 29.1, 39.2, 126.1, 128.2, 129.5, 134.9, 165.8. MALDI-TOF (matrix: 2,5-dihydroxybenzoic acid, solvent acetonitrile:TFA): m/z = 700 to 5932 Da. The following peaks were observed: 5932 (**3c** (n=23)+24), 5918 (**3c** (n=23)+10), 5685 (**3c** (n=22)+23), 5671 (**3c** (n=22)+9), 5439 (**3c** (n=21)+23), 5425 (**3c** (n=21)+9), 5192 (**3c** (n=20)+22), 5178 (**3c** (n=20)+8), 4946 (**3c** (n=19)+22), 4932 (**3c** (n=19)+8), 4699 (**3c** (n=18)+21), 4685 (**3c** (n=18)+7), 4453 (**3c** (n=17)+21), 4439 (**3c** (n=17)+7), 4207 (**3c** (n=16)+21), 4193 (**3c** (n=16)+7), 3961 (**3c** (n=15)+21), 3947 (**3c** (n=15)+7), 3714 (**3c** (n=14)+20), 3700 (**3c** (n=14)+6), 3468 (**3c** (n=13)+20), 3454 (**3c** (n=13)+6), 3219 (**3c** (n=12)+17), 3205 (**3c** (n=12)+3), 2973 (**3c** (n=11)+17), 2959 (**3c** (n=11)+3), 2727 (**3c** (n=10)+17), 2713 (**3c** (n=10)+3), 2481 (**3c** (n=9)+17), 2467 (**3c** (n=9)+3), 2234 (**3c** (n=8)+16), 2220 (**3c** (n=8)+2), 1988 (**3c** (n=7)+16), 1974 (**3c** (n=7)+2), 1742 (**3c** (n=6)+16), 1728 (**3c** (n=6)+2), 1496 (**3c** (n=5)+16), 1482 (**3c** (n=5)+2). The excess mass units are due to the protonation of the amine functionality in TFA.

Polyamide 3d:

[0177]

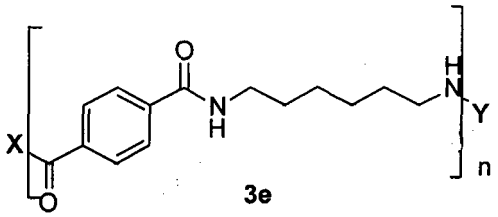


3d

[0178] ^{1}H NMR (DMSO-d_6): 1.32 (broad s, 4H, CH_2), 1.51 (broad s, 4H, CH_2), 3.15 (s, 2H, NCH_2), 3.38 (broad s, 2H, NCH_2), 3.82 (s, 3H, OCH_3), 7.48 (s, 2H, =C*H*), 7.88 (s, 1H, =C*H*), 8.53 (broad s, 2H, N*H*); ^{13}C{^{1}H}NMR (DMSO-d_6): 26.3, 29.1, 48.6, 55.6, 66.4, 115.0, 119.1, 136.3, 159.1, 165.6;
GPC (0.1% LiBr in DMF): *M*n = 18.7×10^3 g/mol, *M*w = 39.1×10^3 g/mol
MALDI-TOF (matrix: 2,5-dihydroxybenzoic acid+NaI, solvent dichloromethane:TFA): m/z = 1116 to 7199 Da. The MALDI-TOF exhibited a series of oligomeric peaks at 1116 (**3d** (n=4)+8H$^+$, NH_2/OH), 1386 (**3d** (n=5)+2H$^+$, NH_2/OH), 1661 (**3d** (n=6)+ H$^+$, NH_2/OH), 1935 (**3c**(n=7)+3H$^+$, cyclic), 2210 (**3d** (n=8)+2H$^+$, cyclic), 2484 (**3d** (n=9), cyclic), 2762 (**3d** (n=10)+2H$^+$, cyclic), 3034, 3309, 3582, 3861, 4144 (**3d** (n=15), NH_2/OH), 4410, 4682, 4974 (**3d** (n=18)+2H$^+$, NH_2/OH), 5254 (**3d** (n=19)+6H$^+$, NH_2/OH), 5526 (**3d** (n=20)+2H$^+$, NH_2/OH), 6102 (**3d** (n=22)+Na+3H$^+$, NH_2/OH), 6351 (**3d** (n=23)+3, cyclic), 6641 (**3d** (n=24)+13, NH_2/OH), 6904 (**3d** (n=25), NH_2/OH) and 7199 (**3d** (n=26)+23, cyclic).

Polyamide 3e:

[0179]

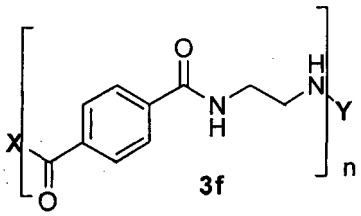


3e

[0180] IR (KBr pellet): 3312, 2936, 2857, 1626, 1540, 1498, 1287 cm^{-1}. ^{1}H NMR (DMSO-d_6): 1.29-1.51 (m, 8H), 3.23 (broad s, 4H), 4.52 (s), 5.32 (broad s), 7.36 (d), 7.78 (d), 7.87 (s), 8.38 (t), 8.54 (broad s).
MALDI-TOF (matrix= DHB, solvent acetonitrile: TFA): m/z = 743 to 2322 Da. The oligomeric peaks are 743 (**3e** (n=3)+H$^+$), 989 (**3e** (n=4)+H$^+$), 1235 (**3e** (n=5)+H$^+$), 1482 (**3e** (n=6)+2H$^+$), 1728 (**3e** (n=7)+H$^+$), 1973 (**3e** (n=8)+H$^+$), 2221 (**3e** (n=9)+3H$^+$), 2464 (**3e** (n=10)+3H$^+$).

Polyamide 3f:

[0181]

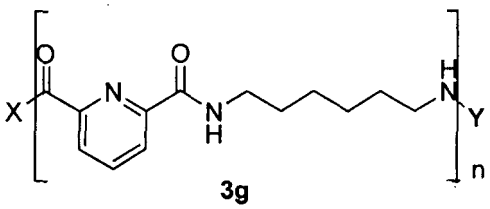


3f

[0182] ^{1}H NMR (DMSO-d_6): 2.67 (t), 3.44 (broad s), 4.53 (s), 7.37 (d), 7.80 (d), 7.90 (s), 8.56 (broad s), 8.71 (broad s). MALDI-TOF (matrix: 2,5-dihydroxybenzoic acid, solvent: acetonitrile: TFA): m/z = 765 to 1835 Da. Oligomeric peaks were observed at 765 (**3f** (n=4)+H$^+$), 955 (**3f** (n=5)+H$^+$), 1145 (**3f** (n=6)+H$^+$), 1335 (**3f** (n=7)+H$^+$), 1525 (**3f** (n=8)+H$^+$), 1715 (**3f** (n=9)+H$^+$), 1849 (**3f** (n=9)+H$^+$, ending with OH/OH groups).

Polyamide 3g:

[0183]

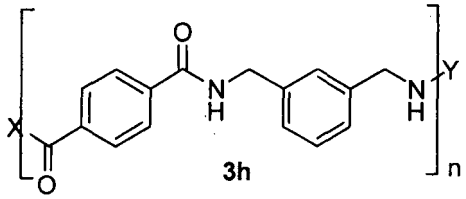


3g

[0184] IR (KBr pellet): 3325, 2932, 2859, 1662, 1538, 1445, 1243 cm^{-1}; ^1H NMR (DMSO-d_6): 1.27 (broad m, 4H, CH_2), 1.50 (broad m, 4H, CH_2), 3.29 (broad s, 4H, NCH_2), 8.13 (m, 3H, =C*H*), 9.28 (broad s); ^{13}C NMR (DMSO-d_6): 13.9, 22.1, 26.1, 29.4, 30.9, 40.1, 124.1, 139.3, 148.8, 163;
GPC (0.1% LiBr in DMF): $Mn = 26.9\times10^3$ g/mol, $Mw = 53.3\times10^3$ g/mol
MALDI-TOF (matrix: 2,5-dihydroxybenzoic acid, solvent acetonitrile: TFA): m/z = 610 to 4583 Da. The spectrum exhibits a series of oligomeric peaks at 610 (**3g** (n = 2), NH_2/NH_2), 742 (**3g** (n = 3) $+H^+$, cyclic), 907 (**3g** (n = 3) $+Na^+ +3H^+$, OH/OH), 989 (**3g** (n = 4) $+H^+$, cyclic), 1203, 1236 (**3g** (n = 5) $+H^+$, cyclic), 1484 (**3g** (n = 6) $+2H^+$, cyclic), 1500, 1732 (**3g** (n = 7) $+3H^+$, cyclic), 1781, 1796, 1914, 1978 (**3g** (n = 8) $+2H^+$, cyclic), 2063, 2079, 2092, 2210, 2226 (**3g** (n = 9) $+3H^+$, cyclic), 2242, 2360, 2374, 2389, 2473 (**3g** (n = 10) $+3H^+$, cyclic), 2492, 2507, 2657, 2671, 2685, 2789, 2803, 2836, 2953, 2968, 2981, 3085, 3100, 3132, 3250, 3264, 3278, 3396 (**3g** (n = 13) $+3Na^+$, NH_2/NH_2), 3427 (**3g** (n = 13) +KK, OK/OH), 3561, 3576 (**3g** (n = 14) $+2H^+$, NH_2/NH_2), 3679, 3709 (**3g** (n = 15) $+3H^+$, cyclic), 3726, 3844 (**3g** (n = 15) $+Na^+$, NH_2/NH_2), 3975 (**3g** (n = 16) $+Na^+$, cyclic), 4449 (**3g** (n = 18) $+3H^+$, cyclic), 4569 (**3g** (n = 18) $+7H^+$, NH_2/NH_2).

Polyamide 3h:

[0185]

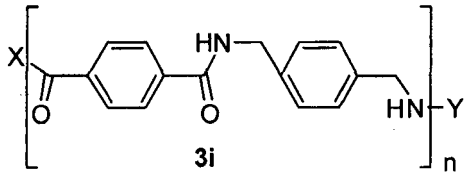


3h

[0186] IR (KBr pellet): 3285, 2921, 1638, 1540, 1439, 1318 cm^{-1}. ^1H NMR (DMSO-d_6): 3.68 (s), 4.47 (broad s), 7.21-7.37 (broad m), 7.92-7.94 (m), 9.15 (broad s); $^{13}C\{^1H\}$NMR (DMSO-d_6): 42.7, 45.5, 62.6, 125.2, 125.8, 126.1, 127.2, 136.6, 139.6, 165.6; MALDI-TOF (matrix: 2,5-dihydroxybenzoic acid, solvent acetonitrile: TFA): m/z = 668 to 3861 Da.

Polyamide 3i:

[0187]

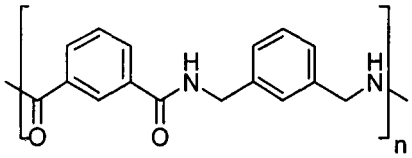


3i

[0188] IR (KBr pellet): 3346, 3056, 2923, 1640, 1540, 1496, 1317 cm^{-1}; ^1H NMR (DMSO-d_6): 3.59 (s), 4.43 (broad m), 7.23-7.27 (broad m), 7.37 (d), 7.83 (d), 7.94 (m), 9.13 (broad s); $^{13}C\{^1H\}$NMR (DMSO-d_6): 42.4, 45.1, 62.4, 126.0, 127.1, 132.7, 137.5, 137.9, 138.0, 138.3, 142.1, 145.9, 165.5, 166.1; MALDI-TOF (matrix: 2,5-dihydroxybenzoic acid, solvent ACETONITRILE: TFA): m/z = 400 to 3734 Da

Polyamide 3j:

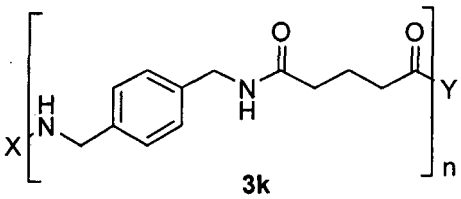
[0189]



[0190] IR (KBr pellet): 3290, 3061, 2920, 1640, 1533, 1478, 1272 cm^{-1}; ^{1}H NMR (DMSO-d_6): 4.45-4.47 (m, 4H), 7.17-7.28 (m, 4H), 7.50 (t, 1H), 7.97 (d, 2H), 8.36 (s, 1H), 9.13 (broad m, 2H); $^{13}C\{^{1}H\}$NMR (DMSO-d_6): 42.8, 66.4, 125.6, 126.5, 126.7, 128.5, 128.7, 129.9, 134.6, 139.7, 165.9.
GPC (0.1% LiBr in DMF): $Mn = 1.4\times10^{3}$ g/mol, $Mw = 5.01\times10^{3}$ g/mol
MALDI-TOF (matrix: 2,5-dihydroxybenzoic acid, solvent acetonitrile: TFA): m/z = 500 to 1467 Da

Polyamide 3k:

[0191]

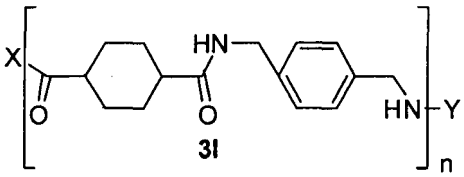


3k

[0192] IR (KBr pellet): 3245, 3069, 2964, 2944, 1629, 1556, 1424, 1262 cm^{-1}; ^{1}H NMR (DMSO-d_6): 1.35-1.79 (m, 2H), 2.07-2.15 (m, 4H), 4.19-4.21 (broad m, 4H), 7.16 (broad s, 4H), 8.27 (broad m); $^{13}C\{^{1}H\}$NMR (DMSO-d_6): 21.3, 21.9, 32.9, 35.0, 41.7, 46.8, 61.1, 127.0, 127.3, 138.1, 171.6. MALDI-TOF (matrix= DHB, solvent acetonitrile: TFA): m/z = 500 to 5200 Da

Polyamide 3l:

[0193]

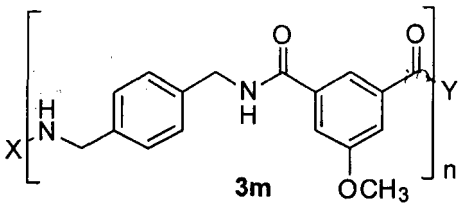


3l

[0194] IR (KBr pellet): 3282, 3060, 2934, 2860, 1633, 1551, 1443, 1386 cm^{-1}; ^{1}H NMR (TFA-d): 7.26 (d), 7.19 (d), 7.11 (broad s), 4.44 (broad s), 4.18 (s), 3.83 (s), 2.56 (broad s), 2.00 (broad s), 0.92-1.82 (m); $^{13}C\{^{1}H\}$NMR (TFA-d): 29.3, 45.2, 46.9, 130.6, 131.0, 131.9, 139.2, 182.7. MALDI-TOF (matrix= DHB, solvent acetonitrile: TFA): m/z = 400 to 1912 Da

Polyamide 3m:

[0195]

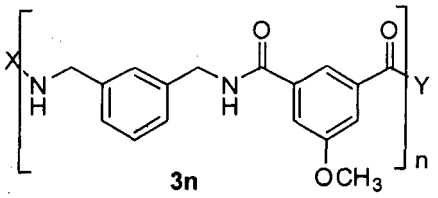


3m

[0196] IR(KBr pellet): 3294, 3063, 2935, 1642, 1593, 1536, 1423, 1283, 1061 cm^{-1}. ^1H NMR (DMSO-d_6): 3.56 (s), 3.81 (s), 4.42 (broad s), 7.24 (broad s), 7.54 (s), 7.96 (s), 9.11 (broad s); $^{13}C\{^1H\}$NMR (DMSO-d_6): 42.5, 55.6, 66.3, 115.3, 118.7, 127.3, 135.9, 138.0, 159.1, 165.5, 165.8;
GPC (0.1% LiBr in DMF): $Mn = 5.39\times10^3$ g/mol, $Mw = 17.3737\times10^3$ g/mol
MALDI-TOF (matrix: 2,5-dihydroxybenzoic acid, solvent acetonitrile: TFA): m/z = 600 to 4450 Da

Polyamide 3n:

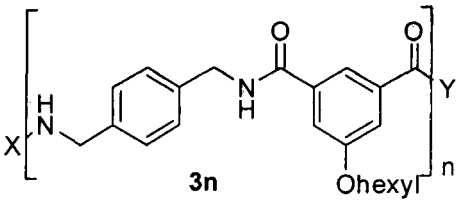
[0197]



[0198] ^1H NMR (TFA-D): 3.74 (s, 2H, NCH_2), 3.88 (s, 2H, NCH_2), 4.60 (s, 3H, OCH_3), 7.19-7.23 (m, 4H, Arom-H), 7.44 (s, 2H, Arom-*H*), 7.77 (s, 1H, Arom-*H*); $^{13}C\{^1H\}$NMR (TFA-D): 47.2, 57.6, 68.7, 119.7, 121.1, 129.0, 129.8, 131.9, 136.3, 138.5, 162.3, 173.0; GPC (0.1% LiBr in DMF): $Mn = 11.3\times10^3$ g/mol, $Mw = 24.71\times10^3$ g/mol

Polyamide 3o:

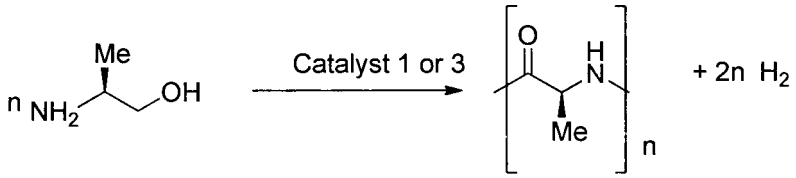
[0199]



[0200] IR (KBr pellet): 3325, 3079, 2929, 2869, 1644, 1592, 1532, 1434, 1333, 1062 cm^{-1}; ^1H NMR (TFA-d): 7.78 (s, 1H), 7.46 (s, 2H), 7.21 (s, 4H), 4.56 (broad s, 4H), 3.94 (broad s, 2H), 1.65 (broad s, 2H), 1.26 (broad s, 2H), 1.15 (broad s, 4H), 0.70 (broad s, 3H); $^{13}C\{^1H\}$NMR (TFA-d): 14.5, 24.1, 27.1, 30.5, 33.2, 47.0, 72.1, 120.4, 121.0, 130.5, 136.0, 137.8, 162.1, 173.0.
GPC (0.1% LiBr in DMF): $Mn = 5.4\times10^3$ g/mol, $Mw = 13.76\times10^3$ g/mol MALDI-TOF (matrix= DHB, solvent acetonitrile: TFA): up to m/z = 3052 Da

Example 6: Dehydrogenation of L-alaninol to form poly(alanine) catalyzed by Ruthenium complexes 1 or 3

[0201]



Scheme 28

[0202] Complex **3** (0.01 mmol), L-alaninol (1 mmol), and 1,4-dioxane (2 mL) were taken in a Schlenk flask under an atmosphere of purified nitrogen in a glove box. The flask was taken out the glove box, and equipped with a condenser. The solution was refluxed with stirring in an open system under argon for 48 h. After cooling to room temperature, the

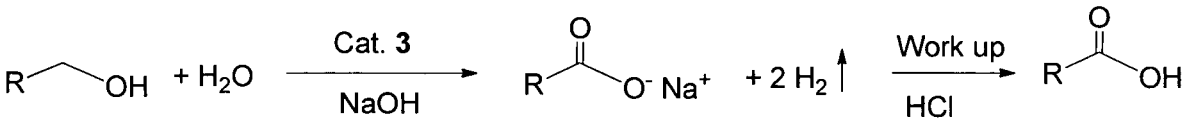
solvent was concentrated (~0.5 mL) under reduced vacuum followed by addition of CH_2Cl_2 (in order to remove the unreacted starting material). The white solid precipitated out from the solution at ~5 °C (after 30 min) and was collected by simple filtration and washed with toluene and dried under vacuum at 80 °C for about 14 h to yield 77% of polypeptide. Using Complex **1** under the same procedure, 72% yield was obtained.

Poly(alanine):

[0203] mp: 190-194°C (decompose) ^{1}H NMR (400 MHz, DMSO-d_6): 0.93 (broad s, 3H, C*H*$_3$), 4.22-4.26 (m, 1H, NC*H*), 8.00 (1H, CON*H*). ^{13}C{^{1}H}NMR (300 MHz, TFA-d_4): 20.0 (*C*H$_3$), 21.7 (*C*H$_3$), 53.1 (NCH), 53.4 (NCH), 174.9 (*C*=O). MS (ES$^+$): 165.3 (100%, cycloala-ala+Na,$^+$), 240 (18%, M (n=1)+Na), 311 (65%, M (n=2)+Na), 382 (32%, M (n=3)+Na)), 453 (10%, M (n=4)+Na)), 524 (6%, M (n=5)+Na)). Maldi-Tof: 754 ((M (n=8)+K+H)), 903 ((M (n=10)+2Na+H)), 1001 ((M (n=12)+3H)), 1150 ((M (n=14)+10H)), 1248, 1396 ((M (n=17)+K+3H)), 1494 ((M (cyclic, n=21)+3H), 1644 ((M (n=23)+7H)). [α] = -105° (50 mg/5mL, Acetic Acid)

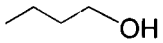
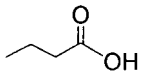
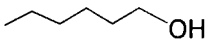
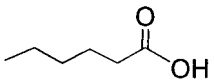
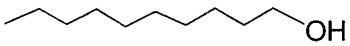
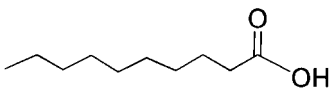
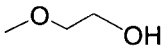
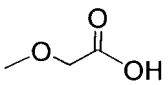
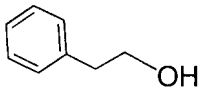
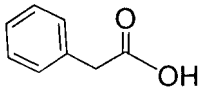
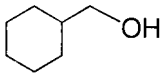
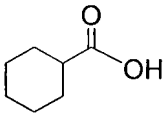
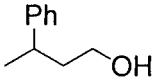
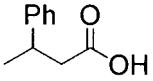
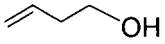
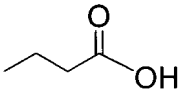
Example 7: Coupling of Alcohols with water to form Acids with Liberation of H_2

[0204]

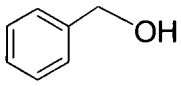
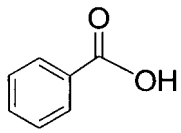
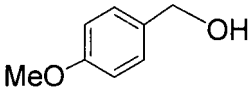
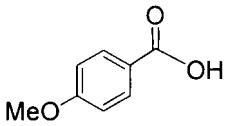
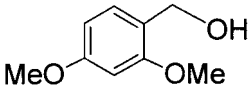
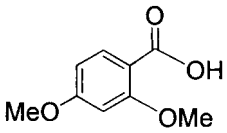


Scheme 29

Table 21. Direct Transformation of Alcohols to Acids Using Water

Entry	Alcohols	Acids	Yield (%) isolated
1			84
2			88
3			78
4			73
5			78
6			80
7			74
8			63

(continued)

Entry	Alcohols	Acids	Yield (%) isolated
9			91
10			89
11			83

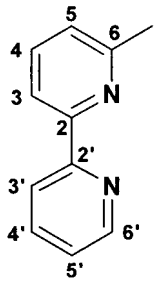
[0205] General procedure for the dehydrogenation of alcohols to acids catalyzed by 3: A mixture of an alcohol (10 mmol), degassed double distilled water (2 mL) and sodium hydroxide (11 mmol) were combined in a Schlenk-flask under argon atmosphere. The biphasic mixture was degassed by purging with argon for 10 min. Complex **3** (0.02 mmol) was added and the reaction mixture was refluxed under a stream of argon. After 18 h water was added (10 mL), and the mixture was extracted with diethyl ether (2 X 10 mL). The aqueous phase was acidified with 5N HCl and extracted with ethyl acetate (5 X 20 mL).The combined extracts were washed with brine (25 mL), dried over Na_2SO_4, and evaporated under reduced pressure, affording the pure acid.

Example 8 - General Experimental (Ruthenium complex)

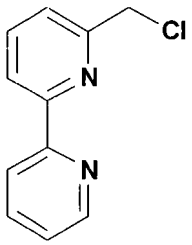
[0206] All experiments with metal complexes and phosphine ligands were carried out under an atmosphere of purified nitrogen in a Vacuum Atmospheres glove box equipped with a MO 40-2 inert gas purifier or using standard Schlenk techniques. All solvents were reagent grade or better. All non-deuterated solvents were refluxed over sodium/benzophenone ketyl and distilled under argon atmosphere. Deuterated solvents were used as received. All solvents were degassed with argon and kept in the glove box over 4Å molecular sieves. Most of the chemicals used in catalysis reactions were purified according to standard procedure (or by vacuum distillation/sublimation). The 6-methyl-2,2'-bipyridine (BPy-Me) and 6-chloromethyl-2,2'-bipyridine (BPy-CH_2Cl) precursors (Schubert et al.; Smith et al.), and RuHCl$(PPh_3)_3$(CO) (Ahmad et al.) were prepared according to literature procedures.
Thin layer chromatography (TLC) was performed on Merck 1.05554 aluminum sheets precoated with silica gel 60 F254 and the spots visualized with UV light at 254 nm or under iodine. Column chromatography purifications were performed by flash chromatography using Merck silica gel 60 (0.063-0.200 mm). ^1H, ^{13}C and ^{31}P NMR spectra were recorded at 300, 75, and 122 MHz, respectively, using Bruker AMX-300 NMR spectrometers. ^1H and $^{13}C[^1H\}$ NMR chemical shifts are reported in ppm downfield from tetramethylsilane. ^{31}P NMR chemical shifts are reported in parts per million downfield from H_3PO_4 and referenced to an external 85% solution of phosphoric acid in D_2O. Abbreviations used in the NMR follow-up experiments: br, broad; s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. IR spectra were recorded on a Nicolet FT-IR spectrophotometer. Mass spectra were recorded on Micromass Platform LCZ 4000, using Electro Spray Ionization (ESI) mode. Elemental analysis were performed on Thermo Finnigan Italia S.p.A-FlashEA 1112 CHN Elemental Analyzer (manufactured by Thermo Finnigam Italia S.p.A).

Synthesis of Ligand 5:

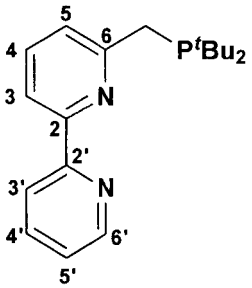
[0207] 6-methyl-2,2'-bipyridine (BPy-Me): Prepared according to procedure described in *Org. Lett.* **2000,** 3373 (Schubert et al.). ^1H NMR ($CDCl_3$): 2.61 (s, 3H, CH_3), 7.13 (d, 1H, J_{HH} = 7.80 Hz, *H*-5), 7.26 - 7.27 (m, 1H, *H-5'),* 7.57 (t, 1H, J_{HH} = 7.80 Hz, *H*-4), 7.74 - 7.79 (m, 1H, *H*-4'), 8.17 (d, 1H, J_{HH} = 7.50 Hz, *H-3),* 8.40 (d, 1H, J_{HH} = 8.10 Hz, *H-3'),* 8.64 - 8.67 (m, 1H, *H*-6').



[0208] 6-chloromethyl-2,2'-bipyridine (BPy-CH_2Cl): Prepared according to procedure described in *Org. Synth.* **2002,** 78, 82 (Smith et al.). ^1H NMR ($CDCl_3$): 4.75 (s, 2H, CH_2), 7.27 - 7.32 (m, 1H), 7.49 (d, 1H, J_{HH} = 7.50 Hz), 7.77 - 7.86 (m, 2H), 8.33 (d, 1H, J_{HH} = 7.80 Hz), 8.43 (d, 1H, J_{HH} = 8.10 Hz), 8.66 - 8.68 (m, 1H).



[0209] 6-di-*tert*-butylphosphinomethyl-2,2'-bipyridine (BPy-^{t}PNN) 5: To an oven dried 50 mL pressure vessel equipped with magnetic stirring bar was added 6-chloromethyl-2,2'-bipyridine (BPy-CH_2Cl) (2.05 g, 10.00 mmol), di-*tert*-butyl phosphine (1.75g, 12.00 mmol), and 30 mL MeOH in a nitrogen glove box. The flask was sealed and heated at 50 °C for 48 hrs with stirring outside the glove box. After cooling, it was reintroduced to the glove box, triethylamine (1.82g, 18.00 mmol) was added and the reaction mixture was stirred at room temperature for 1 hr. The solvents were removed under reduced pressure to obtain a white solid. The residue was washed with ether (3 × 20 mL) and the ether filtered and was removed under reduced pressure to yield a white solid. It was recrystallized from MeOH at *ca.* -30 °C to yield 2.67 g (85%) of 6-di-*tert*-butylphosphinomethyl-2,2'-bipyridine (BPy-^{t}PNN).



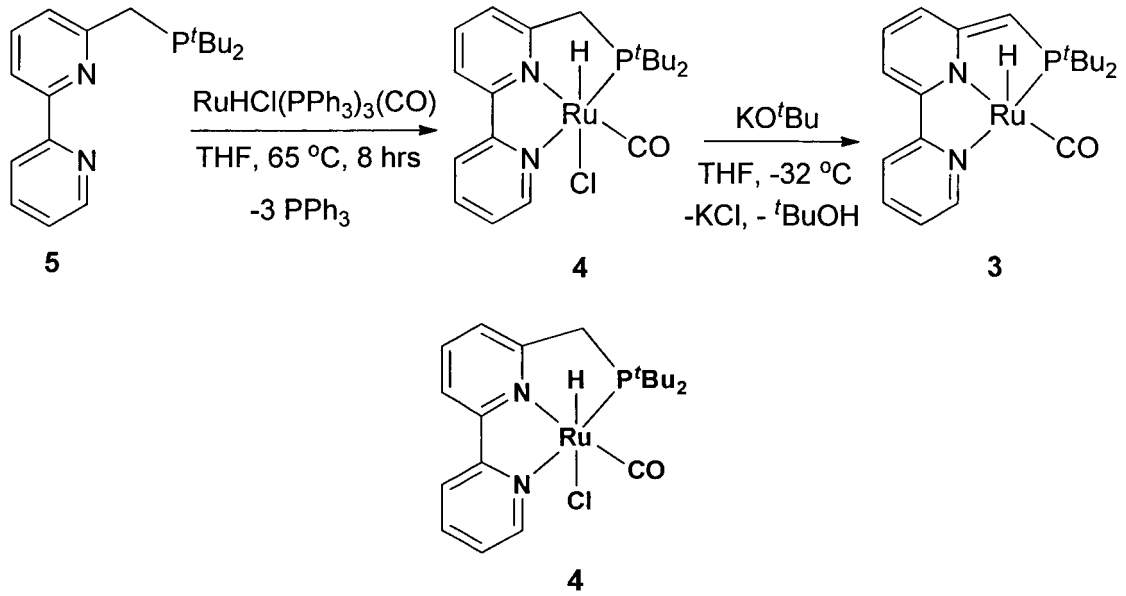
5

[0210] Alternative method for the preparation of BPy-^{t}PNN (5): An oven-dried 500 mL three-necked round bottom flask equipped with an argon inlet, a stirring bar, dropping funnel and one rubber septum was cooled under a stream of argon. The flask was then charged with 6-methyl-2,2'-bipyridine (3.40 g, 20 mmol) in 80 mL dry ether. The solution was cooled to 0 °C and 13.4 mL of a 1.8 M solution of commercial lithium diisopropylamide (LDA) in heptane/THF/ethylbenzene (24 mmol) was added dropwise *via* syringe during 15 minutes. The resulting brown colored mixture was stirred for 1 hr at 0 °C and then cooled to -78 °C and a solution of di-*tert*-butylchlorophosphine (4.34 g, 24 mmol) in 30 mL dry ether was added dropwise (~ 30 min) to it. The stirring was continued for a further 1 hr at -78 °C and the mixture was allowed to slowly warm up to room temperature and stirred overnight. To this reaction mixture was added 40 mL of degassed water and the ether phase was separated under N_2 atmosphere. The aqueous phase was extracted with ether (2 × 50 mL). The combined ether solutions were dried over anhydrous Na_2SO_4, filtered under N_2 pressure, and the solvent was removed under vacuum to get brownish-white solid. This was purified by column chromatography in the nitrogen glove box (basic alumina; hexane: ether (10:1) as eluent) to yield 4.46 g (71%) of 6-di-*tert*-butylphosphinomethyl-2,2'-bipyridine (BPy-^{t}PNN) as a white solid.

$^{31}P\{^1H\}$NMR (CD_2Cl_2): 37.57 (s). ^1H NMR (CD_2Cl_2): 1.17 (d, J_{PH} = 11.0 Hz, 18H, $P(C(CH_3)_3)_2$), 3.12 (d, J_{PH} = 3.3 Hz, 2H, P-CH_2), 7.24 (ddd, J_{HH} = 7.5 Hz, J_{HH} = 4.8 H, J_{PH} = 1.2 Hz, 1H, *H*-5'), 7.40 (td, J_{HH} = 7.8 Hz, J_{PH} = 1.0 H, 1H, *H*-5), 7.67 (t, J_{HH} = 7.8 Hz,, 1H, *H*-4), 7.76 (dt, J_{HH} = 7.8 Hz, J_{HH} = 1.8 H, 1H, *H*-4'), 8.14 (br d, J_{HH} = 7.8 Hz, 1H, *H*-3), 8.40 (td, J_{HH} = 8.0 Hz, J_{HH} = 1.0 Hz, 1H, *H*-3'), 8.62 - 8.64 (m, 1H, *H*-6'). $^{13}C\{^1H\}$NMR ($CDCl_3$): 29.61 (s, $P(C(C_aH_3)_3)$, 29.74 (s, $P(C(C_bH_3)_3)$, 31.77 (d, J_{PC} = 24.0 Hz, PCH_2), 31.93 (d, J_{PC} = 21.8, $P(C(CH_3)_3)_2$), 117.72 (s, C-3), 121.04 (s, *C*-3'), 123.38 (s, *C*-5'), 123.85 (d, J_{PC} = 8.4 Hz, *C-5),* 136.75, (s, C-4'), 136.91 (s, C-4), 148.98 (s, C-6'), 154.97 (s, C-2), 156.49 (s, C-2'), 161.43 (d, J_{PC} = 13.8, *C*-6). Assignment of signals was confirmed by DEPT 135, COSY, and HSQC. Anal. Calcd. for $C_{19}H_{27}N_2P$: C, 72.58; H, 8.66. Found: C, 72.75, H, 8.83.

Synthesis of complexes 4 and 3:

[0211]



[0212] Synthesis of RuHCl(CO)(BPy-^{t}PNN) 4: To an oven dried 25 mL pressure vessel equipped with magnetic stirring bar was added ligand, BPy-^{t}PNN (**5**) (157 mg, 0.52 mmol), $RuHCl(CO)(PPh_3)_3$ (476 mg, 0.5 mmol), and 12 mL dry THF in a nitrogen glove box. The flask was sealed and heated at 65 °C for 8 hrs with stirring outside the glove box, then cooled to room temperature to lead to reddish-brown solid. It was reintroduced to the glove box, and the solvent was decanted and the solid thus obtained was washed with ether (3 × 3mL), then dried under vacuum to give pure complex **4** (212 mg, 88%).

[0213] $^{31}P\{^1H\}$NMR (CD_2Cl_2): 107.01 (s). ^1H NMR (CD_2Cl_2): -15.26 (d, $^2J_{PH}$ = 24.6 Hz, 1H, Ru-*H*), 1.27 (d, J_{PH} = 13.2 Hz, 9H, $P(C(CH_{a3})_3)$, 1.49 (d, J_{PH} = 13.8 Hz, 9H, $P(C(CH_{b3})_3)$, AB system centered at 3.06 and 3.75 (ABq, J_{HH} = 16.8 Hz and J_{PH} = 10.2 Hz, 2H, PCH_aH_b), 7.44 - 7.46 (m, 1H, *H*-5'), 7.57 (d, J_{HH} = 7.8 Hz, 1H, *H*-5), 7.83 - 7.90 (m, 2H, *H*-4 and *H*-4'), 7.97 (d, J_{HH} = 8.1 Hz, 1H, *H*-3), 8.05 (d, J_{HH} = 7.8 Hz, 1H, *H*-3'), 9.12 - 9.15 (br m, 1H, *H*-6'). $^{13}C\{^1H\}$NMR (CD_2Cl_2): 28.63 (d, J_{PC} = 3.8 Hz, $P(C(C_aH_3)_3)$, 29.79 (d, J_{PC} = 4.5 Hz, $P(C(C_bH_3)_3)$, 36.20 (d, J_{PC} = 24.0 Hz, PCH_2), 37.21 (d, J_{PC} = 15.0 Hz, $P(C_a(CH_3)_3)$, 37.27 (d, J_{PC} = 15.8 Hz, $P(C_b(CH_3)_3)$, 119.39 (s, *C*-3), 121.31 (s, *C*-3'), 122.82 (d, J_{PC} = 9.0 Hz, *C*-5), 126.11 (s, *C*-5'), 136.30, (s, *C*-4'), 137.26 (s, *C*-4), 153.19 (s, *C*-6'), 154.80 (s, *C*-2), 155.89 (s, *C*-2'), 161.72 (br d, J_{PH} = 14 Hz, *C*-6), 207.37 (d, J_{PC} = 15.0 Hz, Ru-*C*O). IR (KBr, pellet): 1990 (vRu-H), 1906 (vCO) cm^{-1}. Anal. Calcd. for $C_{20}H_{28}N_2OPClRu$: C, 50.05; H, 5.88. Found: C, 50.28, H, 6.01. MS (ESI, MeOH): 446 (100%, $(M-Cl)^+$). The crystal suitable for a single-crystal X-ray diffraction was obtained from CD_2Cl_2 (20 mg in 0.3 mL) at -32 °C after several days.

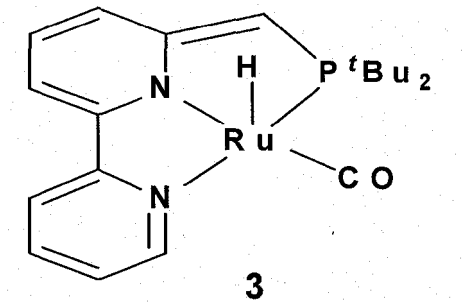
[0214] X-ray Crystal Structure Determination of 4: A crystal was mounted in a MiTeGen loop and flash frozen in a nitrogen stream at 120K. Data were collected on a Nonius Kappa CCD diffractometer mounted on a FR590 generator equipped with a sealed tube with Mo$K\alpha$ radiation (λ = 0.71073 Å) and a graphite monochromator. The structure was solved using direct methods with SHELXS-97 based on F^2.

[0215] Complex 4: $C_{20}H_{28}N_2OPClRu$, Orange, prism, 0.16 ×0.16 × 0.12 mm^3, monoclinic, $P2_1/c$, a = 8.1380(2) Å, b = 14.3161(2) Å, c = 17.5802(3) Å, β = 92.253(1) deg., V = 2046.59(7) $Å^3$, Z = 4, fw = 479.93, D_c = 1.558 Mg/m^3, μ = 0.986 mm^{-1}. Full matrix least-squares of refinement based on F^2 gave an agreement factor R = 0.0326 for data with $I>2\sigma(I)$ and R = 0.0435 for all data (4691 reflections) with a goodness-of-fit of 0.994. Idealized hydrogen atoms were

placed and refined in the riding mode, with the exception of the hydride ligand H1-Ru, which was located in the difference map and refined independently.

Synthesis of [RuH(CO)(BPy-^{t}PNN*)] 3.

[0216]



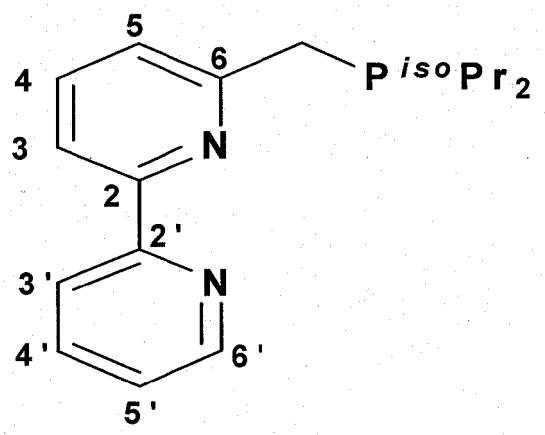
(a) To a suspension of complex **4** (48 mg, 0.1 mmol) in dry THF (5 ml) in a nitrogen glove box was added KO^{t}Bu (11.2 mg, 0.1 mmol) at *ca.*-32 °C and the mixture was stirred at -32 °C for 3 hrs and the solvent was removed under vacuum. The product was extracted using a benzene: pentane (3:7) mixture (3 x 5mL) and passed through celite. The resulting solution was concentrated under vacuum to *ca.* 0.5 mL and 5 mL pentane was added to cause precipitation of a greenish-block solid, which was filtered and washed with pentane (3 × 2mL), then dried under vacuum (42 mg, 94%).

(b) 9.6 mg. of RuHCl(CO)(BPy-^{t}PNN) **4** (0.02 mmol) were placed in to a J.Young NMR tube, dissolved in ~0.4 mL of C_6D_6 and 1 eq. of potassium bis(trimethylsilyl)amide (KHMDS, 4.0 mg) was added to generate dark-green/black complex **3.** The resulting complex **3** exhibits a broad singlet at 92.70 in $^{31}P\{^1H\}$NMR, and the hydride ligand appears as broad doublet at-25.73 ppm ($^2J_{PH}$ = 23 Hz) in the ^{1}HNMR spectrum.

$^{31}P\{^1H\}$NMR (THF-*d*; 202 MHz): 95.64 (s). ^{1}H NMR (THF-*d*; 500 MHz): -20.93 (d, $^2J_{PH}$ = 25.0 Hz, 1H, Ru-*H*), 1.25 (d, J_{PH} = 13.0 Hz, 9H, P(C(CH_{a3})$_3$), 1.28 (d, J_{PH} = 12.5 Hz, 9H, P(C(CH_{b3})$_3$), 3.36 (s, 1H, =C*H*P), 6.00 (d, 1H, *H*-3), 6.12 (d, J_{HH} = 9.0 Hz, 1H, *H*-5), 6.37 (d, J_{HH} = 8.0 Hz, 1H, *H*-4), 7.19 (t, J_{HH} = 6.0 Hz, 1H, *H*-5'), 7.65 - 7.71 (m, 2H, *H*-3' and *H*-4'), 8.89 - 8.90 (br m, 1H, *H*-6'). $^{13}C\{^1H\}$NMR (THF-*d*; 125 MHz): 30.09 (d, J_{PC} = 5.0 Hz, P(C(C_aH$_3$)$_3$), 30.19 (d, J_{PC} = 3.8 Hz, P(C(C_bH$_3$)$_3$), 36.20 (d, J_{PC} = 22.5 Hz, P(C_a(CH$_3$)$_3$), 37.45 (d, J_{PC} = 27.5 Hz, P(C_b(CH$_3$)$_3$), 66.56 (d, J_{PC} = 48.8 Hz, =CHP), 99.87 (s, *C*-3), 117.64 (d, J_{PC} = 17.5 Hz, *C*-5), 121.47 (s, *C*-3'), 124.60, (s, *C*-5'), 131.81 (s, *C*-4), 136.92 (s, *C*-4'), 153.21 (s, *C*-6'), 155.06 (s, *C*-2), 161.55 (s, *C*-2'), 168.97 (d, J_{PC} = 16.3 Hz, *C*-6), 208.1 (d, J_{PC} = 13.8 Hz, Ru-*C*O). Assignment of signals was confirmed by DEPT 135, COSY, and HSQC. IR (KBr, pellet): 2017 (vRu-H), 1907 (vCO) cm^{-1}. Anal. Calcd. for $C_{20}H_{27}N_2OPRu$: C, 54.17; H, 6.14. Found: C, 54.32, H, 6.37. MS (ESI, CH_3CN): 445 (100%, (M+1)$^+$).

Synthesis of 6-di-*iso*-propylphosphinomethyl-2,2'-bipyridine (BPy-^{iso}(Pr)PNN) 6:

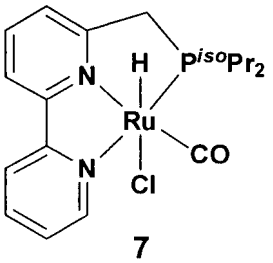
[0217] To an oven dried 50 mL pressure vessel equipped with magnetic



6

stirring bar was added 6-chloromethyl-2,2'-bipyridine (BPy-CH_2Cl) (1.03 g, 5.00 mmol), di-*iso*-propyl phosphine (710 mg, 6.00 mmol), and 15 mL MeOH in nitrogen glove box. The flask was sealed and heated at 50 °C for 48 hrs with stirring outside the glove box. After cooling, it was reintroduced to the glove box, triethylamine (910 mg, 9.00 mmol) was added and the reaction mixture was stirred at room temperature for 1 hr. The solvents were removed under reduced pressure to obtain a white solid. The residue was washed with ether (2 × 10 mL), filtered and was removed under reduced pressure to yield a pale yellow liquid. It was further purified by basic alumina chromatography under the glove box using hexane as an eluent to yield pure **6.**

[0218] Yield = 874 mg (61 %). $^{31}P\{^1H\}$NMR (CD_2Cl_2): 15.84 (s). ^1H NMR (CD_2Cl_2): 1.11 (dd, J_{PH} = 13.8 Hz, J_{HH} = 7.2 Hz, 6H, P(CH(CH_{a3})$_2$), 1.17 (dd, J_{PH} = 14.4 Hz, J_{HH} = 7.2 Hz, 6H, P(CH(CH_{b3})$_2$), 1.89 (sep d, J_{HH} = 7.2 Hz, J_{PH} = 2.1 Hz, 2H, P(C*H*(C$H_{a/b3}$)$_2$), 3.12 (d, J_{PH} = 1.8 Hz, 2H, P-CH_2), 7.28 - 7.34 (m, 1H, *H*-5'), 7.33 (d merged with m, 1H, J_{HH} = 7.8 Hz, *H*-5), 7.73 (t, J_{HH} = 7.8 Hz,, 1H, *H*-4), 7.82 (dt, J_{HH} = 7.8 Hz, J_{HH} = 1.8 H, 1H, *H*-4'), 8.21 (d, J_{HH} = 7.8 Hz, 1H, *H*-3), 8.46 (br d, J_{HH} = 8.1 Hz, 1H, *H*-3'), 8.67 - 8.69 (m, 1H, *H*-6'). $^{13}C\{^1H\}$NMR (CD_2Cl_2): 18.89 (d, J_{PC} = 10.5 Hz, P(C(C_aH$_3$)$_2$), 19.62 (d, J_{PC} = 15.0 Hz, P(C(C_bH$_3$)$_2$), 23.62 (d, J_{PC} = 15.0 Hz, P*C*H$_2$), 32.45 (d, J_{PC} = 22.5, P(*C*(C$_{a/b}$H$_3$)$_2$), 117.63 (s, *C*-3), 120.77 (s, *C*-3'), 123.50 (s, *C*-5'), 123.60 (s, *C-5*), 136.68, (s, *C*-4'), 136.90 (s, *C*-4), 149.06 (s, *C*-6'), 155.18 (s, *C*-2), 156.38 (s, *C*-2'), 161.34 (d, J_{PC} = 9.0, *C*-6). Assignment of signals was confirmed by DEPT 135. Anal. Calcd. for $C_{17}H_{23}N_2P$: C, 71.30; H, 8.10. Found: C, 71.52, H, 8.34.



7

[0219] Synthesis of RuHCl(CO)(BPy-*iso*(Pr)PNN) 7: To a suspension of RuHCl(CO)(PPh_3)$_3$ (476 mg, 0.5 mmol) in dry THF (12 ml) in a nitrogen glove box was added ligand, BPy-*iso*(Pr)PNN (**6**) (143 mg, 0.5 mmol), and the mixture was stirred for overnight at room temperature to obtain reddish-brown solid. The solvent was decanted and the solid thus obtained was washed with pentane (3 × 5 mL), then dried under vacuum to give pure complex **7** (206 mg, 91%).

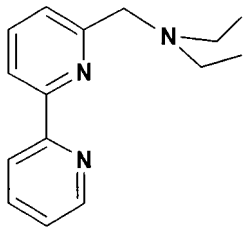
$^{31}P\{^1H\}$ NMR (see below) of complex shows a singlet at 95.38 ppm. The ^1H NMR spectrum of the complex exhibits a doublet resonance at -15.26 ppm ($^2J_{PH}$ = 24.6 Hz) for Ru-H. The "arm" methylene protons give rise ABq system centered at 3.65 and 3.77 ppm with J_{HH} = 17.4 Hz and J_{PH} = 10.2 Hz. The BPy-C6'H appears as multiplet at 9.18 - 9.26 ppm, representing an upfield shift of *ca.* 0.53 ppm relative to the corresponding proton of the ligand (8.67 - 8.69 ppm), upon complexation with ruthenium.

$^{31}P\{^1H\}$NMR (CD_2Cl_2): 95.38 (s). ^1H NMR (CD_2Cl_2): -14.75 (d, J_{PH} = 23.7 Hz, 1H, Ru-*H*), 0.95 (dd, J_{PH} = 15.3 Hz, J_{HH} = 6.9 Hz, 3H, P(CH(CH_{a3})$_2$), 1.12 (dd, J_{PH} = 17.1 Hz, J_{HH} = 6.9 Hz, 3H, P(CH(C$H_{a'3}$)$_2$), 1.38 (dd, J_{PH} = 13.2 Hz, J_{HH} = 7.2 Hz, 3H, P(CH(CH_{b3})$_2$), 1.49 (dd, J_{PH} = 16.8 Hz, J_{HH} = 7.2 Hz, 3H, P(CH(C$H_{b'3}$)$_2$), 2.16 - 2.33 (m, 1H, P(C*H*(CH$_{a,a'3}$)$_2$),

2.66 - 2.82 (m, 1H, P(C*H*($CH_{b,b'3}$)$_2$), AB system centered at 3.65 and 3.77 (ABq, J_{HH} = 17.4 Hz and J_{PH} = 10.2 Hz, 2H, PCH_aH_b), 7.44 - 7.48 (m, 1H, *H*-5'), 7.53 (d, J_{HH} = 7.8 Hz, 1H, *H*-5), 7.83 - 7.94 (m, 2H, *H*-4 and *H*-4'), 7.97 (d merged with m, J_{HH} = 8.1 Hz, 1H, *H*-3), 8.06 (d, J_{HH} = 8.1 Hz, 1H, *H*-3'), 9.18 - 9.26 (br m, 1H, *H*-6'). ^{13}C{^{1}H}NMR (CD_2Cl_2): 17.35 (d, J_{PC} = 4.5 Hz, P(C(C_aH$_3$)$_2$), 18.21 (s, P(C($C_{a'}$H$_3$)$_2$), 19.24 (d, J_{PC} = 5.3 Hz, P(C(C_bH$_3$)$_2$), 20.15 (d, J_{PC} = 4.5 Hz, P(C($C_{b'}$H$_3$)$_2$), 24.58 (d, J_{PC} = 29.3 Hz, P(C_a(CH$_3$)$_2$), 28.12 (d, J_{PC} = 24.0 Hz, P(C_b(CH$_3$)$_2$), 40.94 (d, J_{PC} = 21.8 Hz, PCH_2), 119.63 (s, *C*-3), 122.59 (s, *C*-3'), 122.80 (d, J_{PC} = 9.8 Hz, *C*-5), 126.00 (s, *C*-5'), 136.25, (s, *C*-4'), 137.02 (s, *C*-4), 153.06 (s, *C*-6'), 154.47 (s, *C*-2), 155.99 (s, *C*-2'), 161.11 (d, J_{PC} = 4.5, *C*-6). 207.31 (d, J_{PC} = 15.0 Hz, Ru-*C*O). IR (KBr, pellet): 1962 (vRu-H), 1915 (vCO) cm^{-1}. Anal. Calcd. for $C_{18}H_{24}N_2OPClRu$: C, 47.84; H, 5.35. Found: C, 48.01, H, 5.54.

Synthesis of 6-(N,N-diethyl)aminomethyl-2,2'-bipyridine (BPy-NNN) 8:

[0220]

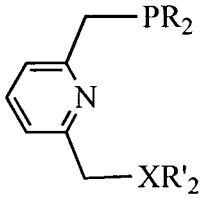


8

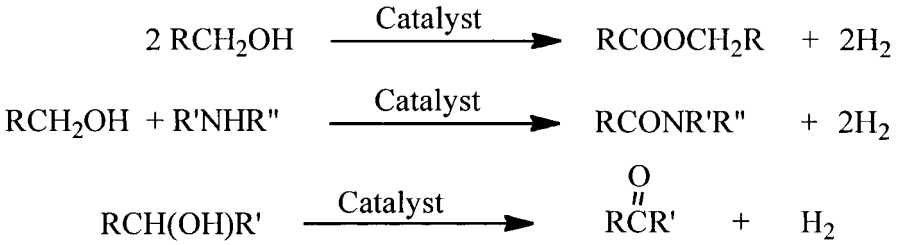
[0221] A solution of 6-chloromethyl-2,2'-bipyridine (BPy-CH_2Cl) in 20 mL of dry THF was cooled to 0 °C and a solution diethylamine (5 mL) in THF (10 mL) was added to it dropwise over 10 min. The mixture was allowed to slowly warm up to room temperature and refluxed under N_2 for 6 hrs. The solvent was removed under vacuum and the residue was dissolved in 50 mL of diethyl ether and washed with 2 × 10 mL of a 10 % aqueous KOH solution. The organic phase was separated and dried over Na_2SO_4 and the ether was removed under vacuum. The residue was purified by flash chromatography (silica gel; EtOAc: Hexane as eluent), yielding (78% yield) 6-(N,N-diethyl)aminomethyl-2,2'-bipyridine (BPy-NNN) **8** as a yellow-brown oil.
^{1}H NMR ($CDCl_3$): 1.15 (t, J_{HH} = 7.2 Hz, 6H, N(CH_2CH_3)$_2$), 2.70 (q, J_{HH} = 7.2 Hz, 4H, N(CH_2CH$_3$)$_2$), 7.28 - 7.32 (m, 1H, *H*-5'), 7.54 (d, J_{HH} = 7.8 Hz, 1H, *H*-5), 7.77 - 7.84 (m, 2H, *H*-4 and *H*-4'), 8.26 (d, J_{HH} = 8.1 Hz, 1H, *H*-3), 8.41 (br d, J_{HH} = 8.1 Hz, 1H, *H*-3'), 8.67 - 8.69 (m, 1H, *H*-6'). ^{13}C{H}NMR ($CDCl_3$): 11.69 (s, N(CH_2CH$_3$)$_2$), 47.36 (s, N(CH_2CH$_3$)$_2$), 58.81 (s, Arm-CH_2), 119.33 (s, *C*-3), 121.17 (s, *C*-3'), 123.26 (s, *C*-5'), 123.58 (s, *C*-5), 136.87, (s, *C*-4'), 137.33 (s, *C*-4), 149.14 (s, *C*-6'), 155.34 (s, *C*-2), 156.33 (s, *C*-2'), 158.68 (br s, *C*-6). Assignment of signals was confirmed by DEPT 135. Anal. Calcd. for $C_{15}H_{19}N_3$: C, 74.65; H, 7.94. Found: C, 74.81, H, 8.08.

Example 9 - Borohydride Complexes

[0222] As contemplated herein, certain reactions described herein, such as novel ester synthesis, novel amide synthesis, as well as the dehydrogenation of secondary alcohols to ketones, and hydrogenation of esters to alcohols, can be effectively accomplished also with stable, readily synthesized PNN- and PNP Ru borohydride complexes, in absence of base, under neutral conditions, and in absence of hydrogen acceptor.



^{t}Bu-PNP: R = R' = Bu^t, X = P;
PNN : R = Bu^t, R' = Et, X = N;
^{i}Pr-PNP: R = R' = ^{i}Pr, X = P

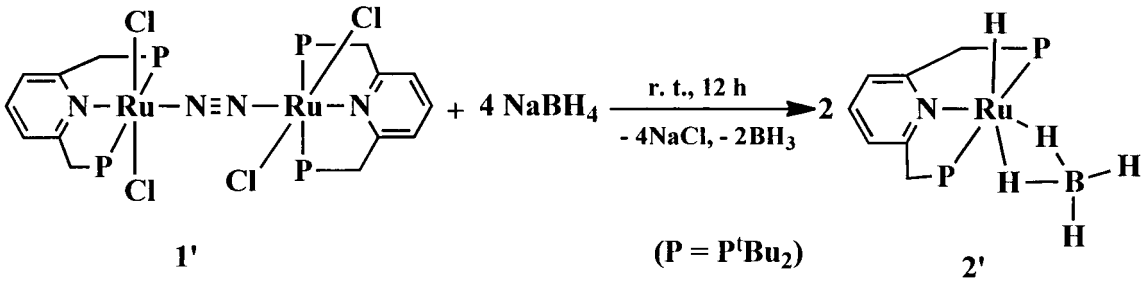


(R, R', R" can be alkyl, aryl, H)

Scheme 30

Synthesis and Characterization of [RuH(η^2-BH$_4$)(^{t}Bu-PNP] 2'

[0223] The N_2-bridged binuclear Ru(II) complex [(^{t}Bu-PNP)RuCl$_2$]$_2$(μ-N$_2$) **1'** was prepared by the reaction of RuCl$_2$(PPh$_3$)$_3$ with one equivalent of ^{t}Bu-PNP (Zhang et al. 2004). Treatment of **1'** with an excess (5 equiv) of NaBH$_4$ in 2-propanol for 12 hrs resulted in formation of the Ru(II) hydrido borohydride complex **2'** in almost quantitative yield (by NMR) (Scheme 25). The ^{31}P{^{1}H} NMR spectrum of **2'** exhibits a singlet peak at 86.3 ppm, representing a downfield shift of 21 ppm relative to **1'** (65.0 ppm). In the ^{1}H NMR spectrum, the hydride ligand gives rise to a triplet peak at -16.09 ppm with J_{PH} = 18.0 Hz. In addition, two broad signals are observed for the two bridging hydrides at -16.01 and -4.48 ppm and another broad feature at 5.49 ppm belonging to the terminal boron hydrides. The IR spectrum of **2'** indicates two strong bands in the terminal B-H region at 2395 and 2327 cm^{-1} and two bands in the bridging M-H-B region at 2104 and 2024 cm,$^{-1}$ consistent with the bidentate η^2-BH$_4$ binding mode (Marks et al.).



Scheme 31

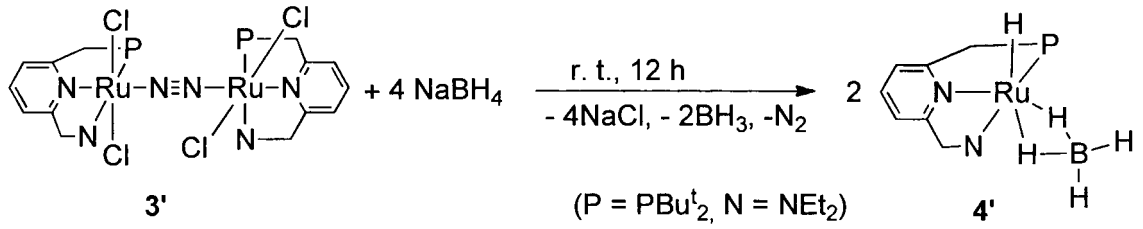
[0224] Single crystals suitable for an X-ray diffraction study were obtained by slow evaporation of a pentane solution of **2'** at -32' °C. The crystal structure of **2'** (Fig. 3) displays a distorted octahedral geometry around the ruthenium center, including the ^{t}Bu-PNP, hydride and BH$_4$ units. The hydride ligand is bound to the Ru center *cis* to the pyridine nitrogen (N1-Ru1-Hru, 81 (2)°), while the BH$_4$ unit is coordinated to Ru(II) center in a $\eta^{2'}$ mode. The two Ru-H bonds to the chelating BH$_4$ unit are not equal (1.67(5) and 1.85(6) Å, respectively), while the corresponding Ru-H bonds in the structure of RuH(BH$_4$)(PMe$_3$)$_3$ (Statler et al.) are of equal length. The difference in the case of **2'** is a result of the larger *trans* effect of hydride relative to that of the pyridinic nitrogen atom. Because of the meridional coordination geometry of the ^{t}Bu-PNP framework and lack of a plane of symmetry involving the P, N, P atoms, the protons of the four *tert*-butyl and two methylene groups are magnetically inequivalent.

Table 22. Selected Bond Distances (Å) and Angles (deg) of Complex 2'

Ru1 - N1	2.123 (3)	Ru1 - P1	2.311 (1)
Ru1 - P2	2.322 (1)	Ru1 - HRu	1.57 (5)
Ru1 - HB2	1.67 (5)	Ru1-HB4	1.85 (6)
N1 - Ru1 - HRu	81 (2)	HRu - Ru1 - HB4	166 (2)
P1 - Ru1 - P2	159.6 (1)	HB2 - Ru1 - N1	177 (2)
N1 - Ru1 - P2	83.0 (1)	P1 - Ru1 - N1	82.5 (1)
P2 - Ru1 - HRU	79 (2)	HRU - Ru1 - P1	85 (2)
HB2 - Ru1 - HB4	70 (2)	HB3 - B1 - HB1	113 (3)
HB2 - B1 - HB4	104 (3)		

Synthesis and Characterization of [RuH(η^2-BH_4)(PNN)] 4'

[0225] The N_2-bridged binuclear Ru(II) complex [($RuCl_2$(PNN))$_2$](μ-N_2) **3'** was prepared by the reaction of $RuCl_2(PPh_3)_3$ with one equivalent of PNN, employing a similar method to the one used for the preparation of **1.** Treatment of **3'** with an excess (5 equiv) of $NaBH_4$ in 2-propanol for 12 hrs resulted in the formation of the ruthenium(II) hydrido borohydride complex **4'** in excellent yield as indicated by $^{31}P\{^1H\}$ NMR spectroscopy (Scheme 26). The $^{31}P\{^1H\}$ NMR spectrum of **4'** shows a singlet peak at 116.7 ppm, representing a downfield shift of 29 ppm relative to **3'.** The hydride ligand gives rise to a doublet at -16.24 ppm with J_{PH} = 28.0 Hz in the ^1H NMR spectrum. The IR spectrum of **4'** exhibits two strong bands in the terminal B-H region at 2378 and 2311 cm^{-1} and two bands in the bridging M-H-B region at 2096 and 1956 cm,$^{-1}$ similar to the IR spectrum of complex **2',** consistent with the bidentate η^2-BH_4 binding mode (Marks et al.).



Scheme 32

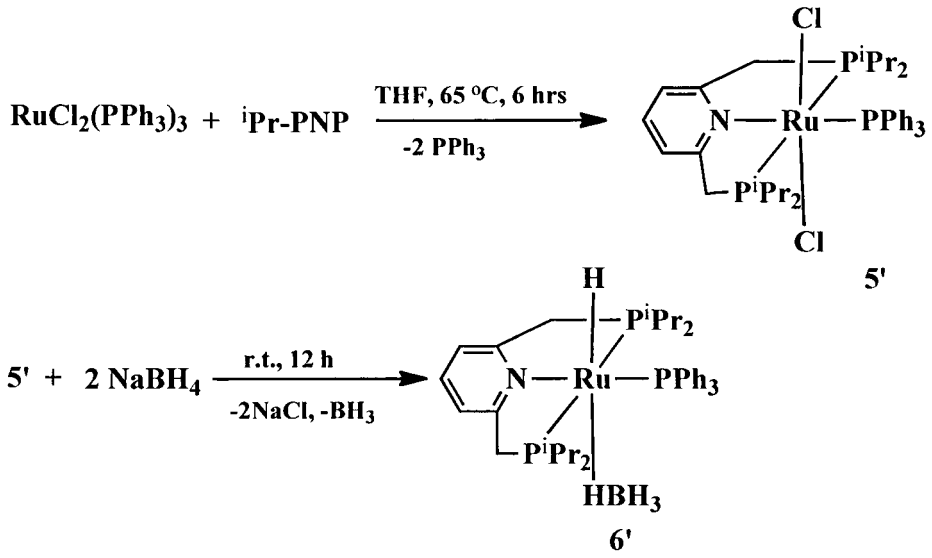
[0226] At room temperature, one broad singlet peak at -13.01 ppm is observed in the ^1H NMR spectrum of **4'** for one proton of BH_4^-. A variable-temperature ^1H NMR study of **4'** in toluene-d_8 is shown in Fig. 2, revealing interesting fluxional behavior of the BH_4^- ligand. At 213K, two singlets are observed at -13.21 and -4.33 ppm for the bridging hydrides and two broad singlets at 4.70 and 5.13 ppm for the two terminal hydrides of the BH_4^- ligand, respectively. Upon raising the temperature to 248K, the signals for the two terminal hydrides coalesce while the signal at -4.33 ppm collapses. At 263K, the signals (~ 5 ppm) for the two terminal hydrides and the signal at -4.33 ppm for one bridging hydride disappear in the baseline and the signal (-13.21 ppm) of another bridging hydride also collapses. Upon temperature increase to 323K, the resonance at -13.21 ppm also disappears into the baseline. Upon raising the temperature to 353K, a very broad singlet peak appears at -2 ppm, indicating that the four hydrides of BH_4^- start to coalesce. The signal of the terminal Ru-H ligand appears as a doublet peak throughout the 213-373K temperature range, indicating that it does not participate in the fluxional process of the BH_4^- ligand. These variable-temperature ^1H NMR spectra of complex **4'** are similar to those reported for the complexes RuH(BH_4)$(PMe)_3$ (Statler et al.) and RuH(BH_4)(ttp) (ttp = $PhP(CH_2CH_2CH_2PPh_2)_2$) (Letts et al.). The bridging hydride (-4.33 ppm) *trans* to the terminal Ru-H exchanges positions with the two terminal hydrides on the boron at 263K. These hydrogen atoms further exchange with the bridging hydride (-13.21 ppm) *trans* to pyridinic nitrogen above 323K and the calculated coalescence frequency at -2.0 ppm was observed at 353K.

Synthesis and Characterization of [$RuCl_2(PPh_3)$(^{i}Pr-PNP)] 5 and [RuH(η^1-BH_4)(PPh_3)(^{i}Pr-PNP)] 6'.

[0227] Heating of $RuCl_2(PPh_3)_3$ with one equivalent of ^{i}Pr-PNP (^{i}Pr-PNP = 2,6-bis(di-iso-propylphosphinomethyl)pyridine) in THF at 65 °C for 6 hrs resulted in formation of the PPh_3 complex **5'** in 75% yield (Scheme 27). The $^{31}P\{^1H\}$ NMR spectrum of **5'** exhibits one doublet at 46.4 ppm and one triplet peak at 43.2 ppm, indicating that triphenylphosphine

is coordinated to the Ru(II) center, as observed also with the reported Ph-PNP-Ru(II) dichloride complex (Ph-PNP = 2,6-bis(diphenylphosphinomethyl)pyridine) (Jia et al.). In contrast, the ^{t}Bu complexes **1'** and **3'** do not contain coordinated PPh_3, under similar preparation conditions, probably because of the steric bulk of the *tert*-butyl group of ^{t}Bu-PNP and PNN ligands. The two methylene groups of ^{i}Pr-PNP give rise to one triplet peak at 3.92 ppm with J_{PH}= 4.0 Hz, indicating the existence of a symmetric plane involving the P, N, P atoms. The PPh_3 ligand is coordinated to the Ru(II) center *trans* to the nitrogen atom of ^{i}Pr-PNP and the chloride ligands are coordinated to metal center *trans* to each other.

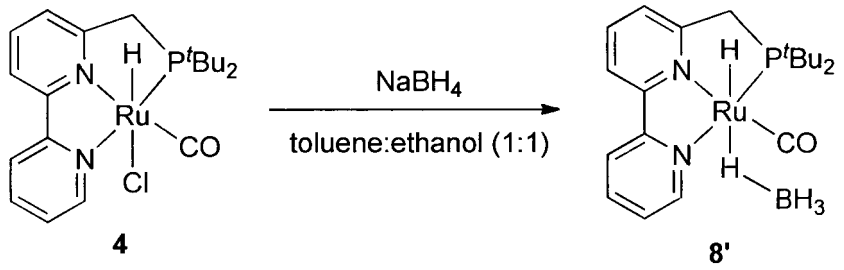
[0228] In analogy to the preparation of complexes **2'** and **4',** treatment of complex **5'** with excess (2.5 equiv) of $NaBH_4$ in isopropanol at room temperature resulted in precipitation of the Ru(II) hydrido borohydride complex **6'** as a yellow solid in 85 % yield (Scheme 27). The $^{31}P\{^{1}H\}$ NMR spectrum of **6'** exhibits a doublet signal at 61.6 ppm and a triplet signal at 67.9 ppm, corresponding to the two phosphorus atoms of ^{i}Pr-PNP and one phosphorus atom of PPh_3, respectively. It is noted that the signal of the PPh_3 ligand of **6'** is downfield shifted relative to that of ^{i}Pr-PNP, unlike the corresponding signals of complex **5.** The Ru-H gives rise in the ^{1}H NMR of **6'** to a quartet signal at -14.00 ppm with J_{PH} = $J_{P'H}$ = 28.0 Hz. A broad peak at -0.84 ppm is assigned to the four protons of the BH_4 ligand, which is probably coordinated to the Ru(II) center in a η^1 mode, similar to the reported bonding of ruthenium borohydride complexes by Ohkuma et al. and Guo et al. The IR spectrum of **6'** exhibits strong absorptions at 2361, 2292 and a strong broad peak at 1884 cm,$^{-1}$ consistent with the monodentate η^1-BH_4 bonding mode (Marks et al.).



Scheme 33

Synthesis of Borohydride Complex 8'

[0229]



Scheme 34

[0230] RuHCl(CO)(BPy-^{t}PNN) complex **4** (82 mg, 0.17 mmol) and $NaBH_4$ (32 mg, 0.85 mmol) were placed in a 20 mL Schlenk flask equipped with a Teflon-coated magnetic stirring bar. A 1:1 mixture of toluene and ethanol (4 mL) was added to the flask. It was then stirred at 65 °C for 5 min (to get homogeneous solution) then at room temperature for 2 hr to give a reddish yellow solution. The solvent was removed *in vacuo.* The resulting residue was dissolved in CH_2Cl_2

(6 mL) and the remaining insoluble materials were removed by filtration through a Celite pad (0.5 g). The filtrate was concentrated to *ca.* 0.5 mL and 5 mL of pentane was added to cause precipitation of a orange-yellow solid, which was filtered and dried under vacuum to give 72 mg (92%) of analytically pure RuH(CO)(η^1BH4)BPy-^{t}PNN) complex **8'.** ^{31}P{^{1}H}NMR (202 MHz, CD_2Cl_2): 110.67 (s). ^{1}H NMR (500 MHz, CD_2Cl_2): -12.27 (d, $^2J_{PH}$ = 21.5 Hz, 1H, Ru-*H*), -2.34 - -1.90 (br d, 4 H, Ru-HBH_3), 1.31 (d, J_{PH} = 13.0 Hz, 9H, P(C(CH_{a3})$_3$), 1.43 (d, J_{PH} = 13.5 Hz, 9H, P(C(CH_{b3})$_3$), ABX system centred at 3.62 and 3.69 (2H, PCH_aH_b), 7.41 - 7.43 (m, 1H, *H*-5'), 7.56 (d, J_{HH} = 8.0 Hz, 1H, *H*-5), 7.85 - 7.89 (m, 2H, *H*-4 and *H*-4'), 7.96 (d, J_{HH} = 7.5 Hz, 1H, *H*-3), 8.04 (d, J_{HH} = 8.0 Hz, 1H, *H*-3'), 9.12 - 9.13 (br m, 1H, *H*-6'). ^{13}C{^{1}H}NMR (125 MHz, CD_2Cl_2): 28.43 (d, J_{PC} = 3.8 Hz, P(C(C_aH_3)$_3$), 29.63 (d, J_{PC} = 3.8 Hz, P(C(C_bH_3)$_3$), 35.87 (d, J_{PC} = 16.3 Hz, P($C_{a/b}$(CH_3)$_3$), 37.34 (d, J_{PC} = 16.3 Hz, PCH_2), 119.26 (s, *C*-3), 121.16 (s, *C*-3'), 122.53 (d, J_{PC} = 8.8 Hz, *C*-5), 125.71 (s, *C*-5'), 135.97, (s, *C*-4'), 137.07 (s, *C*-4), 153.69 (s, *C*-6'), 154.79 (br s, *C*-2), 155.91 (s, *C*-2'), 163.95 (d, J_{PC} = 3.78 Hz, *C*-6), 206.90 (br d, J_{PC} = 15 Hz, Ru-*C*O). IR (KBr disc, CH_2Cl_2): 2313 (B-H stretching), 1988 (Ru-H stretching), 1046 (BH_3 deformation), 1019 (BH_3 deformation). Assignment of signals was confirmed by DEPT 135, COSY, and HSQC.

Dehydrogenation of Alcohols Using Complexes 2', 4', 6' and 8' as Catalysts.

[0231] As some of the inventors of the present invention have demonstrated (Zhang 2004, Zhang 2005), PNP and PNN Ru(II) complexes catalyze the dehydrogenation of secondary alcohols to ketones and primary alcohols to esters. It has now been discovered that the ruthenium hydrido borohydride complexes of **2', 4',** and **6'** and **8'** catalyze the dehydrogenation of alcohols under base-free conditions and in absence of hydrogen acceptors. Indeed, when complex **2'** was heated with 1000 equivalents of 1-phenyl-1-ethanol in toluene for 24 hrs, 28.6% of the alcohol were converted to acetophenone, accompanied by the evolution of hydrogen gas (Table 23, entry 1). Similarly, upon heating of 1-phenyl-1-ethanol with 0.1 % **4'** or **6'** in toluene for 24 hrs, acetophenone was formed in 86.5 % and 76.5 % yield, respectively (Table 23, entry 2 and 3), indicating that the catalytic activity of **4'** was significantly higher than that of complexes **2'** and **6',** probably as a result of the potentially "hemilabile" amine arm of **4',** which can play an important role in the catalytic cycle (Zhang 2005). A longer reaction time resulted in a higher yield of the ketone (Table 23, entry 4). Other secondary alcohols can also be dehydrogenated to the corresponding ketones using **4'** as catalyst in good yields (Table 23, entries 5-8). The catalysis by **4'** was quite sensitive to the reaction temperature, and when 2-propanol was heated at 83 °C with 0.1 % **4',** acetone was formed in only 12.6 % yield after 48 hrs (TON = 126), while when heated in toluene at 105 °C, 89.9 % of acetone were formed during the same reaction period (TON = 899).

Table 23. Dehydrogenation of secondary alcohols to the corresponding ketones with complexes **2', 4', 6'** as catalysts

entry	Cat.	Alcohol	Temp. (°C)	Time (h)	Conversion (%)	Yield of ketone (%)[a]
1	**2'**	1-phenyl-1-ethanol	115	24	28.6	28.6
2	**4'**	1-phenyl-1-ethanol	115	24	86.5	86.5
3	**6'**	1-phenyl-1-ethanol	115	24	77	76.5
4	**4'**	1-phenyl-1-ethanol	115	48	93	93
5	**4'**	2-hexanol	115	48	83.2	83
6	**4'**	2-butanol	110	48	88.8	88.7
7	**4'**	cyclohexanol	115	48	56.5	56.5
8	**4'**	2-propanol	105	48	90	89.9
9	**4'**	2-propanol	83[b]	48	12.6	12.6

(a) reaction conditions: catalyst 0.01 mmol, alcohol 10 mmol, toluene 2 mL, reflux under argon flow (b) reflux in neat 2-propanol under argon.

[0232] In comparison to the dehydrogenation of secondary alcohols to the corresponding ketones, homogeneous systems capable of dehydrogenation of primary alcohols to the corresponding aldehydes or esters are very rare (Zhang 2005, Murahashi et al., Blum et al., Lin et al. and Zhao et al), probably because of decarbonylation of the product (or intermediate) aldehyde to form an inactive carbonyl complex.

[0233] When a toluene solution of benzyl alcohol and 0.1% complex **2'** was refluxed for 24 hrs in an open system, benzyl benzoate was formed in 70% yield, accompanied by a small amount of benzaldehyde (4%) (Table 24, entry 1).

Refluxing 1-hexanol with 0.1% **2** in toluene (115 °C) or neat (157 °C) for 24 hrs resulted in formation of 60 -70% of hexyl hexanoate, accompanied by 2.5 -10 % hexanal (Table 24, entries 2 and 3). Complex **6'** was slightly less catalytically active than **2** (Table 24, entry 7). The PNN complex **4'** exhibited significantly higher catalytic activity than that of the PNP complexes **2'** and **6';** benzyl alcohol, 1-hexanol and 1-butanol were dehydrogenated to the corresponding esters in over 90% yield after heating with 0.1% **4'** in toluene (Table 24, entry 4-6).

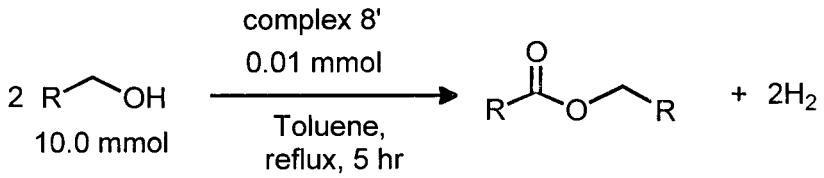
Table 24. Dehydrogenation of primary alcohols to esters and aldehydes with complexes **2', 4', 6'** as catalysts

entry	Cat.	Alcohol	Temp. (°C)	Conversion (%)	Yield of Aldehyde (%)	Yield of ester (%)[a]
1	**2'**	benzyl alcohol	115	75	4	70
2	**2'**	1-hexanol	115	72	2.5	69
3	**2'**	1-hexanol	157[a]	70	10	59.4
4	**4'**	benzyl alcohol	115	99	0	99
5	**4'**	1-hexanol	115	94	0	94
6	**4'**	1-butanol	110	96	0.2	95.5
7	**6'**	benzyl alcohol	115	62	3.4	58.6
8	**6'**	1-hexanol	157[b]	57.5	9.5	47.4

(a) reaction conditions: catalyst 0.01mmol, alcohol 10 mmol and toluene 2 mL heated under reflux for 24 hrs under argon flow (b) reflux in neat 1-hexanol under argon flow

Dehydrogenation of alcohols to esters using complex 8' as catalyst

[0234]



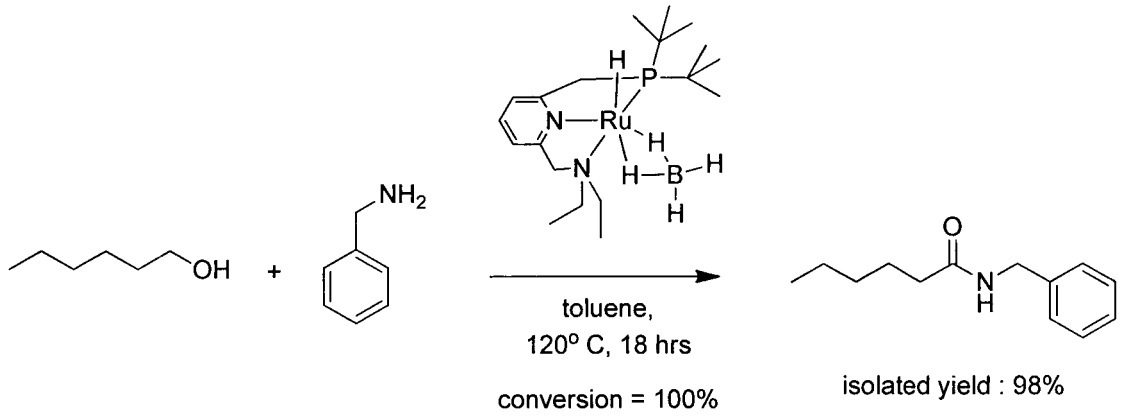
Scheme 35

Table 25. Dehydrogenation of alcohols to esters using complex 8' as catalyst

Entry	Alcohols	Esters	Conv. (%)	Yield (%)[a]
1	1-Hexanol	Hexyl hexanoate	99.8	99.0
2	Benzyl alcohol	Benzyl benzoate	~100	99.3
(a) Complete conversion of alcohol was observed and no formation of aldehyde (by GC).				

Amidation Using Complex 4' as a Catalyst

[0235]

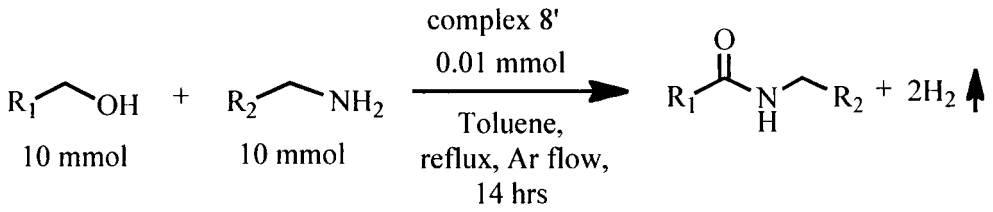


Scheme 36

Complex **4'** (4.4 mg, 0.01 mmol), 1-hexanol (1.02 g, 10 mmol), benzyl amine (1.07 g, 10 mmol) and toluene (3 mL) were taken in a Schlenk flask under an atmosphere of purified nitrogen in a glove box. The flask was equipped with a condenser and the solution was refluxed with stirring in an open system under argon for 18 h. After cooling to room temperature, the consumption of starting materials was checked by GC using a Carboxen 1000 column on a HP 690 series GC system and shows that 100% conversion of the 1-hexanol. To the reaction mixture, hexane (30 mL) was added to precipitate out the *N*-benzylhexanamide as white coloured solid and filtered off the solid to get the pure product in 98% yield.

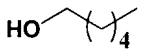
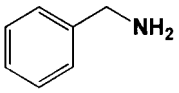
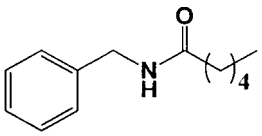
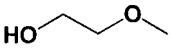
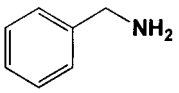
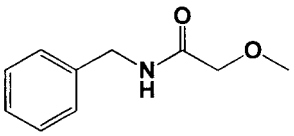
Amidation using complex 8' as catalyst

[0236]



Scheme 37

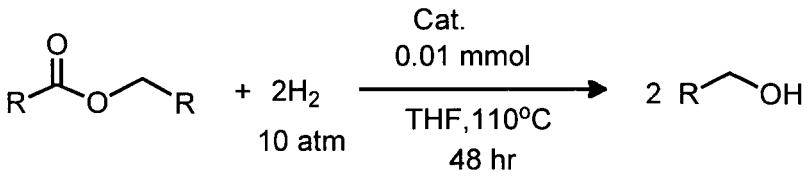
Table 26. Amidation using complex 8' as a catalyst

Entry	Alcohols	Amines	Amides	Yield (isolated)
1				59[a]
3				71[b]

(a) Conversion of alcohol is 87.8%. Other products are Ester (5.2%) and Imine (17%) also formed (by GC).
(b) Conversion of alcohol is 91.1%. Other products are Ester (3.5%) and Imine (12%) also formed (by GC).

Ester hydrogenation using complexes as catalysts

[0237]



Scheme 38

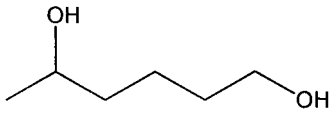
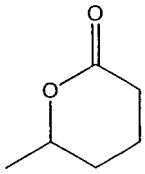
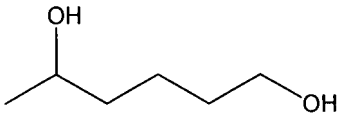
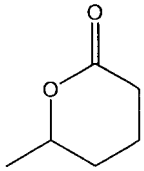
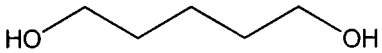
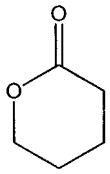
Table 27. Ester hydrogenation

Entry	Cat.	Esters	Alcohols	Conv. (%)	Yield (%)
1	8'	Hexyl hexanoate (2 mmol)	1-Hexanol	99.8	98.9
2	8'	Methyl formate (15 mmol)	MeOH	96.5	94.7
3	4'	Hexyl hexanoate (2 mmol)	1-Hexanol	~100	99.4
4	4'	Butyl butyrate (2 mmol)	1-Butanol	~100	98.0
5	6'	Butyl butyrate (2 mmol)	1-Butanol	9.8	9.0

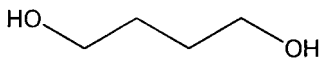
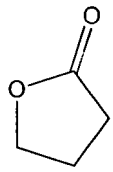
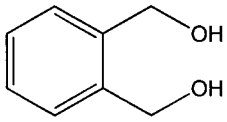
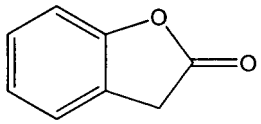
Dehydrogenation of diols to the corresponding lactones catalyzed by complexes 2' **and** 4'[a]

[0238]

Table 28 - Dehydrogenation of esters to lactones

entry	cat.	diol	Lactone yield (%)[b]
1	2'		 **(33)**
2	4'		 **(72)**
3	4'		 **(81)**

(continued)

entry	cat.	diol	Lactone yield (%)[b]
4	4'		 **(86)**
5	4'		 **(90) and 76[c]**

[a]Reaction conditions: catalyst (0.01 mmol), diol (3 mmol) and 2 mL of toluene were refluxed in an open system under argon for 48 hrs. [b]Yields of the lactones were analyzed by ^{1}H NMR of the reaction mixture. [C]Isolated yield.

General procedure for the catalytic dehydrogenation of diols to lactones. Complexes 2' or 4' (0.01 mmol), diol (3 mmol), and toluene (2 mL) were taken in a Schlenk flask under an atmosphere of purified nitrogen in a Vacuum Atmospheres glove box. The flask was equipped with a condenser and the solution was refluxed with stirring in an open system under argon for 48 hrs. After cooling to room temperature, the yield of the lactones was determined by ^{1}H NMR spectroscopy from the reaction mixture. The resulting mixture was concentrated in vacuo for about 3-4 h. The purification was performed on silica gel column using hexane - ethylacetate mixture as eluent. The products were analyzed by ^{1}H NMR and the spectra were identical with the authentic samples.

Example 10: Experimental Section - Borohydride Complexes

General Procedures

[0239] All experiments with metal complexes and phosphine ligands were carried out under an atmosphere of purified nitrogen in a Vacuum Atmospheres glove box equipped with a MO 40-2 inert gas purifier or using standard Schlenk techniques. All solvents were reagent grade or better. All non-deuterated solvents were refluxed over sodium/benzophenone ketyl and distilled under argon atmosphere. Deuterated solvents were used as received. All solvents were degassed with argon and kept in the glove box over 4Å molecular sieves. Complexes 1' and 3' were prepared as reported previously (Zhang 2004, Milstein). ^{i}Pr-PNP (2,-6-bis-(di-iso-propylphosphinomethyl)pyridine) (Jansen et al.), $RuCl_2(PPh_3)_3$, (Holm et al.) were prepared according to literature procedures.

[0240] ^{1}H, ^{13}C and ^{31}P NMR spectra were recorded at 400 or 500, 100 or 126, and 162 or 202 MHz, respectively, using a Bruker AMX-400 and AMX-500 NMR spectrometers. ^{1}H and ^{13}C(^{1}H} NMR chemical shifts are reported in ppm downfield from tetramethylsilane. ^{31}P NMR chemical shifts are reported in parts per million downfield from H_3PO_4 and referenced to an external 85% solution of phosphoric acid in D_2O. Abbreviations used in the NMR follow-up experiments: b, broad; s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet, v, virtual. Elemental analyses were performed at Kolbe Laboratorium, Mulheim, Germany.

Synthesis of [RuH(BH_4)(^{t}Bu-PNP)] 2'.

[0241] To a suspension of complex **1'** (58 mg, 0.05 mmol) in 2-propanol (10 ml) was added a very fine powder of $NaBH_4$ (9.5 mg, 0.25 mmol), and the mixture was stirred at room temperature for 12 hrs. The mixture was filtered and the orange filtrate was taken to dryness under vacuum. The residue was extracted with diethyl ether (3 × 5 mL). The ether solution was evaporated under vacuum to yield complex **2'** as an orange solid. The complex was dried under vacuum overnight. Yield: 50 mg (98%).

^{31}P{^{1}H} NMR (C_6D_6): 86.3 (s); ^{1}H NMR (C_6D_6): -16.09 (t, 1H, J_{PH} = 18.0 Hz, Ru-H), -16.01 (br s, 1H, BH_4), -4.48 (br s, 1H, BH_4), 1.45 (t, 18H, J_{PH} = 6.0 Hz, P(C(CH_3)$_3$)), 1.56 (t, 18H, J_{PH} = 6.0 Hz, P(C(CH_3)$_3$)$_2$), 3.08 (dt, 2H, J_{HH} = 16.0 Hz, J_{PH} = 4.0 Hz, -C*H*HP), 3.19 (dt, 2H, J_{HH} = 16.0 Hz, J_{PH} = 4.0 Hz, -CH*H*P), 5.49 (br s, 2H, BH_4), 6.52 (d, 2H, J_{HH} = 8.0 Hz, pyridine-H3, H5), 6.76 (t, 1H, J_{HH} = 8.0 Hz, pyridine-H4). ^{13}C{^{1}H} NMR (C_6D_6): 29.7 (s, P(CH(*C*H$_3$)$_2$)$_2$), 30.2 (s,

P(C(CH_3)$_3$)$_2$), 35.0 (t, J_{PC} = 6.5 Hz, P(*C*(CH_3)$_3$)$_2$), 35.6 (t, J_{PC} = 5.0 Hz, P(*C*(CH_3)$_3$)$_2$), 39.0 (t, J_{PC} = 7.0 Hz, CH_2P), 118.2 (t, J_{PC} = 4.0 Hz, pyridine-C3, C5), 131.0 (s, Pyridine-C4), 165.1 (t, J_{PC} = 4.5 Hz, Pyridine-C2, C6).
IR (KBr pellets): 2395, 2327, 2104, 2024, 1461, 1184 cm^{-1}.
Anal. Calcd. for $C_{23}H_{48}BNP_2Ru$: C, 53.90; H, 9.45; Found: C. 53.86, H, 9.49.

Synthesis of [RuH(BH_4)(PNN)] 4'.

[0242] To a suspension of complex **3'** (51 mg, 0.05 mmol) in 2-propanol (10 ml) was added a very fine powder of $NaBH_4$ (9.5 mg, 0.25 mmol), and the mixture was stirred at room temperature for 12 hrs. The mixture was filtered and the orange filtrate was taken to dryness under vacuum. The orange solid residue was extracted with diethyl ether (3 × 5 mL). The ether solution was evaporated under vacuum yielding complex **4'** as a red-orange solid, which was dried under vacuum overnight. Yield: 40 mg (91%).
$^{31}P\{^1H\}$ NMR (C_6D_6): 116.7 (s); ^1H NMR (C_6D_6, 298 K): -16.24 (t, 1H, J_{PH} = 28.0 Hz, Ru-H), -13.10 (Br s, 1H, BH_4), 0.84 (t, 3H, J_{HH} = 6.0 Hz, N(CH_2C*H*$_3$)$_2$), 0.99 (t, 3H, J_{HH} = 6.0 Hz, N(CH_2C*H*$_3$)$_2$), 1.28 (d, 9H, J_{PH} = 12.0 Hz, P(C(CH_3)$_3$)), 1.43 (d, 9H, J_{PH} = 12.0 Hz, P(C(CH_3)$_3$)$_2$), 2.31 (m, 1H, N(C*H*$_2$$CH_3$)$_2$), 2.49 (m, 1H, N(C*H*$_2$$CH_3$)$_2$), 2.71 (dd, 1H, J_{HH} = 16.0 Hz, J_{PH} = 8.0 Hz, -C*H*HP), 2.98 (dd, 1H, J_{HH} = 16.0 Hz, J_{PH} = 12.0 Hz, -CH*H*P), 3.05 (m, 1H, N(C*H*$_2$$CH_3$)$_2$), 3.41 (d, 1H, J_{HH} = 14.0 Hz, NCH*H*-py), 3.54 (d, 1H, J_{HH} = 14.0 Hz, NC*H*H-py), 3.73 (m, 1H, N(C*H*$_2$$CH_3$)$_2$), 6.30 (d, 1H, J_{HH} = 8.0 Hz, pyridine-H5), 6.51 (d, 1H, J_{HH} = 8.0 Hz, pyridine-H3), 6.71 (t, 1H, J_{HH} = 8.0 Hz, pyridine-H4). ^1H NMR (Toluene-d_8, 243 K): -16.30 (t, 1H, J_{PH} = 28.0 Hz, Ru-H), -13.21 (Br s, 1H, BH_4), -4.33 (br s, 1H, BH_4), 0.71 (br s, 3H, N(CH_2C*H*$_3$)$_2$), 0.92 (br s, 3H, N(CH_2C*H*$_3$)$_2$), 1.18 (d, 9H, J_{PH} = 12.0 Hz, P(C(CH_3)$_3$)), 1.35 (d, 9H, J_{PH} = 12.0 Hz, P(C(CH_3)$_3$)$_2$), 2.10 (m, 1H, N(C*H*$_2$$CH_3$)$_2$), 2.31 (m, 1H, N(C*H*$_2$$CH_3$)$_2$), 2.53 (dd, 1H, J_{HH} = 16.0 Hz, J_{PH} = 8.0 Hz, -C*H*HP), 2.82 (dd, 1H, J_{HH} = 16.0 Hz, J_{PH} = 8.0 Hz, -CH*H*P), 2.93 (br m, 1H, N(C*H*$_2$$CH_3$)$_2$), 3.15 (d, 1H, J_{HH} = 16.0 Hz, NCH*H*-py), 3.33 (d, 1H, J_{HH} = 16.0 Hz, NC*H*H-py), 3.37 (m, 1H, N(C*H*$_2$$CH_3$)$_2$), 4.69 (br s, 1H, BH_4), 5.00 (br s, 1H, BH_4), 6.16 (d, 1H, J_{HH} = 8.0 Hz, pyridine-H5), 6.38 (d, 1H, J_{HH} = 8.0 Hz, pyridine-H3), 6.62 (t, 1H, J_{HH} = 8.0 Hz, pyridine-H4). $^{13}C\{^1H\}$ NMR (C_6D_6): 8.8 (s, N(CH_2*C*H$_3$)$_2$), 11.0 (s, N(CH_2*C*H$_3$)$_2$), 29.0 (d, J_{PC} = 4.0 Hz, P(C(*C*H$_3$)$_3$)$_2$), 34.2 (d, J_{PC} = 15.1 Hz, P(*C*(CH_3)$_3$)$_2$), 37.0 (d, J_{PC} = 10.0 Hz, P(*C*(CH_3)$_3$)$_2$), 38.9 (d, J_{PC} = 19.1 Hz, PCH_2-), 51.1 (s, N(*C*H$_2$Me)$_2$), 51.2 (s, N(*C*H$_2$Me)$_2$), 63.7 (s, py-CH_2N), 117.5 (s, Py-C3), 118.5 (s, Py-C5), 128.8 (s, Py-C4), 159.9 (s, Py-C6), 163.7 (d, J_{PC} = 4.0 Hz, py-C2).
IR (KBr pellets): 2378, 2311, 2096, 1956, 1469, 1177 cm^{-1}.
Anal. Calcd. for $C_{19}H_{40}BN_2PRu$: C, 51.93; H, 9.18; Found: C. 51.86, H, 9.24.

Synthesis of [RuCl$_2$(PPh$_3$)(^{i}Pr-PNP)] 5'.

[0243] To a suspension of Ru(PPh_3)$_3$$Cl_2$ (480 mg, 0.5 mmol) in dry THF (20 ml) was added ^{i}Pr-PNP (170 mg, 0.5 mmol) and the mixture was stirred and heated at 65 °C for 6 hrs. The yellow solution was concentrated to 4 mL under vacuum and 20 mL of pentane were added to precipitate a yellow solid. The solid was isolated by filtration, washed with pentane (3 × 2 mL) and dried under vacuum to give 290 mg (75 % yield) of **5** as a yellow solid.
$^{31}P\{^1H\}$ NMR (CD_2Cl_2): 46.4 (d, J_{PP} = 27.5 Hz), 43.2 (t, J_{PP} = 27.5 Hz). ^1H NMR (CD_2Cl_2): 0.87 (q, 12H, J_{PH} = J_{HH} = 8.0 Hz, P(CH(C*H*$_3$)$_2$)$_2$), 1.13 (q, 12H, J_{PH} = J_{HH} = 8.0 Hz, P(CH(C*H*$_3$)$_2$)$_2$), 2.43 (m, 4H, P(C*H*(CH_3)$_2$)$_2$), 3.92 (t, 4H, J_{PH} = 4.0 Hz, -CH_2P), 7.26 (m, 9H, P(C_6H_5)$_3$), 7.30 (d, 2H, J_{HH} = 8.0 Hz, pyridine-H3, 5), 7.53 (t, 1H, J_{HH} = 8.0 Hz, pyridine-H4), 7.91 (m, 6H, P(C_6H_5)$_3$). $^{13}C\{^1H\}$ NMR (CD_2Cl_2): 19.6 (s, P(CH(*C*H$_3$)$_2$)$_2$), 20.7 (s, P(CH(*C*H$_3$)$_2$)$_2$), 25.1 (t, J_{PC} = 8.0 Hz, P(*C*H(CH_3)$_2$)$_2$), 38.9 (t, J_{PC} = 10.1 Hz, CH_2P), 119.9 (s, Py-C3,5), 127.2 (d, J_{PC} = 9.0 Hz, *m*-C_6H_5-P), 128.8 (s, *p*-C_6H_5-P), 135.0 (d, J_{PC} = 9.0 Hz, *o*-C_6H_5-P), 136.7 (s, Py-C4), 140.4 (d, J_{PC} = 36.2 Hz, *ipso*-C_6H_5-P), 164.8 (t, J_{PC} = 4.0 Hz, py-C2,6).
Anal. Calcd. for $C_{37}H_{50}NP_3Cl_2Ru$: C, 57.44; H, 6.52. Found: C, 57.28; H, 6.53.

Synthesis of [RuH(BH_4)(PPh$_3$)(^{i}Pr-PNP)] 6'.

[0244] To a suspension of complex **5** (77 mg, 0.1 mmol) in 2-propanol (10 ml) was added a fine powder of $NaBH_4$ (9.5 mg, 0.25 mmol). The mixture was stirred at room temperature for 12 hrs and then filtered. The resulting yellow solid was washed with 2-propanol (3 × 1.5 mL) and then dissolved in benzene (10 mL) and the solution was filtered. The yellow filtrate was evaporated to dryness under vacuum, yielding complex **6'** as a yellow solid which was dried under vacuum overnight to give 61 mg (85 % yield). $^{31}P\{^1H\}$ NMR (C_6D_6): 61.6 (d, J_{PP} = 29.2 Hz), 67.9 (t, J_{PP} = 29.2 Hz). ^1H NMR (C_6D_6): -14.0 (q, 1H, J_{PH} = 28.0 Hz, Ru-H), -0.84 (br s, 4H, BH_4), 0.91 (q, 6H, J_{PH} = J_{HH} = 8.0 Hz, P(CH(C*H*$_3$)$_2$)$_2$), 0.87 (m, 12H, J_{PH} = J_{HH} = 8.0 Hz, P(CH(C*H*$_3$)$_2$)$_2$), 1.18 (q, J_{PH} = J_{HH} = 8.0 Hz, 6H, P(CH(C*H*$_3$)$_2$)$_2$), 1.44 (m, 2H, P(C*H*(CH_3)$_2$)$_2$), 1.77 (m, 2H, P(C*H*(CH_3)$_2$)$_2$), 2.85 (dt, 2H, J_{HH} = 16.0 Hz, J_{PH} = 4.0 Hz,-CH*H*P), 3.92 (dt, 2H, J_{HH} = 16.0 Hz, J_{PH} = 4.0 Hz, -C*H*HP), 6.56 (d, 2H, J_{HH} = 8.0 Hz, pyridine-H3, 5), 6.79 (t, 1H, J_{HH} = 8.0 Hz, pyridine-H4), 7.01 (d, 3H, J_{HH} = 8.0 Hz, P(C_6H_5)$_3$), 7.12 (t, 6H, J_{HH} = 8.0 Hz, P(C_6H_5)$_3$), 8.18 (t, 6H, J_{HH} = 8.0 Hz, P(C_6H_5)$_3$). $^{13}C\{^1H\}$ NMR (C_6D_6): 18.0 (s, P(CH(*C*H$_3$)$_2$)$_2$), 18.5 (s, P(CH(*C*H$_3$)$_2$)$_2$), 19.6 (s, P(CH(*C*H$_3$)$_2$)$_2$), 20.8 (s, P(CH(*C*H$_3$)$_2$)$_2$), 25.6 (t, J_{PC} =

8.0 Hz, P($CH(CH_3)_2)_2$), 26.4 (t, J_{PC} = 11.6 Hz, CH_2P), 39.2 (t, J_{PC} = 6.0 Hz, P($CH(CH_3)_2)_2$), 118.4 (t, J_{PC} = 2.5 Hz, Py-C3,5), 127.1 (d, J_{PC} = 9.0 Hz, *m*-C_6H_5-P), 128.8 (s, *p*-C_6H_5-P), 134.2 (s, Py-C4), 135.7 (d, J_{PC} = 10.1 Hz, *o*-C_6H_5-P), 142.0 (d, J_{PC} = 36.2 Hz, *ipso*-C_6H_5-P), 163.7 (t, J_{PC} = 4.5Hz, py-C2,6).
IR (KBr pellet): 2361, 2293, 2246, 1884, 1458, 1060 cm^{-1}.
Anal. Calcd. for $C_{37}H_{55}BNP_3Ru$: C, 61.84; H, 7.72. Found: C, 61.98; H, 7.66.

Typical procedures for the catalytic dehydrogenation of alcohols

[0245]

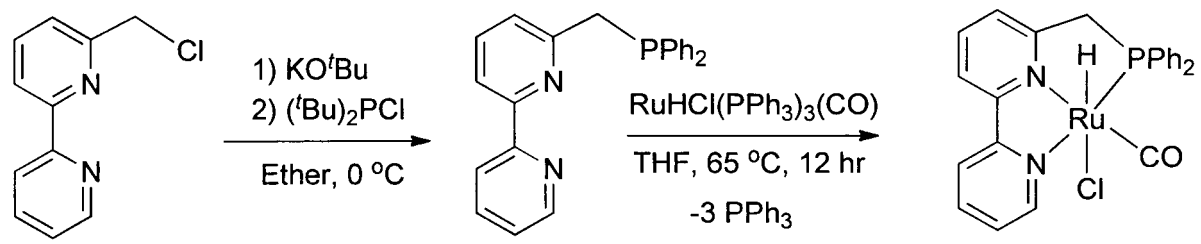
(a) Complexes **2'** (0.01 mmol), **4'** (0.01 mmol) or **6'** (0.01 mmol) were dissolved in the neat primary or secondary alcohol (10 mmol). The flask was equipped with a condenser and the solution was heated with stirring in an open system under argon at the specified temperature and time (Tables 18 and 19). After cooling to room temperature, the product aldehydes, esters or ketones were determined by GC, using mesitylene or (in the case of 1-butanol) benzene as internal standards, employing a Carboxen 1000 column on a HP 690 series GC system.
(b) A solution containing the catalyst (0.01 mmol) (complexes **2', 4'** or **6'**) and the alcohol (10 mmol) in toluene (2 mL) was heated in a flask equipped with a reflux condenser under argon in an open system at the specified temperatures and times (Tables 2 and 3). After cooling to room temperature, the products were determined by GC using mesitylene or benzene (for 1-butanol) as internal standards, employing a Carboxen 1000 column on a HP 690 series GC system.

X-ray Crystal Structure Determination of 2'.

[0246] The crystal was mounted on a nylon loop and flash frozen in a nitrogen stream at 120 K. Data were collected on a Nonius Kappa CCD diffractometer mounted on a FR590 generator equipped with a sealed tube with Mo $K\alpha$ radiation (λ = 0.71073 Å) and a graphite monochromator. The four structures were solved using direct methods with SHELXS-97 based on F^2.
[0247] **Complex 2':** $C_{23}H_{48}BNP_2Ru$, yellow plate, 0.40 × 0.40 × 0.30 mm^3, monoclinic, $P2_1$ (No.4), *a* = 12.541 (3) Å, *b* = 15.314 (3) Å, *c* = 15.131 (3) Å, β = 111.85 (3)°, *V* = 2697.3 (9) $Å^3$, *Z* = 4, fw = 512.4, *F(000)* = 1088, D_c = 1.262 Mg/m^3, μ = 0.709 mm^{-1}. The final cycle of refinement based on F^2 gave an agreement factor *R* = 0.027 for data with $I > 2\sigma(I)$ and *R* = 0.030 for all data (6375 reflections) with a goodness-of-fit of 1.080. Idealized hydrogen atoms were placed and refined in the riding mode, with the exception of Hru and Hb1 - Hb4 which were located in the difference map and refined independently.

Example 11 - Synthesis of Complex 9 and Catalysis by It

[0248]



BPy-(Ph)PNN

Scheme 39

(a) Synthesis of the ligand BPy-(Ph)PNN (10)

[0249] An oven-dried 250 mL three-necked round bottom flask equipped with an argon inlet, a stirring bar, dropping funnel and one rubber septum was cooled under a stream of argon. The flask was then charged with chlorodiphenylphosphine (1.08 g, 6 mmol) in 30 mL dry ether. The solution was cooled to 0 °C and a THF solution (5 mL) of potassium tert-butoxide (74 mg, 6.6 mmol) was added dropwise via syringe during 10 min. The resulting brown coloured mixture was stirred for 1 hr at 0 °C and then a solution of 6-chlorometyl-2,2'-bipyridine (1.02 g, 5 mmol) in 20 mL dry ether was

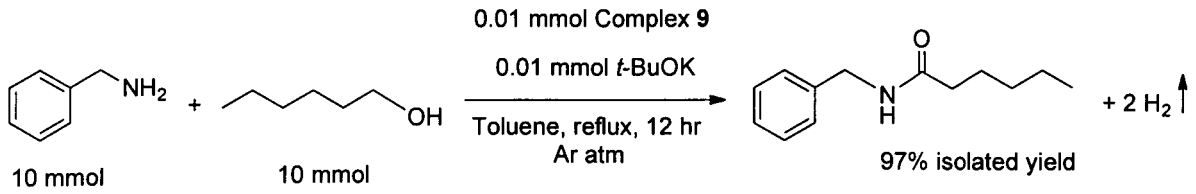
added dropwise (~15 min) to it. The stirring was continued for a further 1 hr at the same temperature and the mixture was allowed to slowly warm up to room temperature and stirred overnight. To this reaction mixture was added 20 mL of degassed water and the ether phase was separated under N_2 atmosphere. The aqueous phase was extracted with ether (2 × 20 mL). The combined ether solutions were dried over anhydrous Na_2SO_4, filtered under N_2 pressure, and the solvent was removed under vacuum to get brownish-white solid. This was purified by column chromatography in the nitrogen glove box (basic alumina; hexane: ether (10:1) as eluent) to yield 1.08 g (61%) of 6-di-phenyphosphinomethyl-2,2'-bipyridine (BPy-(Ph)PNN) as a white crystalline solid. $^{31}P\{1H\}$NMR (122 MHz, CD_2Cl_2): -8.28 (s). ^1H NMR (300 MHz, CD_2Cl_2): 3.81 (s, 2H, P-CH2), 7.13 (d, JHH = 7.5 Hz, 1H, H-5), 7.32 (ddd, JHH = 7.5 Hz, JHH = 4.8 H, JPH = 1.2 Hz, 1H, H-5'), 7.40 - 7.45 (m, 6H, Ph-H), 7.58 - 7.63 (m, 4H, Ph-H), 7.69 (t, JHH = 7.8 Hz,, 1H, H-4), 7.80 (dt, JHH = 7.8 Hz, JHH = 2.1 Hz, 1H, H-4'), 8.28 (br d, JHH = 8 Hz, 2H, H-3 and H-3'), 8.68 - 8.70 (m, 1H, H-6'). $^{13}C\{1H\}$NMR (125 MHz, CD2Cl2): 38.35 (d, JPC = 16.3 Hz, P-CH2), 118.07 (s, C-3), 121.02 (s, C-3'), 123.55 (s, C-5'), 123.61 (d, JPC = 8.4 Hz, C-5), 128.34 (s, Ph-C), 128.40 (Ph-C), 128.65 (s, Ph-C), 132.90 (s, Ph-C), 133.05 (s, Ph-C), 136.61, (s, C-4'), 136.97 (s, C-4), 138.72 (d, JPC = 15.0 Hz, Ph-C(quar)), 149.02 (s, C-6'), 155.49 (s, C-2), 156.22 (s, C-2'), 157.64 (d, JPC = 7.5, C-6). Anal. Calcd. for C23H19N2P: C, 77.95; H, 5.40. Found: C, 78.13, H, 5.61. MS (ESI, MeOH): 355 (100%, M+1)+). Assignment of signals was confirmed by DEPT 135, COSY, and HSQC.

(b) Synthesis of Complex **9**

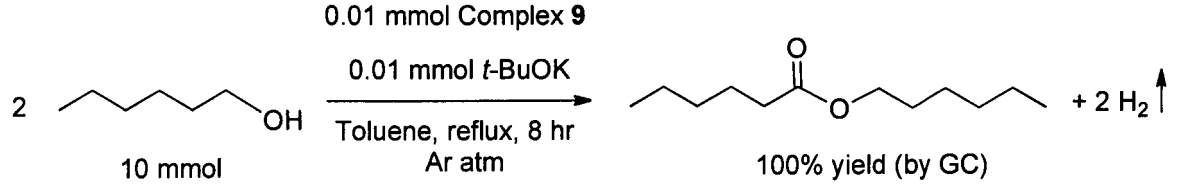
[0250] To an oven dried 25 mL pressure vessel equipped with magnetic stirring bar was added ligand, BPy-(Ph)PNN (**10**) (148 mg, 0.42 mmol), $RuHCl(CO)(PPh_3)_3$ (382 mg, 0.4 mmol), and 8 mL dry THF in a nitrogen glove box. The flask was sealed and heated at 65 °C for 12 hr with stirring outside the glove box, then cooled to room temperature to lead to reddish-brown solid. It was reintroduced to the glove box, and the solvent was decanted and the solid thus obtained was washed with ether (3 × 5 mL), then dried under vacuum to give analytically pure complex RuHCl(CO)(BPy-(Ph)PNN) (184 mg, 84%). $^{31}P\{1H\}$NMR (202 MHz, CD_2Cl_2): 69.44 (s). ^1H NMR (500 MHz, CD_2Cl_2): -14.09 (d, JPH = 25.5 Hz, 1H, Ru-H), 4.38 - 4.50 (m, 2H, P-CH2), 7.39 - 7.40 (m, 3H, Ph-H), 7.46 - 7.51 (m, 4H, Ph-H), 7.60 - 7.64 (m, 3H, Ph-H), 7.87 - 7.90 (m, 2H, H-5 and H-5'), 7.57 (d, JHH = 7.8 Hz, 1H, H-5), 7.93 - 7.97 (m, 2H, H-4 and H-4'), 8.04 (d, JHH = 8.0 Hz, 1H, H-3), 8.10 (d, JHH = 8.0 Hz, 1H, H-3'), 9.22 (br s, 1H, H-6'). $^{13}C\{1H\}$NMR (125 MHz, CD2Cl2): 45.52 (d, JPC = 26.3 Hz, P-CH2), 120.04 (s, C-3), 122.65 (s, C-3'), 123.09 (d, JPC = 11.3, C-5), 126.21 (s, C-5'), 128.16 (s, Ph-C), 128.24 (s, Ph-C), 128.28 (s, Ph-C), 128.37 (s, Ph-C), 129.82 (s, Ph-C), 130.37 (s, Ph-C), 131.60 (d, JPC = 11.3 Hz, Ph-Ca(ortho)), 133.46 (d, JPC = 11.3 Hz, Ph-Cb(ortho)), 133.78 (d, JPC = 43.8 Hz, Ph-Cb(quar)), (136.64, (s, C-4'), 137.39 (s, C-4), 139.86 (d, JPC = 50.0 Hz, Ph-Ca(quar)), 153.39 (s, C-6'), 154.67 (s, C-2), 156.05 (s, C-2'), 160.04 (d, JPC = 6.3, C-6). 206.53 (d, JPC = 7.5 Hz, Ru-CO). IR (KBr, pellet): 1915 (vCO) cm-1. MS (ESI, CH3CN): 519 (100%, (M-1)+) and MS (ESI, CH3OH): 485 (100%, (M-Cl)+).

Some Examples of Reactions Catalyzed by Complex 9:

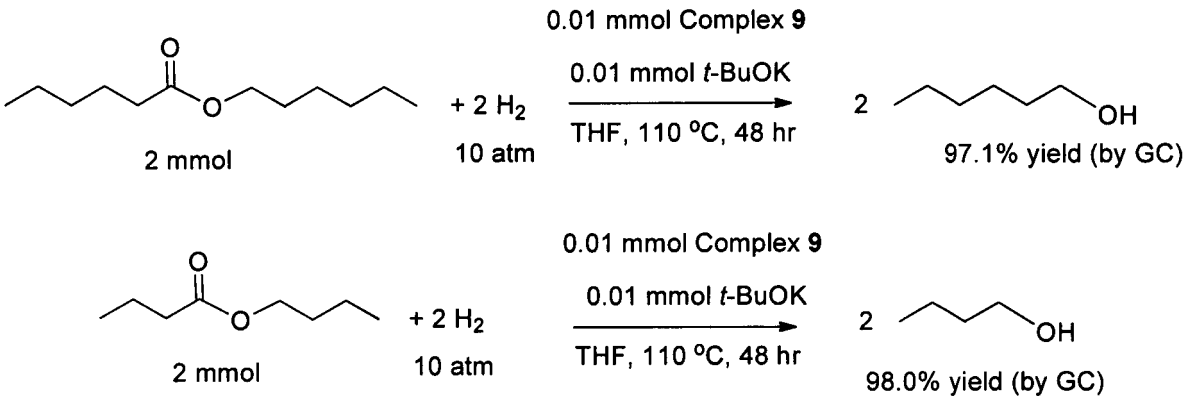
[0251]



Scheme 40



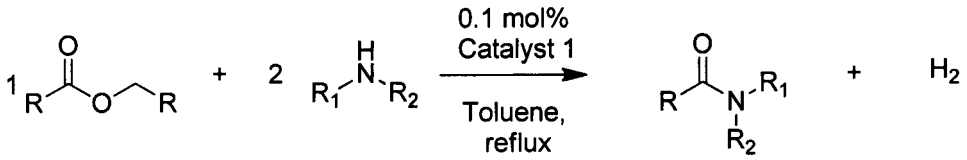
Scheme 41



Scheme 42

Example 12: Direct Synthesis of Amides from Esters using Ruthenium-Pincer Catalyst with Liberation of H_2 under Neutral Conditions

[0252] PNN- type pincer ruthenium complexes used for catalytic conversion of esters and amines into amides:



Scheme 43

[0253] The applicants of the present invention have discovered that amide synthesis from esters and amines can be achieved using the ruthenium PNN catalyst **1.** The reaction is general, efficient, environmentally benign and atom economical. It proceeds under neutral conditions without acid/base/activators/promoters. Notably, this reaction affords with amide in high TON (1000) and H_2 as the only byproduct (Scheme 43).

[0254] When a benzene solution containing 10 mmol of pyrrolidine, 10 mmol of ethyl acetate and 0.01 mmol of complex **1** was refluxed under Argon atmosphere, quantitative conversion of pyrrolidine was observed by GC after 28 hrs, to yield 98% of N-acetyl pyrrolidine after column purification (Table 29, entry 1). The N-acetyl pyrrolidine was characterized by NMR and GC-MS. Similar results were obtained in toluene. Reaction of ethyl acetate with morpholine in benzene under reflux resulted after 36 hrs in 79% conversion with the isolation of the corresponding amide in 77% yield (Table 29, entry 2). Refluxing of 1-methyl piperazine, ethyl acetate and benzene in the presence of complex **1** provides the corresponding amide in 56% yield with the conversion of the ester being 59% (Table 29, entry 3).

[0255] Various esters and amines reacted similarly. Refluxing a toluene solution containing butyl butyrate (5 mmol), piperidine (10mmol) and 0.1 mol% of the PNN complex **1** under argon atmosphere for 19 hrs resulted in 100% conversion of piperidine as observed by GC analysis, with the exclusive formation of the 1-(piperidin-1-yl)butan-1-one in 94% yield after isolation from alumina column chromatography (Table 29, entry 4). The product was completely characterized by NMR spectroscopy. Unlike the traditional methods, this reaction does not form any alcohol as by-product, resulting in the irreversible, unique incorporation of both the acyl and alkoxo parts of the starting ester into the product amide. Significantly the TON of ester-amide exchange reaction was high (1000). Similarly, refluxing the toluene solution containing butyl butyrate, morpholine or N-methyl piperazine in the presence of complex **1** resulted in 100% conversion of the amine with the isolation of the amides in 95 and 94% yields, respectively. Refluxing of excess of butyl butyrate and piperazine in toluene led to bis-acylation of the piperazine, providing the corresponding amide in 61% yield.

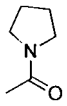
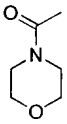
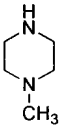
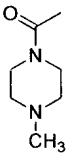
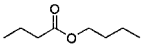
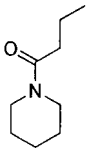
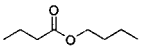
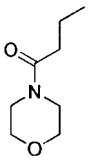
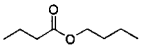
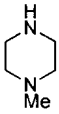
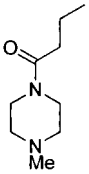
[0256] To explore the synthetic utility of this reaction, pentyl pentanoate was reacted with various amines. The reaction of pentyl pentanoate with piperidine gave 100% conversion with the isolation of the amide in 96% yield. Morpholine and N-methyl piperazine furnished the respective amide in 96 and 94% isolated yield.

[0257] Next, reactions were studied with primary amines. The reaction of ethyl butyrate and hexyl amine in the presence of 0.1mol% of **1** in refluxing toluene led to 100% conversion of the hexyl amine with the isolation of 97% of the corresponding amide as the only product. Similarly, reaction of pentyl pentanoate and 4-methylbenzyl amine in refluxing

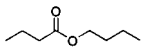
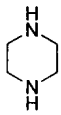
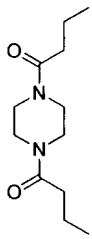
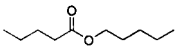
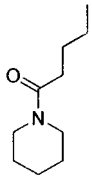
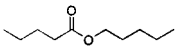
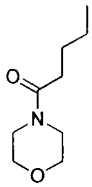
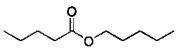
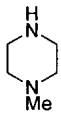
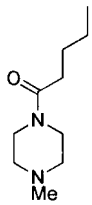
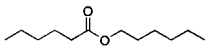
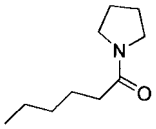
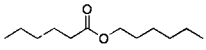
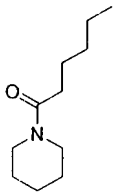
toluene resulted in 100% conversion with isolation of corresponding amide in 98% yield. These reactions did not lead any alcohol as waste product.

[0258] The reactions were also studied in absence of solvent. Thus, heating pentylpentanoate, piperidine and complex **1** at 135°C resulted in 52% conversion.

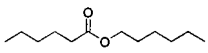
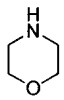
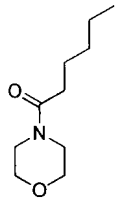
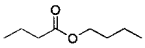
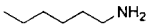
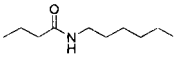
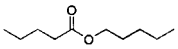
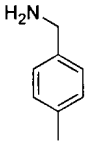
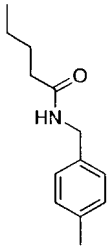
Table 29. Amination of esters catalyzed by the ruthenium complex **1**[a]

Entry	Ester	Amine	Time (hrs)	Conv. of amine	Isolated Yield (%)
1			26	100	 99
2			36	79	 77
3			24	59	 56
4			19	100	 94
5			21	100	 95
6			24	100	 94

(continued)

Entry	Ester	Amine	Time (hrs)	Conv. of amine	Isolated Yield (%)
6			36	100	 61
7			19	100	 96
8			26	100	 92
9			24	100	 94
10			18	100	 97
11			26	100	 94

(continued)

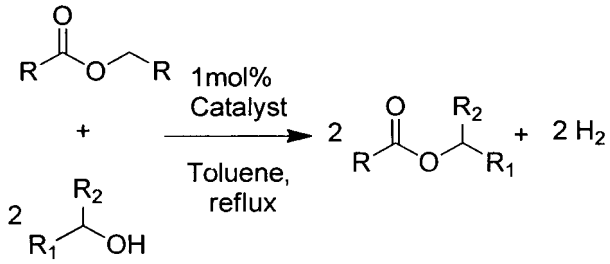
Entry	Ester	Amine	Time (hrs)	Conv. of amine	Isolated Yield (%)
12			18	100	 93
13			24	100	 97
14			18	100	 98

[a] Complex **1** (0.01 mmol), ester (5 mmol), amine (10 mmol) and toluene/benzene (3 ml) were refluxed at an oil bath temperature of 135°C in a Schlenk tube. Conversion of amine was analyzed by GC using *m*-xylene as internal standard.

In summary, acylation of amines using esters as the acylating partner is efficiently catalyzed by complex **1** under neutral conditions. The use of symmetrical esters results in the incorporation of both the acyl and alkoxo parts of the substrate ester into the product amide with liberation of H_2. This offers an environmentally benign, atom economical method for amide synthesis from esters without any waste generation. This catalytic cycle produces a high turnover number (1000) and both primary and secondary amines can be used.

Example 13: Ruthenium-Pincer Catalyzed Acylation of Alcohols Using Esters with Liberation of H_2 under Neutral Conditions

[0259] The acylation of esters with secondary alcohols can be carried out selectively to give the mixed ester using the PNN catalyst **1.** The reaction is general, efficient, and environmentally benign. It proceeds under neutral conditions without acids or bases, activators, or molecular sieves. Uniquely, when a symmetrical ester (such as ethyl acetate) is reacted with a secondary alcohol, the only co-product is molecular hydrogen, unlike the generally employed transesterification reaction which gives an alcohol co-product (or its derivative) (Scheme 44).



Scheme 44. Acylation of alcohols using esters.

[0260] When a benzene solution containing 15 mmols of cyclohexanol, 5 mmols of ethyl acetate and 0.05 mmols of complex **1** was refluxed under argon atmosphere, GC analysis after 28 hrs showed that all of the ethyl acetate disappeared and cyclohexyl acetate was formed as a single product (Table 30, entry 1). ^{1}H NMR and GC-MS of the isolated product were identical to cyclohexyl acetate prepared by refluxing neat acetic anhydride with cyclohexanol.

[0261] Likewise, refluxing a toluene solution containing one equivalent of hexyl hexanoate, 2 equivalents of cyclohexanol and 1 mol% of the PNN complex **1** under argon atmosphere for 20 h resulted in 84% conversion of hexyl hexanoate as determined by GC analysis, with the exclusive formation of the ester cyclohexyl hexanoate in 83% yield (Table 30, entry 2). Notably, unlike the traditional transesterification methods, this reaction does not form an alcohol product; rather, an irreversible incorporation of both the acyl and alkoxo parts of the starting ester into the product ester takes place. While 2 equivalents of the alcohol with respect to the ester are sufficient, somewhat higher yields are obtained when 3 equivalents of alcohol were used. Thus, reaction of 3 equivalents of cyclohexanol with hexyl hexanoate resulted after 26 h in 96% conversion with 95% yield of cyclohexyl hexanoate, as observed by GC, and confirmed by GC-MS by comparison with an authentic sample (Table 30, entry 3). The pure product was isolated by evaporation of the solvent followed by passing through a basic alumina plug and analysis by NMR and GC-MS. Use of the PNP complexes **2** or **3** resulted after 20 h in 58% or 17% yield of cyclohexyl hexanoate, respectively. Studying the scope of this new reaction with regard to the secondary alcohol, reaction of hexyl hexanoate with cyclopentanol in the presence of 1 mol% **1** was carried out. After 26 h reflux in toluene, cyclopentyl hexanoate (70% yield) was formed, with 71% conversion of hexyl hexanoate (Table 30, entry 4). Similarly, upon reaction of hexyl hexanoate with excess of 1-phenylethanol, 50% conversion of hexyl hexanoate with the formation of 49% of the acylated product was observed (Table 30, entry 5). The lower conversion of the ester is a result of facile dehydrogenation of 1-phenylethanol to acetophenone (49%). Because of the expected easy dehydrogenation of the isopropyl alcohol to acetone, transesterification with this alcohol was performed in a closed vessel, to retard this dehydrogenation process. Thus, heating hexyl hexanoate with excess of isopropyl alcohol resulted after 19 h in 83% conversion of hexyl hexanoate with the formation of isopropyl hexanoate in 67% yield (entry 6). The reaction of hexyl hexanoate and 3-pentanol led to 91% conversion of the ester with formation of 3-pentyl hexanoate in 90% yield after 26 h reflux (entry 7).

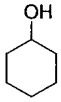
[0262] Exploring further the scope with regard to the ester substrate, pentyl pentanoate was reacted with cyclohexanol, resulting in 93% conversion with the formation of 93% cyclohexyl pentanoate (entry 8). Like in the case of hexyl hexanoate, the presumably formed pentanol intermediate is converted into pentyl pentanoate with the liberation of H_2. Similarly, treatment of pentyl pentanoate with cyclopentanol, 1-phenylethanol and 3-pentanol, furnished 87, 51, 91% conversion of pentyl pentanoate, respectively, with the predominant formation of the corresponding cross-ester as the product in 85, 49, 90% yields, respectively (entries 9-11).

[0263] Next we studied the reaction of butyl butyrate with various secondary alcohols. Reaction of 5 mmol of butyl butyrate with 15 mmol of cyclohexanol led to 93% conversion of the ester with the formation of 92% of cyclohexyl butyrate after 34 h (entry 12). Upon refluxing of butyl butyrate with cyclopentanol, after 28 hrs 75 % conversion of the ester, with formation of 74% cyclopentyl butyrate were observed (entry 13). In a similar reaction with 1-phenylethanol or 3-pentanol, 41 and 77% conversion, respectively, into the product was noted by GC analysis after 36 h (entries 14 and 15).

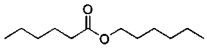
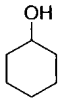
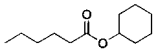
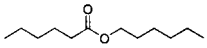
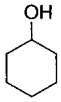
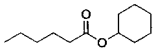
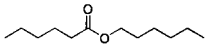
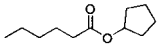
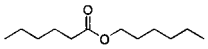
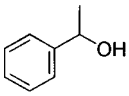
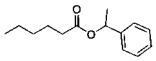
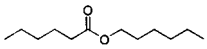
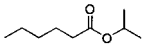
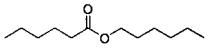
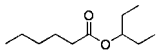
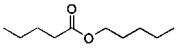
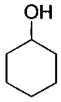
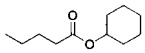
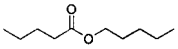
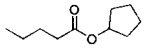
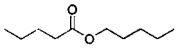
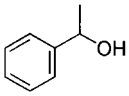
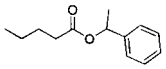
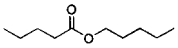
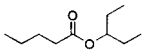
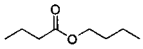
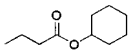
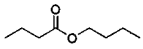
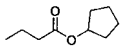
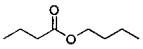
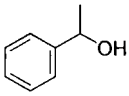
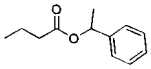
[0264] These reactions were also studied with unsymmetrical esters. The reaction of ethyl butyrate with 3-pentanol in the presence of 1 mol% of **1** under refluxing toluene led to 75% conversion of ethyl butyrate with the formation of 73% of 3-pentyl butyrate as the exclusive product (entry 16). Traces of 3-pentyl acetate, resulting from reaction with the formed ethanol, were also observed. The remaining ethanol probably evaporated from the reaction mixture under the reflux conditions. Similarly, the reaction of methyl hexanoate with cyclohexanol results in 42% conversion after 17 h with the formation of 42% of cyclohexyl hexanoate (entry 17).

[0265] Since the dehydrogenation of the secondary alcohol to ketone is slower than the dehydrogenative coupling of the primary alcohol to ester, most of the secondary alcohol reacts with the ester, although some ketone resulting from excess alcohol was observed. The slow reaction of the secondary alcohol with PNN complex may be due to the steric hindrance.

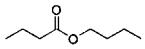
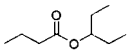
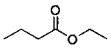
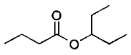
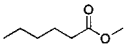
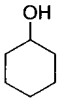
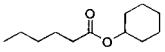
Table 30. Acylation of alcohols catalyzed by the ruthenium complex **1**[a)]

Entry	Ester	alcohol	Time (hrs)	Conv. of ester %	Yield %
1[b)]			28	100	95

(continued)

Entry	Ester	alcohol	Time (hrs)	Conv. of ester %	Yield %
2[c)]			20	84	 83
3			26	96 (cat **1**) 58 (cat. **2**) 17 (cat. **3**)	 95 (cat **1**)
4			26	71	 70
5			36	50	 49
6[d)]			19	83	 67
7			26	91	 90
8			36	93	 93
9			36	87	 85
10			18	51	 49
11			26	91	 90
12			34	93	 92
13			28	75	 74
14			36	41	 39

(continued)

Entry	Ester	alcohol	Time (hrs)	Conv. of ester %	Yield %
15			18	77	 76
16[e)]			20	75	 73
17			17	42	 42

[a)] Complex **1** (0.05 mmol), ester (5 mmol), alcohol (15 mmol) and toluene (3 ml) were refluxed/heated at an oil bath temperature of 135°C under argon. Conversion of ester and yield of product were analyzed by GC using *m*-xylene or benzene as internal standards. A small amount of the secondary alcohol was converted into the corresponding ketone. [b)] Benzene was used as solvent. Efficient cooling of the reflux condenser is required to avoid losses of ethyl formate. [c)] **1** (0.05 mmol), hexyl hexanoate (5 mmol), cyclohexanol (10 mmol) and toluene (3 ml) were used. [d)] a closed system and 3 ml of 2-propanol were used. An equivalent amount of 1-hexanol (67%) was also detected. [e)] *m*-xylene was used as solvent and benzene as internal standard.

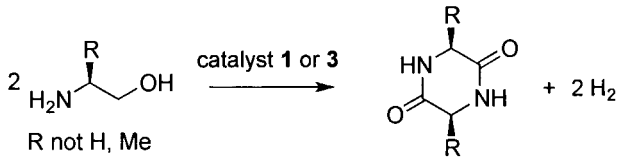
Experimental Section

[0266] General procedure for the catalytic acylation of alcohols: Complex **1** (0.05 mmol), ester (5 mmol), alcohol (15 mmol) and toluene (3 mL) were added to Schlenk flask under an atmosphere of nitrogen in a glove box. The flask was equipped with a condenser and the solution was refluxed with stirring in an open system under argon for the specified time (Table 30). In the case of isopropanol, the reactions were performed in a closed system at 135° C. The reaction products were analyzed by GC-MS. After cooling to room temperature, *m*-xylene (1 mmol) or benzene (1 mmol) were added as internal standards to the reaction mixture and the products were quantitatively analyzed by GC using a Carboxen 1000 column on a HP 690 series GC system or HP-5 cross linked 5% PH ME Siloxane column (30m × 0.32mm × 0.25 μm film thickness) on a HP 6890 series GC system. In the reaction of cyclohexanol and esters, evaporation of the solvent, followed by purification over basic alumina column chromatography afforded the pure transesters. ^{1}H NMR of the products isolated from the catalysis was identical with the literature.

Example 14: Synthesis of Cyclic Dipeptides and Pyrazines from β-Aminoalcohols

A. Formation of cyclic dipeptides

[0267] Dehydrogenative coupling of β-aminoalcohols can lead to cyclic dipeptide formation (Scheme 45), except in case of R=H, Me (in which case linear polypeptides are the main products; in case of R=Me, a small amount of cyclic dipeptide is also formed).



Scheme 45

[0268] Refluxing a dioxane solution of (S)-2-amino-4-methylpentan-1-ol with complex 1 (1 mol%) led to 64% isolated yield of the cyclic dipeptide, 3,6-diisobutylpiperazine-2,5-dione 7b after workup (Table 31, entry 1). The product structure was confirmed by MS, NMR spectroscopies.

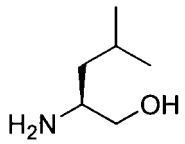
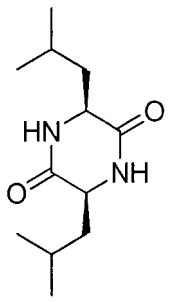
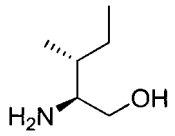
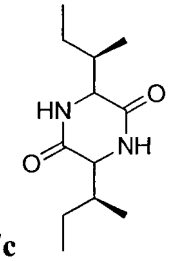
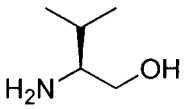
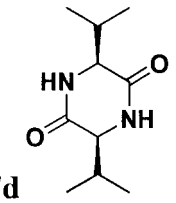
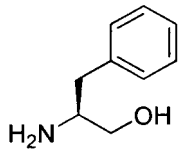
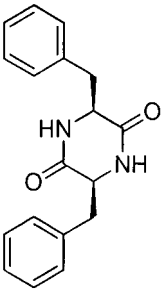
[0269] Upon refluxing a dioxane solution containing 2 mmol of (2S,3S)-2-amino-3-methylpentan-1-ol and 0.02 mmol of catalyst **1** for 19 hrs and cooling the reaction mixture, the solid product precipitated and was filtered off and dried

under vacuum to give pure 3-(sec-butyl)-6-(sec-butyl)piperazine-2,5-dione **7c** in 72% yield (Table 31, entry 2). The structure was confirmed by NMR and MS spectroscopies. Under the same conditions, cyclic peptidation of (S)-2-amino-3-methylbutan-1-ol led to 3,6-diisopropylpiperazine-2,5-dione **7d** as an insoluble solid which separated from the reaction mixture and was isolated by filtration and dried under vacuum to give 78% of (3S,6S)-3,6-diisopropylpiperazine-2,5-dione **7d** (Table 31, entry 3). The optical rotation of the pure product (-52°) was essentially the same as reported in the literature (-54°). Thus, under these experimental condition, no racemization took place.

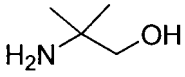
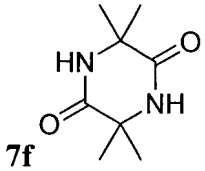
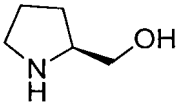
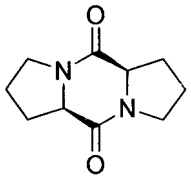
[0270] The reaction of (S)-2-amino-3-phenylpropan-1-ol and 1 in refluxing dioxane led to 90% conversion with the isolation of the corresponding 3,6-dibenzylpiperazine-2,5-dione 7e in 72% yield (Table 31, entry 4). Reaction of 2-amino-2-methylpropan-1-ol under the same conditions yielded 100% conversion with isolation of the corresponding cyclic dipeptide 3,3,6,6-tetramethylpiperazine-2,5-dione 7f in 92% yield (Table 31, entry 5).

[0271] Tricyclic ring systems represent an important structural motif in many naturally existing alkaloids. Refluxing a dioxane solution of (S)-pyrrolidin-2-yl-methanol in the presence of catalyst 1 followed by solvent evaporation, hexane addition to the crude solid, and its isolation by filtration and washing with hexane led to octahydrodipyrrolo[1,2-a:1',2'-d]pyrazine-5,10-dione 7g in 99% isolated yield (Table 31, entry 6).

Table 31. Synthesis of cyclic dipeptides from β-aminoalcohols catalyzed by complex **1.**

Entry	Catalyst	Aminoalcohol	cyclic dipeptide	Isolated Yields (%)
1	**1**		 **7b**	64
2	**1**		 **7c**	72
3	**3**		 **7d**	87
4	**3**		 **7e**	82

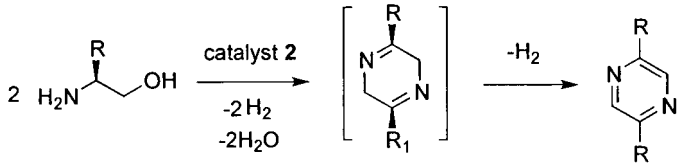
(continued)

Entry	Catalyst	Aminoalcohol	cyclic dipeptide	Isolated Yields (%)
5	**1**		 **7f**	92
6	**1**		 **7g**	99

[a] Complex 1 or 3 (0.02 mmol), aminoalcohol (2 mmol) and dioxane (2 ml) were refluxed under argon (oil bath temperature of 135 °C) for 19 h.

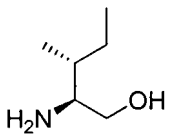
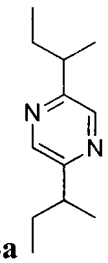
B. Formation of pyrazines

[0272] Pyrazines are biologically important organic compounds and their synthesis is of industrial significance. When the RuPNP complex 2 was used as catalyst, pyrazine derivatives were obtained from β-amino alcohols (Scheme 46). Thus, a toluene solution of isoleucinol with complex 2 (1 mol%) was vigorously refluxed under argon for 24 hrs resulting in complete conversion of isoleucinol. The solvent was evaporated under vacuum and the residue was subjected to silica-gel column chromatography to afford 2,6-diiso-butyl pyrazine 8a in 53% yield (Table 32, Entry 1). ^{1}H NMR exhibits the characteristic aromatic CH at 8.27 ppm and GC-MS confirms the respective molecular weight. The same reaction was also conducted by reflux under air using complex 2, resulting in 48% isolated yield of 8a. The similarity in yields of 8a under argon and under air indicates that air does not play a role as oxidant in the dehydrogenation of the presumed intermediate 1,4-dihydropyrazine to form the pyrazine. Significantly, no cyclic dipeptide was obtained under these conditions. Similar results were obtained with other aminoalcohols. Thus, toluene solutions of (S)-2-amino-3-methylbutan-1-ol, (S)-2-amino-4-methylpentan-1-ol, and (S)-2-amino-2-phenylethanol, were vigorously refluxed (bath temperature 165 °C) for 24 hrs while monitoring reaction progress by GC-MS. After complete disappearance of the amino alcohol, the crude product was purified by column chromatography to get the corresponding pyrazine products 8b-d (Table 32).

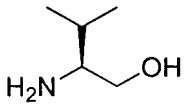
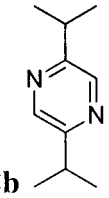
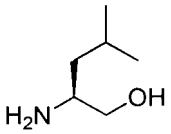
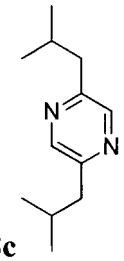
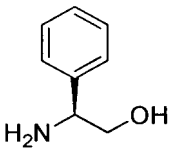
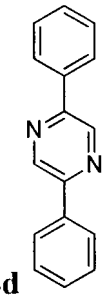
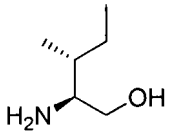
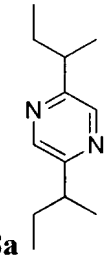


Scheme 46

Table 32. Synthesis of pyrazines from β-aminoalcohols catalyzed by the ruthenium PNP complex 2.(a)

Entry	β-Aminoalcohol	Pyrazine	Isolated Yields (%)
1		 **8a**	53

(continued)

Entry	β-Aminoalcohol	Pyrazine	Isolated Yields (%)
2		 **8b**	35
3[(b)]		 **8c**	38
4		 **8d**	45
5[(c)]		 **8a**	48

(a) Complex 2 (0.02 mmol), aminoalcohol (2 mmol) and toluene (2 ml) were vigorously refluxed (oil bath temperature at 165 °C for 24 h). (b) Heated in absence of solvent (oil bath temperature at 165 °C). (c) Reaction performed under air.

[0273] General procedure for the synthesis of cyclic dipeptides from β-aminoalcohols: Complex **1** (0.02 mmol), aminoalcohol (2 mmol) and dioxane (2 mL) were added to Schlenk flask under an atmosphere of nitrogen in a glovebox. The flask was equipped with a condenser and the solution was refluxed with stirring in an open system under argon for 19 hrs. The reaction products were analyzed by GC-MS on Agilent 7820A GC coupled with 5975 MSD system. The reaction mixture was cooled; the solid obtained was filtered off, washed with hexane and dried to give the pure cyclic dipeptide.

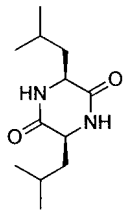
[0274] General procedure for the synthesis of pyrazines from β-aminoalcohols: Complex **2** (0.02 mmol), aminoalcohol (2 mmol) and toluene (2 mL) were added to Schlenk flask under an atmosphere of nitrogen in a glovebox. The flask was equipped with a condenser and the solution was refluxed with stirring under argon in an open system for the 24 hrs. The reaction products were analyzed by GC-MS on Agilent 7820A GC coupled with 5975 MSD system.

[0275] The solvent was evaporated from the reaction mixture and the crude product was subjected to silica-gel column chromatography using EtOAc:hexane to afford the pyrazine derivatives.

Characterization data of cyclic dipeptides

(3S,6S)-3,6-diisobutylpiperazine-2,5-dione

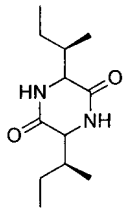
[0276]



mp: 270-272°C
^{1}H NMR (300 MHz, CD_3COOD): 0.84 (broad s, 12H, C*H*$_3$), 1.7 (broad s, 6H, C*H*$_2$, CH), 4.23 (broad s, 2H, NC*H*).
^{13}C{^{1}H}NMR (300 MHz, $CDCl_3$): 21.3 (*C*H$_3$), 21.6 (*C*H$_3$), 23.7 (*C*H$_3$), 23.8 (*C*H$_3$), 26.0 (CH), 26.2 (*C*H), 43.7 (*C*H$_2$), 46.4 (*C*H$_2$), 55.4 (NCH), 55.8 (NCH), 174.9 (*C*=O), 175.0 (*C*=O).
MS (ES$^+$, CH_2Cl_2+TFA): 227 (60%, M+H$^+$), 249 (100%, M+Na), 475 (70%, 2M+Na).

3-((R)-sec-butyl)-6-((S)-sec-butyl)piperazine-2,5-dione:

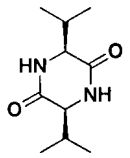
[0277]



mp: 276-280°C (decompose)
^{1}H NMR (300 MHz, $CDCl_3$): 0.86-1.02 (m, 12H, C*H*$_3$), 1.19-1.47(m, 4H, C*H*$_2$), 2.10-2.26 (m, 2H, C*H*$_2$), 3.91-4.07 (m, 2H, NC*H*), 6.11-6.31 (m, 2H, NH).
MS (ES$^+$, CH_2Cl_2+TFA): 227 (40%, M+H), 244 (100%), 249 (40%, M+Na), 467 (80%), 475 (5%, 2M+Na).

(3S,6S)-3,6-diisopropylpiperazine-2,5-dione:

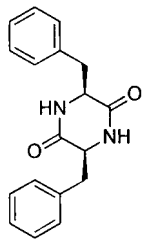
[0278]



mp: 290-294°C (decompose)
^{1}H NMR (300 MHz, $CDCl_3$ and CD_3COOD): 0.91 (d, *J*= 6.6 Hz, 6H, C*H*$_3$), 1.01 (d, *J*= 6.6 Hz, 6H, C*H*$_3$), 2.44-2.53 (m, 2H, C*H*), 4.11 (m, 2H, NC*H*).
^{13}C{^{1}H}NMR (300 MHz, $CDCl_3$): 15.7 (*C*H$_3$), 18.2 (*C*H$_3$), 32.3 (CH), 59.8 (NCH), 171.2 (*C*=O).
MS (ES$^+$, CH_2Cl_2+TFA): 199 (100%, M+H$^+$), 221 (60%, M+Na), 419 (15%, 2M+Na).
[α] = -52° (c=0.01, AcOH)

(3S,6S)-3,6-dibenzylpiperazine-2,5-dione:

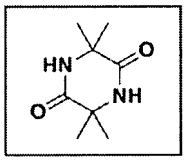
[0279]



mp: 299-302°C (decompose)
^{1}H NMR (300 MHz, $CDCl_3$ and CD_3COOD): 2.15-2.22 (m, 2H, CH_2), 2.95-3.01 (m, 2H, CH_2), 4.39-4.43 (m, 2H, NC*H*), 7.03(d, *J*= 6.9Hz, 4H, =C*H*), 7.31-7.39 (m, 6H, =C*H*).
^{13}C{^{1}H}NMR (300 MHz, CD_3COOD): 39.6 (CH_2), 56.2 (NCH), 128.4 (=*C*H), 129.4 (=*C*H), 129.9 (=CH), 133.5 *(quat-C),* 169.9, 173.0 (*C*=O).
MS (ES^{+}, CH_2Cl_2+TFA): 295 (80%, M+H), 317 (100%, M+Na), 611 (60%, 2M+Na).

3,3,6,6-tetramethylpiperazine-2,5-dione:

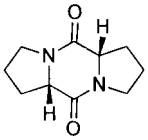
[0280]



^{1}H NMR (300 MHz, DMSO-d_6): 1.30 (s, 12H, CH_3), 8.09
(s, 2H, N*H*).
^{13}C{^{1}H}NMR (300 MHz, DMSO-d_6): 28.6 (CH_3), 55.7 (*quat-C*), 170.2 (*C*=O). MS (ES^{+}): 170 (100%, M^{+}), 192(30%), 200(25%).

(5aS,10aS)-octahydrodipyrrolol[1,2-a:1',2'-d]pyrazine-5,10-dione:

[0281]

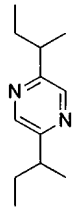


mp: 146-148°C
^{1}H NMR (300 MHz, $CDCl_3$): 1.88-2.33 (m, 8H, CH_2), 3.49-3.54 (m, 4H, NCH_2), 4.16 (t, 2H, NC*H*).
^{13}C{^{1}H}NMR (300 MHz, $CDCl_3$): 23.3 (CH_2), 27.6 (CH_2), 45.1 (NCH_2), 60.5 (NCH), 166.3 (*C*=O).
MS (ES^{+}): 194 (70%, M^{+}), 216 (100%, M+Na-1), 217 (10%, M+Na).

Characterization data of pyrazines

2,5-di-sec-butylpyrazine:

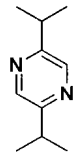
[0282]



[0283] ^{1}H NMR (300 MHz, $CDCl_3$): 0.77 (t, 6H, C*H*$_3$, *J* = 7.2 *Hz),* 1.22(d, 6H, *CH*$_3$, *J* = 6.9*Hz*), 1.52-1.74 (m, 4H, C*H*$_2$), 2.68-2.76 (m, 2H, C*H*), 8.27 (s, 2H, =CH).
^{13}C{^{1}H}NMR (300 MHz, $CDCl_3$): 11.6 (*C*H$_3$), 19.6 (*C*H$_3$), 29.3 (*C*H$_2$), 40.2 (*C*H), 142.4 (=*C*H), 158.1 (*quat-C*).

2,5-diisopropylpyrazine:

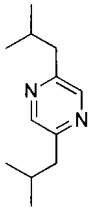
[0284]



[0285] ^{1}H NMR (300 MHz, $CDCl_3$): 1.23 (d, 12H, C*H*$_3$, *J* = 7.2 *Hz*), 2.95 -3.04 (m, 2H, C*H*), 8.30 (s, 2H, =CH).
^{13}C{^{1}H}NMR (300 MHz, $CDCl_3$): 21.8 (*C*H$_3$), 33.1 (*C*H), 141.4 (=*C*H), 158.9 (*quat-C*).

2,5-diisobutylpyrazine:

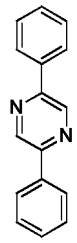
[0286]



[0287] ^{1}H NMR (300 MHz, $CDCl_3$): 0.94 (d, 12H, C*H*$_3$, *J = 6.6 Hz*), 2.04-2.13 (m, 2H, C*H*), 2.63 (d, 4H, C*H*$_2$, *J* = 7.2 *Hz*), 8.32 (s, *J*= 6.9 Hz, 2H, =C*H*).
^{13}C{^{1}H}NMR (300 MHz, $CDCl_3$): 21.9 (*C*H$_3$), 28.6 (*C*H), 43.6 (*C*H$_2$), 143.5 (=*C*H), 153.4 (*quat-C*).

2,5-diphenylpyrazine:

[0288]



[0289] ^{1}H NMR (300 MHz, $CDCl_3$): 7.48-7.57 (m, 6H, =C*H*$_3$), 8.07-8.10 (m, 4H, =C*H*), 9.09 (s, 2H, =C*H*).
^{13}C{^{1}H}NMR (300 MHz, $CDCl_3$): 126.8 (=CH), 129.1 (=*C*H), 129.7 (=*C*H), 136.3 (*quat-C*), 141.2 (=CH), 150.6 (*quat-C*).
[0290] While certain embodiments of the invention have been illustrated and described, it will be clear that the invention is not limited to the embodiments described herein. Numerous modifications, changes, variations, substitutions and

equivalents will be apparent to those skilled in the art without departing from the scope of the present invention as described by the claims, which follow.

References and Notes

(A) References Related to Ruthenium Complexes:

[0291]

(1) Seyden-Penne, J. Reductions by the Alumino and Borohydrides in Organic Synthesis; 2nd ed.; Wiley-VCH: New York, 1997.
(2) (a) Rylander, P. M. Hydrogenation Methods; Academic Press: London, 1985. (b) Hartwig, J. Organotransition Metal Chemistry; University Science Books: Sausalito, CA, 2010; pp 651-655.
(3) (a) Hirosawa, C.; Wakasa, N.; Fuchikami, T. Tetrahedron, Lett. 1996, 37, 6749. (b) Núñez Magro, A. A.; Eastham, G. R.; Cole-Hamilton, D. J. Chem. Commun. 2007, 3154. (c) Beamson, G.; Papworth, A. J.; Philipps, C.; Smith, A. M.; Whyman, R. Adv. Synth. Catal. 2010, 352, 869. (d) Beamson, G.; Papworth, A. J.; Philipps, C.; Smith, A. M.; Whyman, R. J. Catal. 2010, 269, 93.
(4) (a) Fernandes, A. C.; Romao, C. C. J. Mol. Catal. A., 2007, 272, 60. (b) Das, S.; Addis, D.; Zhou, S.; Junge, K.; Beller, M. J. Am. Chem. Soc. 2010, 132, 1770.
(5) Ito, M.; Koo, L. W.; Himizu, A.; Kobayashi, C.; Sakaguchi, A.; Ikariya, T. Angew. Chem. Int. Ed. 2009, 48, 1324.
(7) (a) Lawrence, S. A. Amines: Synthesis, Properties and Applications; Cambridge University Press: Cambridge, 2005. (b) Ricci, A. Amino Group Chemistry: From Synthesis to the Life Sciences; Wiley-VCH: Weinheim, 2008. (c) Kumara Swamy, K. C.; Bhuvan Kumar, N. N.; Balaraman, E.; Pavan Kumar, K. V. P. Chem. Rev. 2009, 109, 2551.
(8) (a) Zhang, J.; Gandelman, M.; Shimon, L. J. W.; Milstein, D. Organometallics 2004, 23, 4026. (b) Zhang, J.; Leitus, G.; Ben-David, Y.; Milstein, D. J. Am. Chem. Soc. 2005, 127, 10840. (c) Zhang, J.; Leitus, G.; Ben-David, Y.; Milstein, D. Angew. Chem. Int. Ed. 2006, 45, 1113. (d) Zhang, J.; Gandelman, M.; Shimon, L. J. W.; Milstein, D. Dalton Trans. 2007, 107. (e) Gunanathan, C.; Ben-David, Y.; Milstein, D. Science 2007, 317, 790. (f) Gnanaprakasam, B.; Zhang, J.; Milstein, D. Angew. Chem. Int. Ed. 2010, 49, 1. (g) Milstein, D. Top. Catal. 2010, 53, 915.
(9) (a) Gunanathan, C.; Shimon, L. J. W.; Milstein, D. J. Am. Chem. Soc. 2009, 131, 3146. (b) Gunanathan, C.; Milstein, D. Angew. Chem. Int. Ed. 2008, 47, 8661.
(10) Khaskin, E.; Iron, M. A.; Shimon, L. J. W.; Zhang, J.; Milstein, D. J. Am. Chem. Soc. 2010, 132, 8542.
(11) Kohl, S.W.; Weiner, L.; Schwartsburd, L.; Konstantinovski, L.; Shimon, L. J. W.; Ben-David, Y.; Iron, M. A.; Milstein, D. Science 2009, 324, 74.
(12) (a) Schubert. U. S.; Eschbaumer. C.; Heller. M. Org. Lett. 2000, 3373. (b) Smith. A. P.; Lamba. J. J. S.; Fraser. C. L. Org. Synth. 2002, 78, 82.
(13) Ahmad, N.; Levison, J. J.; Robinson, S. D.; Uttley, M. F. Inorg. Synth. 1974, 15, 45.
(14). Balaraman, E.; Gnanaprakasam, B.; Shimon, L. J. W.; Milstein, D. J. Am. Chem. Soc. 2010, 132, 16756-16758.

(B) References Relates to Formation of Amides:

[0292]

(1) N. Sewald, H. -D. Jakubke, Peptides: Chemistry and Biology (Wiley-VCH, 2002).
(2a) A. Greenberg, C. M. Breneman, J. F. Liebman, The Amide Lingkage: Selected Structural Aspects in Chemistry, Biochemistry, and Material Science (Wiley, New York, 2000).
(2b) M. B. Smith, J. March, Advanced Organic Chemistry (Wiley, New York, ed. 5, 2001).
(3) B. L. Bray, Nat. Rev. 2, 587-93 (2003).
(4) R. C. Larock, Comprehensive Organic Transformations (VCH, New York, ed. 2, 1999).
(5) M. B. Smith, Compendium of Organic Synthetic Methods (Wiley, 2001), Vol. 9, Pp 100-116.
(6) C. J. Cobley, M. van den Heuvel, A. Abbadi, J. G. de Vries, Tetrahedron Lett. 41, 2467-2470 (2000).
(7) S. I. Murahashi, T. Naota, E. Saito, J. Am. Chem. Soc. 108, 7846-7847 (1986).
(8) S. I. Murahashi, S. Sasao, E. Saito, T. Naota, J. Org. Chem. 57, 2521-2523 (1992).
(9) Y. Tamaru, Y. Yamada, Z. Yoshida, Synthesis 1983, 474-476 (1983).
(10) A. Tillack, I. Rudloff, M. Beller, Eur. J. Org. Chem. 2001, 523-528 (2001).
(11) W. K. Chan, C. M, Ho, M. K. Wong, C. M. Che, J. Am. Chem. Soc. 128, 14796-14797 (2006).
(12) S. H. Cho, E. J. Yoo, I. Bae, S. Chang, J. Am. Chem. Soc. 127, 16046-16047 (2005).
(13) M. P. Cassidy, J. Raushel, V. V. Fokin, Angew. Chem. Int. Ed. 45, 3154-3157 (2006).
(14) Nordstrom, L. U.; Vogt, H.; Madsen, R. J. Am. Chem. Soc. 2008, 130, 17672

(15) Shimizu, K.; Ohshima, K.; Satsuma, A. Chem. Eur. J. 2009, 15, 9977
(16) Ghosh, S.C., Muthaia, S.; Zhang, Y.; Xu, X.; Hong, S.H; A Adv. Synth. Catal. 2009, 351, 2643
(17) Zweifel, T.; .; Naubron, J. V.; Grutzmacher, H. Angew. Chem. Int. Ed. 2009, 48, 559
(18) Watson, A.J.A.; Maxwell, A. C.; Williams, J. M. J. Org. Lett. 2009, 11, 2667.
(19) Zeng, H.; Guan, Z. J. Am. Chem. Soc. 2011, 133, 1159.

References related to Borohydrides:

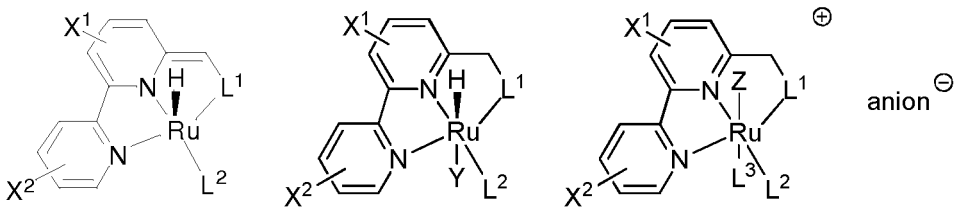
[0293]

(1) a) D. G. Dick, R. Duchateau, J. H. Edema, S. Gambarotta, Inorg. Chem. 1993, 32, 1959-1962 and references therein; b) J. P. White III, H. Deng, S. G. Shore, Inorg. Chem. 1991, 30, 2337-2342.
(2) a) K. Burgess, W. A. van der Donk, J. Am. Chem. Soc. 1994, 116, 6561-6569; b) K. Isagawa, H. Sano, M. Hattori, Y. Otsuji, Chem. Lett. 1979, 1069-1072; c) H. S. Lee, I K. sagawa, Y. Otsuji, Chem. Lett. 1984, 363-366; d) H. S. Lee, K. Isagawa, H. Toyoda, Y. Otsuji, Chem. Lett. 1984, 673-676.
(3) a) D. Barbier-Baudry, O. Blacque, A. Hafid, A. Nyassi, H. Sitzmann, M. Visseaux, Eur. J. Inorg. Chem. 2000, 2333-2336; b) F. Bonnet, A. C. Hillier, A. Collins, S. R. Dubberley, P. Mountford, J. Chem. Soc., Dalton Trans. 2005, 421-423; c) T. J. Marks, J. R. Kolb, Chem. Rev. 1977, 77, 263-293.
(4) I. Palard, A. Soum, S. M. Guillaume, Chem. Eur. J. 2004, 10, 4054-4062.
(5) T. Ohkuma, M. Koizumi, K. Muniz, G. Hilt, C. Kabuto, R. Noyori, J. Am. Chem. Soc, 2002, 124, 6508-6509; b) C. A. Sandoval, T. Ohkuma, K. Muniz, R. Noyori, J. Am. Chem. Soc. 2003, 125, 13490-13503.
(6) R. Guo, X. Chen, C. Elpelt, D. Song, R Morris, Org. Lett. 2005, 7, 1757-1759.
(7) (a) J. A. Jensen, S. R. Wilson, G. S. Girolami, J. Am. Chem. Soc. 1988, 110, 4977-4982; b) J. A. Jensen, G. S. Girolami, J. Chem. Soc., Chem. Commun. 1986, 1160-1162.
(8) Recent reviews: a) M. E. van der Boom, D. Milstein, Chem. Rev. 2003, 103, 1759-1792; b) M. Albrecht, G. van Koten, Angew. Chem. Int. Ed. 2001, 40, 3750-3781; c) A. Vigalok, D. Milstein, Acc. Chem. Res. 2001, 34, 798-807; d) C. M. Jensen, Chem. Commun. 1999, 2443-2449; e) B. Rybtchinski, D. Milstein, Angew. Chem. Int. Ed. 1999, 38, 870-883.
(9) a) M. Kawatsura, J. F. Hartwig, Organometallics 2001, 20, 1960-1964; b) J. P. Stambuli, S. R. Shaun, K. H. Shaughnessy, J. F. Hartwig, J. Am. Chem. Soc., 2001, 123, 2677-2678.
(10) D. H. Gibson, C. Pariya, M. S. Mashuta, Organometallics 2004, 23, 2510-2513.
(11) S. M. Kloek, M. D. Heinekey, K. I. Goldberg, Organometallics, 2006, 25, 3007-3011.
(12) a) D. Hermann, M. Gandelman, H. Rozenberg, L. J. W. Shimon, D. Milstein, Organometallics 2002, 21, 812-818; b) E. Ben-Ari, M. Gandelman, H. Rozenberg, L. J. W. Shimon, D. Milstein, J. Am. Chem. Soc. 2003, 125, 4714-4715; c) J. Zhang, M. Gandelman, L. J. W. Shimon, H. Rozenberg, D. Milstein, Organometallics 2004, 23, 4026-4033; d) J. Zhang, M. Gandelman, D. Herrman, G. Leitus, L. J. W. Shimon, Y. Ben David, D. Milstein, Inorg. Chim. Acta 2006, 359, 1955-1960; e) E. Ben-Ari, R. Cohen, M. Gandelman, L. J. W. Shimon, J. M. L. Martin, D. Milstein, Organometallics 2006, 25, 3190-3210; f) J. Zhang, G. Leitus, Y. Ben-David, D. Milstein, Angew. Chem. Int. Ed. 2006, 45, 1113-1115; g) M. Feller, A. Karton, G. Leitus, J. M. L. Martin, D. Milstein, J. Am. Chem. Soc. 2006, 127, ASAP
(13) J. Zhang, G. Leitus, Y. Ben-David, D. Milstein, J. Am. Chem. Soc. 2005, 127, 10840-10841.
(14) S. I. Murahashi, T. Naota, K. Ito, Y. Maeda, H. Taki, J. Org. Chem. 1987, 52, 4319-4327. Heating $Ru(H)_2(PPh_3)_4$ with 1-butanol at 180 °C in toluene (sealed tube) resulted in 40 turnovers of butyl butyrate after 24 hrs.
(15) a) H. B. Charman, J. Chem. Soc. B, 1970, 584-587; b) D. Morton, D. J. Cole-Hamilton Chem. Comm. 1988, 1154-1156.
(16) a) A. Dobson, S. D. Robinson, Inorg. Chem., 1977, 16, 137-142; b) C. W. Jung, P. E. Garrou, Organometallics 1982, 1, 658-666; c) G. B. W. L. Ligthart, R. H. Meijer, M. P. Donners, J., J. Meuldijk, V. J. A. J. M. Ekemans, L. A. Hulshof, Tetrahedron Lett. 2003, 44, 1507-1509.
(17) (a) S. Shinoda, T. Kojima, Y. Saito, J. Mol. Cat., 1983, 18, 99-104; (b) T. Matsubara, Y. Saito, J. Mol. Cat., 1994, 92, 1-8.
(18) G. R. A. Adair and J. M. J. Williams, Tetrahedron Lett. 2005, 46, 8233-8235.
(19) Y. Lin, D. Ma, X. Lu, Tetrahedron Lett., 1987, 28, 3115-3118.
(20) Y. Blum, Y. Shvo, J. Organomet. Chem. 1985, 282, C7-C10; Yields and reaction times were not reported.
(21) Homogeneous catalytic dehydrogenative lactonization of diols: (a) Y. Lin, X. Zhu, Y. Zhou, J. Organometal. Chem. 1992, 429, 269-274; Attempted use of primary alcohols resulted in no catalysis (b) J. Zhao, J. F. Hartwig, Organometallics 2005, 24, 2441
(22) a) J. A. Statler, G. Wilkinson, M. Thornton-Pett, M. B. Hursthousee, J. Chem. Soc., Dalton Trans. 1984, 1731-1738; b) J. B. Letts, T. J. Mazanec, D. W. Meek, J. Am. Chem. Soc. 1982, 104, 3898-3905.
(23) G. Jia, H. M. Lee, I. D. Williams, C.-P. Lau, Y. Chen, Organometallics 1997, 16, 3941-3949.

(24) a) R. Pierantozzi, G. L. Geoffroy, Inorg. Chem. 1980, 19, 1821-1822; b) G. Geoffroy, L. R. Pierantozzi, J. Am. Chem. Soc. 1976, 98, 8054-8059.
(25) N. Menashe, Y. Shvo, Organometallics 1991, 10, 3885-3891.
(26) T. Ito, H. Horino, Y. Koshiro, A. Yamamoto, Bull. Chem. Soc. Jpn. 1982, 55, 504-512.
(27) A. Jansen, S. Pitter, Monatsch. Chem. 1999, 130, 783-794.
(28) R. Holm, Inorg. Synth. 1970, 12, 238-240.

Claims

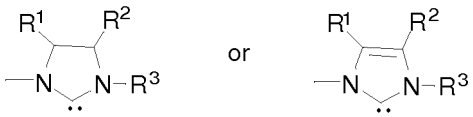
1. A Ruthenium complex represented by the structure of any of formulae B1, B2 or A3:



B1 **B2** **A3**

wherein

L^1 is selected from the group consisting of phosphine (PR^aR^b), and a N-heterocyclic carbene represented by the structures:



;

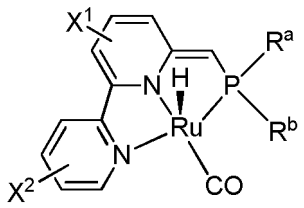
L^2 is a mono-dentate two-electron donor selected from the group consisting of CO, $P(OR^a)(OR^b)(OR^c)$, NO^+, isonitrile (RNC), PF_3, and CS;
L^3 is absent or is **L^2;**
Y and **Z** are each independently H or an anionic ligand selected from the group consisting of halogen, OCOR, $OCOCF_3$, OSO_2R, and OSO_2CF_3;
R^a, R^b and **R^c** are each independently C_1 to C_{12} linear or branched substituted or unsubstituted alkyl, C_3 to C_8 saturated or unsaturated substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl system containing 6-14 ring carbon atoms, 5-8 membered saturated or unsaturated heterocyclyl that have 1 to 4 heteroatoms selected from O, S and N, heteroaryl containing 5 or more ring atoms, wherein at least one ring atom is selected from N, S and O, or combinations thereof selected from: alkylcycloalkyl, alkylaryl, alkylheterocyclyl or alkylheteroaryl; wherein substitutions are one or more selected from the group consisting of halogen, hydroxy, alkoxy, aryloxy, alkylaryloxy, heteroaryloxy, oxo, cycloalkyl, phenyl, heteroaryls, heterocyclyl, naphthyl, amino, alkylamino, arylamino, heteroarylamino, dialkylamino, diarylamino, alkylarylamino, alkylheteroarylamino, arylheteroarylamino, acyl, acyloxy, nitro, carboxy, carbamoyl, carboxamide, cyano, sulfonyl, sulfonylamino, sulfinyl, sulfinylamino, thiol, alkylthio, arylthio, or alkylsulfonyl groups;
R, R^1, R^2 and **R^3** are each independently H, C_1 to C_{12} linear or branched substituted or unsubstituted alkyl, C_3 to C_8 saturated or unsaturated substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl system containing 6-14 ring carbon atoms, 5-8 membered saturated or unsaturated heterocyclyl that have 1 to 4 heteroatoms selected from O, S and N, heteroaryl containing 5 or more ring atoms, wherein at least one ring atom is selected from N, S and O, or combinations thereof selected from: alkylcycloalkyl, alkylaryl, alkylheterocyclyl or alkylheteroaryl; wherein substitutions are one or more selected from the group consisting of halogen, hydroxy, alkoxy, aryloxy, alkylaryloxy, heteroaryloxy, oxo, cycloalkyl, phenyl, heteroaryls, heterocyclyl, naphthyl, amino, alkylamino, arylamino, heteroarylamino, dialkylamino, diarylamino, alkylarylamino, alkylheteroarylamino, arylheteroarylamino, acyl, acyloxy, nitro, carboxy, carbamoyl, carboxamide, cyano, sulfonyl, sulfonylamino, sulfinyl, sulfinylamino, thiol, alkylthio, arylthio, or alkylsulfonyl groups;

X^1 represents zero, one, two or three substituents and **X^2** represents zero, one, two, three or four substituents, wherein each such substituent is independently selected from the group consisting of C_1 to C_{12} linear or branched substituted or unsubstituted alkyl, C_3 to C_8 saturated or unsaturated substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl system containing 6-14 ring carbon atoms, 5-8 membered saturated or unsaturated heterocyclyl that have 1 to 4 heteroatoms selected from O, S and N, heteroaryl containing 5 or more ring atoms, wherein at least one ring atom is selected from N, S and O, or combinations thereof selected from: alkylcycloalkyl, alkylaryl, alkylheterocyclyl or alkylheteroaryl; wherein substitutions are one or more selected from the group consisting of halogen, hydroxy, alkoxy, aryloxy, alkylaryloxy, heteroaryloxy, oxo, cycloalkyl, phenyl, heteroaryls, heterocyclyl, naphthyl, amino, alkylamino, arylamino, heteroarylamino, dialkylamino, diarylamino, alkylarylamino, alkylheteroarylamino, arylheteroarylamino, acyl, acyloxy, nitro, carboxy, carbamoyl, carboxamide, cyano, sulfonyl, sulfonylamino, sulfinyl, sulfinylamino, thiol, alkylthio, arylthio, or alkylsulfonyl groups,, halogen, nitro, amide, ester, cyano, alkoxy, alkylamino, arylamino, an inorganic support and a polymeric moiety; and

anion represents a group bearing a single negative charge; or
a borane derivative of said complex.

2. The complex according to claim 1,

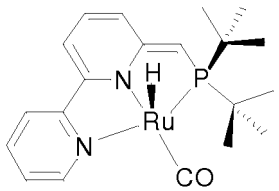
wherein X^1 and X^2 are each absent, and the bipyridine moiety is unsubstituted; or
wherein L^1 is phosphine (PR^aR^b); or
wherein L^2 is CO; or
wherein Z and Y are H or halogen; or
wherein the complex is represented by formula **C1:**



C1

wherein each of X^1, X^2 R^a and R^b are as defined in claim 1,

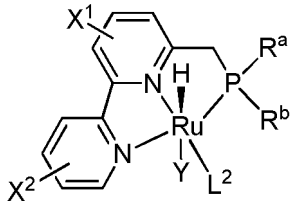
preferably wherein the Ruthenium complex is represented by the structure of formula **3:**



3

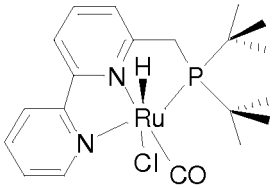
;

or
wherein the complex is represented by formula **C2**:

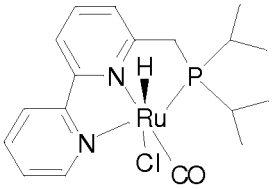


C2

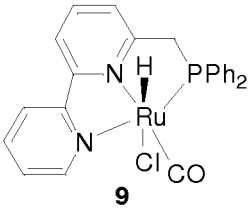
wherein each of L^2, X^1, X^2, Y, R^a and R^b are as defined in claim 1,
preferably wherein Y is halogen or wherein L^2 is CO, more preferably wherein the Ruthenium complex is represented by the structure of formulae 4, 7 or 9:



4



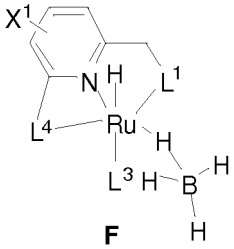
7



9

.

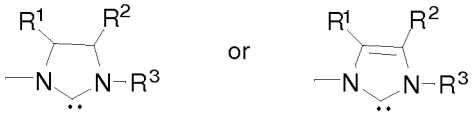
3. A borane derivative of a Ruthenium complex, wherein said borane derivative is represented by the structure of formula F:



F

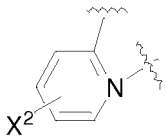
wherein

each **L^1** is independently selected from the group consisting of phosphine (PR^aR^b), and a N-heterocyclic carbene represented by the structures:



;

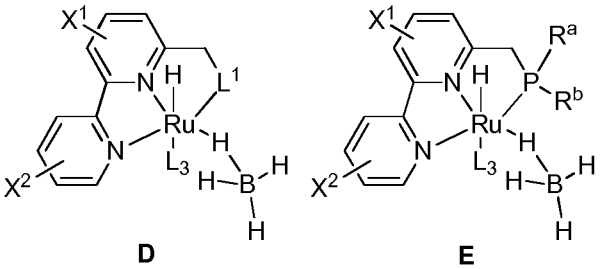
L^3 is absent or is a mono-dentate two-electron donor selected from the group consisting of CO, $P(OR^a)(OR^b)(OR^c)$, NO^+, isonitrile (RNC), PF_3, and CS;
L^4 is a group of the formula:



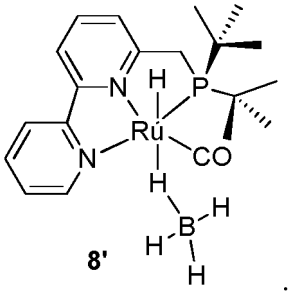
R^a, R^b and **R^c** are each independently alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkylcycloalkyl, alkylaryl, alkylheterocyclyl or alkylheteroaryl;
R, R^1, R^2 and **R^3** are each independently H, alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkylcycloalkyl,

alkylaryl, alkylheterocyclyl or alkylheteroaryl;
X^1 represents zero, one, two or three substituents and **X**^{2} represents zero, one, two, three or four substituents, wherein each such substituent is independently selected from the group consisting of alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, alkylcycloalkyl, alkylaryl, alkylheterocyclyl, alkylheteroaryl, halogen, nitro, amide, ester, cyano, alkoxy, alkylamino, arylamino, an inorganic support and a polymeric moiety,

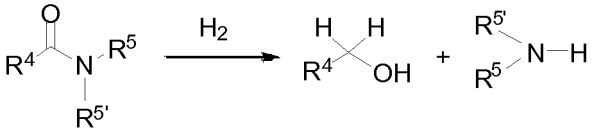
preferably wherein the Ruthenium complex is represented by the structure of any of formula:



more preferably wherein the Ruthenium complex is represented by the structure of formula 8':



4. A process for hydrogenating an amide to an alcohol and an amine, comprising the step of reacting the amide represented by the formula $R^4C(=O)\text{-}N\text{-}R^5R^{5'}$ with molecular hydrogen (H_2), to generate an alcohol of formula R^4CH_2OH and amine of formula $R^5R^{5'}NH$:

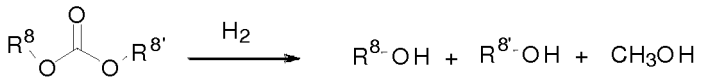


wherein R^4, R^5 and $R^{5'}$ are each independently selected from the group consisting of H, an unsubstituted or substituted alkyl, alkoxyalkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl;
wherein the process is conducted in the presence of the Ruthenium complex according to any of claims 1 or 2, preferably wherein the amide is selected from the group consisting of N-benzyl-2-methoxyacetamide, N-hexyl-2-methoxyacetamide, N-hexyl- 3-methyloxetane-3-carboxamide, N-hexyl-2-furanylcarboxamide, N-benzylbenzamide, N- ethylacetamide, N-methylpropionamide, N-cyclohexyl-2-methoxyacetamide, N- phenylacetamide, N-phenylhexylamide, 2-methoxy-N-phenylacetamide, N-phenylbenzamide, Ethylenediamine-N,N'-(2-methoxyacetamide), N-hexanoylmorpholine, N-butanoylmorpholine, N-2-metoxyacetylpyrrolidine, N-formylmorpholine, N,N-dimethylformamide, N,N- diethylbenzamide, benzamide, 4-methylbenzamide, cyclohexanecarboxamide, hexanamide, acetamide, acrylamide and pivalamide; and
optionally wherein the amide is a cyclic amide (lactam) and the process results in an amino alcohol, or optionally wherein the amide is a polyamide, or wherein the amide is a polypeptide.

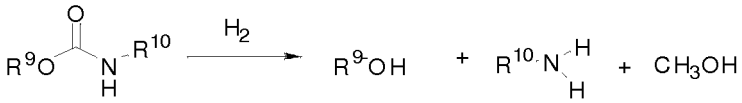
5. A process for hydrogenating an ester, organic carbonate, carbamate or urea derivative, comprising the step of reacting the ester, organic carbonate, carbamate or urea derivative with molecular hydrogen (H_2) in the presence of the Ruthenium complex according to any of claims 1 to 3, thereby hydrogenating the ester, organic carbonate, carbamate or urea derivative and generating at least one alcohol, amine or combination thereof;

(I) preferably wherein the process is selected from the group consisting of:

a. a process comprising the step of hydrogenating a carbonate represented by the formula R^8O-C(=O)-$OR^{8'}$ to the corresponding alcohols(s) and methanol:

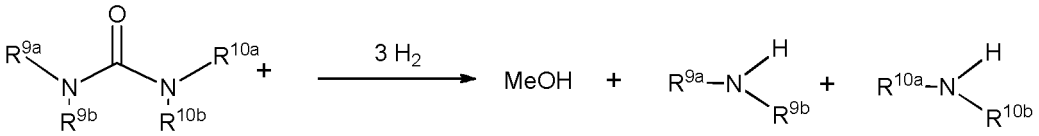


wherein R^8 and R^8 are the same or different and are selected from the group consisting of an unsubstituted or substituted alkyl, alkoxyalkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl, wherein the carbonate is preferably dimethyl carbonate, diethyl carbonate, dipropyl carbonate or dibutyl carbonate;
b. a process comprising the step of hydrogenating a carbamate represented by the formula R^9O-C(=O)-NHR^{10} to the corresponding amine, alcohol and methanol:



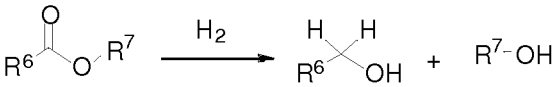
wherein R^9 is selected from the group consisting of an unsubstituted or substituted alkyl, alkoxyalkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl; and
R^{10} is selected from the group consisting of H or an unsubstituted or substituted alkyl, alkoxyalkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl,

wherein the carbamate is preferably methyl benzylcarbamate or methyl 4-methoxybenzylcarbamate; and
c. a process comprising the step of hydrogenating a urea derivative to the corresponding amine and methanol:



or;

(II) preferably wherein said process comprising the step of hydrogenating an ester represented by the formula R^6C(=O)-OR^7 to the corresponding alcohol or alcohols:

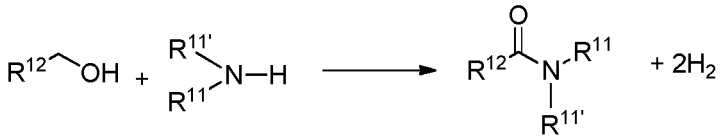


wherein

R^6 is selected from the group consisting of H, an unsubstituted or substituted alkyl, alkoxyalkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl; and
R^7 is selected from the group consisting of an unsubstituted or substituted alkyl, alkoxyalkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl;

preferably wherein R^6 is H and the process comprises hydrogenating a formate ester of formula H-C(=O)-OR^7 to methanol and an alcohol of formula R^7-OH;
more preferably wherein the ester is selected from the group consisting of hexyl hexanoate, butyl butyrate, methyl formate, ethyl formate, propyl formate and butyl formate; or wherein the ester is a polyester, or whererin the ester is cyclic ester (lactone), or wherein the ester is a cyclic di-ester (di-lactone), and the process results in the formation of a diol; preferably wherein the cyclic di-ester is biomass-derived, preferably wherein the cyclic di-ester is glycolide or lactide.

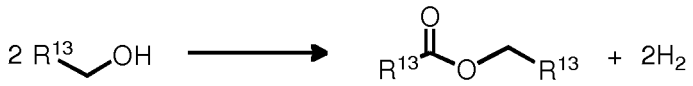
6. A process for preparing an amide, comprising the step of reacting a primary or secondary amine with a primary alcohol in the presence of the Ruthenium complex according to any of claims 1 to 3, thereby generating the amide and molecular hydrogen,
wherein the process comprises the step of reacting an amine represented by formula $R^{11}R^{11'}NH$ with an alcohol represented by the formula $R^{12}CH_2OH$ to generate an amide represented by the structure R^{12}-C(=O)-$NR^{11}R^{11'}$:



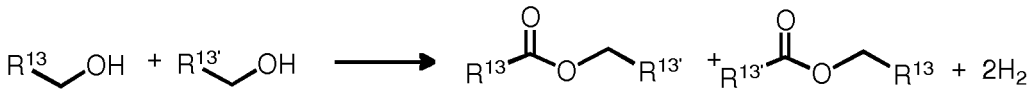
wherein R^{10}, R^{11} and R^{12} are each independently selected from the group consisting of H an unsubstituted or substituted alkyl, alkoxyalkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl;
preferably wherein the alcohol is selected from the group consisting of methanol, ethanol, propanol, butanol, pentanol, hexanol, 2-methoxyethanol, and 2-methyl-1-butanol; or wherein the amine is selected from the group consisting of benzylamine, 1-hexylamine, 1-pentylamine, 1-(2-furyl)methylamine, aniline, morpholine, pyrrolidine, 2-methylhexylamine, cyclohexylamine, ethylenediamine, diethylenetriamine and 1,6-diaminohexane; and
optionally, wherein (a) the amine is a diamine or the alcohol is a dialcohol, and the process results in a diamide; or (b) the amine is a diamine and the alcohol is a dialcohol, and the process results in a polyamide; or (c) the amine and alcohol are present in the same molecule, and the process is an intra-molecular process which results in a lactam; or (d) the amine and the alcohol are present in the same molecule, and the process is an inter-molecular process which results in a polyamide; or (e) the amine and alcohol together represent a beta-amino alcohol, and the process results in a polypeptide; or (f) the amine and alcohol together represent a beta-amino alcohol, and the process results in a cyclic dipeptide.

7. A process for preparing an ester by dehydrogenative coupling of primary alcohols, or by dehydrogenative coupling of a primary alcohol and a secondary alcohol, comprising the step of reacting the alcohols in the presence of the Ruthenium complex according to any of claims 1 to 3, thereby generating the ester and molecular hydrogen, wherein the process is selected from the group consisting of:

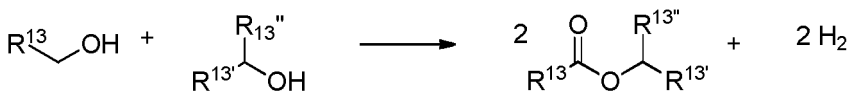
(a) a process comprising the step of converting a primary alcohol represented by formula $R^{13}CH_2OH$ to an ester by the structure R^{13}-C(=O)-OCH_2R^{13}:



wherein R^{13} is selected from the group consisting of H, an unsubstituted or substituted alkyl, alkoxyalkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl;
(b) a process comprising the step of reacting a first primary alcohol represented by formula $R^{13}CH_2OH$ with a second alcohol represented by formula $R^{13'}CH_2OH$ so as to generate an ester by the structure R^{13}-C(=O)-$OCH_2R^{13'}$ or an ester of formula $R^{13'}$-C(=O)-OCH_2R^{13}

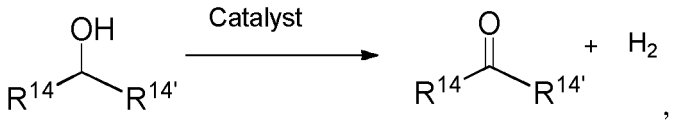


wherein R^{13} and $R^{13'}$ are the same or different from each other and are each independently selected is from the group consisting of H, an unsubstituted or substituted alkyl, alkoxyalkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl; and
(c) a process comprising the step of reacting a primary alcohol represented by formula $R^{13}CH_2OH$ with a secondary alcohol of formula $R^{13'}R^{13''}CHOH$ so as to generate an ester by the structure R^{13}-C(=O)-$OCHR^{13'}R^{13''}$:



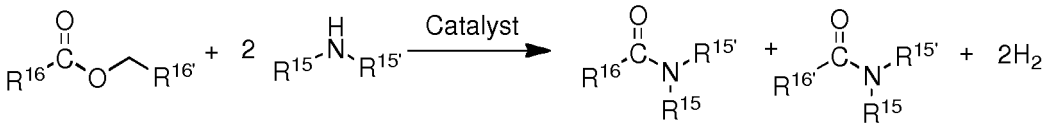
wherein R^{13}, $R^{13'}$ and $R^{13''}$ are each independently selected from the group consisting of H, an unsubstituted or substituted alkyl, alkoxyalkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl;
preferably wherein the alcohol is selected from the group consisting of methanol, ethanol, propanol, butanol, pentanol, hexanol, 2-methoxyethanol, 2-methyl-1-butanol, benzyl alcohol, 1-phenylethanol and cyclohexane methanol; or
wherein the alcohol is a dialcohol, and the process results in a polyester or a lactone.

8. A process for preparing a ketone by dehydrogenation of a secondary alcohol, comprising the step of reacting the secondary alcohol in the presence of the Ruthenium complex according to any of claims 1 to 3, thereby generating the ester and molecular hydrogen; wherein the process comprises the step of converting a secondary alcohol represented by formula $R^{14}CH(OH)R^{14'}$ to a ketone represented by the structure R^{14}-C(=O)-$R^{14'}$:



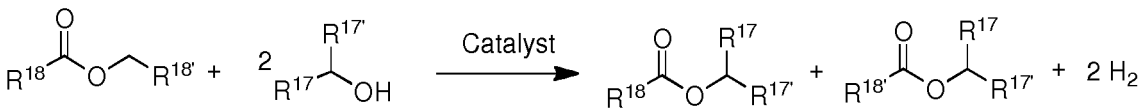
preferably
wherein the secondary alcohol is selected from the group consisting of 1-phenyl-1-ethanol, 2-hexanol, cyclohexanol and 2-propanol.

9. A process for preparing an amide, comprising the step of reacting a primary or secondary amine with an ester in the presence of the Ruthenium complex according to any of claims 1 to 3, thereby generating the amide and molecular hydrogen, wherein the process comprises the step of reacting an amine represented by formula $R^{15}R^{15'}NH$ with an ester represented by the formula R^{16}-C(=O)-$OCH_2R^{16'}$ to generate an amide represented by the structure R^{16}-C(=O)-$NR^{15}R^{15'}$:



wherein R^{15}, $R^{15'}$, R^{16} and $R^{16'}$ are each independently selected from the group consisting of H an unsubstituted or substituted alkyl, alkoxyalkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl;
preferably wherein the ester is selected from the group consisting of ethyl acetate, butyl butyrate, pentyl pentanoate and hexyl hexanoate.; orwherein the amine is selected from the group consisting of pyrrolidine, morpholine, 1-methyl piperazine, piperidine, piperazine, 1-hexylamine and p-tolylmethanamine.

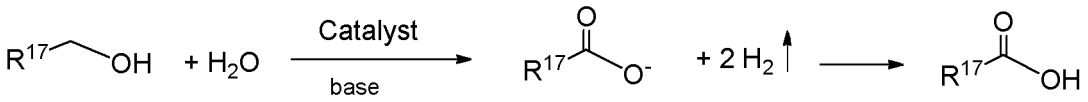
10. A process for preparing an ester by reacting a primary or secondary alcohol with an ester in the presence of the Ruthenium complex according to any of claims 1 to 3, thereby generating the ester and molecular hydrogen, wherein the process comprises the step of reacting a primary or secondary alcohol represented by formula $R^{17}R^{17'}CHOH$ with an ester by the structure R^{18}-C(=O)-$OCH_2R^{18'}$:



wherein R^{17}, $R^{17'}$, R^{18} and $R^{18'}$ are each independently selected from the group consisting of H, an unsubstituted or substituted alkyl, alkoxyalkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl;
preferably wherein the alcohol is selected from the group consisting of cyclohexanol, cyclopentanol, 1-phenylethanol, isopropanol and 3-pentanol; or wherein the ester is selected from the group consisting of ethyl acetate, hexyl hexanoate, pentyl pentanoate, butyl butyrate, ethyl butyrate and methyl hexanoate.

11. A process for preparing a carboxylic acid comprising the step of reacting a primary alcohol with water and a base in the presence of the Ruthenium complex according to any of claims 1 to 3,
thereby generating the carboxylic acid and molecular hydrogen,

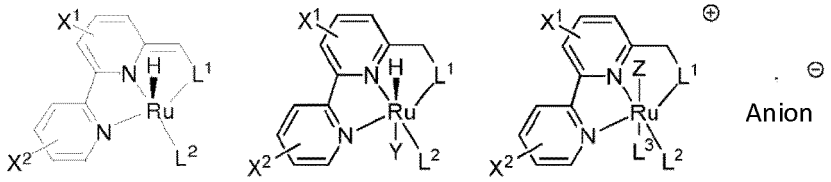
wherein the process comprises the step of reacting a primary alcohol represented by formula $R^{17}CH_2OH$ with water in the presence of a base so as to generate a carboxylic acid salt represented by the structure R^{17}-C(=O)O^- and, optionally, if desired, converting the carboxylic acid salt to the corresponding carboxylic acid of formula R^{17}-C(=O)OH.



wherein R^{17} is selected from the group consisting of H, an unsubstituted or substituted alkyl, alkoxyalkyl, cycloalkyl, aryl, alkylaryl, heterocyclyl and heteroaryl;
preferably wherein the alcohol is selected from the group consisting of butanol, pentanol, decanol, 2-methoxyethanol, 2-phenylethanol, cyclohexylmethanol, 3-phenylbutan-1-ol, but-3-en-1-ol, (4-methoxyphenyl)methanol, and (2,4-dimethoxyphenyl)methanol.

Patentansprüche

1. Rutheniumkomplex, der durch die Struktur einer der Formeln B1, B2 oder A3 dargestellt wird:



B1 **B2** **A3**

wobei

L^1 aus der Gruppe bestehend aus Phosphin (PR^aR^b) und einem N-Heterocyclischen Carben, die durch die folgenden Strukturen dargestellt werden, ausgewählt ist:

L^2 ist ein Monodentat-Zwei-Elektronendonor, der aus der Gruppe bestehend aus CO, $P(OR^a)(OR^b)(OR^c)$, NO^+, Isonitril (RNC), PF_3 und CS ausgewählt ist;
L^3 fehlt oder ist **L^2;**
Y und **Z** sind jeweils unabhängig H oder ein anionischer Ligand, jeweils aus der Gruppe bestehend aus Halogen, OCOR, $OCOCF_3$, OSO_2R und OSO_2CF_3 ausgewählt;
R^a, R^b und **R^c** sind jeweils unabhängig C_1 bis C_{12} lineares oder verzweigtes, substituiertes oder nicht substituiertes Alkyl, C_3 bis C_8 gesättigtes oder ungesättigtes, substituiertes oder nicht substituiertes Cycloalkyl, substituiertes oder nicht substituiertes Arylsystem mit 6 bis 14 Ring-Kohlenstoffatomen, 5- bis 8-gliedriges, gesättigtes oder ungesättigtes Heterocyclyl mit 1 bis 4 Heteroatomen, die von O, S und N ausgewählt sind, Heteroaryl mit 5 oder mehr Ringatomen, wobei mindestens ein Ringatom von N, S und O ausgewählt ist, oder Kombinationen davon, die ausgewählt sind von: Alkylcycloalkyl, Alkylaryl, Alkylheterocyclyl oder Alkylheteroaryl; wobei eine oder mehr Substitutionen aus der folgenden Gruppe Substituenten ausgewählt wird: Halogen, Hydroxy, Alkoxy, Aryloxy, Alkylaryloxy, Heteroaryloxy, Oxo, Cycloalkyl, Phenyl, Heteroaryl, Heterocyclyl, Naphthyl, Amino, Alkylamino, Arylamino, Heteroarylamino, Dialkylamino, Diarylamino, Alkylarylamino, Alkylheteroarylamino, Arylheteroarylamino, Acyl, Acyloxy, Nitro, Carboxy, Carbamoyl, Carboxamide, Cyano, Sulfonyl, Sulfonylamino, Sulfinyl, Sulfinylamino, Thiol, Alkylthio, Arylthio oder Alkylsulfonyl;
R, R^1, R^2 und **R^3** sind jeweils unabhängig H, C_1 bis C_{12} lineares oder verzweigtes, substituiertes oder nicht substituiertes Alkyl, C_3 bis C_3 gesättigtes oder ungesättigtes, substituiertes oder nicht substituiertes Cycloalkyl,

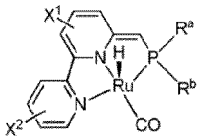
substituiertes oder nicht substituiertes Arylsystem mit 6 bis 14 Ring-Kohlenstoffatomen, 5- bis 8-gliedriges, gesättigtes oder ungesättigtes Heterocyclyl mit 1 bis 4 Heteroatomen, die von O, S und N ausgewählt sind, Heteroaryl mit 5 oder mehr Ringatomen, wobei mindestens ein Ringatom von N, S und O ausgewählt ist, oder Kombinationen davon, die ausgewählt sind von: Alkylcycloalkyl, Alkylaryl, Alkylheterocyclyl oder Alkylheteroaryl; wobei für eine oder mehr Substitutionen aus der folgenden Gruppe Substituenten ausgewählt wird: Halogen, Hydroxy, Alkoxy, Aryloxy, Alkylaryloxy, Heteroaryloxy, Oxo, Cycloalkyl, Phenyl, Heteroaryls, Heterocyclyl, Naphthyl, Amino, Alkylamino, Arylamino, Heteroarylamino, Dialkylamino, Diarylamino, Alkylarylamino, Alkylheteroarylamino, Arylheteroarylamino, Acyl, Acyloxy, Nitro, Carboxy, Carbamoyl, Carboxamide, Cyano, Sulfonyl, Sulfonylamino, Sulfinyl, Sulfinylamino, Thiol, Alkylthio, Arylthio oder Alkylsulfonyl;

X^1 steht für null, einen, zwei oder drei Substituenten; und **X^2** steht für null, einen, zwei, drei oder vier Substituenten, wobei jeder Substituent jeweils unabhängig aus der Gruppe ausgewählt wird von C_1 bis C_{12} lineares oder verzweigtes, substituiertes oder nicht substituiertes Alkyl, C_3 bis C_8 gesättigtes oder ungesättigtes, substituiertes oder nicht substituiertes Cycloalkyl, substituiertes oder nicht substituiertes Arylsystem mit 6 bis 14 Ring-Kohlenstoffatomen, 5- bis 8-gliedrigem, gesättigtem oder ungesättigtem Heterocyclyl mit 1 bis 4 Heteroatomen, die von O, S und N ausgewählt sind, Heteroaryl mit 5 oder mehr Ringatomen, wobei mindestens ein Ringatom von N, S und O ausgewählt ist, oder Kombinationen davon, die von den folgenden ausgewählt sind: Alkylcycloalkyl, Alkylaryl, Alkylheterocyclyl oder Alkylheteroaryl; wobei für eine oder mehr Substitutionen aus der folgenden Gruppe Substituenten ausgewählt wird: Halogen, Hydroxy, Alkoxy, Aryloxy, Alkylaryloxy, Heteroaryloxy, Oxo, Cycloalkyl, Phenyl, Heteroaryl, Heterocyclyl, Naphthyl, Amino, Alkylamino, Arylamino, Heteroarylamino, Dialkylamino, Diarylamino, Alkylarylamino, Alkylheteroarylamino, Arylheteroarylamino, Acyl, Acyloxy, Nitro, Carboxy, Carbamoyl, Carboxamid, Cyano, Sulfonyl, Sulfonylamino, Sulfinyl, Sulfinylamino, Thiol, Alkylthio, Arylthio oder Alkylsulfonylgruppen, Halogen, Nitro, Amid, Ester, Cyano, Alkoxy, Alkylamino, Arylamino, ein anorganischer Träger und ein polymerischer Rest; und Anion steht für eine Gruppe, die eine negative Einzelladung trägt; oder

ein Boranderivat des Komplexes.

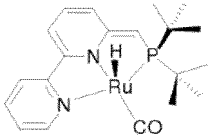
2. Komplex nach Anspruch 1,

wobei X^1 und X^2 jeweils fehlen, und der Bipyridinrest ist nicht substituiert; oder
wobei L^1 Phosphin (PR^aR^b) ist; oder
wobei L^2 CO ist; oder
wobei Z und Y H oder Halogen sind; oder
wobei der Komplex durch die Formel **C1** dargestellt wird:



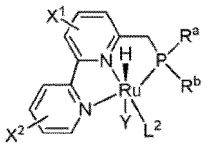
C1

wobei X^1, X^2, R^a und R^b jeweils wie im Anspruch 1 definiert werden, wobei der Rutheniumkomplex bevorzugt durch die Strukturformel 3 dargestellt wird:



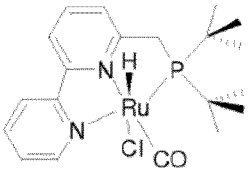
3

oder
wobei der Komplex durch die Formel **C2** dargestellt wird:

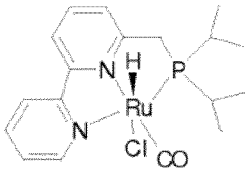


C2

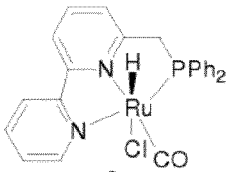
wobei L^2, X^1, X^2, Y, R^a und R^b jeweils wie in Anspruch 1 definiert werden, wobei
Y bevorzugt ein Halogen ist, oder wobei L^2 CO ist, wobei der Rutheniumkomplex noch bevorzugter durch die Strukturformeln 4, 7 oder 9 dargestellt wird:



4

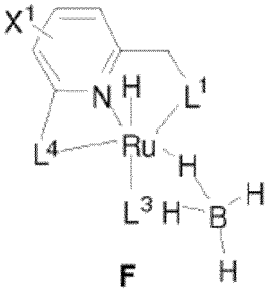


7



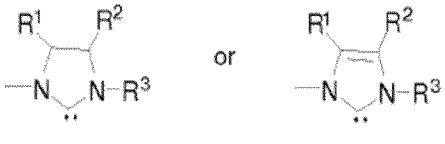
9

3. Boranderivat von einem Rutheniumkomplex, wobei das Boranderivat durch die Strukturformel **F** dargestellt wird:

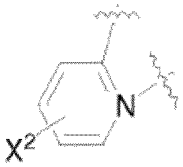


F

wobei
jedes $\mathbf{L^1}$ jeweils unabhängig aus der Gruppe bestehend von Phosphin (PR^aP^b) und einem N-Heterocyclischen Carben besteht, wie dies in den folgenden Strukturformeln dargestellt ist:



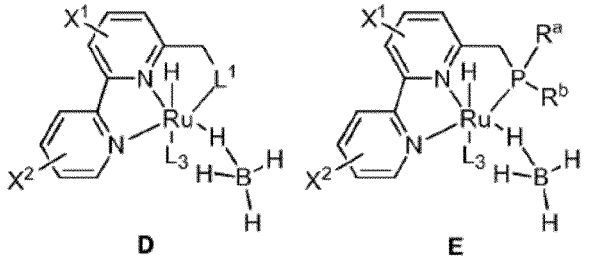
wobei $\mathbf{L^3}$ fehlt oder ein Monodentat-Zweielektronen-Donor ist, ausgewählt aus der Gruppe bestehend aus CO, $P(OR^3)(OR^b)(OR^a)$, NO^+, Isonitril (RNC), PF_3, und CS;
$\mathbf{L^4}$ ist eine Gruppe der Formel:



$\mathbf{R^a}$, $\mathbf{R^b}$ und $\mathbf{R^c}$ stehen jeweils unabhängig für Alkyl, Cycloalkyl, Aryl, Heterocyclyl, Heteroaryl, Alkylcycloalkyl, Alkylaryl, Alkylheterocyclyl oder Alkylheteroaryl;
R, $\mathbf{R^1}$, $\mathbf{R^2}$ und $\mathbf{R^3}$ stehen jeweils unabhängig für H, Alkyl, Cycloalkyl, Aryl, Heterocyclyl Heteroaryl, Alkylcycloalkyl, Alkylaryl, Alkylheterocyclyl oder Alkylheteroaryl;
$\mathbf{X^1}$ steht für null, einen, zwei der drei Substituenten und $\mathbf{X^2}$ steht für null, einen, zwei, drei oder vier Substituenten,

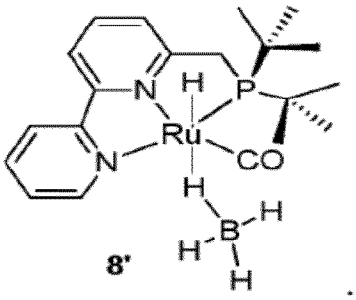
wobei jeder der Substituenten jeweils unabhängig aus der Gruppe bestehend aus folgenden ausgewählt wird: Alkyl, Cycloalkyl, Aryl, Heterocyclyl, Heteroaryl, Alkylcycloalkyl, Alkylaryl, Alkylheterocyclyl, Alkylheteroaryl, Halogen, Nitro, Amid, Ester, Cyano, Alkoxy, Alkylamino, Arylamino, einem anorganischen Träger und einem polymerischen Rest,

wobei der Rutheniumkomplex bevorzugt durch eine dieser Strukturformeln dargestellt wird:



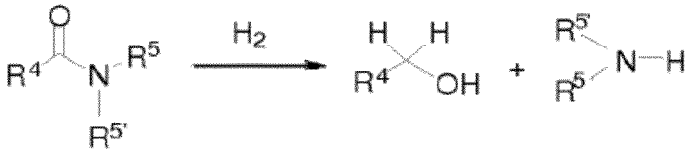
D E

wobei der Rutheniumkomplex bevorzugter durch die Strukturformel 8' dargestellt wird:



8'

4. Prozess zum Hydrieren eines Amids zu einem Alkohol und einem Amin, umfassend den Schritt des Umsetzens des durch Formel $R^4C(=O)\text{-}N\text{-}R^5R^{5'}$ dargestellten Amids mit molekularem Wasserstoff (H_2), um einen Alkohol der Formel R^4CH_2OH und ein Amin der Formel $R^5R^{5'}NH$ zu erhalten.

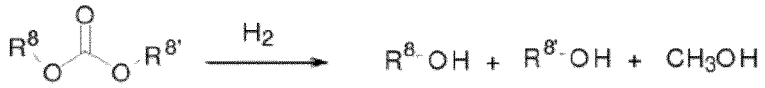


wobei R^4, R^5 and $R^{5'}$ jeweils unabhängig aus der Gruppe bestehend aus H, einem nicht substituierten oder substituierten Alkyl, Alkoxyalkyl, Cycloalkyl, Aryl, Alkylaryl, Heterocyclyl und Heteroaryl ausgewählt werden;
wobei der Prozess bei Anwesenheit des Rutheniumkomplexes nach einem der Ansprüche 1 oder 2 durchgeführt wird, wobei das Amid bevorzugt aus der Gruppe bestehend aus folgenden ausgewählt wird: N-Benzyl-2-methoxyacetamid, N-Hexyl-2-methoxyacetamid, N-Hexyl-3-methyloxetan-3-carboxamid, N-Hexyl-2-furanylcarboxamid, N-Benzylbenzamid, N-Ethylacetamid, N-Methylpropionamid, N-Cyclohexyl-2-methoxyacetamid, N-Phenylacetamid, N-Phenylhexylamid, 2-Methoxy-N-phenylacetamid, N-Phenylbenzamid, Ethylendiamin-N,N'-(2-methoxyacetamid), N-Hexanoylmorpholin, N-Butanoylmorpholin, N-2-Metoxyacetylpyrrolidin, N-Formylmorpholin, N,N-Dimethylformamid, N,N-Diethylbenzamid, Benzamid, 4-Methylbenzamid, Cyclohexancarboxamid, Hexanamid, Acetamid, Acrylamid und Pivalamid; und
wobei das Amid wahlweise ein cyclisches Amid (Lactam) ist, und der Prozess führt zu einem Aminalkohol, oder wobei das Amid wahlweise ein Polyamid ist, oder wobei das Amid ein Polypeptid ist.

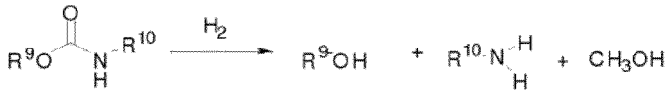
5. Prozess zum Hydrieren eines Esters, organischen Carbonats, Carbamats oder Harnstoffderivats, umfassend den Schritt des Umsetzens des Esters, organischen Carbonats, Carbamats oder Harnstoffderivates mit molekularem Wasserstoff (H_2) bei Anwesenheit des Rutheniumkomplexes nach einem der Ansprüche 1 bis 3, wodurch der Ester, das organische Carbonat, Carbamat oder Harnstoffderivat hydriert wird und mindestens ein Alkohol, Amin oder eine Kombination davon erhalten wird;

(I) wobei der Prozess bevorzugt aus der Gruppe bestehend aus den folgenden ausgewählt wird:

a. einem Prozess, umfassend den Schritt des Hydrierens eines Carbonats, was durch die Formel R^8O-C(=O)-$OR^{8'}$ dargestellt wird, zu dem(den) entsprechenden Alkohol(en) und Methanol:

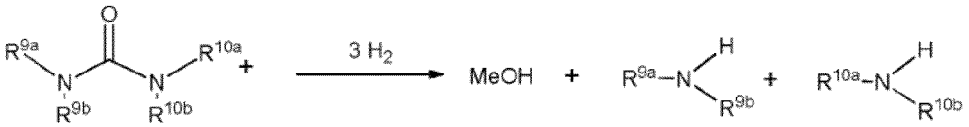


wobei R^8 and R^8 gleich oder unterschiedlich sind und aus der Gruppe bestehend aus folgenden ausgewählt sind: einem nicht substituierten oder substituierten Alkyl, Alkoxyalkyl, Cycloalkyl, Aryl, Alkylaryl, Heterocyclyl und Heteroaryl, wobei das Carbonat bevorzugt Dimethylcarbonat, Diethylcarbonat, Dipropylcarbonat oder Dibutylcarbonat ist;
b. einem Prozess, umfassend den Schritt des Hydrierens eines Carbamats, dargestellt durch die Formel R^9O-C(=O)-NHR^{10}, zum entsprechenden Amin, Alkohol und Methanol:



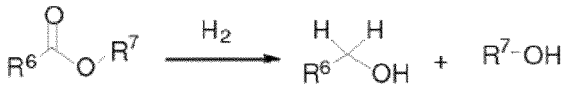
wobei R^9 aus der Gruppe bestehend aus einem nicht substituierten oder substituierten Alkyl, Alkoxyalkyl, Cycloalkyl, Aryl, Alkylaryl, Heterocyclyl und Heteroaryl ausgewählt ist; und
R^{10} wird aus der Gruppe bestehend aus H oder einem nicht substituierten oder substituierten Alkyl, Alkoxyalkyl, Cycloalkyl, Aryl, Alkylaryl, Heterocyclyl und Heteroaryl ausgewählt,

wobei das Carbamat bevorzugt Methylbenzylcarbamat oder Methyl 4-methoxybenzylcarbamat ist; und
c. einem Prozess, umfassend den Schritt des Hydrierens eines Harnstoffderivats zu dem entsprechenden Amin und Methanol:



oder;

(II) wobei der Prozess bevorzugt den Schritt des Hydrierens eines Esters, der durch die Formel R^6C(=O)-OR^7 dargestellt ist, zu dem entsprechenden Alkohol oder den entsprechenden Alkoholen umfasst:



wobei

R^6 aus der Gruppe bestehend aus H, einem nicht substituierten oder substituierten Alkyl, Alkoxyalkyl, Cycloalkyl, Aryl, Alkylaryl, Heterocyclyl und Heteroaryl ausgewählt ist; und
R^7 aus der Gruppe bestehend aus nicht substituiertem oder substituiertem Alkyl, Alkoxyalkyl, Cycloalkyl, Aryl, Alkylaryl, Heterocyclyl und Heteroaryl ausgewählt ist;

wobei R^6 bevorzugt H ist, und der Prozess das Hydrieren eines Ameisensäureesters der Formel H- C(=O)-OR^7 zu Methanol und einem Alkohol der Formel R^7-OH umfasst;
wobei das Ester bevorzugter aus der Gruppe bestehend aus Hexylhexanoat, Butylbutyrat, Methylformiat, Ethylformiat, Propylformiat und Butylformiat ausgewählt ist;
oder wobei der Ester ein Polyester ist, oder wobei der Ester ein cyclischer Ester (Lacton) ist, oder wobei der Ester ein cyclischer Diester (Dilacton) ist, und wobei der Prozess zur Bildung eines Diols führt;

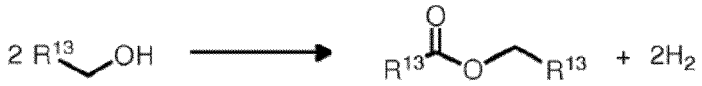
wobei der cyclische Diester bevorzugt von Biomasse abgeleitet ist, wobei dies vorliegend bevorzugt cyclischer Diester, Glycolid oder Lactid ist.

6. Prozess zum Herstellen eines Amids, umfassend den Schritt des Umsetzens von einem primären Amin oder sekundären Amin mit einem primären Alkohol bei Anwesenheit eines Rutheniumkomplexes nach einem der Ansprüche 1 bis 3, um dadurch das Amid und den molekularen Wasserstoff zu erhalten,
wobei der Prozess den Schritt des Umsetzens eines Amins, das durch die Formel $R^{11}R^{11'}NH$ dargestellt wird, mit einem Alkohol, der durch die Formel $R^{12}CH_2OH$ dargestellt wird, umfasst, um ein Amid zu erhalten, das durch die Struktur R^{12}-C(=O)-$NR^{11}R^{11'}$ dargestellt wird:

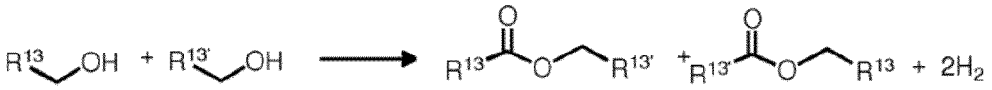
wobei R^{10}, R^{11} and R^{12} jeweils unabhängig aus der Gruppe bestehend aus H, einem nicht substituierten oder substituierten Alkyl, Alkoxyalkyl, Cycloalkyl, Aryl, Alkylaryl, Heterocyclyl und Heteroaryl ausgewählt werden;
wobei der Alkohol bevorzugt aus der Gruppe bestehend aus Methanol, Ethanol, Propanol, Butanol, Pentanol, Hexanol, 2-Methoxyethanol und 2-Methyl-1-butanol ausgewählt wird; oder wobei das Amin aus der Gruppe bestehend aus folgenden ausgewählt wird: Benzylamin, 1-Hexylamin, 1-Pentylamin, 1-(2-Furyl)methylamin, Anilin, Morpholin, Pyrrolidin, 2-Methylhexylamin, Cyclohexylamin, Ethylendiamin, Diethylentriamin und 1,6-Diaminohexan; und
wobei wahlweise Folgendes gilt: (a) das Amin ist ein Diamin oder der Alkohol ist ein Dialkohol, und der Prozess führt zu einem Diamid; oder (b) das Amin ist ein Diamin und der Alkohol ist ein Dialkohol, und der Prozess führt zu einem Polyamid; oder (c) das Amin und der Alkohol liegen in demselben Molekül vor, und der Prozess ist ein intramolekularer Prozess, der zu einem Lactam führt; oder (d) das Amin und der Alkohol liegen in demselben Molekül vor, und der Prozess ist ein intermolekularer Prozess, der zu einem Polyamid führt; oder (e) das Amin und der Alkohol stehen gemeinsam für einen beta-Aminalkohol, und der Prozess führt zu einem Polypeptid; oder (f) das Amin und der Alkohol stehen gemeinsam für einen beta-Aminalkohol, und der Prozess führt zu einem cyclischen Dipeptid.

7. Prozess zum Herstellen eines Esters durch dehydrierendes Koppeln primären Alkohols oder durch dehydrierendes Koppeln eines primären Alkohols und eines sekundären Alkohols, umfassend den Schritt des Umsetzens der Alkohole bei Anwesenheit von dem Rutheniumkomplex nach einem der Ansprüche 1 bis 3, wodurch der Ester und der molekulare Wasserstoff erhalten werden, wobei der Prozess aus der Gruppe bestehend aus folgenden ausgewählt wird:

(a) einem Prozess, umfassend den Schritt des Umwandelns eines primären Alkohols, der durch die Formel $R^{13}CH_2OH$ dargestellt wird, in einen Ester der Struktur R^{13}-C(=O)-OCH_2R^{13}:



wobei R^{13} aus der Gruppe bestehend aus H, einem nicht substituierten oder substituierten Alkyl, Alkoxyalkyl, Cycloalkyl, Aryl, Alkylaryl, Heterocyclyl und Heteroaryl ausgewählt ist;
(b) einem Prozess, umfassend den Schritt des Umsetzen eines ersten primären Alkohols, der durch die Formel $R^{13}CH_2OH$ dargestellt ist, mit einem zweiten Alkohol, der durch die Formel $R^{13'}CH_2OH$ dargestellt ist, sodass ein Ester der Struktur R^{13}-C(=O)-$OCH_2R^{13'}$



oder ein Ester der Formel $R^{13'}$-C(=O)-OCH_2R^{13} erhalten wird:
wobei R^{13} und $R^{13'}$ gleich oder unterschiedlich sind, und jedes wird jeweils unabhängig aus der Gruppe bestehend aus H, einem nicht substitutierten oder substituierten Alkyl, Alkoxyalkyl, Cycloalkyl, Aryl, Alkylaryl, Hete-

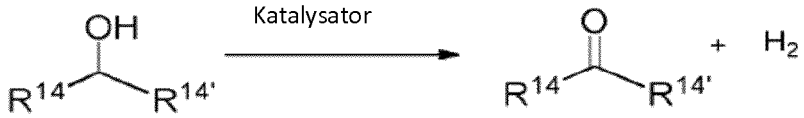
rocyclyl und Heteroaryl ausgewählt; und

(c) einem Prozess, umfassend den Schritt des Umsetzens eines primären Alkohols, der durch die Formel $R^{13}CH_2OH$ dargestellt wird, mit einem sekundären Alkohol der Formel $R^{13'}R^{13''}CHOH$, um einen Ester der Struktur R^{13}-C(=O)-$OCHR^{13'}R^{13''}$ zu erhalten:

wobei R^{13}, $R^{13'}$ und $R^{13''}$ jeweils unabhängig aus der Gruppe bestehend aus H, einem nicht substituierten oder substituierten Alkyl, Alkoxyalkyl, Cycloalkyl, Aryl, Alkylaryl, Heterocyclyl und Heteroaryl ausgewählt ist; wobei der Alkohol bevorzugt aus der Gruppe bestehend aus Methanol, Ethanol, Propanol, Butanol, Pentanol, Hexanol, 2-Methoxyethanol, 2-Methyl-1-butanol, Benzylalkohol, 1-Phenylethanol und Cyclohexanmethanol ausgewählt ist; oder

wobei der Alkohol ein Dialkohol ist und der Prozess führt zu einem Polyester oder einem Lacton.

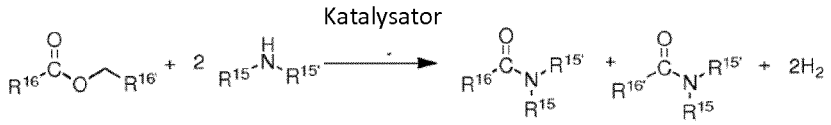
8. Prozess zum Herstellen eines Ketons durch Dehydrieren eines sekundären Alkohols, umfassend den Schritt des Umsetzens des sekundären Alkohols bei Anwesenheit des Rutheniumkomplexes nach einem der Ansprüche 1 bis 3, um dadurch den Ester und den molekularen Wasserstoff herzustellen; wobei der Prozess den Schritt des Umwandelns eines sekundären Alkohols der Formel $R^{14}CH(OH)R^{14'}$ zu einem Keton, das durch die Struktur R^{14}-C(=O)-$R^{14'}$ dargestellt ist, umfasst:



wobei der sekundäre Alkohol bevorzugt aus der Gruppe bestehend aus 1-Phenyl-1-ethanol, 2-hexanol, Cyclohexanol und 2-Propanol ausgewählt ist.

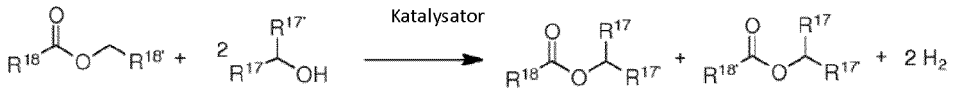
9. Prozess zum Herstellen eines Amids, umfassend den Schritt des Umsetzens eines primären oder sekundären Amins mit einem Ester bei Anwesenheit des Rutheniumkomplexes nach einem der Ansprüche 1 bis 3, wodurch das Amid und molekularer Wasserstoff erhalten werden,

wobei der Prozess den Schritt des Umsetzens eines Amins, das durch die Formel $R^{15}R^{15'}NH$ dargestellt ist, mit einem Ester, der durch die Formel R^{16}-C(=O)-$OCH_2R^{16'}$ dargestellt ist, umfasst, um ein Amid zu erhalten, das durch die Struktur R^{16}-C(=O)-$NR^{15}R^{15'}$ dargestellt wird:



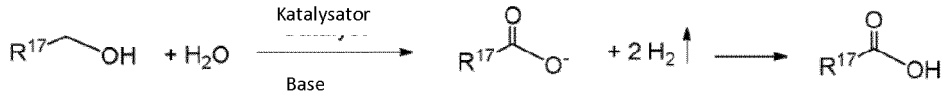
wobei R^{15}, $R^{15'}$, R^{16} und $R^{16'}$ jeweils unabhängig aus der Gruppe bestehend aus H, einem nicht substituierten oder substituierten Alkyl, Alkoxyalkyl, Cycloalkyl, Aryl, Alkylaryl, Heterocyclyl und Heteroaryl ausgewählt ist; wobei der Ester bevorzugt aus der Gruppe bestehend aus Ethylacetat, Butylbutyrat, Pentylpentanoat und Hexylhexanoat ausgewählt ist; oder wobei das Amin aus der Gruppe bestehend aus Pyrrolidin, Morpholin, 1-Methylpiperazin, Piperidin, Piperazin, 1-Hexylamin und p-Tolylmethanamin ausgewählt ist.

10. Prozess zum Herstellen eines Esters, umfassend ein Umsetzen eines primären oder sekundären Alkohols mit einem Ester bei Anwesenheit des Rutheniumkomplexes nach einem der Ansprüche 1 bis 3, wodurch der Ester und der molekulare Wasserstoff erhalten werden, wobei der Prozess den Schritt des Umsetzens eines primären oder sekundären Alkohols, der durch die Formel $R17^{17}R^{17'}$ CHOH dargestellt wird, mit einem Ester der Struktur R^{18}-C(=O)-$OCH_2R^{18'}$ umfasst:



wobei R^{17}, $R^{17'}$, R^{18} und $R^{18'}$ jeweils unabhängig aus der Gruppe bestehend aus H, einem nicht substituierten oder substituierten Alkyl, Alkoxyalkyl, Cycloalkyl, Aryl, Alkylaryl, Heterocyclyl und Heteroaryl ausgewählt sind;
wobei der Alkohol bevorzugt aus der Gruppe bestehend aus Cyclohexanol, Cyclopentanol, 1-Phenylethanol, Isopropanol und 3-Pentanol ausgewählt ist; oder wobei der Ester aus der Gruppe bestehend aus Ethylacetat, Hexylhexanoat, Pentylpentanoat, Butylbutyrat, Ethylbutyrat und Methylhexanoat ausgewählt ist.

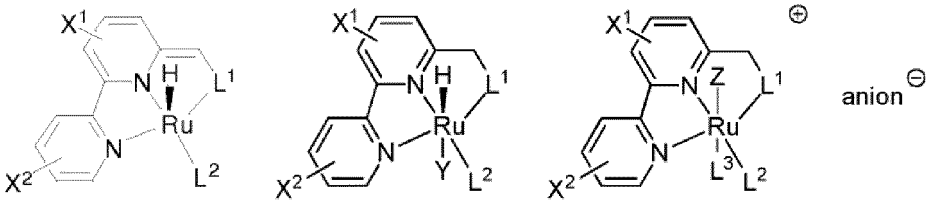
11. Prozess zum Herstellen einer Carbonsäure, umfassend die Schritte des Umsetzens eines primären Alkohols mit Wasser und einer Base bei Anwesenheit des Rutheniumkomplexes nach einem der Ansprüche 1 bis 3, wodurch die Carbonsäure und der molekulare Wasserstoff erhalten werden,
wobei der Prozess den Schritt des Umsetzens eines primären Alkohols, der durch die Formel $R^{17}CH_2OH$ dargestellt ist, mit Wasser bei Anwesenheit einer Base umfasst, sodass ein Carbonsäuresalz, das durch die Struktur R^{17}-C(=O)O' dargestellt ist, erhalten wird, und wahlweises, sofern erwünscht, Umwandeln der Carbonsäure in die entsprechenden Carbonsäuren der Formel R^{17}-C(=O)OH.



wobei R^{17} aus der Gruppe bestehend aus H, einem nicht substituierten oder substituierten Alkyl, Alkoxyalkyl, Cycloalkyl, Aryl, Alkylaryl, Heterocyclyl und Heteroaryl ausgewählt ist;
wobei der Alkohol bevorzugt aus der Gruppe bestehend aus Butanol, Pentanol, Decanol, 2-Methoxyethanol, 2-Phenylethanol, Cyclohexylmethanol, 3-Phenylbutan-1-ol, But-3-en-1-ol, (4-Methoxyphenyl)methanol und (2,4-Dimethoxyphenyl)methanol ausgewählt ist.

Revendications

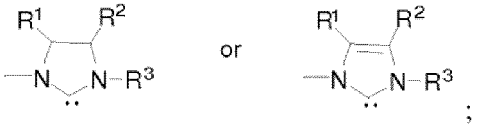
1. Un complexe ruthénium représenté par la structure de l'une des formules B1, B2 ou A3 :



B1 **B2** **A3**

dans laquelle

L^1 est choisi dans le groupe constitué par la phosphine (PR^aR^b) et un carbène N-hétérocyclique représenté par les structures :



;

L^2 est un donneur mono-denté à deux électrons choisi dans le groupe constitué par CO, $P(OR^a)(OR^b)(OR^c)$, NO^+, isonitrile (RNC), PF_3 et CS ;
L^3 est absent ou est L^2;
Y et Z sont chacun indépendamment H ou un ligand anionique choisi dans le groupe constitué par les atomes d'halogène, OCOR, $OCOCF_3$, OSO_2R et OSO_2CF_3 ;
R^a, R^b et R^c sont chacun indépendamment alkyle C_1 à C_{12} substitué ou non substitué, linéaire ou ramifié, cycloalkyle C_3 à C_8 substitué ou non substitué, système aryle substitué ou non substitué contenant 6 à 14

atomes de carbone en anneau, hétérocyclyle à 5 ou 8 chaînons saturés ou non saturés ayant 1 à 4 hétéroatomes choisis parmi O, S et N, hétéroaryle contenant 5 atomes de cycle ou plus, où au moins un atome de cycle est choisi parmi N, S et O, ou des combinaisons de ceux-ci choisis parmi : les groupes alkylcycloalkyle, alkylaryle, alkylhétérocyclyle ou alkylhétéroaryle ; dans lesquels les substitutions se font par un ou plusieurs choisis dans le groupe comprenant halogène, hydroxy, alcoxy, aryloxy, alkylaryloxy, hétéroaryloxy, oxo, cycloalkyle, phényle, hétéroaryles, hétérocyclyle, naphtyle, amino, alkylamino, arylamino, arylamino, hétéroarylamino, dialkylamino, diarylamino, alkylarylamino, alkylhétéroarylamino, arylhétéroarylamino, acyle, acyloxy, nitro, carboxy, carbamoyle, carboxamide, cyano, sulfonyle, sulfonylamino, sulfinyl, sulfinylamino, thiol, alkylthio, arylthio ou alkylsulfonyle ;

R, R^1, R^2 et R^3 sont chacun indépendamment H, alkyle C_1 à C_{12} substitué ou non substitué, linéaire ou ramifié, cycloalkyle C_3 à C_8 substitué ou non substitué, système aryle substitué ou non substitué contenant 6 à 14 atomes de carbone en anneau, hétérocyclyle à 5 ou 8 chaînons saturés ou non saturés ayant 1 à 4 hétéroatomes choisis parmi O, S et N, hétéroaryle contenant 5 atomes ou plus en anneau, dans lequel au moins un atome de cycle est choisi parmi N, S et O, ou des combinaisons de ceux-ci choisis parmi : les groupes alkylcycloalkyle, alkylaryle, alkylhétérocyclyle ou alkylhétéroaryle ; dans lesquels les substitutions se font par un ou plusieurs choisis dans le groupe comprenant halogène, hydroxy, alcoxy, aryloxy, alkylaryloxy, hétéroaryloxy, oxo, cycloalkyle, phényle, hétéroaryles, hétérocyclyle, naphtyle, amino, alkylamino, arylamino, hétéroarylamino, dialkylamino, diarylamino, alkylarylamino, alkylhétéroarylamino, arylhétéroarylamino, acyle, acyloxy, nitro, carboxy, carbamoyle, carboxamide, cyano, sulfonyle, sulfonylamino, sulfinyl, sulfinylamino, thiol, alkylthio, arylthio ou alkylsulfonyle ;

X^1 représente zéro, un, deux ou trois substituants et X^2 représente zéro, un, deux, trois ou quatre substituants, chacun de ces substituants étant indépendamment choisi dans le groupe constitué d'alkyle C_1 à C_{12} linéaires ou ramifiés, substitués ou non substitués, de cycloalkyle C_3 à C_8 saturé ou non saturé, substitué ou non substitué, de système aryle substitué ou non substitué contenant 6-14 atomes de cycle carbone, d'hétérocyclyle saturé ou insaturé de 5 à 8 chaînons ayant 1 à 4 hétéroatomes choisis parmi O, S et N, d'hétérocyclyle contenant 5 ou plus de cycles d'atomes, dans lesquels au moins un atome du cycle est choisi parmi N, S et O, ou des combinaisons de ceux-ci choisis parmi : alkylcycloalkyle, alkylaryle, alkylhétérocyclyle ou alkylhétéroaryle ; où les substitutions sont un ou plusieurs choisis dans les groupes constitués par halogène, hydroxy, alcoxy, aryloxy, alkylaryloxy, hétéroaryloxy, 0X0, cycloalkyle, phényle, hétéroaryles, hétérocyclyle, naphtyle, amino, alkylamino, arylamino, arylamino, hétéroarylamino, dialkylamino, diarylamino alkylarylamino, alkylhétéroarylamino, arylhétéroarylamino, acyle, acyloxy, nitro, carboxy, carbamoyle, carbamamide, cyano, sulfonyle, sulfonylamino, sulfinyle, sulfinylamino, thiol, alkylthio, arylthio ou alkylsulfonyle, halogène, nitro, amide, ester, cyano, alcoxy, alkylamino, arylamino, un support inorganique et un fragment polymère ; et

l'anion représente un groupe portant une seule charge négative ; ou

un dérivé du borane dudit complexe.

2. Complexe selon la revendication 1,

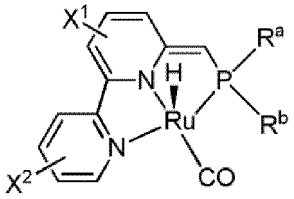
où X^1 et X^2 sont chacun absents, et le fragment bipyridine est non substitué ; ou

dans lequel L^1 est la phosphine (PR^aR^b); ou

dans lequel L^2 est CO ; ou

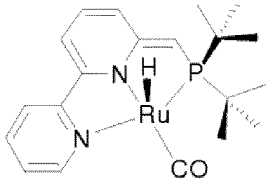
dans lesquels Z et Y sont H ou halogène ; ou

dans lequel le complexe est représenté par la formule C1 :



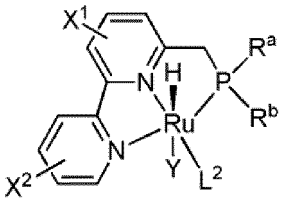
C1

dans lesquels chacun de X^1, X^2, R^a et R^b est tel que défini dans la revendication 1, de préférence dans lequel le complexe de ruthénium est représenté par la structure de formule 3



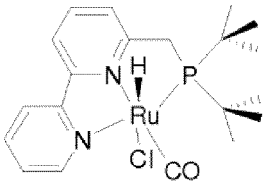
3 ;

ou
dans lequel le complexe est représenté par la formule C2 :

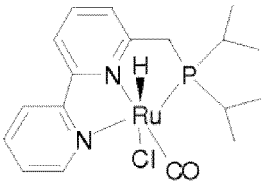


C2

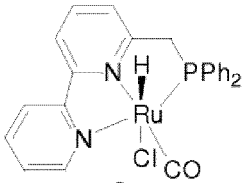
dans laquelle L^2, X^1, X^2, Y, R^a et R^b sont tels que définis dans la revendication 1,
de préférence dans lequel Y est halogène ou dans laquelle L^2 est un groupe CO, encore plus préférablement dans laquelle le complexe ruthénium est représenté par la structure des formules 4, 7 ou 9 :



4

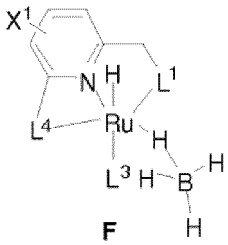


7



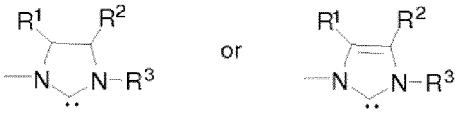
9

3. Dérivé de borane d'un complexe de ruthénium, dans lequel ledit dérivé de borane est représenté par la structure de formule F :

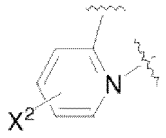


F

dans laquelle
chaque L^1 est indépendamment choisi dans le groupe constitué de phosphine (PR^aR^b) et carbène N-hétérocyclique représentés par les structures :

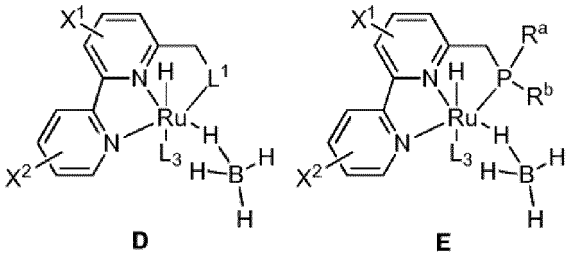


L^3 est absent ou est un donneur mono-denté de deux électrons choisi dans le groupe comprenant CO, $P(OR^a)(OR^b)(OR^c)$, NO +, isonitrile (RNC), PF_3 et CS ;
L^4 est un groupe de formule :



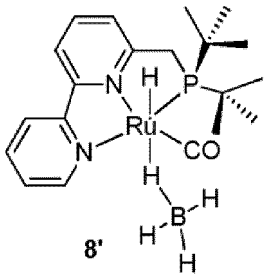
R^a, R^b et **R^c** représentent chacun indépendamment un groupe alkyle, cycloalkyle, aryle, hétérocyclyle, hétéroaryle, alkylcycloalkyle, alkylaryle, alkylhétérocyclyle ou alkylhétéroaryle;
R, **R^1, R^2** et **R^3** représentent chacun indépendamment H, alkyle, cycloalkyle, aryle, hétérocyclyle, hétéroaryle, alkylcycloalkyle, alkylaryle, alkylhétérocyclyle ou alkylhétéroaryle ;
X^1 représente zéro, un, deux ou trois substituants et **X^2** représente zéro, un, deux, trois ou quatre substituants, chacun de ces substituants étant indépendamment choisi dans le groupe constitué de alkyle, cycloalkyle, aryle, hétérocyclyle, hétéroaryle, alkylcycloalkyle, alkylaryle, alkylhétérocyclyle, alkylhétéroaryle, halogène, nitro, amide, ester, cyano, alcoxy, alkylamino, arylamino, un support inorganique et un fragment polymère,

de préférence dans lequel le complexe de ruthénium est représenté par la structure de l'une quelconque de la formule :



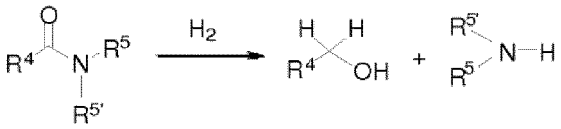
D **E**

encore plus préférablement dans laquelle le complexe de ruthénium est représenté par la structure de formule 8' :



8'

4. Procédé d'hydrogénation d'un amide en un alcool et une amine, comprenant l'étape consistant à faire réagir l'amide représenté par la formule $R^4C(=0)\text{-}N\text{-}R^5R^{5'}$ avec de l'hydrogène moléculaire (H_2), pour générer un alcool de formule R^4CH_2OH et une amine de formule $R^5R^{5'}NH$:



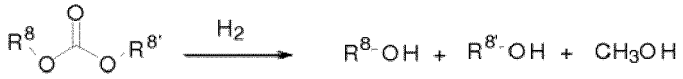
où R^4, R^5 et $R^{5'}$ sont chacun indépendamment choisis dans le groupe constitué de H, d'un alkyle, alcoxyalkyle, cycloalkyle, aryle, alkylaryle, hétérocyclyle et hétéroaryle non substitué ou substitué ;
dans lequel le processus est effectué en présence du complexe de ruthénium selon l'une quelconque des revendications 1 ou 2, de préférence dans lequel l'amide est choisi dans le groupe constitué par le N-benzyl-2-méthoxyacétamide, N-hexyl-2-méthoxyacétamide, N-hexyl-3-méthyloxétane-3-carboxamide, N-hexyl-2, furanylcarboxamide, N-benzylbenzamide, N-éthylacétamide, N-méthylpropionamide, N-cyclohexyl-2-méthoxyacétamide, N-phénylacétamide, N-phénylhexylamide, 2-méthoxy-N-phénylacétamide, N-phénylbenzamide, éthylènediamine-N,N'-(2-méthoxyacétamide), N-hexanoylmorpholine, N-butanoylmorpholine, N-2-métoxyacétylpyrrolidine, N-for-

mylmorpholine, N,N-diméthylformamide, N,N-diéthylbenzamide, benzamide, 4-méthylbenzamide, cyclohexanecarboxylate, hexanamide, acétamide, acrylamide et pivalamide ; et
éventuellement dans lequel l'amide est un amide cyclique (lactame) et le procédé conduit à un amino-alcool, ou éventuellement dans lequel l'amide est un polyamide, ou dans lequel l'amide est un polypeptide.

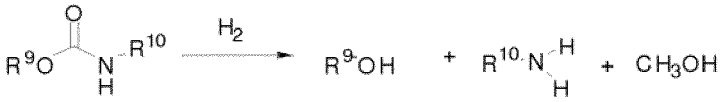
5. Procédé d'hydrogénation d'un ester, carbonate, carbamate ou urée organique, comprenant l'étape consistant à faire réagir l'ester, le carbonate, le carbamate ou l'urée organique avec de l'hydrogène moléculaire (H_2) en présence du complexe ruthénium selon l'une quelconque des revendications 1 à 3, hydrogénant ainsi l'ester, le carbonate organique, le carbamate ou le dérivé d'urée et générant au moins un alcool, une amine ou une combinaison de ceux-ci ;

(I) de préférence dans lequel le procédé est choisi dans le groupe constitué :

a. d'un procédé comprenant l'étape d'hydrogénation d'un carbonate représenté par la formule R^8O-C(=O)-$OR^{8'}$ en un ou plusieurs alcools correspondants et en méthanol :

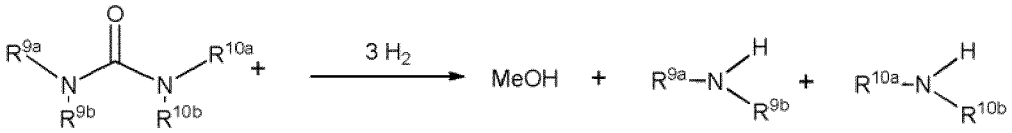


dans lequel R^8 et R^8 sont identiques ou différents et sont choisis dans le groupe constitué d'un alkyle, un alcoxyalkyle, un cycloalkyle, un aryle, un alkylaryle, un hétérocyclyle et un hétéroaryle substitué ou non substitué, où le carbonate est de preference le carbonate de diméthyle, le carbonate de diéthyle, le carbonate de dipropyle ou le carbonate de dibutyle ;
b. un procédé comprenant l'étape d'hydrogénation d'un carbamate représenté par la formule $R^9$0-C(=O)-NHR^{10} en l'amine, l'alcool et le méthanol correspondants :



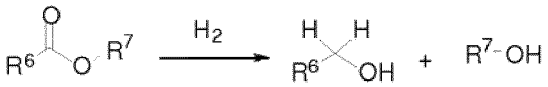
où R^9 est choisi dans le groupe constitué par un alkyle, un alcoxyalkyle, un cycloalkyle, un aryle, un alkylaryle, un hétérocyclyle et un hétéroaryle substitué ou non substitué; et
R^{10} est choisi dans le groupe constitué par H ou un alkyle, un alcoxyalkyle, un cycloalkyle, un aryle, un alkylaryle, un hétérocyclyle et un hétéroaryle substitué ou non substitué.

dans lequel le carbamate est de préférence le benzylcarbamate de méthyl ou le 4-méthoxybenzylcarbamate de méthyl ; et
c. un procédé comprenant l'étape consistant à hydrogéner un dérivé d'urée en l'amine et le méthanol correspondants :



ou ;

(II) de préférence dans lequel ledit procédé comprenant l'étape d'hydrogénation d'un ester représenté par la formule R^6C(=O)-OR^7 en un ou plusieurs alcools correspondants :



dans laquelle

R^6 est choisi dans le groupe constitué par H ou un alkyle, un alcoxyalkyle, un cycloalkyle, un aryle, un alkylaryle, un hétérocyclyle et un hétéroaryle substitué ou non substitué ; et
R^7 est choisi dans le groupe constitué par H ou un alkyle, un alcoxyalkyle, un cycloalkyle, un aryle, un alkylaryle, un hétérocyclyle et un hétéroaryle substitué ou non substitué ;

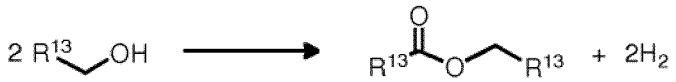
de préférence dans lequel R^6 est H et le procédé comprend l'hydrogénation d'un ester de formiate de formule H-C(=O)-OR^7 en méthanol et un alcool de formule R^7-OH ;
plus préférentiellement dans lequel l'ester est choisi dans le groupe constitué d'hexylhexanoate, de butyl butyrate, formiate de méthyle, formiate d'éthyle, formiate de propyle et formiate de butyle ; ou dans lequel l'ester est un polyester, ou dans lequel l'ester est un ester cyclique (lactone), ou dans lequel l'ester est un diester (dilactone) cyclique, et le procédé conduit à la formation d'un diol ; de préférence dans lequel le di-ester cyclique est dérivé de la biomasse, de préférence dans lequel le di-ester cyclique est un glycolide ou un lactide.

6. Procédé de préparation d'un amide, comprenant l'étape consistant à faire réagir une amine primaire ou secondaire avec un alcool primaire en présence du complexe de ruthénium selon l'une quelconque des revendications 1 à 3, générant ainsi l'amide et de l'hydrogène moléculaire,
dans lequel le procédé comprend l'étape consistant à faire réagir une amine représentée par la formule $R^{11}R^{11'}NH$ avec un alcool représenté par la formule $R^{12}CH_2OH$ pour générer un amide représenté par la structure R^{12}-C(=O)-$NR^{11}R^{11'}$:

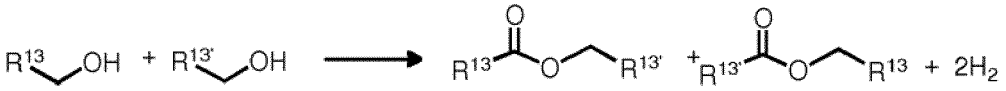
où R^{10}, R^{11} et R^{12} sont chacun indépendamment choisis dans le groupe constitué de H, d'un alkyle, alcoxyalkyle, cycloalkyle, aryle, alkylaryle, hétérocyclyle et hétéroaryle substitué ou non substitué ;
de préférence dans lequel l'alcool est choisi dans le groupe constitué de méthanol, éthanol, propanol, butanol, pentanol, hexanol, 2-méthoxyéthanol et 2-méthyl-l-butanol ; ou dans lequel l'amine est choisie dans le groupe comprenant benzylamine, 1-hexylamine, 1-pentylamine, 1-(2-furyl)méthylamine, aniline, morpholine, pyrrolidine, 2-méthylhexylamine, cyclohexylamine, éthylènediamine, diéthylènetriamine et 1,6-diaminohexane ; et
éventuellement, dans lequel (a) l'amine est une diamine ou l'alcool est un dialcool, et le procédé conduit à un diamide ; ou (b) l'amine est une diamine et l'alcool est un dialcool, et le procédé conduit à un polyamide ; ou (c) l'amine et l'alcool sont présents dans la même molécule et le procédé est un procédé intramoléculaire qui conduit à un lactame ; ou (d) l'amine et l'alcool sont présents dans la même molécule et le procédé est un procédé intermoléculaire qui conduit à un polyamide ; ou (e) l'amine et l'alcool représentent ensemble un bêta-aminoalcool et le procédé conduit à un polypeptide ; ou (f) l'amine et l'alcool représentent ensemble un bêta-aminoalcool et le procédé conduit à un dipeptide cyclique.

7. Procédé de préparation d'un ester par couplage par déshydrogénation d'alcools primaires ou par couplage par déshydrogénation d'un alcool primaire et d'un alcool secondaire, comprenant l'étape consistant à faire réagir les alcools en présence du complexe ruthénium selon l'une quelconque des revendications 1 à 3, permettant générer l'ester et l'hydrogène moléculaire, dans lequel le procédé est choisi dans le groupe comprenant :

(a) un procédé comprenant l'étape consistant à convertir un alcool primaire représenté par la formule $R^{13}CH_2OH$ en un ester de structure R^{13}-C(=O)-OCH_2R^{13} :



dans lequel R^{13} est choisi dans le groupe constitué par H ou un alkyle, un alcoxyalkyle, un cycloalkyle, un aryle, un alkylaryle, un hétérocyclyle et un hétéroaryle substitué ou non substitué ;
(b) un procédé comprenant l'étape consistant à faire réagir un premier alcool primaire représenté par la formule $R^{13}CH_2OH$ avec un deuxième alcool représenté par la formule $R^{13}CH_2OH$ afin de générer un ester de structure R^{13}-C(=O)-$OCH_2R^{13'}$ ou un ester de formule $R^{13'}$-C(=O)-OCH_2R^{13}



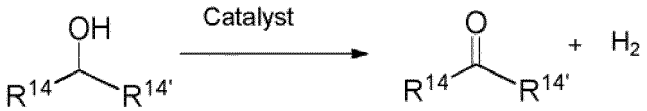
où R^{13} et R^{13} 'sont identiques ou différents l'un de l'autre et sont chacun indépendamment choisis dans le groupe constitué de H, un alkyle, alcoxyalkyle, un cycloalkyle, un cycloalkyle, un aryle, un alkylaryle, un hétérocyclyle et un hétéroaryle substitué ou non substitué ; et

(c) un procédé comprenant l'étape consistant à faire réagir un alcool primaire représenté par la formule $R^{13}CH_2OH$ avec un alcool secondaire de formule $R^{13'}R^{13''}CHOH$ afin de générer un ester de la structure R^{13}-C(=O)-OCH$R^{13'}$RI$^{3''}$:

où R^{13}, $R^{13'}$ et $R^{13''}$ sont chacun indépendamment choisis dans le groupe constitué par H, un alkyle, un alcoxyalkyle, un cycloalkyle, un aryle, un alkylaryle, un hétérocyclyle et un hétéroaryle substitué ou non substitué ; de préférence dans lequel l'alcool est choisi dans le groupe constitué par méthanol, éthanol, propanol, butanol, pentanol, hexanol, 2-méthoxyéthanol, 2-méthyl-l-butanol, alcool benzylique, 1-phényléthanol et cyclohexane méthanol ; ou

dans lequel l'alcool est un dialcool et le procédé conduit à un polyester ou une lactone

8. Procédé de préparation d'une cétone par déshydrogénation d'un alcool secondaire, comprenant l'étape consistant à faire réagir l'alcool secondaire en présence du complexe de ruthénium selon l'une quelconque des revendications 1 à 3, générant ainsi l'ester et de l'hydrogène moléculaire ; dans lequel le procédé comprend l'étape consistant à convertir un alcool secondaire représenté par la formule $R^{14}CH(OH)R^{14'}$ en une cétone représentée par la structure R^{14}-C(=O)-$R^{14'}$:

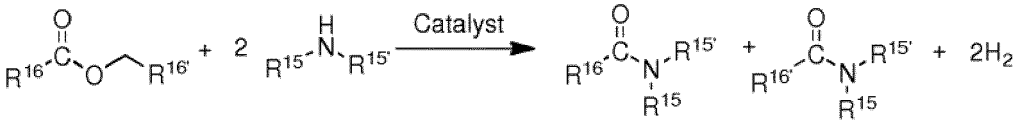


de préférence

dans lequel l'alcool secondaire est choisi dans le groupe constitué par 1-phényl-1-éthanol, 2-hexanol, cyclohexanol et 2-propanol.

9. Procédé de préparation d'un amide, comprenant l'étape consistant à faire réagir une amine primaire ou secondaire avec un ester en présence du complexe ruthénium selon l'une quelconque des revendications 1 à 3, générant ainsi l'amide et de l'hydrogène moléculaire,

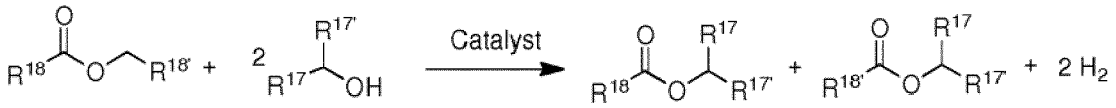
dans lequel le procédé comprend l'étape consistant à faire réagir une amine représentée par la formule $R^{15}R^{15'}NH$ avec un ester représenté par la formule R^{16}-C(=O)-OCH$_2R^{16'}$ pour générer un amide représenté par la structure R^{16}-C(=O)-N$R^{15}R^{15'}$:



où R^{15}, $R^{15'}$, R^{16} et $R^{16'}$ sont chacun indépendamment choisis dans le groupe constitué de H, d'un alkyle, un alcoxyalkyle, un cycloalkyle, un aryle, un alkylaryle, un hétérocyclyle et un hétéroaryle substitué ou non substitué ; de préférence dans lequel l'ester est choisi dans le groupe constitué par acétate d'éthyle, butyrate de butyle, pentanoate de pentyle et hexanoate d'hexyle ; ou dans lequel l'amine est choisie dans le groupe constitué par pyrrolidine, morpholine, 1-méthyl pipérazine, pipéridine, pipérazine, 1-hexylamine et p-tolylméthanamine.

10. Procédé de préparation d'un ester consistant à faire réagir un alcool primaire ou secondaire avec un ester en présence du complexe ruthénium selon l'une quelconque des revendications 1 à 3, générant ainsi l'ester et de l'hydrogène moléculaire, dans lequel le procédé comprend l'étape consistant à faire réagir un alcool primaire ou

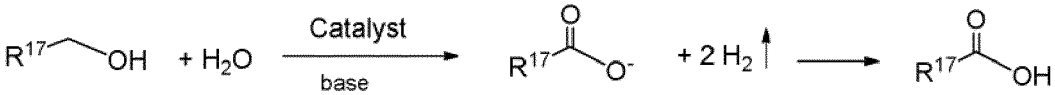
secondaire représenté par la formule $R^{17}R^{17'}CHOH$ avec un ester de structure R^{18}-C(=O)-$OCH_2R^{18'}$:



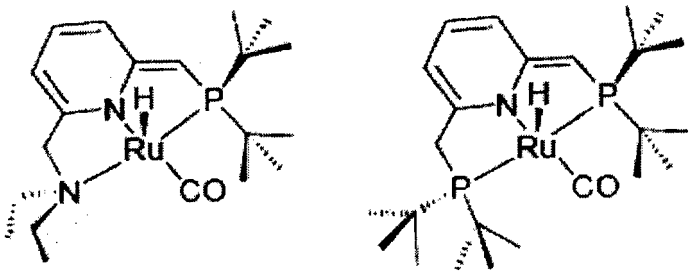
où R^{17}, $R^{17'}$, R^{18} et $R^{18'}$ sont chacun indépendamment choisis dans le groupe constitué de H, d'un alkyle, un alcoxyalkyle, un cycloalkyle, un aryle, un alkylaryle, un hétérocyclyle et un hétéroaryle substitué ou non substitué ; de préférence dans lequel l'alcool est choisi dans le groupe constitué par le cyclohexanol, le cyclopentanol, le 1-phényléthanol, l'isopropanol et le 3-pentanol ; ou dans lequel l'ester est choisi dans le groupe comprenant l'acétate d'éthyle, l'hexylhexanoate de pentyle, le pentanoate de pentyle, le butyrate de butyle, le butyrate d'éthyle et l'hexanoate de méthyle.

11. Procédé de préparation d'un acide carboxylique comprenant l'étape de réaction d'un alcool primaire avec de l'eau et une base en présence du complexe ruthénium selon l'une quelconque des revendications 1 à 3,

générant ainsi de l'acide carboxylique et de l'hydrogène moléculaire,
dans lequel le procédé comprend l'étape consistant à faire réagir un alcool primaire représenté par la formule $R^{17}CH_2OH$ avec de l'eau en présence d'une base afin de générer un sel d'acide carboxylique représenté par la structure R^{17}-C(=O)O^- et éventuellement, si désiré, de convertir du sel d'acide carboxylique en l'acide carboxylique correspondant de formule R^{17}-C(=O)OH.

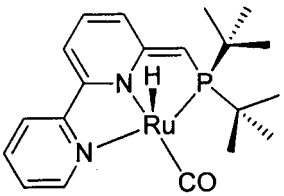


dans lequel R^{17} est choisi dans le groupe constitué par H ou un alkyle, un alcoxyalkyle, un cycloalkyle, un aryle, un alkylaryle, un hétérocyclyle et un hétéroaryle substitué ou non substitué ;
de préférence dans lequel l'alcool est choisi dans le groupe constitué par du butanol, pentanol, décanol, 2-méthoxyéthanol, 2-phényléthanol, cyclohexylméthanol, 3-phénylbutanol-1, but-3-èn-1-ol, (4-méthoxyphényl) méthanol et (2,4-diméthoxyphényl) méthanol.



1 2

Figure 1A



3

Figure 1B

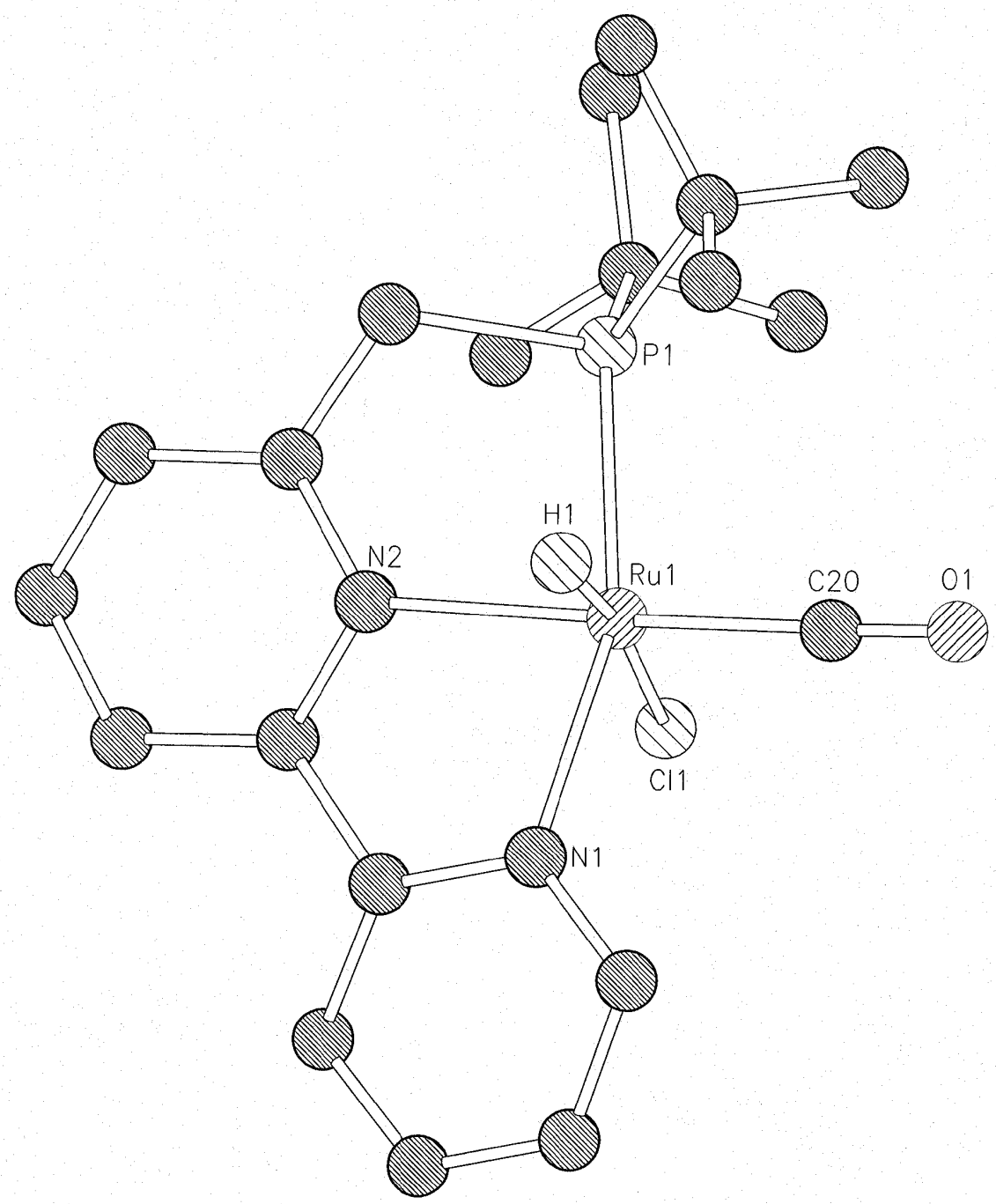


FIG.2

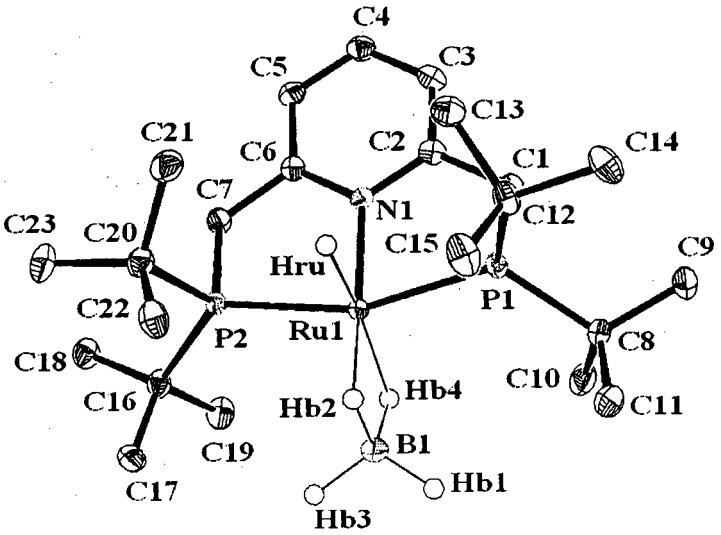

C4
C5
C3
C13
C21
C6
C2
C1
C14
C7
N1
C12
C23
C20
C15
C9
Hru
P1
C22
P2
Ru1
C8
C18
C10
C16
Hb2
Hb4
C11
C19
B1
C17
Hb1
Hb3

Figure 3

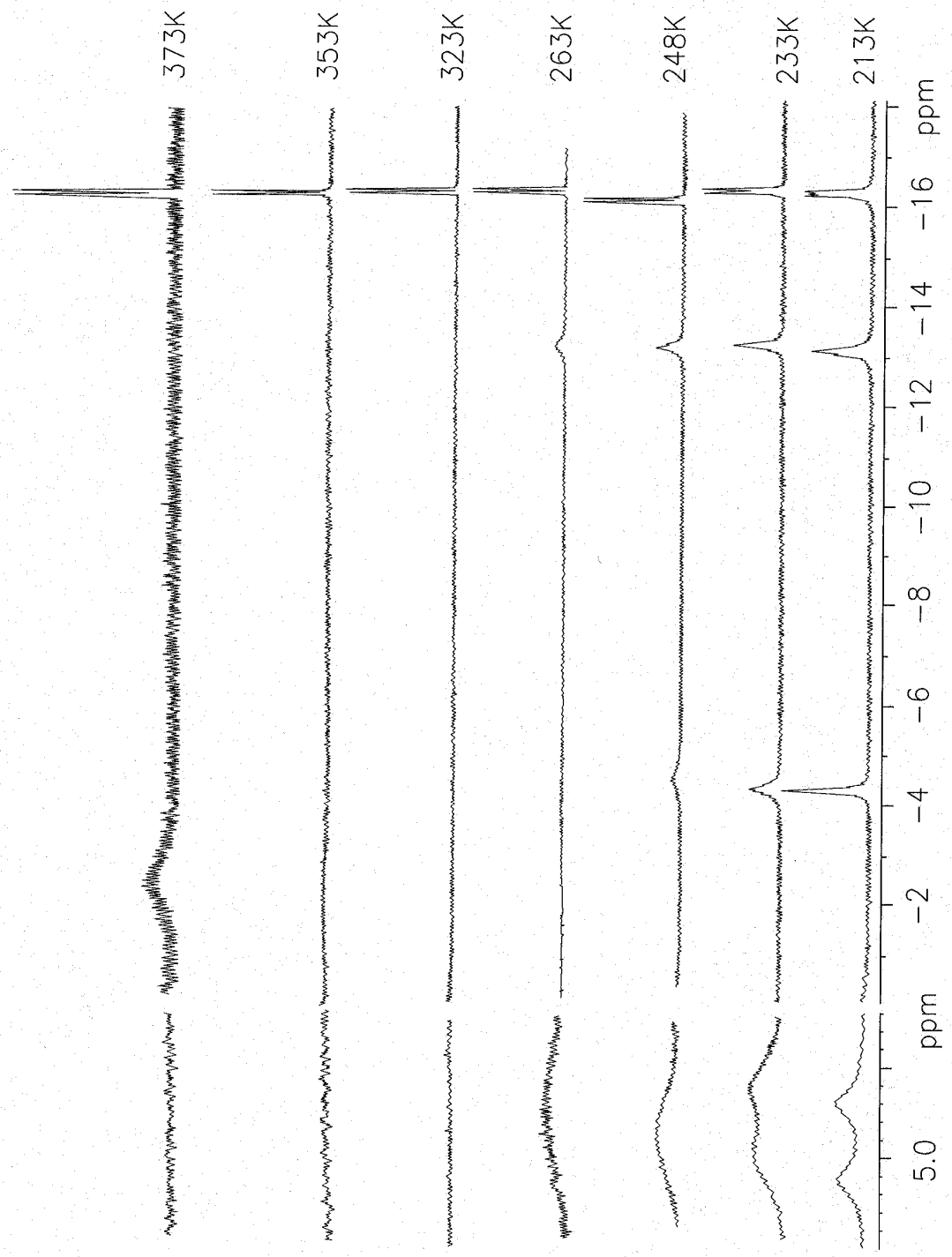


FIG.4

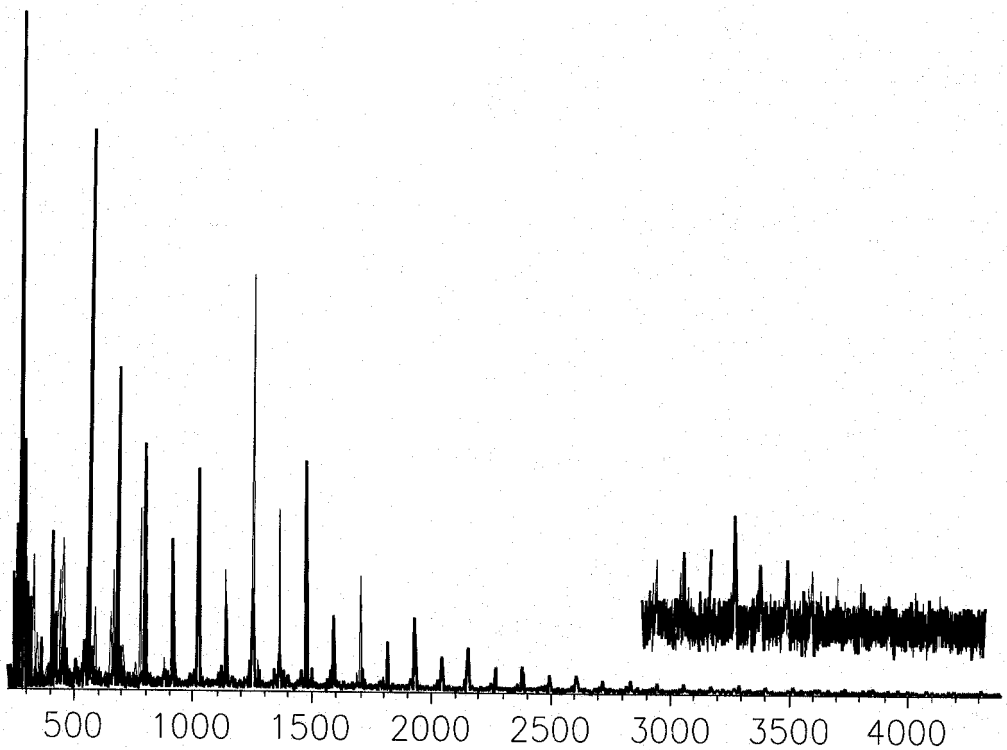

500
1000
1500
2000
2500
3000
3500
4000

FIG.5A

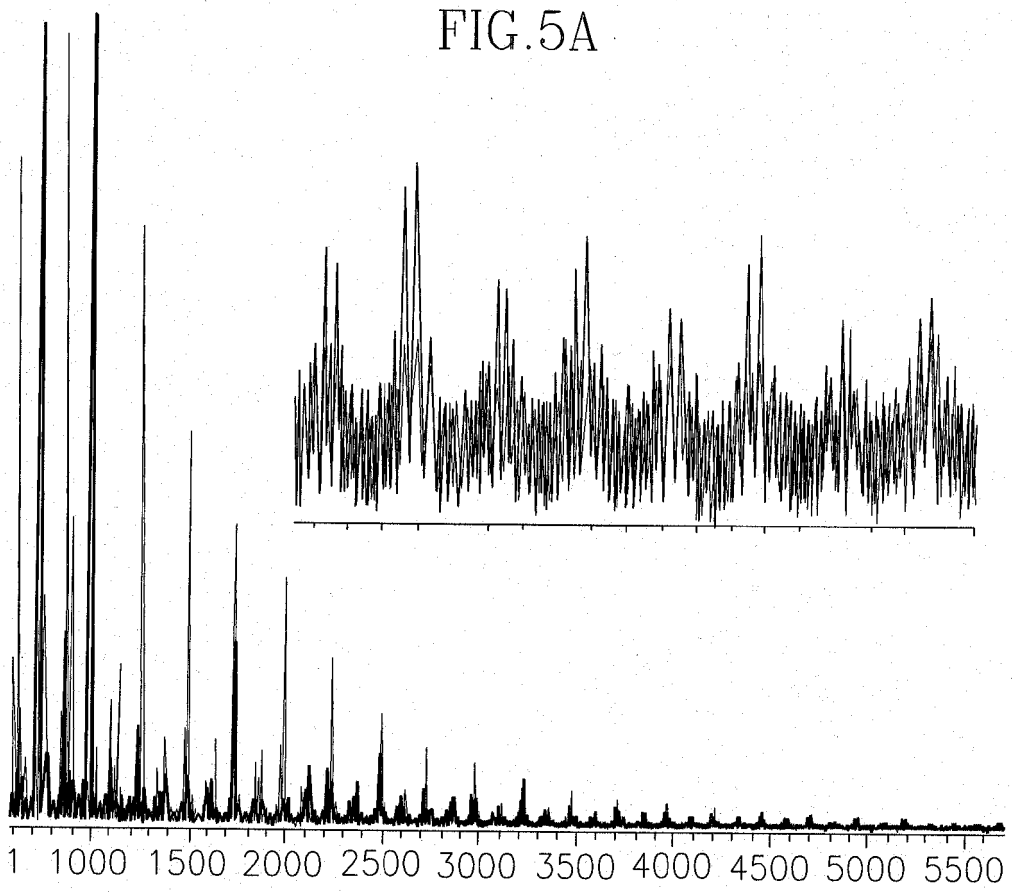

1
1000
1500
2000
2500
3000
3500
4000
4500
5000
5500

FIG.5B

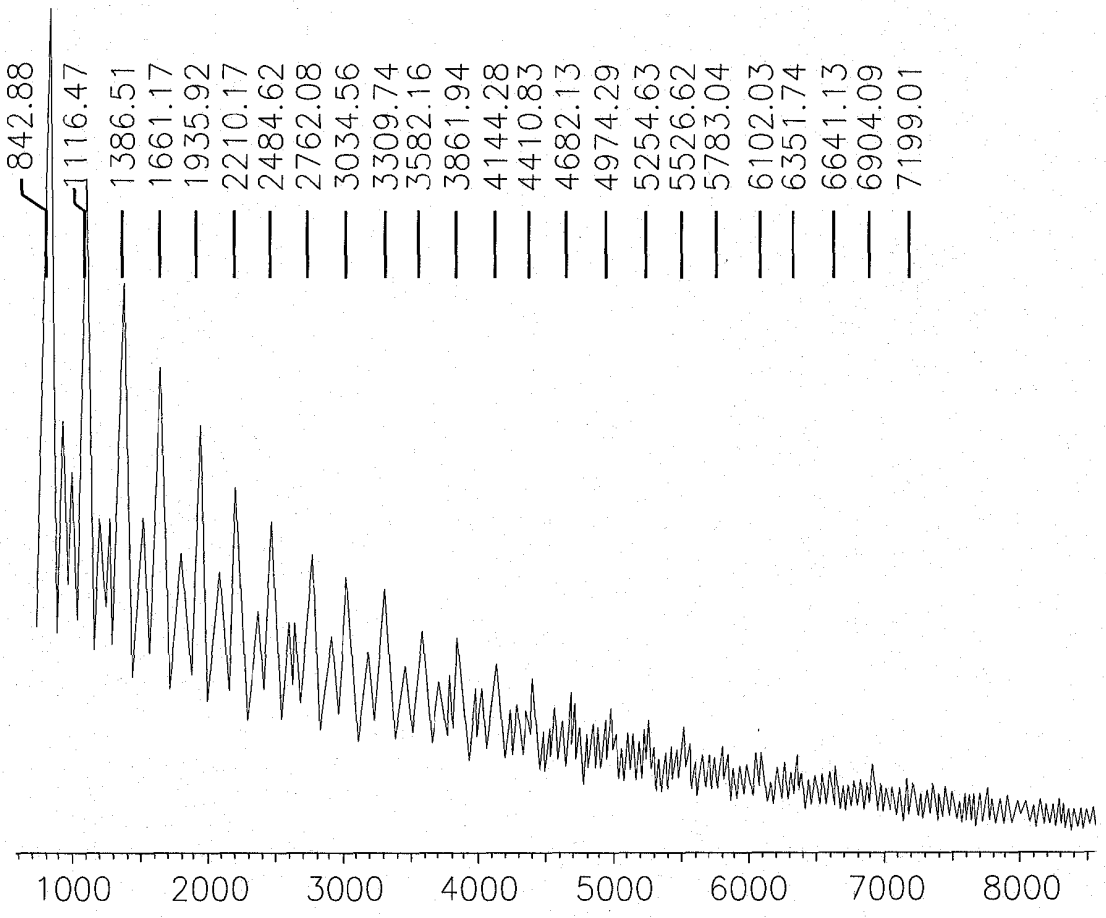

842.88
1116.47
1386.51
1661.17
1935.92
2210.17
2484.62
2762.08
3034.56
3309.74
3582.16
3861.94
4144.28
4410.83
4682.13
4974.29
5254.63
5526.62
5783.04
6102.03
6351.74
6641.13
6904.09
7199.01
1000
2000
3000
4000
5000
6000
7000
8000

FIG.5C

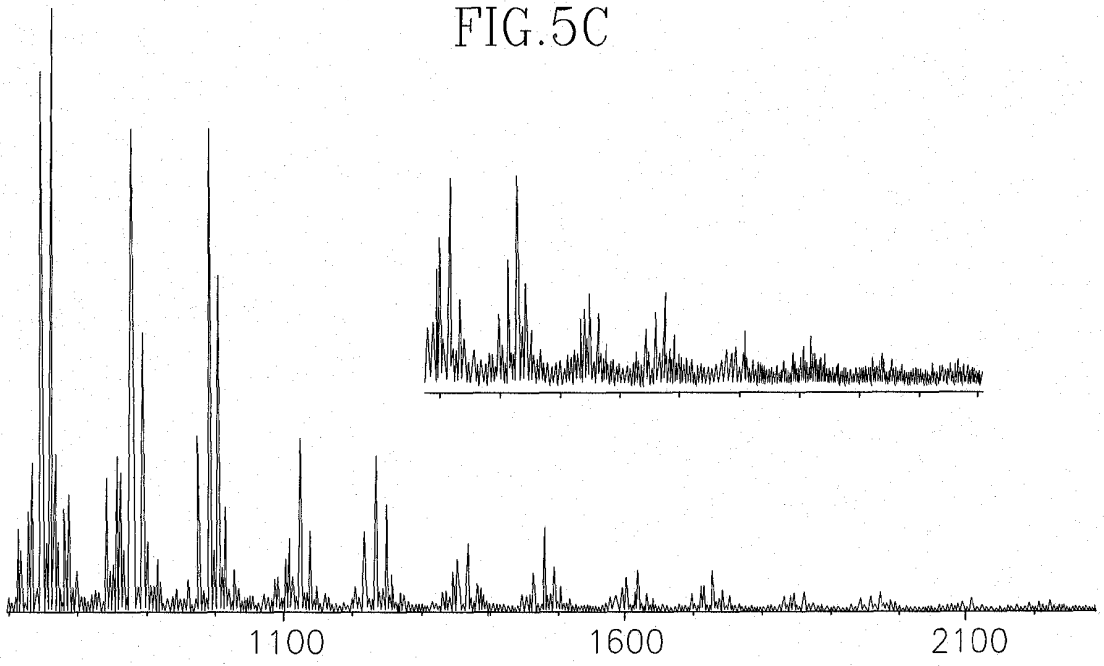

1100
1600
2100

FIG.5D

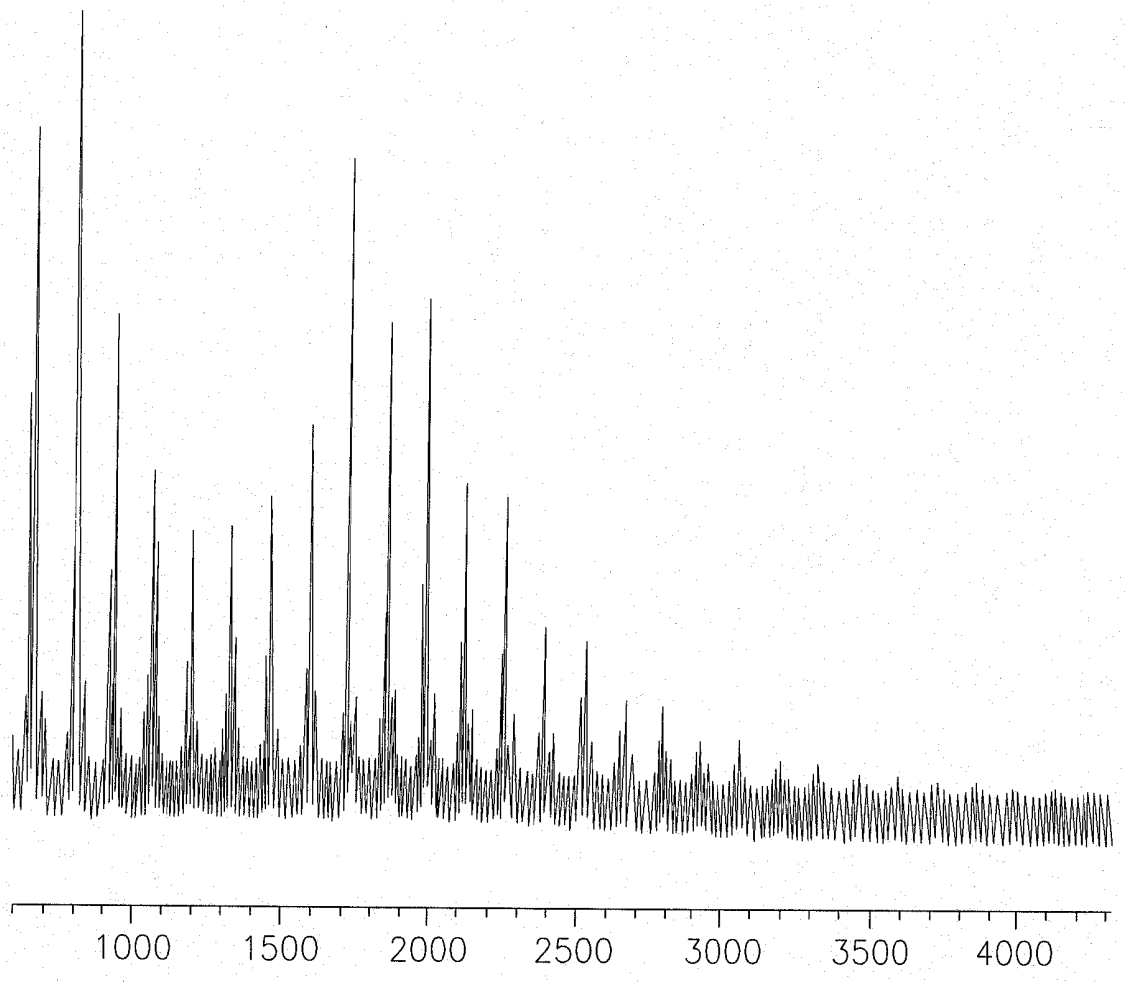


FIG.5E

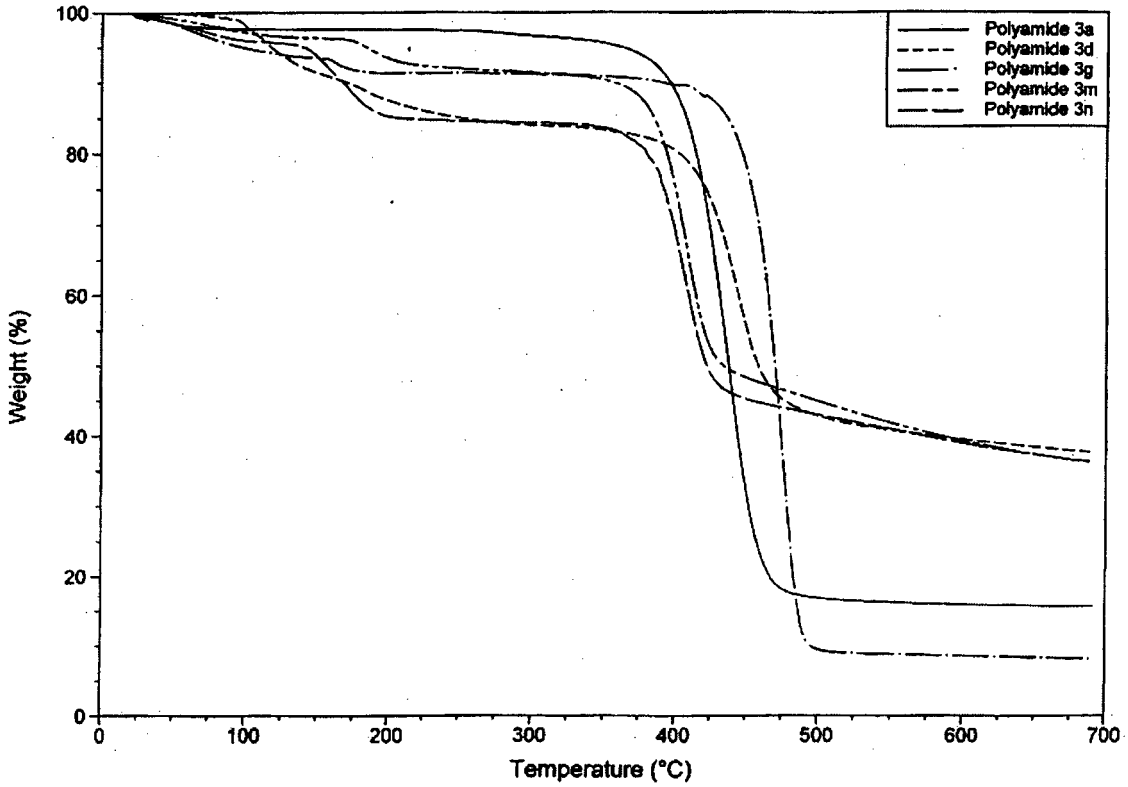

Polyamide 3a
Polyamide 3d
Polyamide 3g
Polyamide 3m
Polyamide 3n
Weight (%)
Temperature (°C)
0
20
40
60
80
100
0
100
200
300
400
500
600
700

Figure 6

REFERENCES CITED IN THE DESCRIPTION

This list of references cited by the applicant is for the reader's convenience only. It does not form part of the European patent document. Even though great care has been taken in compiling the references, errors or omissions cannot be excluded and the EPO disclaims all liability in this regard.

Patent documents cited in the description

- US 20090112005 A **[0015] [0065] [0071] [0094] [0095] [0096] [0116]**
- WO 2010018570 A **[0016]**
- FR 590 **[0246]**

Non-patent literature cited in the description

- **E. FOGLER ; E. BALARAMAN ; Y. BEN-DAVID ; G. LEITUS ; L. J. W. SHIMON ; D. MILSTEIN.** *Organometallics,* 2011, vol. 30, 3826 **[0145]**
- **SEYDEN-PENNE, J.** Reductions by the Alumino and Borohydrides in Organic Synthesis. Wiley-VCH, 1997 **[0291]**
- **RYLANDER, P. M.** Hydrogenation Methods. Academic Press, 1985 **[0291]**
- **HARTWIG, J.** Organotransition Metal Chemistry. University Science Books, 2010, 651-655 **[0291]**
- **HIROSAWA, C. ; WAKASA, N. ; FUCHIKAMI, T.** *Tetrahedron, Lett.,* 1996, vol. 37, 6749 **[0291]**
- **NÚÑEZ MAGRO, A. A. ; EASTHAM, G. R. ; COLE-HAMILTON, D. J.** *Chem. Commun.,* 2007, vol. 3154 **[0291]**
- **BEAMSON, G. ; PAPWORTH, A. J. ; PHILIPPS, C. ; SMITH, A. M. ; WHYMAN, R.** *Adv. Synth. Catal.,* 2010, vol. 352, 869 **[0291]**
- **BEAMSON, G. ; PAPWORTH, A. J. ; PHILIPPS, C. ; SMITH, A. M. ; WHYMAN, R.** *J. Catal.,* 2010, vol. 269, 93 **[0291]**
- **FERNANDES, A. C. ; ROMAO, C. C.** *J. Mol. Catal. A.,* 2007, vol. 272, 60 **[0291]**
- **DAS, S. ; ADDIS, D. ; ZHOU, S. ; JUNGE, K. ; BELLER, M.** *J. Am. Chem. Soc.,* 2010, vol. 132, 1770 **[0291]**
- **ITO, M. ; KOO, L. W. ; HIMIZU, A. ; KOBAYASHI, C. ; SAKAGUCHI, A. ; IKARIYA, T.** *Angew. Chem. Int. Ed.,* 2009, vol. 48, 1324 **[0291]**
- **LAWRENCE, S. A.** Amines: Synthesis, Properties and Applications. Cambridge University Press, 2005 **[0291]**
- **RICCI, A.** Amino Group Chemistry: From Synthesis to the Life Sciences. Wiley-VCH, 2008 **[0291]**
- **KUMARA SWAMY, K. C. ; BHUVAN KUMAR, N. N. ; BALARAMAN, E. ; PAVAN KUMAR, K. V. P.** *Chem. Rev.,* 2009, vol. 109, 2551 **[0291]**
- **ZHANG, J. ; GANDELMAN, M. ; SHIMON, L. J. W. ; MILSTEIN, D.** *Organometallics,* 2004, vol. 23, 4026 **[0291]**
- **ZHANG, J. ; LEITUS, G. ; BEN-DAVID, Y. ; MILSTEIN, D.** *J. Am. Chem. Soc.,* 2005, vol. 127, 10840 **[0291]**
- **ZHANG, J. ; LEITUS, G. ; BEN-DAVID, Y. ; MILSTEIN, D.** *Angew. Chem. Int. Ed.,* 2006, vol. 45, 1113 **[0291]**
- **ZHANG, J. ; GANDELMAN, M. ; SHIMON, L. J. W. ; MILSTEIN, D.** *Dalton Trans.,* 2007, 107 **[0291]**
- **GUNANATHAN, C. ; BEN-DAVID, Y. ; MILSTEIN, D.** *Science,* 2007, vol. 317, 790 **[0291]**
- **GNANAPRAKASAM, B. ; ZHANG, J. ; MILSTEIN, D.** *Angew. Chem. Int. Ed.,* 2010, vol. 49, 1 **[0291]**
- **MILSTEIN, D.** *Top. Catal.,* 2010, vol. 53, 915 **[0291]**
- **GUNANATHAN, C. ; SHIMON, L. J. W. ; MILSTEIN, D.** *J. Am. Chem. Soc.,* 2009, vol. 131, 3146 **[0291]**
- **GUNANATHAN, C. ; MILSTEIN, D.** *Angew. Chem. Int. Ed.,* 2008, vol. 47, 8661 **[0291]**
- **KHASKIN, E. ; IRON, M. A. ; SHIMON, L. J. W. ; ZHANG, J. ; MILSTEIN, D.** *J. Am. Chem. Soc.,* 2010, vol. 132, 8542 **[0291]**
- **KOHL, S.W. ; WEINER, L. ; SCHWARTSBURD, L. ; KONSTANTINOVSKI, L. ; SHIMON, L. J. W. ; BEN-DAVID, Y. ; IRON, M. A. ; MILSTEIN, D.** *Science,* 2009, vol. 324, 74 **[0291]**
- **SCHUBERT. U. S. ; ESCHBAUMER. C. ; HELLER. M.** *Org. Lett.,* 2000, 3373 **[0291]**
- **SMITH. A. P. ; LAMBA. J. J. S. ; FRASER. C. L.** *Org. Synth.,* 2002, vol. 78, 82 **[0291]**
- **AHMAD, N. ; LEVISON, J. J. ; ROBINSON, S. D. ; UTTLEY, M. F.** *Inorg. Synth.,* 1974, vol. 15, 45 **[0291]**
- **BALARAMAN, E. ; GNANAPRAKASAM, B. ; SHIMON, L. J. W. ; MILSTEIN, D.** *J. Am. Chem. Soc.,* 2010, vol. 132, 16756-16758 **[0291]**
- **N. SEWALD ; H.-D. JAKUBKE.** Peptides: Chemistry and Biology. Wiley-VCH, 2002 **[0292]**
- **A. GREENBERG ; C. M. BRENEMAN ; J. F. LIEBMAN.** The Amide Lingkage: Selected Structural Aspects in Chemistry, Biochemistry, and Material Science. Wiley, 2000 **[0292]**
- **M. B. SMITH ; J. MARCH.** Advanced Organic Chemistry. Wiley, 2001 **[0292]**
- **B. L. BRAY.** *Nat. Rev.,* 2003, vol. 2, 587-93 **[0292]**
- **R. C. LAROCK.** Comprehensive Organic Transformations. VCH, 1999 **[0292]**
- **M. B. SMITH.** Compendium of Organic Synthetic Methods. Wiley, 2001, vol. 9, 100-116 **[0292]**

- **C. J. COBLEY ; M. VAN DEN HEUVEL ; A. ABBADI ; J. G. DE VRIES.** *Tetrahedron Lett.,* 2000, vol. 41, 2467-2470 **[0292]**
- **S. I. MURAHASHI ; T. NAOTA ; E. SAITO.** *J. Am. Chem. Soc.,* 1986, vol. 108, 7846-7847 **[0292]**
- **S. I. MURAHASHI ; S. SASAO ; E. SAITO ; T. NAOTA.** *J. Org. Chem.,* 1992, vol. 57, 2521-2523 **[0292]**
- **Y. TAMARU ; Y. YAMADA ; Z. YOSHIDA.** *Synthesis,* 1983, 474-476 **[0292]**
- **A. TILLACK ; I. RUDLOFF ; M. BELLER.** *Eur. J. Org. Chem.,* 2001, 523-528 **[0292]**
- **W. K. CHAN ; C. M, HO ; M. K. WONG ; C. M. CHE.** *J. Am. Chem. Soc.,* 2006, vol. 128, 14796-14797 **[0292]**
- **S. H. CHO ; E. J. YOO ; I. BAE ; S. CHANG.** *J. Am. Chem. Soc.,* 2005, vol. 127, 16046-16047 **[0292]**
- **M. P. CASSIDY ; J. RAUSHEL ; V. V. FOKIN.** *Angew. Chem.,* 2006, vol. 45, 3154-3157 **[0292]**
- **NORDSTROM, L. U. ; VOGT, H. ; MADSEN, R.** *J. Am. Chem. Soc.,* 2008, vol. 130, 17672 **[0292]**
- **SHIMIZU, K. ; OHSHIMA, K. ; SATSUMA, A.** *Chem. Eur. J.,* 2009, vol. 15, 9977 **[0292]**
- **GHOSH, S.C. ; MUTHAIA, S. ; ZHANG, Y. ; XU, X. ; HONG, S.H.** *A Adv. Synth. Catal.,* 2009, vol. 351, 2643 **[0292]**
- **ZWEIFEL, T. ; NAUBRON, J. V. ; GRUTZMACHER, H.** *Angew. Chem. Int. Ed.,* 2009, vol. 48, 559 **[0292]**
- **WATSON, A.J.A. ; MAXWELL, A. C. ; WILLIAMS, J. M.** *J. Org. Lett.,* 2009, vol. 11, 2667 **[0292]**
- **ZENG, H. ; GUAN, Z.** *J. Am. Chem. Soc.,* 2011, vol. 133, 1159 **[0292]**
- **D. G. DICK ; R. DUCHATEAU ; J. H. EDEMA ; S. GAMBAROTTA.** *Inorg. Chem.,* 1993, vol. 32, 1959-1962 **[0293]**
- **J. P. WHITE III ; H. DENG ; S. G. SHORE.** *Inorg. Chem.,* 1991, vol. 30, 2337-2342 **[0293]**
- **K. BURGESS ; W. A. VAN DER DONK.** *J. Am. Chem. Soc.,* 1994, vol. 116, 6561-6569 **[0293]**
- **K. ISAGAWA ; H. SANO ; M. HATTORI ; Y. OTSUJI.** *Chem. Lett.,* 1979, 1069-1072 **[0293]**
- **H. S. LEE ; I K. SAGAWA ; Y. OTSUJI.** *Chem. Lett.,* 1984, 363-366 **[0293]**
- **H. S. LEE ; K. ISAGAWA ; H. TOYODA ; Y. OTSUJI.** *Chem. Lett.,* 1984, 673-676 **[0293]**
- **D. BARBIER-BAUDRY ; O. BLACQUE ; A. HAFID ; A. NYASSI ; H. SITZMANN ; M. VISSEAUX.** *Eur. J. Inorg. Chem.,* 2000, 2333-2336 **[0293]**
- **F. BONNET ; A. C. HILLIER ; A. COLLINS ; S. R. DUBBERLEY ; P. MOUNTFORD.** *J. Chem. Soc., Dalton Trans.,* 2005, 421-423 **[0293]**
- **T. J. MARKS ; J. R. KOLB.** *Chem. Rev.,* 1977, vol. 77, 263-293 **[0293]**
- **I. PALARD ; A. SOUM ; S. M. GUILLAUME.** *Chem. Eur. J.,* 2004, vol. 10, 4054-4062 **[0293]**
- **T. OHKUMA ; M. KOIZUMI ; K. MUNIZ ; G. HILT ; C. KABUTO ; R. NOYORI.** *J. Am. Chem. Soc,* 2002, vol. 124, 6508-6509 **[0293]**
- **C. A. SANDOVAL ; T. OHKUMA ; K. MUNIZ ; R. NOYORI.** *J. Am. Chem. Soc.,* 2003, vol. 125, 13490-13503 **[0293]**
- **R. GUO ; X. CHEN ; C. ELPELT ; D. SONG ; R MORRIS.** *Org. Lett.,* 2005, vol. 7, 1757-1759 **[0293]**
- **J. A. JENSEN ; S. R. WILSON ; G. S. GIROLAMI.** *J. Am. Chem. Soc.,* 1988, vol. 110, 4977-4982 **[0293]**
- **J. A. JENSEN ; G. S. GIROLAMI.** *J. Chem. Soc., Chem. Commun.,* 1986, 1160-1162 **[0293]**
- **M. E. VAN DER BOOM ; D. MILSTEIN.** *Chem. Rev.,* 2003, vol. 103, 1759-1792 **[0293]**
- **M. ALBRECHT ; G. VAN KOTEN.** *Angew. Chem. Int. Ed.,* 2001, vol. 40, 3750-3781 **[0293]**
- **A. VIGALOK ; D. MILSTEIN.** *Acc. Chem. Res.,* 2001, vol. 34, 798-807 **[0293]**
- **C. M. JENSEN.** *Chem. Commun.,* 1999, 2443-2449 **[0293]**
- **B. RYBTCHINSKI ; D. MILSTEIN.** *Angew. Chem. Int. Ed.,* 1999, vol. 38, 870-883 **[0293]**
- **M. KAWATSURA ; J. F. HARTWIG.** *Organometallics,* 2001, vol. 20, 1960-1964 **[0293]**
- **J. P. STAMBULI ; S. R. SHAUN ; K. H. SHAUGHNESSY ; J. F. HARTWIG.** *J. Am. Chem. Soc.,* 2001, vol. 123, 2677-2678 **[0293]**
- **D. H. GIBSON ; C. PARIYA ; M. S. MASHUTA.** *Organometallics,* 2004, vol. 23, 2510-2513 **[0293]**
- **S. M. KLOEK ; M. D. HEINEKEY ; K. I. GOLDBERG.** *Organometallics,* 2006, vol. 25, 3007-3011 **[0293]**
- **D. HERMANN ; M. GANDELMAN ; H. ROZENBERG ; L. J. W. SHIMON ; D. MILSTEIN.** *Organometallics,* 2002, vol. 21, 812-818 **[0293]**
- **E. BEN-ARI ; M. GANDELMAN ; H. ROZENBERG ; L. J. W. SHIMON ; D. MILSTEIN.** *J. Am. Chem. Soc.,* 2003, vol. 125, 4714-4715 **[0293]**
- **J. ZHANG ; M. GANDELMAN ; L. J. W. SHIMON ; H. ROZENBERG ; D. MILSTEIN.** *Organometallics,* 2004, vol. 23, 4026-4033 **[0293]**
- **J. ZHANG ; M. GANDELMAN ; D. HERRMAN ; G. LEITUS ; L. J. W. SHIMON ; Y. BEN DAVID ; D. MILSTEIN.** *Inorg. Chim. Acta,* 2006, vol. 359, 1955-1960 **[0293]**
- **E. BEN-ARI ; R. COHEN ; M. GANDELMAN ; L. J. W. SHIMON ; J. M. L. MARTIN ; D. MILSTEIN.** *Organometallics,* 2006, vol. 25, 3190-3210 **[0293]**
- **J. ZHANG ; G. LEITUS ; Y. BEN-DAVID ; D. MILSTEIN.** *Angew. Chem. Int. Ed.,* 2006, vol. 45, 1113-1115 **[0293]**
- **M. FELLER ; A. KARTON ; G. LEITUS ; J. M. L. MARTIN ; D. MILSTEIN.** *J. Am. Chem. Soc.,* 2006, vol. 127 **[0293]**
- **J. ZHANG ; G. LEITUS ; Y. BEN-DAVID ; D. MILSTEIN.** *J. Am. Chem. Soc.,* 2005, vol. 127, 10840-10841 **[0293]**
- **S. I. MURAHASHI ; T. NAOTA ; K. ITO ; Y. MAEDA ; H. TAKI.** *J. Org. Chem.,* 1987, vol. 52, 4319-4327 **[0293]**
- **H. B. CHARMAN.** *J. Chem. Soc. B,* 1970, 584-587 **[0293]**

- **D. MORTON ; D. J. COLE-HAMILTON.** *Chem. Comm.,* 1988, 1154-1156 **[0293]**
- **A. DOBSON ; S. D. ROBINSON.** *Inorg. Chem.,* 1977, vol. 16, 137-142 **[0293]**
- **C. W. JUNG ; P. E. GARROU.** *Organometallics,* 1982, vol. 1, 658-666 **[0293]**
- **G. B. W. L. LIGTHART ; R. H. MEIJER ; M. P. DONNERS ; J., J. MEULDIJK ; V. J. A. J. M. EKEMANS ; L. A. HULSHOF.** *Tetrahedron Lett.,* 2003, vol. 44, 1507-1509 **[0293]**
- **S. SHINODA ; T. KOJIMA ; Y. SAITO.** *J. Mol. Cat.,* 1983, vol. 18, 99-104 **[0293]**
- **T. MATSUBARA ; Y. SAITO.** *J. Mol. Cat.,* 1994, vol. 92, 1-8 **[0293]**
- **G. R. A. ADAIR ; J. M. J. WILLIAMS.** *Tetrahedron Lett.,* 2005, vol. 46, 8233-8235 **[0293]**
- **Y. LIN ; D. MA ; X. LU.** *Tetrahedron Lett.,* 1987, vol. 28, 3115-3118 **[0293]**
- **Y. BLUM ; Y. SHVO.** *J. Organomet. Chem.,* 1985, vol. 282, C7-C10 **[0293]**
- **Y. LIN ; X. ZHU ; Y. ZHOU.** Homogeneous catalytic dehydrogenative lactonization of diols. *J. Organometal. Chem.,* 1992, vol. 429, 269-274 **[0293]**
- **J. ZHAO ; J. F. HARTWIG.** Attempted use of primary alcohols resulted in no catalysis. *Organometallics,* 2005, vol. 24, 2441 **[0293]**
- **J. A. STATLER ; G. WILKINSON ; M. THORNTON-PETT ; M. B. HURSTHOUSEE.** *J. Chem. Soc., Dalton Trans.,* 1984, 1731-1738 **[0293]**
- **J. B. LETTS ; T. J. MAZANEC ; D. W. MEEK.** *J. Am. Chem. Soc.,* 1982, vol. 104, 3898-3905 **[0293]**
- **G. JIA ; H. M. LEE ; I. D. WILLIAMS ; C.-P. LAU ; Y. CHEN.** *Organometallics,* 1997, vol. 16, 3941-3949 **[0293]**
- **R. PIERANTOZZI ; G. L. GEOFFROY.** *Inorg. Chem.,* 1980, vol. 19, 1821-1822 **[0293]**
- **G. GEOFFROY ; L. R. PIERANTOZZI.** *J. Am. Chem. Soc.,* 1976, vol. 98, 8054-8059 **[0293]**
- **N. MENASHE ; Y. SHVO.** *Organometallics,* 1991, vol. 10, 3885-3891 **[0293]**
- **T. ITO ; H. HORINO ; Y. KOSHIRO ; A. YAMAMOTO.** *Bull. Chem. Soc. Jpn.,* 1982, vol. 55, 504-512 **[0293]**
- **A. JANSEN ; S. PITTER.** *Monatsch. Chem.,* 1999, vol. 130, 783-794 **[0293]**
- **R. HOLM.** *Inorg. Synth.,* 1970, vol. 12, 238-240 **[0293]**