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(54) Title: PROCESS OF FORMING A CYCLIC IMIDE

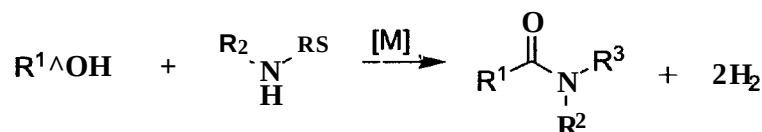
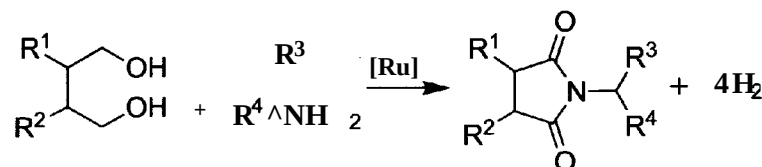
prior art*this invention*

Fig. 2

(57) **Abstract:** A process is provided for the synthesis of a cyclic imide. A primary amine and a diol compound are contacted in the presence of a Ruthenium (II) complex. The Ruthenium (II) catalyst includes at least one of an alicyclic ligand, an aromatic ligand, an arylalicyclic ligand, an arylaliphatic ligand and a phosphine ligand.

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PROCESS OF FORMING A CYCLIC IMIDE**CROSS REFERENCE TO RELATED APPLICATIONS**

[0001] This application makes reference to and claims the benefit of priority of United States Provisional Patent Application No. 61/361,119, filed on 02 July 2010 and United States Provisional Patent Application No. 61/384,555, filed on 20 September 2010, the contents of which being hereby incorporated by reference for all purposes, including an incorporation of any element or part of the description, claims or drawings not contained herein and referred to in Rule 20.5(a) of the PCT, pursuant to Rule 4.18 of the PCT.

FIELD OF THE INVENTION

[0002] The present invention relates to a process of forming a cyclic imide. In the process a primary amine and a primary diol are contacted in the presence of Ruthenium (II) catalyst.

BACKGROUND OF THE INVENTION

[0003] Imide derivatives are widely used organic compounds with numerous applications in biological, medicinal, synthetic, and polymer chemistry (Hargreaves, MK, et al., Chem. Rev. (1970) 70, 439; Kamitori, Y, et al., J. Org. Chem. (1986) 51, 1427; Rad-Moghadam, K, & Kheyrkhah, L, Synth. Commun. (2009) 39, 2108; Abell, AD, & Oldham, MD, J. Org. Chem. (1997) 62, 1509; Barker, D, et al., Bioorg. Med. Chem. (2005), 13, 4565; de Figueiredo, RM, et al., Synlett (2007) 391; Luzzio, FA, Science of Synthesis (2005) 21, 259; Reddy, PY, et al., J. Org. Chem. (1997) 62, 2652). Especially, cyclic imides are important building blocks for natural products and drugs such as palasimide (Peter, MG, et al., Helv. Chim. Acta (1974) 57, 32; Bochis, RJ, & Fisher, MH, Tetrahedron Lett. (1968) 1971) salfredins (Matsumoto, K, et al., J. Antibiot. (1995) 48, 439), thalidomide (a) A. Shoji, M. Kuwahara, H. Ozaki, H. Sawai, J. Am. Chem. Soc. 2007, 129, 1456; Luzzio, FA, et al., J. Org. Chem. (2005) 70, 10117; Franks, ME, et al., Lancet (2004) 363, 1802), julocrotine (Nakano, T, et al., J. Org. Chem. (1961) 26, 1184), lamprolobine (Hart, NK, et al., Chem. Commun. (1968) 302), migrastatin (Gaul, C, et al., J. Am. Chem. Soc. (2004) 126, 11326), and phensuximide (Hargreaves et al., 1970, supra; Kamitori et al., 1986, supra; Rad-Moghadam & Kheyrkhah, 2009, supra; Abell & Oldham, 1997, supra; Barker et al., 2005, supra; de Figueiredo et al., 2007, supra; Luzzio, 2005, supra; Reddy et al., 1997, supra; Figure 1). Despite their wide applicability, available routes for the synthesis of the cyclic imides from readily available starting materials are limited (Reddy et al., 1997, supra).

The typical methods are the dehydrative condensation of an anhydride and an amine at high temperature or with help of a Lewis acid (Hargreaves et al., 1970, supra; Kamitori et al., 1986, supra; Rad-Moghadam & Kheyrkhah, 2009, supra; Abell & Oldham, 1997, supra; Barker et al., 2005, supra; de Figueiredo et al., 2007, supra; Luzzio, 2005, supra; Reddy et al., 1997, supra; Da Settimo, A, et al., Eur. J. Med. Chem. (1996) 31, 49), and the cyclization of the amic acid in the presence of acidic reagents (Hargreaves et al., 1970, supra; Kamitori et al., 1986, supra; Rad-Moghadam & Kheyrkhah, 2009, supra; Abell & Oldham, 1997, supra; Barker et al., 2005, supra; de Figueiredo et al., 2007, supra; Luzzio, 2005, supra; Reddy et al., 1997, supra; Mehta, NB, et al., J. Org. Chem. (1960) 25, 1012), which are not atom economical, usually generating stoichiometric amount of by-products (Li, CJ, & Trost, BM, Proc. Natl. Acad. Sci. U.S.A. (2008), 105, 13197; Trost, BM, Science (1991) 254, 1471). Some recent approaches are Ir catalyzed multicomponent synthesis of glutarimides (Takaya, H, et al., Angew. Chem., Int. Ed. (2003) 42, 3302), ring expansion of 4-formyl- β -lactams for the synthesis of succinimide derivatives (Domingo, LR, et al., Tetrahedron (2009) 65, 3432; Li, GQ, et al., Adv. Synth. Catal. (2008) 350, 1258; Li, GQ, et al., Org. Lett. (2007) 9, 3519; Alcaide, B, et al., Chem. Commun. (2007) 4788), iron catalyzed carbonylative succinimide synthesis with alkyne, CO, and NH₃ (Driller, KM, et al., Angew. Chem., Int. Ed. (2009), 48, 6041), Ru or Pd catalyzed carbonylation of aromatic compounds leading to phthalimides (Inoue, S, al., J. Am. Chem. Soc. (2009) 131, 6898; Worlikar, SA, & Larock, RC, J. Org. Chem. (2008) 73, 7175), and Rh catalyzed 1,4-addition of aryl boronic acids to maleimides for the synthesis of chiral 3-substituted succinimide derivatives (Shintani, R, et al., Angew. Chem., Int. Ed. (2005) 44, 4611; Shintani, R, et al., J. Am. Chem. Soc. (2006) 128, 5628; Iyer, PS, et al., Tetrahedron Lett. (2007) 48, 4413). However, each of these routes has its own synthetic problems especially when applied to a range of derivatives mostly due to a narrow range of variously functionalized starting materials. Therefore, atom economical synthesis of functionalized imide derivatives from widely used precursors is a challenging goal.

[0004] It is accordingly an object of the present invention to provide a process that is suitable for the production of imides that avoids at least some of the above named difficulties in current processes of imide production. This object is solved by the method of claim 1.

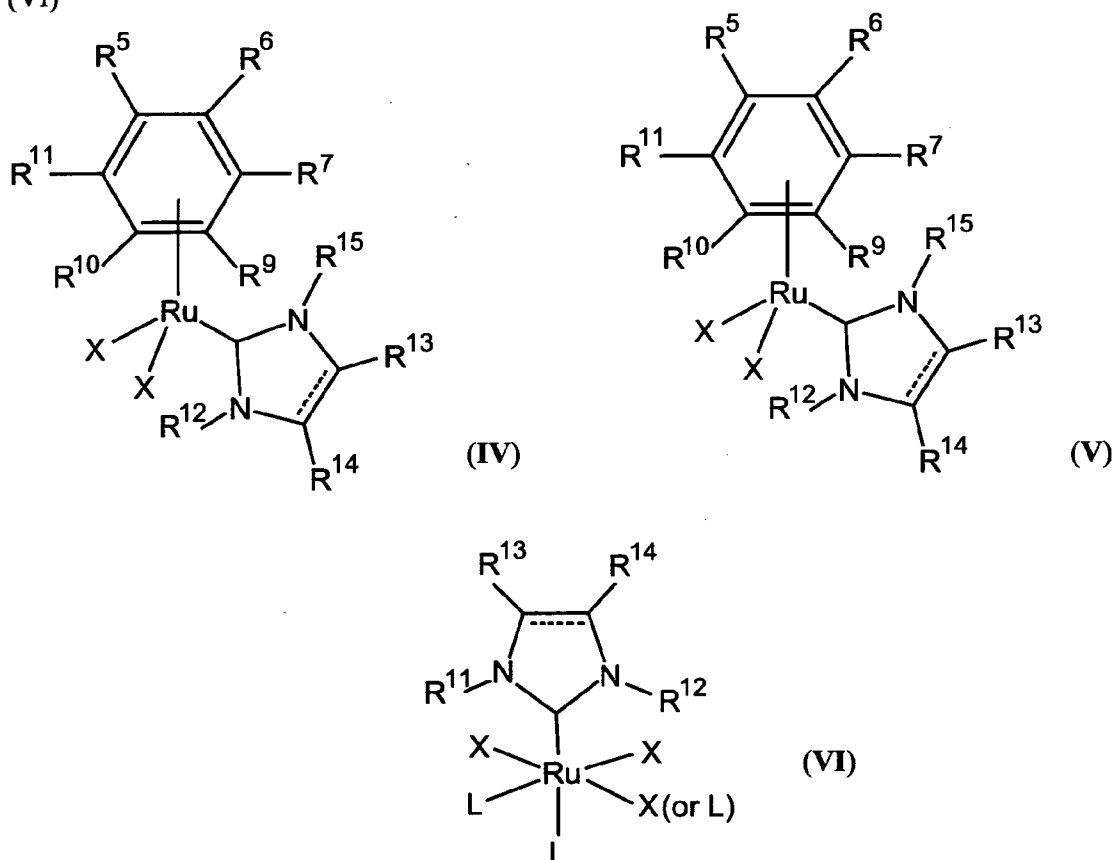
SUMMARY OF THE INVENTION

[0005] The present invention provides a process that involves subjecting an amine and a diol compound to an intermolecular oxidative coupling reaction, whereby a cyclic imide is

formed. The process involves the use of a Ruthenium (II) complex, which may be formed from a Ruthenium (II) precatalyst complex. The use of this Ruthenium (II) complex, in the following also termed the Ruthenium (II) catalyst, may involve providing an N-heterocyclic carbene, which may define a ligand of the Ruthenium (II) complex.

5 [0006] Accordingly, the invention provides a process of forming a cyclic imide. The process includes providing a primary amine. The process also includes providing a diol compound. The process further includes providing a Ruthenium (II) complex. The Ruthenium (II) complex includes one or more of an alicyclic ligand, an aromatic ligand, an arylalicyclic ligand, an arylaliphatic ligand and a phosphine ligand. The process also includes contacting
10 the primary amine and the diol compound in the presence of the Ruthenium (II) complex. Thereby the formation of a cyclic imide from the primary amine and the diol compound is allowed.

15 [0007] Providing the Ruthenium (II) catalyst includes in some embodiments providing an N-heterocyclic carbene. In some embodiments providing the Ruthenium (II) catalyst may involve the formation of one or more Ruthenium (II) complexes of formulae (IV), (V) and (VI)



In these formulae the symbol --- indicates that the respective bond may be a single or a double bond. $R^5 - R^7$ and $R^9 - R^{15}$ are independently from one another selected from the group consisting of a H, an aliphatic, an alicyclic, an aromatic, an arylaliphatic, and an arylalicyclic group. The aliphatic, alicyclic, aromatic, arylaliphatic or arylalicyclic group includes 0 to about 3 heteroatoms. Such a heteroatom may be selected from N, O, S, Se and Si. In the above formulae (I)-(III) X is halogen or $-\text{OR}^{16}$. R^{16} in this moiety $-\text{OR}^{16}$ is one of H, an aliphatic group, an alicyclic group, an aromatic group, an arylaliphatic group, and an arylalicyclic group. The aliphatic, alicyclic, aromatic, arylaliphatic or arylalicyclic group includes 0 to about 3 heteroatoms. Such a heteroatom may be selected from N, O, S, Se and Si. In the above formulae (I)-(III) L is a solvent molecule, pyridine, acetonitrile or an N-heterocyclic carbene.

BRIEF DESCRIPTION OF THE DRAWINGS

[0008] The invention will be better understood with reference to the detailed description when considered in conjunction with the non-limiting examples and the accompanying drawings.

[0009] Figure 1 depicts examples of bioactive compounds containing a cyclic imide moiety.

[0010] Figure 2 illustrates the synthesis of amides and cyclic imides from alcohols and amines.

[0011] Figure 3 shows examples of Ru (II) catalysts that can be used in a process of the invention.

[0012] Figure 4 depicts examples of the reaction of 1,4-butanediol (**3a**) and benzylamine (**4a**). Common reaction conditions: **3a** (0.5 mmol, 1.0 equiv), **4a** (0.55 mmol, 1.1 equiv), a solvent (0.8 mL), reflux, 24 h. [b]: Isolated yields, average of at least two runs. [c]: **1a** (2.5 mol %), 1,3-diisopropylimidazolium bromide (**2**) (5 mol %), NaH (15 mol %), CH_3CN (5 mol %), toluene; [d]: **1b** (2.5 mol %), **2** (5 mol %), NaH (15 mol %), pyridine (5 mol %), toluene. [e]: **1b** (2.5 mol %), dppb (5 mol %), 3-methyl-2-butanone (2.5 equiv), Cs_2CO_3 (10 mol %), tBuOH. [f]: **1c** (5 mol %), 1-hexyne (2.5 equiv), DME; [g]: **1c** (5 mol %), **2** (5 mol %), NaH (20 mol %), CH_3CN (5 mol %), toluene. [h]: **1d** (5 mol %), **2** (5 mol %), PCy_3 (5 mol %), KOtBu (20 mol %), toluene. [i]: **1e** (5 mol %), toluene.

[0013] Figure 5 illustrates the synthesis of succinimides from 1,4-butanediol. Common reaction conditions: **3a** (0.5 mmol, 1.0 equiv), amine (1.1 equiv), **1c** (5 mol %), 1,3-

diisopropylimidazolium bromide (**2**) (5 mol %), NaH (20 mol %), CH₃CN (5 mol %), toluene (0.5 mL), reflux, 24 h. [b]: Isolated yields, average of at least two runs.

[0014] Figure 6 shows further examples of the synthesis of cyclic imides from diols. Common reaction conditions: Diol (0.5 mmol, 1 equiv, 1.0 M), amine (1.1 equiv), **1c** (5 mol %), **2** (5 mol %), NaH (20 mol %), CH₃CN (5 mol %), toluene (0.5 mL), reflux, 24 h. [b]: Isolated yields, average of at least two runs.

[0015] Figure 7 depicts attempts to synthesize imides. Conditions: [Ru] **1c** (5 mol%), **2** (5 mol%), NaH (20 mol%), CH₃CN (5 mol%), toluene (0.8 mL), reflux, 24 h.

[0016] Figure 8 illustrates the proposed mechanism of the formation of the cyclic imide.

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DETAILED DESCRIPTION OF THE INVENTION

[0017] The development leading to the process of the present invention is based on the surprising finding that Ruthenium based complexes can be used to catalyse imide formation from diols and amines.

[0018] The process of the invention includes providing a diol compound. Any diol may be used that is capable of undergoing a cyclisation reaction (see scheme 1 below). Accordingly, the diol usually has a distance of at least two atoms, generally carbon atoms, between the two hydroxyl groups of the diol, that is the two hydroxyl groups of the diol are separated by two or more atoms. As a few illustrative examples, 1,4-butanediol, 2,3-diethyl-1,4-butanediol, 1,5-pentanediol, 2,4-dimethyl-1,5-pentanediol, 2,3,4-trimethyl-1,5-pentanediol, 1,4-pentanediol, 2,3-dimethyl-1,4-pentanediol, 1,6-hexanediol, 1,5-hexanediol, 1,7-heptanediol, (4-hydroxymethyl-phenyl)-methanol, (4-hydroxymethyl-phenyl)-ethanol, (4-hydroxyethyl-phenyl)-ethanol or 2,3-dihydroxymethyl-cyclohexane are suitable diol compounds that can be used in a process of the invention. The diol compound may also be provided in protected form. A large number of protecting groups, which are well known to those skilled in the art, is available for various functional groups. As an illustrative example, hydroxyl groups may be protected by an isopropylidene group. Such a protecting group may easily be removed during or before the process of the invention is carried out and thus the functional group(s) that is/are no longer shielded are available for amide formation. For example, the isopropylidene protective group shielding a hydroxyl group may be removed by acid treatment. Those skilled in the art will furthermore be aware that such protective groups may have to be introduced well in advance during the synthesis of such a bi- or higher functionalized compound.

[0019] Examples of a suitable hydroxy protecting group include, but are not limited to, methyl ethers; substituted methyl ethers (e.g. methoxymethyl, methylthiomethyl, *tert*-butylthiomethyl, (phenyldimethylsilyl)methoxymethyl, benzyloxymethyl, p-methoxybenzyloxymethyl, (4-methoxyphenoxy)methyl, guaiacolmethyl, *tert*-butoxymethyl, 4-pentenylloxymethyl, siloxymethyl, 2-methoxyethoxymethyl, 2,2,2-trichloroethoxymethyl, bis(2-chloroethoxy)methyl, 2-(1-trimethylsilyl)ethoxymethyl, tetrahydropyranyl, 3-bromotetrahydropyranyl, tetrahydropthiopyranyl, 1-methoxycyclohexyl, 4-methoxytetrahydropyranyl, 4-methoxytetrahydrothiopyranyl, 4-methoxytetrahydrothiopyranyl S,S-dioxido, 1-[(2-chloro-4-methyl)phenyl]-4-methoxypiperidin-4-yl, 1,4-dioxan-2-yl, tetrahydrofuranyl, tetrahydrothiofuranyl, 2,3,3a,4,5,6,7,7a-octahydro-7,8,8-trimethyl-4,7-methanobenzofuran-2-yl)); substituted ethyl ethers (1-ethoxyethyl, 1-(2-chloroethoxy)ethyl, 1-methyl-1-methoxyethyl, 1-methyl-1-benzyloxyethyl, 1-methyl-1-benzyloxy-2-fluoroethyl, 2,2,2-trichloroethyl, 2-trimethylsilyl ethyl, 2-(phenylselenyl)ethyl, *tert*-butyl, allyl, p-chlorophenyl, p-methoxyphenyl, 2,4-dinitrophenyl, benzyl); substituted benzyl ethers (p-methoxybenzyl, 3,4-dimethoxybenzyl, o-nitrobenzyl, p-nitrobenzyl, p-halobenzy, 2,6-dichlorobenzy, p-cyanobenzy, p-phenylbenzy, 2- and 4-picolyl, 3-methyl-2-picolyl N-oxido, diphenylmethyl, p,p'-dinitrobenzhydryl, 5-dibenzosuberyl, triphenylmethyl, a-naphthyl diphenylmethyl, p-methoxyphenyl diphenylmethyl, di(p-methoxyphenyl)phenylmethyl, tri(p-methoxyphenyl)methyl, 4-(4'-bromophenacyloxy)phenyl diphenylmethyl, 4,4',4''-tris(4,5-dichlorophthalimidophenyl)methyl, 4,4',4''-tris(levulinoyloxyphenyl)methyl, 4,4',4''-tris(benzoyloxyphenyl)methyl, 3-(imidazol-1-yl)methyl bis(4',4''-dimethoxyphenyl)methyl, 1,1-bis(4-methoxyphenyl)-1'-pyrenylmethyl, 9-anthryl, 9-(9-phenyl)xanthenyl, 9-(9-phenyl-10-oxo)anthryl, 1,3-benzodithiolan-2-yl, benzisothiazolyl S,S-dioxido); silyl ethers (trimethylsilyl, triethylsilyl, triisopropylsilyl, dimethylisopropylsilyl, diethylisopropylsilyl, dimethylhexylsilyl, *tert*-butyldimethylsilyl, t-butyl diphenylsilyl, tribenzylsilyl, tri-p-xylylsilyl, triphenylsilyl, diphenylmethylsilyl, t-butylmethoxyphenylsilyl); carboxylic esters (formate, benzoylformate, acetate, chloroacetate, dichloroacetate, trichloroacetate, trifluoroacetate, methoxyacetate, triphenylmethoxyacetate, phenoxyacetate, p-chlorophenoxyacetate, p-poly-phenylacetate, 3-phenylpropionate, 4-oxopentanoate (Levulinate), 4,4-(ethylenedithio)pentanoate, pivaloate, adamantate, crotonate, 4-methoxycrotonate, benzoate, p-phenylbenzoate, 2,4,6-trimethylbenzoate (mesitoate)); carbonates (methyl, 9-fluorenylmethyl, ethyl, 2,2,2-trichloroethyl, 2-(trimethylsilyl)ethyl, 2-(phenylsulfonyl)ethyl, 2-(triphenylphosphonio)ethyl, isobutyl, vinyl, allyl, p-nitrophenyl, benzyl, p-methoxybenzyl, 3,4-dimethoxybenzyl, o-nitrobenzyl, p-nitrobenzyl, S-benzyl thiocarbonate, 4-ethoxy-1-naphthyl, methyl dithiocarbonate); groups with assisted cleavage (2-iodobenzoate, 4-azidobutyl Tate, 4-nitro-4-methylpentanoate, o-(di-

bromomethyl)benzoate, 2-foimylbenzenesulfonate, 2-(methylthiomethoxy)ethyl carbonate, 4-(memylthiomethoxy)butyrate, 2-(memylthiomethoxymethyl)benzoate); miscellaneous esters (2,6-dichloro-4-methylphenoxyacetate, 2,6-dichloro-4-(1,1,3,3 tetramethylbutyl)phenoxyacetate, 2,4-bis(1,1-dimethylpropyl)phenoxyacetate, chorodiphenylacetate, isobutyrate, monosuccinate, (E)-2-methyl-2-butenolate (Tigloate), o-(methoxycarbonyl)benzoate, p-poly-benzoate, a-naphthoate, alkyl N,N,N',N'-tetramethylphosphorodiamidate, N-phenylcarbamate, 2,4-dinitrophenylsulfonate); and sulfonates (methanesulfonate (mesylate), benzyisulfonate, tosylate).

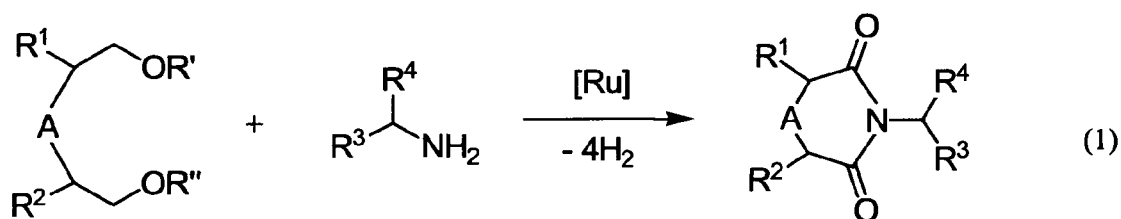
[0020] The process of the invention includes providing an amine. Any primary amine may be used in the process of the invention. The amino group of the primary amine may in some embodiments also be shielded by a protecting group. Examples of a suitable amino protecting group include, but are not limited to, carbamates (methyl and ethyl, 9-fluorenylmethyl, 9-(2-sulfo)fluorenylmethyl, 9-(2,7-dibromo)fluorenylmethyl, 2,7-di-*tert*-buthyl-[9-(10,10-dioxo-10,10,10-tetrahydrothioxanthyl)]methyl, 4-methoxyphenacyl); substituted ethyl (2,2,2-trichloroethyl, 2-trimethylsilylethyl, 2-phenylethyl, 1-(1-adamantyl)-1-methylethyl, 1,1-dimethyl-2-haloethyl, 1,1-dimethyl-2,2-dibromoethyl, 1,1-dimethyl-2,2,2-trichloroethyl, 1-methyl-1-(4-biphenyl)ethyl, 1-(3,5-di-*tert*-butylphenyl)-1-methylethyl, 2-(2'- and 4'-pyridyl)ethyl, 2-(N,N-dicyclohexylcarboxamido)ethyl, *tert*-butyl, 1-adamantyl, vinyl, allyl, 1-isopropylallyl, cinnamyl, 4-nitrocinnamyl, 8-quinolyl, N-hydroxypiperidinyl, alkylidithio, benzyl, p-methoxybenzyl, p-nitrobenzyl, p-bromobenzyl, p-chlorobenzyl, 2,4-dichlorobenzyl, 4-methylsulfinylbenzyl, 9-anthrylmethyl, diphenylmethyl); groups with assisted cleavage (2-methylthioethyl, 2-methylsulfonylethyl, 2-(p-toluenesulfonyl)ethyl, [2-(1,3-dithianyl)]methyl, 4-methylthiophenyl, 2,4-dimethylthiophenyl, 2-phosphonioethyl, 2-triphenylphosphonioisopropyl, 1,1-dimethyl-2-cyanoethyl, m-chloro-p-acyloxybenzyl, p-(dihydroxyboryl)benzyl, 5-benzisoxazolylmethyl, 2-(trifluoromethyl)-6-chromonylmethyl); groups capable of photolytic cleavage (m-nitrophenyl, 3,5-dimethoxybenzyl, o-nitrobenzyl, 3,4-dimethoxy-6-nitrobenzyl, phenyl(o-nitrophenyl)methyl); urea-type derivatives (phenothiazinyl-(10)-carbonyl, N'-p-toluenesulfonylaminocarbonyl, N'-phenylarninothiocarbonyl); miscellaneous carbamates (t-amyl, S-benzyl thiocarbamate, p-cyanobenzyl, cyclobutyl, cyclohexyl, cyclopentyl, cyclopropylmethyl, p-decyloxybenzyl, diisopropylmethyl, 2,2-dimethoxycarbonylvinyl, o-(N,N-dimethylcarboxamido)benzyl, 1,1-dimethyl-3-(N,N-dimethylcarboxamido)propyl, 1,1-dimethylpropynyl, di-(2-pyridyl)methyl, 2-furanylmethyl, 2-Iodoethyl, isobornyl, isobutyl, isonicotinyl, p-(p'-methoxyphenylazo)benzyl, 1-methylcyclobutyl, 1-methylcyclohexyl, 1-methyl-1-cyclopropylmethyl, 1-methyl-1-(3,5-dimethoxyphenyl)ethyl, 1-methyl-1-(p-phenylazophenyl)ethyl, 1-methyl-1-phenylethyl, 1-methyl-1-(4-pyridyl)ethyl, phenyl, p-(phenylazo)benzyl, 2,4,6-tri-*t*-butyl-

phenyl, 4-(trimethylammonium)benzyl, 2,4,6-trimethylbenzyl); amides (N-formyl, N-acetyl, N-chloroacetyl, N-trichloroacetyl, N-trifluoroacetyl, N-phenylacetyl, N-3-phenylpropionyl, N-picolinoyl, N-3-pyridylcarboxamide, N-benzoylphenylalanyl, N-benzoyl, N-p-phenylbenzoyl); amides with assisted cleavage (N-o-nitrophenylacetyl, N-o-nitrophenoxyacetyl, N-acetoacetyl, 5 (N'-dithiobenzyloxycarbonylamino)acetyl, N-3-(p-hydroxyphenyl)propionyl, N-3-(o-nitrophenyl)propionyl, N-2-methyl-2-(o-nitrophenoxy)propionyl, N-2-methyl-2-(o-phenylazophenoxy)propionyl, N-4-chlorobutyryl, N-3-methyl-3-nitrobutyryl, N-o-nitrocinnamoyl, N-acetyl-methionine, N-o-nitrobenzoyl, N-o-(benzoyloxymethyl)benzoyl, 4,5-diphenyl-3-oxazolin-2-one); cyclic imide derivatives (N-phthalimide, N-dithiasuccinoyl, N-2,3-diphenylmaleoyl, N-10 2,5-dimethylpyrrolyl, N-1,1,4,4-tetramethyldisilylazacydopentane adduct, 5-substituted 1,3-dimethyl-1,3,5-triazacyclohexan-2-one, 5-substituted 1,3-dibenzyl-1,3,5-triazacyclohexan-2-one, 1-substituted 3,5-dinitro-4-pyridonyl); N-alkyl and N-aryl amines (N-methyl, N-allyl, N-[2-(trimethylsilyl)ethoxy]methyl, N-3-acetoxypropyl, N-(1-isopropyl-4-nitro-2-oxo-3-pyrrolin-3-yl), quaternary ammonium salts, N-benzyl, N-di(4-methoxyphenyl)methyl, N-5-dibenzo-15 suberyl, N-triphenylmethyl, N-(4-methoxyphenyl)diphenylmethyl, N-9-phenylfluorenyl, N-2,7-dichloro-9-fluorenylmethylene, N-ferrocenylmethyl, N-2-picolylamine N'-oxide), imine derivatives (e.g. N-1,1-dimethylthiomethylene, N-benzylidene, N-p-methoxybenzylidene, N-diphenylmethylene, N-[(2-pyridyl)mesityl]methylene, N,(N',N'-dimethylaminomethylene, N,N'-isopropylidene, N-p-nitrobenzylidene, N-salicylidene, N-5-chlorosalicylidene, N-(5-20 chloro-2-hydroxyphenyl)phenylmethylene, N-cyclohexylidene); enamine derivatives (N-(5,5-dimethyl-3-oxo-1-cyclohexenyl)); N-metal derivatives (N-borane derivatives, N-diphenylborinic acid derivatives, N-[phenyl(pentacarbonylchromium- or -tungsten)]carbenyl, N-copper or N-zinc chelate); N-N derivatives (N-nitro, N-nitroso, N-oxide); N-P derivatives (N-diphenylphosphinyl, N-dimethylthiophosphinyl, N-diphenylthiophosphinyl, N-dialkyl phosphoryl, N-dibenzyl phosphoryl, N-diphenyl phosphoryl); N-Si derivatives; N-S derivatives; N-sulfenyl derivatives (N-benzenesulfenyl, N-o-nitrobenzenesulfenyl, N-2,4-dinitrobenzenesulfenyl, N-pentachlorobenzenesulfenyl, N-2-nitro-4-methoxybenzenesulfenyl, N-triphenylmethylsulfenyl, N-3-nitropyridinesulfenyl); and N-sulfonyl derivatives (N-p-toluenesulfonyl, N-benzenesulfonyl, N-2,3,6-trimethyl-4-methoxybenzenesulfonyl, N-2,4,6-trimethoxybenzenesulfonyl, N-2,6-dimethyl-4-methoxybenzenesulfonyl, N-pentamethylbenzenesulfonyl, N-30 2,3,5,6,-tetramethyl-4-methoxybenzenesulfonyl, N-4-methoxybenzene-sulfonyl, N-2,4,6-trimethylbenzenesulfonyl, N-2,6-dimethoxy-4-methylbenzenesulfonyl, N-2,2,5,7,8-pentamethylchroman-6-sulfonyl, N-methanesulfonyl, N- β -trimethylsilyethanesulfonyl, N-9-anthracene-

sulfonyl, N-4-(4',8'-dimethoxynaphthylmethyl)benzenesulfonyl, N-benzylsulfonyl, N-trifluoromethylsulfonyl, N-phenacylsulfonyl).

[0021] A process according to the invention includes contacting a diol and an amine compound in the presence of a ruthenium based catalyst and in a suitable solvent. The terms "catalyst" and "catalyst system" are used interchangeably herein. As used herein, these terms refer to a compound or component, or combination of compounds or components that that is/are capable of increasing the rate of a chemical reaction. Thereby the catalyst or catalyst system generally facilitate(s) or allow(s) the reaction between one or more other compounds, the catalyst remaining in or returning to its original state. A catalyst may be used in any desired amount relative to the other components whose reactions is facilitated or allowed. Suitable solvents include organic solvents such as, but not limited to, toluene, mesitylene and xylene.

[0022] In some embodiments the method of the invention includes a reaction that can be represented by the following scheme (1):



In this scheme [Ru] is a ruthenium based complex, typically a ruthenium (II) complex. As further explained below, in typical embodiments the ruthenium complex includes an alicyclic, aromatic, arylalicyclic or arylaliphatic ligand and/or a phosphine ligand. Illustrative examples such as dichloro-(1,5-cyclooctadiene)ruthenium(II) or dichloro(benzene)ruthenium(II) are depicted in Fig. 3. Further examples are exemplified below. The moieties R¹ to R⁴ in scheme 1 above may be H, halogen, a silyl group, an aliphatic, an alicyclic, an aromatic, an arylaliphatic or an arylalicyclic group. The aliphatic, alicyclic, aromatic, arylaliphatic or arylalicyclic group may have a main chain of 1 to about 30 carbon atoms. Further, the main chain of such an aliphatic, alicyclic, aromatic, arylaliphatic or arylalicyclic group may include 0 to about 9 heteroatoms. A respective heteroatom may be N, O, S, Se and Si. In some embodiments one of R¹ and R² defines an aliphatic, aromatic or arylaliphatic bridge that is linked to the respective other moiety of R² and R¹. In some embodiments one of R³ and R⁴ defines an aliphatic, aromatic or arylaliphatic bridge that is linked to the respective other moiety of R⁴ and R³. Accordingly, the moieties R¹ and R², and/or the moieties R³ and R⁴ may, independent from one another, in some embodiments define one common cyclic structure.

[0023] R' and R'' may be H or a suitable protecting group (supra). R' and R'' are in some embodiments different from each other. In some embodiments R' and R'' are identical. Examples of a suitable protecting group R' and/or R'' include, but are not limited to, an ether, a silyl ether, an ester, a carbonate, an aryl carbamate, a phosphinate and a sulfonate.

5 Illustrative examples of a suitable ether are a methyl-, a t-butyl-, an isopropyl-, a methoxymethyl-, a benzyl-, a 2,4-dimethylbenzyl-, a 4-methoxybenzyl-, an o-nitrobenzyl-, a p-nitrobenzyl-, a 2,6-dichlorobenzyl-, a 3,4-dichlorobenzyl-, a 4-(dimethylamino)carbonylbenzyl-, a methylsulfinylbenzyl-, a benzyloxymethyl-, a methoxyethoxymethyl-, a (2-trimethylsilyl)ethoxymethyl-, a methylthiomethyl-, a phenylthiomethyl-, an azidomethyl-, a cyanomethyl-, a

10 2,2-dichloro-1,1-difluoroethyl-, a 2-chloroethyl-, a 2-bromoethyl-, a t-butyl-diphenylsilyl-, a tetrahydropyranyl-, a 1-ethoxyethyl-, a phenacyl-, a 4-bromo-phenacyl-, a chloropropylmethyl-, an allyl-, a prenyl-, a cyclohexyl-, a cyclohex-2-en-1-yl-, a propargyl-, an anthrylmethyl-, a 4-picolyl-, a heptafluoro-p-tolyl- and a tetrafluoro-4-pyridyl ether. Illustrative examples of a suitable silyl ether are a trimethylsilyl-, a t-butyl-dimethylsilyl-, a t-butyl-

15 diphenylsilyl- and a triisopropylsilyl ether. Illustrative examples of a suitable ester are a formate-, an acetate-, a levulinate-, a pivaloate-, a benzoate-, a 9-fluorene-carboxylate- and a xanthenecarboxylate group. Illustrative examples of a suitable carbonate are a methyl, a t-butyl-, a vinyl-, a benzyl-, an 1-adamantyl-, a 2,4-dimethylpent-3-yl-, an allyl-, a 4-methylsulfinylbenzyl- and a 2,2,2-trichloroethyl carbonate. Illustrative examples of a suitable phosphinate

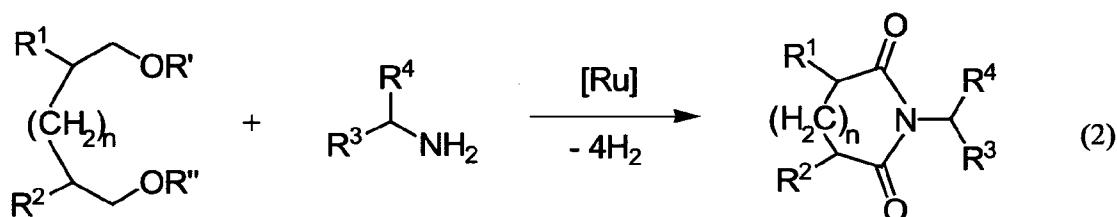
20 are a dimethylphosphinyl-, a dimethylphosphinothioyl- and a diphenylphosphinothioyl group. Illustrative examples of a suitable sulfonate are a methanesulfonate-, a trifluoromethanesulfonate-, a 2-formylbenzenesulfonate, a toluenesulfonate- and a benzylsulfonate group.

[0024] Moiety A in scheme (1) above may be S, Se, O, N-R''', or one of an aliphatic, an alicyclic, an aromatic, an arylaliphatic or an arylalicyclic bridge. The main chain of such an

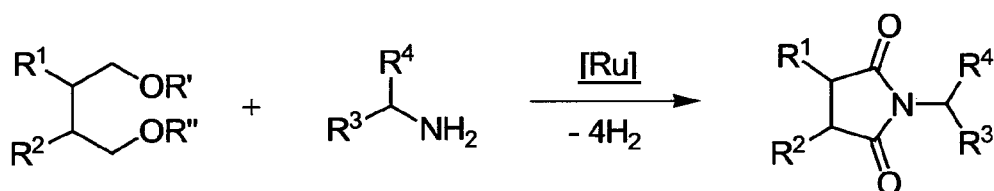
25 aliphatic, alicyclic, aromatic, arylaliphatic or arylalicyclic bridge may have 1 to about 30, such as about 2 to about 30, 1 to about 25, about 2 to about 25, about 3 to about 25, 1 to about 20, about 2 to about 20, 1 to about 15, about 2 to about 15, 1 to about 12, about 2 to about 12, 1 to about 10, about 2 to about 10, 1 to about 8, about 2 to about 8, including 3, 4, 5, 6 or 7 carbon atoms. Further, the main chain of such an aliphatic, alicyclic, aromatic, arylaliphatic or

30 arylalicyclic group may include 0 to about 9 heteroatoms. A respective heteroatom may be N, O, S, Se and Si. R''' may be H, a silyl group, an aliphatic, an alicyclic, an aromatic, an arylaliphatic or an arylalicyclic group.

[0025] In some embodiments the method of the invention includes a reaction that **can be** represented by the following scheme (2):



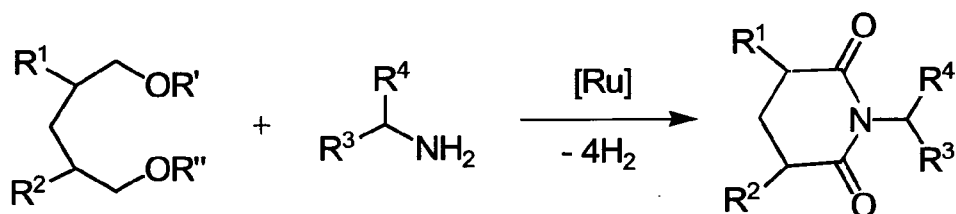
In this scheme [Ru], R¹ to R⁴, R' and R'' are as defined above. As explained above, in some embodiments R' and R'' hydroxy protecting groups may include a substituted methyl ether, a substituted benzyl ether, a silyl ether, and an ester including a sulfonic acid ester, such as a trialkylsilyl ether, a tosylate, a mesylate or an acetate. In the above scheme (2) n is 0, 1 or an integer from 3 to 8, such as 0, 1, 3, 4, 5, 6, 7 or 8. In an embodiment where n is 0, scheme (2) can also be represented as:



scheme (2A).

e.g. a Succinimide,
a Phthalimide,
a Glutarimide

[0026] In an embodiment where n is 1, scheme (2) can also be represented as:



scheme (2B)

[0027] The term "aliphatic" means, unless stated otherwise, a straight or branched hydrocarbon chain, which may be saturated or mono- or poly-unsaturated and include heteroatoms (see below). An unsaturated aliphatic group contains one or more double and/or triple bonds (alkenyl or alkynyl moieties). The branches of the hydrocarbon chain may include linear chains as well as non-aromatic cyclic elements. The respective hydrocarbon chain, which may, unless otherwise stated, be of any length, and contain any number of branches. Typically, the hydrocarbon (main) chain includes 1 to 5, to 10, to 15 or to 20 carbon atoms. Examples of

alkenyl radicals are straight-chain or branched hydrocarbon radicals which contain one or more double bonds. Alkenyl radicals generally contain about two to about twenty carbon atoms and one or more, for instance two, double bonds, such as about two to about ten carbon atoms, and one double bond. Alkynyl radicals normally contain about two to about twenty carbon atoms and one or more, for example two, triple bonds, preferably such as two to ten carbon atoms, and one triple bond. Examples of alkynyl radicals are straight-chain or branched hydrocarbon radicals which contain one or more triple bonds. Examples of alkyl groups are methyl, ethyl, propyl, butyl, pentyl, hexyl, heptyl, octyl, nonyl, decyl, the *n* isomers of these radicals, isopropyl, isobutyl, isopentyl, sec-butyl, *tert*-butyl, neopentyl, 3,3 dimethylbutyl. Both the main chain as well as the branches may furthermore contain heteroatoms as for instance N, O, S, Se or Si, or carbon atoms may be replaced by these heteroatoms.

[0028] The term "alicyclic" may also be referred to as "cycloaliphatic" and means, unless otherwise stated, a non-aromatic cyclic moiety (e.g. hydrocarbon moiety), which may be saturated or mono- or poly-unsaturated. The cyclic hydrocarbon moiety may also include fused cyclic ring systems such as decalin and may also be substituted with non-aromatic cyclic as well as chain elements. The main chain of the cyclic hydrocarbon moiety may, unless otherwise stated, be of any length and contain any number of non-aromatic cyclic and chain elements. Typically, the hydrocarbon (main) chain includes 3, 4, 5, 6, 7 or 8 main chain atoms in one cycle. Examples of such moieties include, but are not limited to, cyclopentyl, cyclohexyl, cycloheptyl, or cyclooctyl. Both the cyclic hydrocarbon moiety and, if present, any cyclic and chain substituents may furthermore contain heteroatoms, as for instance N, O, S, Se or Si, or a carbon atom may be replaced by these heteroatoms. The term "alicyclic" also includes cycloalkenyl moieties that are unsaturated cyclic hydrocarbons, which generally contain about three to about eight ring carbon atoms, for example five or six ring carbon atoms. Cycloalkenyl radicals typically have a double bond in the respective ring system. Cycloalkenyl radicals may in turn be substituted.

[0029] The term "aromatic" means, unless otherwise stated, a planar cyclic hydrocarbon moiety of conjugated double bonds, which may be a single ring or include multiple fused or covalently linked rings, for example, 2, 3 or 4 fused rings. The term aromatic also includes alkylaryl. Typically, the hydrocarbon (main) chain includes 5, 6, 7 or 8 main chain atoms in one cycle. Examples of such moieties include, but are not limited to, cyclopentadienyl, phenyl, naphthalenyl-, [10]annulenyl-(1,3,5,7,9-cyclodecapentaenyl-), [12]annulenyl-, [8]annulenyl-, phenalene (perinaphthene), 1,9-dihydropyrene, chrysene (1,2-benzophenanthrene). An example

of an alkylaryl moiety is benzyl. The main chain of the cyclic hydrocarbon moiety may, unless otherwise stated, be of any length and contain any number of heteroatoms, as for instance N, O and S. Examples of such heteroaromatic moieties (which are known to the person skilled in the art) include, but are not limited to, furanyl-, thiophenyl-, naphthyl-, naphthofuranyl-, anthrathiophenyl-, pyridinyl-, pyrrolyl-, quinolinyl-, naphthoquinolinyl-, quinoxalinyl-, indolyl-, benzindolyl-, imidazolyl-, oxazolyl-, oxoninyl-, oxepinyl-, benzoxepinyl-, azepinyl-, thiepinyl-, selenepinyl-, thioninyl-, azecinyl- (azacyclodecapentaenyl-), diazecinyl-, azacyclododeca-1,3,5,7,9,11-hexaene-5,9-diyl-, azozinyl-, diazocinyl-, benzazocinyl-, azecinyl-, azaundecinyl-, thia[11]annulenyl-, oxacyclotrideca-2,4,6,8,10,12-hexaenyl- or triazaanthracenyl-moieties.

[0030] By the term "arylaliphatic" is meant a hydrocarbon moiety, in which one or more aromatic moieties are substituted with one or more aliphatic groups. Thus the term "arylaliphatic" also includes hydrocarbon moieties, in which two or more aryl groups are connected via one or more aliphatic chain or chains of any length, for instance a methylene group. Typically, the hydrocarbon (main) chain includes 5, 6, 7 or 8 main chain atoms in each ring of the aromatic moiety. Examples of arylaliphatic moieties include, but are not limited to, 1-ethyl-naphthalene, 1,1'-methylenebis-benzene, 9-isopropylanthracene, 1,2,3-trimethyl-benzene, 4-phenyl-2-buten-1-ol, 7-chloro-3-(1-methylethyl)-quinoline, 3-heptyl-furan, 6-[2-(2,5-diethylphenyl)ethyl]-4-ethyl-quinazoline or, 7,8-dibutyl-5,6-diethyl-isoquinoline.

[0031] The term "arylalicyclic" means a hydrocarbon moiety in which an alicyclic moiety is substituted with one or more aromatic groups. Three illustrative example of an arylalicyclic moiety are "phenylcyclohexyl", "phenylcyclopentyl" or "naphthylcyclohexyl". In typical embodiments an arylalicyclic moiety has a main chain of more than about 10 carbon atoms. In some embodiments an arylalicyclic moiety has a main chain of up to about 30 carbon atoms, such as up to about 28, up to about 25, up to about 22, up to about 20, up to about 18 up or to about 14 carbon atoms.

[0032] Each of the terms "aliphatic", "alicyclic", "aromatic", "arylaliphatic" and "arylalicyclic" as used herein is meant to include both substituted and unsubstituted forms of the respective moiety. Substituents may be any functional group, as for example, but not limited to, amino, amido, azido, carbonyl, carboxyl, cyano, isocyano, dithiane, halogen, hydroxyl, nitro, organometal, organoboron, seleno, silyl, silano, sulfonyl, thio, thiocycano, trifluoromethyl sulfonyl, p-toluenesulfonyl, bromobenzenesulfonyl, nitrobenzenesulfonyl, and methane-sulfonyl.

[0033] A heteroatom is any atom that differs from carbon. Examples include, but are not limited to N, O, P, S, and Se. Where several heteroatoms are present within a moiety of a

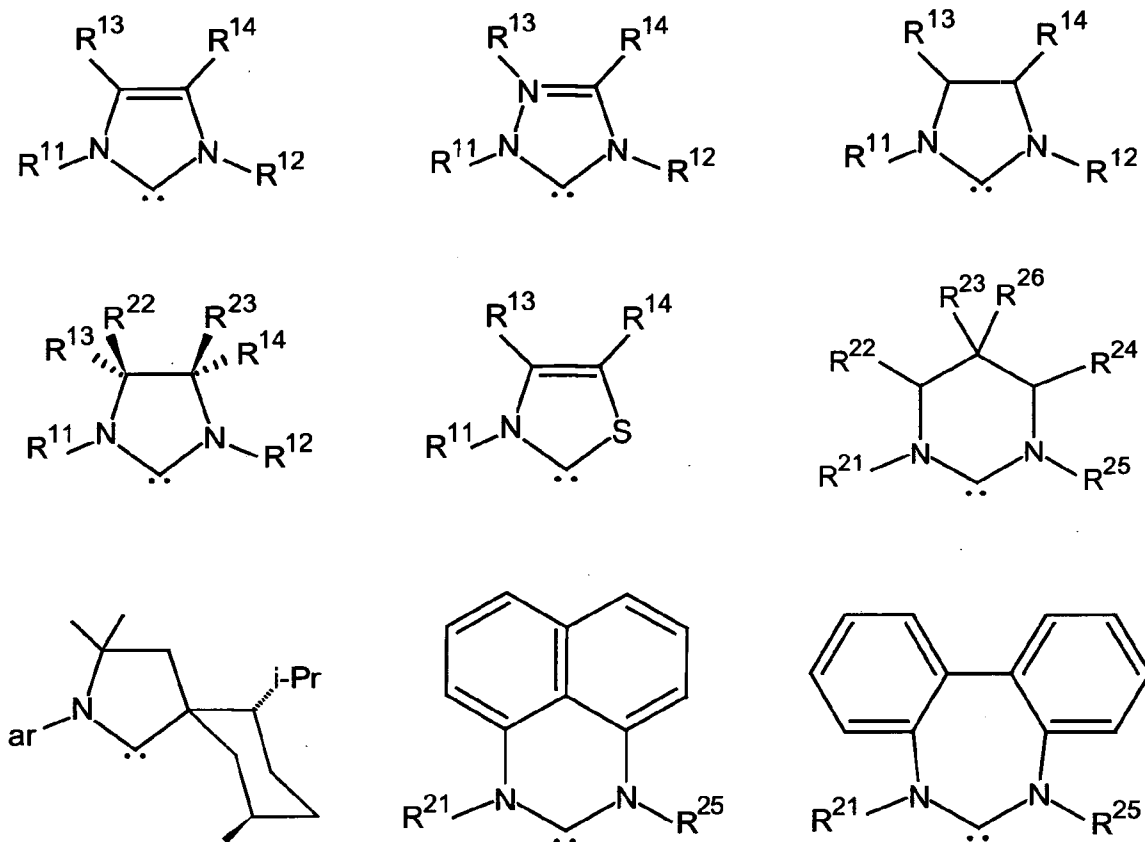
reactant or product of the process of the invention, they are independently selected.

[0034] In a process of the present invention a Ruthenium (II) catalyst is provided. Providing the Ruthenium (II) catalyst in a process according to the invention may in some embodiments include providing an N-heterocyclic carbene. As an example, a Ruthenium (II) precatalyst catalyst complex may be provided and an N-heterocyclic carbene, for example together, at the same time or in sequence, e.g. in a preselected order. In some embodiments the N-heterocyclic carbene may be provided as a complex with a metal halogenide or metal oxide, such as a transition metal halogenide or a transition metal oxide, e.g. a halogenide or oxide of a metal of one of groups 3 to 12 of the periodic table of elements, including group 8, group 9, group 10 or group 11 thereof. An illustrative example of a group 11 halogenide is a silver halogenide, e.g. Ag(I)Cl, Ag(I)Br or Ag(I)I. An illustrative example of a group 11 oxide is copper (II) oxide, CuO.

[0035] An N-heterocyclic carbene is known in the art via the understanding of a molecule with a divalent carbon atom that has six valence electrons. While carbenes in general are typically very short lived, an N-heterocyclic carbene is stable as a ligand, generally a two electron ligand. An N-heterocyclic carbene can be understood as being stabilized by the electron lone pair(s) of one or more nitrogen atoms in the molecule, which can contribute to a resonance effect, which can be depicted in the form of mesomer structures, and be taken to lead to a partial multiple bond character of the additional electrons of the carbene moiety. An N-heterocyclic carbene generally has to be handled under inert gas atmosphere such as argon or nitrogen, prevented from contact with chlorinated solvents and moisture and is then stable even at elevated temperatures such as 200 °C and higher. A brief overview on stable carbenes including N-heterocyclic carbenes has been given by Kirmse (Angew. Chem. Int. Ed (2004) 43, 1767-1769). The formation, reactivity and theoretical aspects of N-heterocyclic carbenes have for example been reviewed by Hahn & Jahnke (Angew. Chem. Int. Ed. (2008) 47, 3122-3172).

[0036] Examples of an N-heterocyclic carbene that is frequently used in the art and that may also be used in the context of the present invention include, but is not limited to one of the following molecules:

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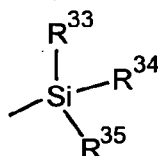
On a general basis an N-heterocyclic carbene can be formed from the corresponding proton-substituted compound using a strong base, i.e. a base such as a metal hydride, e.g. NaH, CaH₂, LiH or TiH₂. Further examples of a strong base include, but are not limited to, lithium diisopropylamide, lithium tetramethylpiperidide or lithium hexamethyldisilazide, each of them having a pK_a of 30 or more in DMSO. In some embodiments an alkoxide can also be used as the respective base, such as NaOCH₃, KOtBu, NaOEt. Yet further examples of a suitable base are Li[N(SiMe₃)₂] and K[N(SiMe₃)₂]. In some embodiments at least one equivalent of the base, at least two or at least three equivalents of the base or more, is/are used relative to the proton-substituted compound (e.g. an imidazole or imidazoline compound), typically being an N-heterocyclic compound.

[0037] In some embodiments the nitrogen atom(s) of the N-heterocyclic carbene is/are included in a 5-membered ring such as an imidazol-based, a triazol-based, a thiazol-based or a benzimidazol-based carbene. An imidazol-based carbene can for example be prepared from an imidazolium salt using a base or by reductive desulfurization of an imidazolin-2-thion (see e.g. chapter 2.3 of Hahn et al., 2008, *supra*). The respective imidazolium salt can for example be obtained via a cyclisation reaction or by a reaction at an N atom of an imidazol compound,

such as alkylation, as summarized by Hahn et al. (ibid.). Imidazol-based N-heterocyclic carbenes have also been reviewed by Ktíhl (Chem. Soc. Rev. (2007) 36, 592-607).

[0038] In the above examples of an N-heterocyclic carbene the moieties R^{11} , R^{12} , R^{13} and R^{14} , where present, may independent from one another be H or an aliphatic, an alicyclic, an aromatic, an arylaliphatic, or an arylalicyclic group, which may include 0 to about 3 heteroatoms. Any two of these moieties, where present, such as R^{13} and R^{14} , R^5 and R^{13} or R^{12} and R^{14} may also be linked to define a bridge, such as an aliphatic, an aromatic, an alicyclic or an arylalicyclic bridge. "ar" in the fourth exemplary compound depicted above represents an aromatic moiety. R^{21} , R^{22} , R^{23} , R^{24} , R^{25} and R^{26} , where present, may also be independent from one another, be H or an aliphatic, an alicyclic, an aromatic, an arylaliphatic, or an arylalicyclic group, which may include 0 to about 3 heteroatoms.

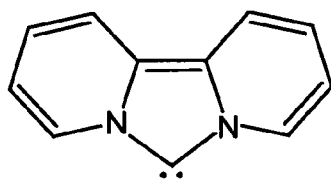
[0039] A respective aliphatic, alicyclic, aromatic, arylaliphatic or arylalicyclic group of any of R^{11} , R^{12} , R^{13} , R^{14} , R^{21} , R^{22} , R^{23} , R^{24} , R^{25} and R^{26} , where present, is typically of a main chain length of 1 to about 10, to about 15 or to about 20 carbon atoms. Each of R^{11} , R^{12} , R^{13} , R^{14} , R^{21} , R^{22} , R^{23} , R^{24} , R^{25} and R^{26} , (as well as R^9 , R^{10} , R^{11} , R^6 , R^7 and R^8 , and R^1 , R^2 and R^3 , see below) may for example include 0 to about 3, such as one or two, heteroatoms selected from the group N, O, S, Se and Si. Any of these aliphatic, alicyclic, aromatic, arylaliphatic or arylalicyclic groups may be substituted (see also below), for example carrying a silyl group, which may be of the structure:



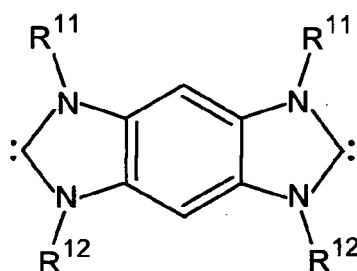
In such a silyl group moieties R^{33} - R^{35} are independently selected aliphatic, alicyclic, aromatic, arylaliphatic, or arylalicyclic groups, typically bonded to the Si-atom via a carbon atom (which is part of the respective group).

[0040] Any two of the moieties R^{21} , R^{22} , R^{23} , R^{24} , R^{25} and R^{26} , where present, such as R^{21} and R^{22} , R^{24} and R^{25} , R^{22} and R^{23} , R^{22} and R^{26} , R^{23} and R^{25} or R^{25} and R^{26} may also be linked to define a bridge, such as an aliphatic, an aromatic, an alicyclic or an arylalicyclic bridge. As an illustrative example of a compound depicted above with two aromatic bridges may serve:

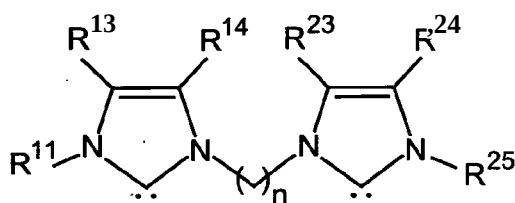
17



As a further illustrative example of a compound depicted above with an aromatic bridge, in which two carbene moieties are present, may serve:

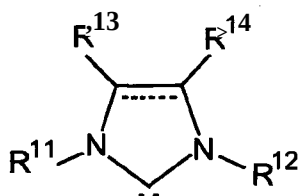


5 A further illustrative example of a compound depicted above with a bridge, in which two carbene moieties are present is a molecule with a moiety R¹² that includes an N-heterocyclic carbene moiety such as:

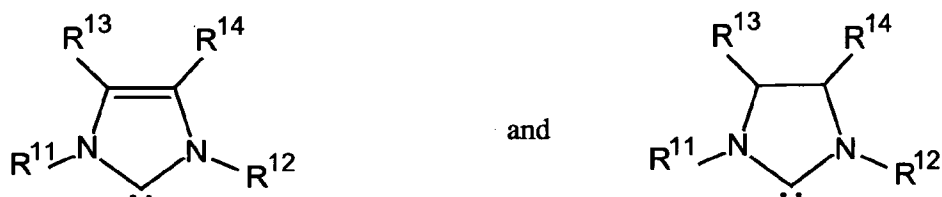


Moieties R²³ to R²⁵ in this example are as defined above, and n may be an integer selected from 1, 2, 3, 4 and 5.

10 [0041] As an illustrative example, the N-heterocyclic carbene may be imidazol- or imidazoline based and have the general formula:



In this formula the symbol 7777 indicates that the respective bond may be a single or a double bond. Accordingly, a corresponding N-heterocyclic carbene may also be represented by one the two formulae



Such an N-heterocyclic carbene may be formed from an imidazole or an imidazoline compound and a base (*supra*). The imidazole compound may be of general formula (I), and the imidazoline compound may be of general formula (II):



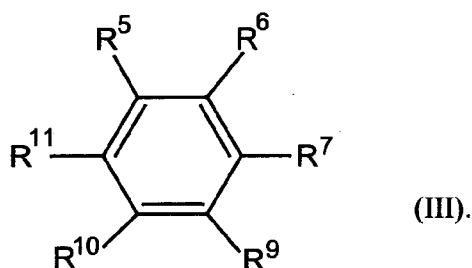
As explained above, R^{11} - R^{13} are independently selected from H, an aliphatic group, an alicyclic group, an aromatic group, an arylaliphatic group, and an arylalicyclic group. A respective aliphatic, alicyclic, aromatic, arylaliphatic or arylalicyclic group may include 0 to about 3 heteroatoms selected from the group N, O, S, Se and Si.

[0042] Providing the Ruthenium (II) catalyst in a method according to the invention may include forming the Ruthenium (II) catalyst, for example forming the Ruthenium (II) catalyst *in situ*. The Ruthenium (II) catalyst may be formed from a Ruthenium (II) precatalyst complex, which may be provided. Forming the Ruthenium (II) catalyst from a Ruthenium (II) precatalyst complex may include allowing a reaction, such as complex formation with the N-heterocyclic carbene. In some embodiments the Ruthenium catalyst is formed in situ from the N-heterocyclic carbene and a $[Ru(A)Cl_2]_2$ precatalyst complex in the presence of the base (*supra*). Moiety A in formula $[Ru(A)Cl_2]_2$ may be an aromatic, an arylaliphatic or an arylalicyclic compound. In some embodiments A is or includes an aromatic moiety that is free of nitrogen as a heteroatom in the respective aromatic ring(s) of the moiety. In some embodiments the ring of the aromatic moiety consists only of carbon atoms. Any such aromatic ring may carry one or more substituents that may include one or more heteroatoms, e.g. 0-3 heteroatoms, such as O, N, Si, S or Se. In some embodiments the moiety A is a hydrocarbon moiety that does not include any heteroatom. In some embodiments the moiety A in formula $[Ru(A)Cl_2]_2$ is a benzene based moiety. The term "benzene based" refers to a

moiety that has a an aromatic moiety, the aromatic moiety being a benzene ring, i.e. an aromatic six-membered ring without a heteroatom. This aromatic ring may carry substituents such as one or more aliphatic or alicyclic groups as well as one or more functional groups such as a hydroxyl group, a seleno group, a thiol group, a silyl group, a silano group, a sulfonyl group, a nitro group, a carboxy group, a halogen, an amino group, an amido group, a cyano group, an isocyano group or a thiocyano group (see also above for examples). The benzene ring may also be linked or fused to an aromatic, an arylaliphatic or an arylalicyclic group.

[0043] In some embodiments a benzene based moiety has a single aromatic moiety, the aromatic moiety being the benzene ring. In such embodiments the aromatic cycle may nevertheless carry substituents such as one or more aliphatic or alicyclic groups as well as one or more functional groups (supra).

[0044] In some **embodiments the benzene based moiety** is of the general formula (III):



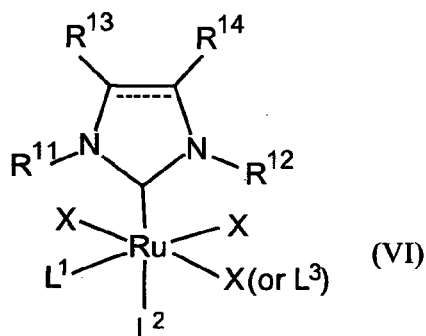
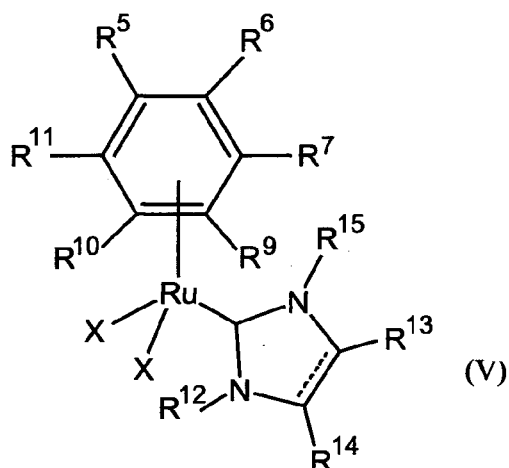
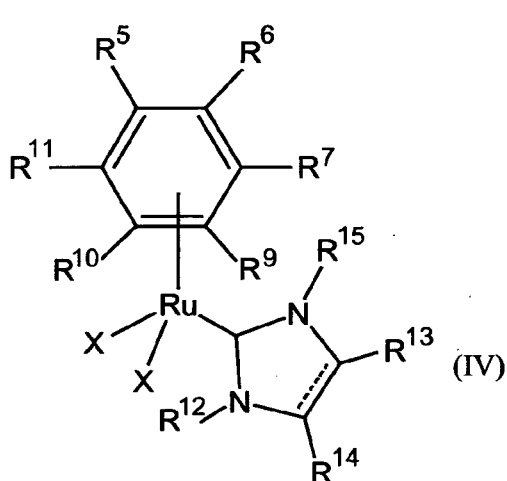
In formula (III) $R^5 - R^7$ and $R^9 - R^{11}$ are independently selected from H, an aliphatic group, an alicyclic group, an aromatic group, an arylaliphatic group, and an arylalicyclic group. A respective aliphatic, alicyclic, aromatic, arylaliphatic or arylalicyclic group may include 0 to about 3 heteroatoms selected from the group N, O, S, Se and Si. As two illustrative examples, the benzene based moiety A may be unsubstituted benzene or cymene.

[0045] In some embodiments providing the Ruthenium catalyst further includes providing a nitrogen containing ligand. In the art an atom or a molecule that is or that can be attached to a central atom, in the present case ruthenium (II), in a coordination or complex compound is called a ligand. Typically a ligand is capable of functioning as an electron-pair donor in a coordinate covalent bond (electron-pair bond) formed with the metal atom. Attachment of the ligand to the ruthenium atom may be through a single atom, e.g. the nitrogen atom, in which case can be called a unidentate ligand, or through two or more atoms, in which case it may be denoted a bidentate or polydentate ligand. In the field of organometallic chemistry, ligands are classified as "L-type", "X-type" and "Z-type". The classification by the symbols L, X, and Z, correspond respectively to 2-electron, 1-electron and 0-electron neutral ligands. X-type ligands

are formed from an anionic precursor molecule and L-type ligands from a charge-neutral precursor molecule. Examples of L-type ligands are CO, a phosphine (e.g. **PPI13**), a phosphite, an ether, a nitrile and an amine. In some embodiments a nitrogen containing ligand provided in a method of the invention is an L-type ligand, such as a nitrile and an amine, e.g. acetonitrile or pyridine.

[0046] In some embodiments, in particular if the ruthenium (II) catalyst is formed from a $[\text{Ru}(\text{A})\text{Cl}_2]_2$ precatalyst complex (supra) and a metal halogenide complex of an N-heterocyclic carbene, a nitrogen containing ligand such as an L-type ligand is not provided. The inventors have found that in such embodiments the formation of an amide proceeds smoothly in the absence of an additional nitrogen containing ligand such as an L-type ligand.

[0047] In some embodiments providing the Ruthenium (II) compound defining the Ruthenium (II) catalyst includes forming one or more Ruthenium (II) complexes of formulae (IV), (V) and (VI)



As defined above, 7777 represents a single or a double bond. $\text{R}^5 - \text{R}^7$ and $\text{R}^9 - \text{R}^{15}$ are independently from one another H or an aliphatic, an alicyclic, an aromatic, an arylaliphatic or an arylalicyclic group. The respective aliphatic, alicyclic, aromatic, arylaliphatic or arylalicyclic group may have 0 to about 3, including 1 or 2, heteroatoms. Such a heteroatom

may be N, O, S, Se or Si. X is halogen or -OR¹⁶. R¹⁶ in -OR¹⁶ is H or an aliphatic, an alicyclic, an aromatic, an arylaliphatic or an arylalicyclic group. The respective aliphatic, alicyclic, aromatic, arylaliphatic or arylalicyclic group may have 0 to about 3, including 1 or 2, heteroatoms, such as N, O, S, Se or Si. L¹, L² and L³ are independently selected from a solvent molecule, the L-type ligand (e.g. pyridine or acetonitrile, supra) and the N-heterocyclic carbene (supra). In some embodiments the Ruthenium catalyst that is provided can be represented by one of the above formulae (IV) to (VI).

[0048] Hence, in some embodiments a Ruthenium (II) catalyst of one or more of formulae (IV) to (VI) is provided, including formed, in a process according to the invention. In some embodiments a catalyst of one of formulae (IV) to (VI) is an intermediate that is formed in situ. In some embodiments a catalyst of one of formulae (IV) to (VI) is used in isolated, enriched or purified form. The term "isolated" means that a respective Ruthenium (II) catalyst is no longer included in a reaction mixture formed by adding e.g. a Ruthenium (II) precatalyst complex, such as a [Ru(A)Cl₂]₂ precatalyst complex, to a solvent, for instance together with an N-heterocyclic carbene. Rather, when isolated, the Ruthenium (II) catalyst has been removed from such solvent or solution, for instance the solution in which it was formed. The term "enriched" means that a respective Ruthenium (II) catalyst constitutes a significantly higher fraction of the total compounds, including the Ruthenium compounds, present in the matter, typically a solid or solution thereof, than in a reaction mixture in which the process of the invention has been carried out. Examples of other means of enrichment are a filtration or a precipitation. The term "purified" means that a respective Ruthenium (II) catalyst constitutes a certain desired portion of the total matter, e.g. solid matter addressed. A purified Ruthenium (II) catalyst may for example be a solid matter, e.g. powder, which contains at least about 50 %, about 60 %, about 60 %, about 70 %, about 80 %, about 90 %, about 95 % or more of Ruthenium (II) catalyst.

[0049] The Ruthenium (II) catalyst may in some embodiments be provided in catalytic amounts. Unless otherwise noted, the term "catalytic amount," as used herein, includes that amount of the Ruthenium (II) catalyst that is sufficient for a reaction of the process of the invention to occur. Accordingly, the quantity that constitutes a catalytic amount is any quantity that serves to allow or to increase the rate of reaction, with larger quantities typically providing a greater increase. The quantity used in any particular application will be determined to a large part by the individual needs of the manufacturing facility. Factors which enter into such a determination include the catalyst cost, recovery costs, desired reaction time, and

system capacity. It will be most convenient to use an amount of Ruthenium (II) catalyst in the range from about 0.001 to about 0.5 equivalents, from about 0.001 to about 0.25 equivalents, from about 0.01 to about 0.25 equivalents, from about 0.001 to about 0.1, from about 0.01 to about 0.1 equivalents, including about 0.005, about 0.05 or about 0.08 equivalents of the primary amine, or in the range from about 0.001 to about 1 equivalents, from about 0.001 to about 0.5 equivalents, from about 0.001 to about 0.25 equivalents, from about 0.001 to about 0.1 equivalents, from about 0.01 to about 0.5 equivalents or from about 0.05 to about 0.1 equivalents, including about 0.015, about 0.02 or about 0.04 equivalents of the diol compound.

[0050] In some embodiments the Ruthenium (II) catalyst used in the invention includes a phosphine ligand. A phosphine typically has the general formula $PR^{40}R^{41}R^{42}$. In this formula R^{40} , R^{41} and R^{42} are independent from one another an aliphatic, an alicyclic, an aromatic, an arylaliphatic, or an arylalicyclic group. A respective aliphatic, alicyclic, aromatic, arylaliphatic or arylalicyclic group may include 0 to about 3 heteroatoms selected from the group N, O, S, Se and Si. In some embodiments one of R^{40} , R^{41} and R^{42} in a phosphine defines an aliphatic, aromatic or arylaliphatic bridge that is linked to a respective further moiety. Hence, e.g. R^{40} may define a bridge with R^{41} or with R^{42} , or R^{41} may define a bridge with R^{40} or R^{42} . Illustrative examples of a suitable phosphine ligand include, but are not limited to, triphenylphosphine, trimethylphosphine, triethylphosphine, tri-n-butylphosphine, tri-n-propyl phosphine, tri-n-butyl phosphine, tri-f-butyl phosphine, tri-p-tolyl phosphine, methyldiphenyl phosphine, phenyldimethyl phosphine ($PPh(Me)_2$), ethyldiphenyl phosphine ($P(Et)(Ph)_2$), tricyclohexyl phosphine (PCy_3), (S)-(2-methoxyphenyl)-[2-[(2-methoxyphenyl)-phenylphosphanyl]ethyl]-phenylphosphane (DIPAMP) or tris(dimethylamino)phosphine. In typical embodiments where the Ruthenium (II) catalyst includes a phosphine ligand providing the Ruthenium (II) catalyst includes providing an N-heterocyclic carbene (supra).

[0051] As noted above, a process according to the present invention may in some embodiments be carried out without adding a phosphine. In particular the Ruthenium (II) catalyst used, including formed in the process of the invention, may be free of a phosphine ligand. In some embodiments the process is carried out in the absence of a phosphine.

[0052] After the ruthenium catalyst has been provided, the primary amine and the diol are provided. The amine and the diol may be different molecules, i.e. reactants. In this case the (primary or secondary) amine and the (primary) alcohol are contacted in the presence of the Ruthenium (II) catalyst. The amine and the diol may also be different moieties of the same molecule. In this case the molecule that includes the amine moiety and the alcohol moiety is

exposed to the Ruthenium (II) catalyst. Contacting the amine and the diol compound in the presence of the catalyst, or exposing the molecule with the corresponding amine and alcohol moieties, respectively, is typically carried out by adding the corresponding molecules into a suitable solvent. Thereby a reaction mixture is formed. The reaction mixture may be brought to an elevated temperature, i.e. a temperature above ambient temperature. Ambient temperature is typically about 18 °C or about 20 °C. The reaction mixture may for example be brought to a temperature above about 30 °C, above about 40 °C, above about 60 °C, above about 80 °C, above about 100 °C, above about 120 °C or above about 140 °C. The temperature may for example be selected in the range from about 25 °C to about 200 °C, such as from about 30 °C to about 180 °C, including about 40 °C to about 180 °C, about 30 °C to about 110 °C, about 40 °C to about 160 °C, about 40 °C to about 110 °C, about 50 °C to about 180 °C or about 60 °C to about 180 °C. The temperature selected may for example be the boiling point of the reaction mixture, which is largely determined by the boiling point of the solvent used. As an illustrative example, if toluene is used as the solvent, the boiling point that may be selected as the temperature is about 120 °C. As a further example, if mesitylene is used as the solvent, the boiling point is about 163 °C.

[0053] Solvents used may be polar or non-polar liquids that are compatible with the catalyst used. Due to the sensitivity of the ruthenium (II) compound used, it may be disadvantageous to use protic polar liquids, which may in some embodiments be avoided. In some embodiments it may also be disadvantageous to use a chlorinated liquid (supra), which may thus in some embodiments be avoided. Accordingly, in some embodiments a non-polar liquid is used that does not have a chlorine substituent. In addition the liquid used is in some embodiments free of substituents, which are capable of coordinating to ruthenium (II) due to the presence of electron lone pair(s). Hence, in some embodiments the liquid used as a solvent is free of substituents that have nitrogen, sulfur or oxygen atoms. Examples of non-polar liquids include, but are not limited to mineral oil, pentane, hexane, heptane, cyclohexane, cyclooctane, benzene, toluene, mesitylene, carbon disulfide, and a non-polar ionic liquid. Examples of a non-polar ionic liquid include, but are not limited to, 1-ethyl-3-methylimidazolium bis[(trifluoromethyl)sulfonyl]amide bis(triflyl)amide, 1-ethyl-3-methylimidazolium bis[(trifluoromethyl)sulfonyl]amide trifluoroacetate, 1-butyl-3-methylimidazolium hexafluorophosphate, 1-hexyl-3-methylimidazolium bis(trifluoromethylsulfonyl)imide, 1-butyl-3-methylimidazolium bis(trifluoromethylsulfonyl)imide, trihexyl(tetradecyl)phosphonium bis[oxalate (2-)]borate, 1-hexyl-3-methylimidazolium tris(pentafluoroethyl)trifluorophosphate, 1-butyl-3-methylimidazolium hexafluorophosphate, tris(pentafluoroethyl)trifluo-

rophosphate, trihexyl (tetradecyl)phosphonium, N''-ethyl-N,N,N',N'-tetramethylguanidinium, 1-butyl-1-methyl pyrroledinium tris(pentafluoroethyl) trifluorophosphate, 1-butyl-1-methyl pyrrolidinium bis (trifluoromethylsulfonyl) imide, 1-butyl-3-methyl imidazolium hexafluorophosphate, 1-ethyl-3-methylimidazolium bis(trifluoromethylsulfonyl)imide and 1-n-butyl-3-methylimidazolium. In some embodiments the solvent used is an aromatic liquid that is free of halogen substituents. Illustrative examples of a respective aromatic liquid include, but are not limited to, benzene, toluene, mesitylene, p-xylene, m-xylene, ethylbenzene, propylbenzene, an ethyl toluene, p-cymene, o-cymene, cumene, naphthalene, phenanthrene or pyrene.

[0054] In order that the invention may be readily understood and put into practical effect, particular embodiments will now be described by way of the following non-limiting examples.

EXAMPLES

[0055] The following examples illustrate the use of catalyst systems using [Ru(p-cymene)Cl₂]₂, [Ru(benzene)Cl₂]₂, RuH₂(PPh₃)₄ or Ru(cyclooctadiene)Cl₂ complexes, in some embodiments with an N-heterocyclic carbene and/or readily available nitrogen containing L-type ligands.

[0056] Synthesis of the imides was carried out directly from alcohols with amines using a similar strategy to the oxidative amide synthesis from alcohols and amines reported as catalyzed by Ru- (Naota, T, & Murahashi, S-I, Synlett (1991) 693; Watson, AJA, et al., Org. Lett. 2009) 11, 2667; Nordstrøm, LU, et al., J. Am. Chem. Soc. 2008, 130, 17672; Gunanathan, C, et al., (Science) 2007, 317, 790; Ghosh, SC, et al., Adv. Synth. Catal. (2009) 351, 2643; Zhang, Y, et al., Organometallics (2010) 29, 1374; Muthaiah, S, et al., J. Org. Chem. (2010) 75, 3002), Rh- (Fujita, K, et al., Org. Lett. (2004) 6, 2785; Zweifel, T, et al., Angew. Chem., Int. Ed. (2009) 48, 559), and Ag-based (Shimizu, K., et al., Chem.-Eur. J. (2009) 15, 9977) complexes (Fig. 2). A recent review has been given by Dobereiner & Crabtree (Chem. Rev. (2010) 110, 681). Without the intend of being bound by theory, the strategy for the amide synthesis is to oxidize alcohol to aldehyde first and then further oxidize the hemiaminal, formed from the aldehyde and the amine, to amide evolving two equivalents of hydrogen gas. Once the possibility of this route for imide synthesis had been discovered, the focus was on identifying an active catalytic system to realize the useful imide synthesis by enabling less nucleophilic nitrogen atom of the amide to react further with alcohols. As a result, the first direct cyclic imide synthesis of imides was developed, starting from simple diols using an in situ generated Ru hydride based catalyst.

[0057] A reaction of 1,4-butanediol (**3a**) and benzylamine (**4a**) to afford N-benzylsuccinimide (**5a**) was chosen to screen the catalytic conditions (Fig. 4). The investigation was started based on the reported Ru catalytic systems for the amide synthesis by others (Naota, T, & Murahashi, SI, Synlett (1991) 693; Watson, AJA, et al., Org. Lett. (2009) 11, 2667; Nordstram, LU, et al., J. Am. Chem. Soc. (2008) 130, 17672; Gunanathan, C, et al., Science (2007) 317, 790) and the present inventors (Ghosh, SC, et al., Adv. Synth. Catal. (2009) 351, 2643; Zhang, Y, et al., Organometallics (2010) 29, 1374; Muthaiah, S, et al., J. Org. Chem. (2010) 75, 3002). [Ru(benzene)Cl₂]₂ (**1a**) (Ghosh, SCS, et al., Adv. Synth. Catal. (2009) 351, 2643) and [Ru(p-cymene)Cl₂]₂ (**1b**) (ibid.) showed limited activity even with the help of an N-heterocyclic carbene (NHC) precursor, 1,3-diisopropylimidazolium bromide (**2**), under basic conditions (entries 1 and 2). Usage of the reported [Ru(p-cymene)Cl₂]₂ with diphenylphosphinobutane (dppb) ligand did not exhibit any activity for the imide synthesis (entry 3) (Watson et al., 2009, supra). Then, the inventors noticed an early example of the use of RuH₂(PPh₃)₄ (**1c**) for the synthesis of cyclic lactam from α,ω-aminoalcohols by Naota and Murahashi (Synlett (1991) 693). Although their original condition using a hydrogen acceptor afforded no amount of **5a** (entry 4), RuH₂(PPh₃)₄ showed good activity (70%) with the help of the NHC precursor **2** (entry 5). Further optimization has been attempted by applying different NHC precursors, however, the reported condition using **2** has been identified most active, see Muthaiah et al. (J. Org. Chem. (2010) 75, 3002) for more detailed screening conditions. The NHC promoted RuH₂(PPh₃)₄ based catalyst was recently reported to be active on the synthesis of amides from either alcohols or aldehydes with amines (ibid.). Other catalytic systems based on **1d** (Nordstram et al., 2008, supra) and **1e** (Gunanathan et al., 2007, supra) exhibited less activity on the cyclic imide synthesis (entries 6 and 7).

[0058] With the identified active catalytic system, various amines were tested with 1,4-butanediol to make N-substituted succinimide derivatives (Fig. 5). Excellent activity was observed with alkyl and benzyl amines (entries 1-5). Noticeably, more electron rich benzyl amines favoured the cyclization reactions than electron poor ones (entry 5, Fig. 4; entries 4-5, Fig. 5). Pyridine and ether groups were tolerant in this reaction (entries 6-9). While 2-aminomethylpyridine (**4g**) exhibited a reduced yield, presumably due to interference of Ru binding to **3a**, reactions of 3-aminomethylpyridine (**4h**) and 4-aminomethylpyridine (**4i**) proceeded smoothly (entries 6-8). Moderately hindered amines proceeded well to generate the corresponding succinimides, although it was sensitive to steric hindrance as reported in the amide synthesis (entries 10-12; Naota, T, & Murahashi, S-I, Synlett (1991) 693; Watson, AJA, Org. Lett. (2009) 11, 2667; Nordstrmn, LU, et al., J. Am. Chem. Soc. (2008) 130, 17672;

Gunanathan, C, et al., Science (2007) 317, 790; Ghosh, SC, et al., Adv. Synth. Catal. (2009) 351, 2643; Zhang, Y, et al., Organometallics (2010) 29, 1374; Muthaiah, S, et al., J. Org. Chem. (2010) 75, 3002). In case of less basic aryl amines such as aniline, the reaction did not proceed well as observed in the amide synthesis (Nordstram et al., 2008, supra; Ghosh et al., 2009, supra; Zhang et al., 2010, supra; Muthaiah, et al., 2010, supra). γ -Butyrolactone was observed especially with low yielding substrates (e.g. 5% with **4g**, and 13% with **4m**), along with unidentified messy by-products presumably from possible inter- and intra-molecular amidation and esterification reactions (Murahashi, S-I, et al., Tetrahedron Lett. (1981) 22, 5327; Murahashi, S-I, et al., J. Org. Chem. (1987) 52, 4319; Ishii, Y, et al., J. Org. Chem. (1986) 51, 2034; Blum, Y, & Shvo, Y, J. Organomet. Chem. (1984) 263, 93; Zhao, J, & Hartwig, JF, Organometallics (2005) 24, 2441; Ito, M, et al., Org. Lett. (2007) 9, 1821; Murahashi, S-I, et al., Tetrahedron Lett. (1982) 23, 229; Abbenhuis, RATM, et al., J. Org. Chem. (1998) 63, 4282). It has been reported that cyclic amines can be formed from diols and primary amines by Ru catalysts. However, in the presented reactions, no cyclic amine was observed as a by-product. For representative examples of cyclic amine formation, see Murahashi et al. (1982, supra) and Abbenhuis et al. (1998, supra).

[0059] Excited by the facile synthesis of succinimide derivatives from **3a**, various diols were screened to synthesize cyclic imides (Fig. 6). 2-aryl or alkyl functionalized 1,4-butanediols generated the corresponding succinimides with good yields (entries 1 and 2). A bicyclic succinimide derivative **5p** was also synthesized smoothly from *cis*-1,2-cyclohexanedimethanol (**3p**) (entry 3). Phthalimide derivatives were obtained from 1,2-benzenedimethanol (**3q**) with good yields (entries 4-7). In a lower concentration (0.3 M), phthalide (61%) was observed as a major product along with **5q** (21%). The effective phthalide synthesis from **3q** was previously reported with Cp*Ru(II) catalyst systems (Ito et al., 2007, supra). Six-membered glutarimides were also formed with moderate yields (entries 8-9). However, 7-membered cyclic imide synthesis from 1,6-hexanediol was not successful. An anticonvulsant drug, phensuximide (**5w**) was synthesized from the corresponding diol **3n** with methylamine with 63% yield (entry 10).

[0060] Synthesis of linear imides from intermolecular reaction from amides or amines with alcohols was attempted (Fig. 7). However, whether the reaction was run from an amide **6** with 1-pentanol (**7**) or an amine **4e** with 2 equiv of **7**, any of the corresponding linear imide **8** was not detected. Only the amide **9** was observed in case of the reaction with **4e** and 2 equiv of **7**. In intramolecular case of **10**, the reaction proceeded well with 70% yield suggesting that the cyclic imide formation may proceed via a stepwise mechanism with favoured intramolecular

5- or 6-membered ring formation.

[0061] On the basis of the observations in Scheme 2 and the reasonably suggested mechanism on the amide formation from alcohols and amines (Naota et al., 1991, supra; Watson et al., 2009, supra; Nordstrom et al., 2008, supra; Gunanathan et al., 2007, supra; Ghosh et al., 2009, supra; Zhang et al., 2010, supra; Muthaiah et al., 2010, supra) a mechanism is proposed that involves the formation of an amide intermediate and further cyclization to the imide product by the intramolecular reaction of the amide intermediate (Fig. 8). The observation of lactones either in low yielding reactions or in lower concentrations can be explained as an intramolecular reaction of an aldehyde intermediate as reported (Murahashi et al., 1981, supra; Murahashi et al., 1987, supra; Ishii et al., 1986, supra; Blum & Shvo, 1984, supra; Zhao & Hartwig, 2005, supra; Ito et al., 2007, supra; Murahashi et al., 1982, supra; Abbenhuis et al., 1998, supra). The involvement of a lactone intermediate for the formation of the cyclic imide was ruled out from a reaction of γ -butyrolactone with **4e**, as a trace amount (<5%) of the corresponding succinimide **5e** was observed. The nature of the exact catalyst structure is under investigation to understand the mechanism fully and expand the reaction scope to the synthesis of linear imides, especially in regards of role of a strong base and possible chelation effect from the intermediates. It has been suggested that a strong base is required to activate precatalysts by reaction with an alkoxide, formed from an alcohol substrate and the strong base, as well as to generate of NHC from its precursor (Ghosh et al., 2009, supra; Zhang et al., 2010, supra; Muthaiah et al., 2010, supra).

[0062] In conclusion, we have demonstrated that cyclic imides can be synthesized directly from simple diols using an *in situ* generated Ru catalytic system. The atom economical and operatively simple method will provide an alternative approach for the synthesis of important cyclic imides.

Experimental Section

General Information

[0063] All reactions were carried out in oven-dried glassware under an inert atmosphere of dry argon. All alcohols and amines were obtained from Aldrich or Alfa Aesar and used as received. Anhydrous acetonitrile was purchased from Aldrich and used without further purification. Commercial 60% sodium hydride in mineral oil was washed with dry pentane to afford white solid and used. Toluene was dried over a Pure Solv solvent purification system.

[0064] Analytical TLC was performed on a Merck 60 F254 silica gel (0.25 mm thickness). Column chromatography was performed on Merck 60 silica gel (230-400 mesh). NMR spectra were recorded on a Bruker 300 MHz spectrometer. Tetramethylsilane was used as reference, and the chemical shifts were reported in ppm and the coupling constants in Hz. GC yield were obtained on a Agilent 7890A instrument equipped with an HP-5 column using dodecane as an internal standard. Mass spectrometry was performed by Waters Q-ToF Premier Micromass instrument, using Electro Spray Ionization (ESI) mode. 1,3-diisopropylimidazolium bromide (Starikova, OV, et al., Russ. J. Org. Chem. (2003) 39, 1467), $\text{RuH}_2(\text{PPh}_3)_4$ (Levison, JJ, & Robinson, SD, J. Chem. Soc. A (1970) 2947), **3n** (Chadha, VK, et al., J. Med. Chem. (1985) 28, 36; Rumero, A, et al., Tetrahedron (1999) 55, 14947), **3o** (Gharpure, MM, & Rao, AS, J. Chem. Soc.-Perkin Trans. 1 (1990) 2759; Gharpure, MM, & Rao, AS, Synthesis (1988) 410), and **10** (Hou, GH, et al., J. Am. Chem. Soc. (2009) 131, 1366) were prepared according to the reported procedures. Complexes **1a**, **1b**, **1d**, and **1e** were purchased from Strem Chemicals and used as received.

15 General Procedure for the Synthesis of Cyclic Imides

[0065] $\text{RuH}_2(\text{PPh}_3)_4$ (28 mg, 0.025 mmol), 1,3-diisopropylimidazolium bromide (5.8 mg, 0.025 mmol), NaH (2.4 mg, 0.10 mmol) and acetonitrile (1.2 mL, 0.025 mmol) were placed in an oven dried Schlenk tube inside the glove box; toluene (0.5 mL) was added to the mixture over there. The Schlenk tube was taken out and heated to reflux in an oil bath under an argon atmosphere. The flask was removed from the oil bath after 20 min and a diol (0.50 mmol) and an amine (0.55 mmol) were added. The reaction mixture was heated to reflux under a flow of argon to facilitate removal of hydrogen for 24 h before being cooled to room temperature. All the volatiles were removed under vacuum. Purification of the crude product was performed by flash chromatography.

25 Characterization of Cyclic Imides 5a-5w

[0066] All reported cyclic imides were identified by spectral comparison with literature data or with analogous literature data.

1-(Phenylmethyl)-2,5-pyrroUdinedione (5a) [Reddy, PY, et al., J. Org. Chem. (1997) 62, 2652]

30 [0067] White solid, isolated yield: 70%.

¹H NMR (CDCl₃, 300MHz): δ = 7.23-7.38 (m, 5H), 4.63 (s, 2H), 2.68 (s, 4H);

¹³C NMR (CDCl₃, 100 MHz): δ = 176.88, 135.82, 128.91, 128.64, 127.97, 42.39, 28.21.

l-Hexyl-2,5-pyrrolidinedione (5b) [Rice, LM, et al., J. Org. Chem. (1954) 19, 884]

[0068] Colorless oil, isolated yield: 81%.

5 ¹H NMR (CDCl₃, 300 MHz): δ = 3.46 (t, *J* = 7.5 Hz, 2H), 2.66 (s, 4H), 1.52 (m, 2H), 1.22-1.25 (m, 6H), 0.84 (t, *J* = 6.9 Hz, 3H);

¹³C NMR (CDCl₃, 100 MHz): δ = 177.3, 38.9, 31.3, 28.1, 27.6, 26.5, 22.5, 14.0;

HR-MS (ESI) calcd. for C₁₀H₁₇N₂O₂: 184.1338. Found: 184.1341 [MH⁺].

l-(2-Phenylethyl)-2,5-pyrrolidinedione (5c) [Reddy et al., 1997, supra]

10 [0069] Colorless oil, isolated yield: 76%.

¹H NMR (CDCl₃, 300 MHz): δ = 7.17-7.28 (m, 5H), 3.69-3.74 (m, 2H), 2.82-2.87 (m, 2H), 2.61 (s, 4H);

¹³C NMR (CDCl₃, 100 MHz): δ = 177.0, 137.8, 128.8, 128.5, 126.7, 39.9, 33.5, 28.1.

HR-MS (ESI) calcd. for C₁₂H₁₃N₂O₂: 204.1025. Found: 204.1028 [MH⁺].

15 **l-(3-Phenylpropyl)-2,5-pyrrolidinedione (5d)**

[0070] White solid, isolated yield: 88%. ¹³C NMR (CDCl₃) δ HRMS (ESI) calcd for C₁₃H₁₅N₂O₂: 218.1181. Found: 218.1185 [MH⁺].

¹H NMR (CDCl₃, 300 MHz): δ = 7.11-7.26 (m, 5 Hz), 3.53 (t, *J* = 7.2 Hz, 2H), 2.61 (t, *J* = 7.5 Hz, 2H), 2.53 (s, 4H), 1.91 (m, 2H);

20 ¹³C NMR (CDCl₃, 100 MHz): δ = 177.3, 141.0, 128.41, 128.2, 126.0, 38.7, 33.2, 28.4, 28.1.

HR-MS (ESI) calcd. for C₁₂H₁₃N₂O₂: 204.1025. Found: 204.1028 [MH⁺].

l-[(4-Methoxyphenyl)methyl]-2,5-pyrrolidinedione (5e) (Daoust, B, & Lessard, J, Tetrahedron (1999) 55, 3495)

[0071] White solid, isolated yield: 87%.

25 ¹H NMR (CDCl₃, 300 MHz): δ = 7.31 (d, *J* = 8.7 Hz, 2H), 6.79 (d, *J* = 8.7 Hz, 2H), 4.57 (s, 2H), 3.75 (s, 3H), 2.65 (s, 4H);

¹³C NMR (CDCl₃, 100 MHz): δ = 176.9, 159.3, 130.4, 128.1, 113.9, 55.3, 41.8, 28.2.

1-[(4-Fluorophenyl)methyl]-2,5-pyrrolidinedione (5f) (Verschueren, WG, et al., J. Med. Chem. 2005, 48, 1930)

[0072] Brown oil, isolated yield: 61%.

¹H NMR (CDCl₃, 300 MHz): δ = 7.33-7.37 (m, 2H), 6.93-6.98 (m, 2H), 4.59 (s, 2H), 2.68 (s, 4H)

¹³C NMR (CDCl₃, 100 MHz): δ = 176.8, 130.9, 130.8, 115.6, 115.4, 41.6, 28.2.

HR-MS (ESI) calcd. for C₁₁H₁₀FNO₂: 208.0774. Found: 208.0773 [MH⁺].

1-(2-Pyridinylmethyl)-2,5-pyrrolidinedione (5g)

[0073] Colorless oil, isolated yield: 44%.

¹H NMR (CDCl₃, 300 MHz): δ = 8.47 (d, *J* = 4.2 Hz, 1H), 7.57-7.63 (m, 1H), 7.22 (brs, 1H), 7.11-7.15 (m, 1H), 4.79 (s, 2H), 2.77 (s, 4H);

¹³C NMR (CDCl₃, 100 MHz): δ = 177.1, 154.5, 149.6, 136.7, 122.6, 122.0, 43.5, 28.3.

HR-MS (ESI) calcd. for C₁₀H₁₀N₂O₂: 191.0821. Found: 191.0816 [MH⁺].

1-(3-Pyridinylmethyl)-2,5-pyrrolidinedione (5h) (Sattler, HJ, et al., Pharmaceutica Acta Helvetiae (1975) 50, 298)

[0074] Colorless oil, isolated yield: 73%. NMR (CDCl₃) δ; ¹³C NMR (CDCl₃) δ. HRMS (ESI) calcd for [MH⁺].

¹H NMR (CDCl₃, 300 MHz): δ = 8.60 (s, 1H), 8.48 (d, *J* = 4.8 Hz, 1H), 7.68 (d, *J* = 7.8 Hz, 1H), 7.17-7.23 (m, 1H), 4.61 (s, 2H), 2.68 (s, 4H);

¹³C NMR (CDCl₃, 100 MHz): δ = 176.6, 150.3, 149.4, 136.7, 131.4, 123.5, 39.9, 28.2.

HR-MS (ESI) calcd. for C₁₀H₁₀N₂O₂: 191.0821. Found: 191.0823 [MH⁺].

1-(4-Pyridinylmethyl)-2,5-pyrrolidinedione (5i) (Verschueren al., 2005, supra)

[0075] White solid, isolated yield: 59%.

¹H NMR (CDCl₃, 300 MHz): δ = 8.51 (dd, *J* = 1.8 Hz, *J* = 4.5 Hz, 2H), 7.21 (dd, *J* = 1.8 Hz, *J* = 4.5 Hz, 2H), 4.61 (s, 2H), 2.72 (s, 4H);

¹³C NMR (CDCl₃, 100 MHz): δ = 176.6, 150.2, 144.1, 123.3, 41.3, 28.2.

HR-MS (ESI) calcd. for C₁₀H₁₀N₂O₂: 191.0821. Found: 190.0824 [MH⁺].

1-(2,2-Dimethoxyethyl)-2,5-pyrrolidinedione (5j)

[0076] White solid, isolated yield: 73%.

¹H NMR (CDCl₃, 300 MHz): δ = 4.64 (t, *J* = 5.7 Hz, 1H), 3.60 (d, *J* = 5.7 Hz, 2H), 3.29 (s, 6H), 2.68 (s, 4H);

5 ¹³C NMR (CDCl₃, 100 MHz): δ = 176.9, 99.1, 52.9, 39.4, 28.1.

HR-MS (ESI) calcd. for C₈H₁₃N₀O₄: 188.0923. Found: 188.0927 [MH⁺].

1-(2-Pyridinylmethyl)-2,5-pyrrolidinedione (5k) (Verschuere al., 2005, supra)

[0077] White solid, isolated yield: 68%. ¹H NMR (CDCl₃)

10 ¹H NMR (CDCl₃, 300 MHz): δ = 4.43 (m, 1H), 2.60 (s, 4H), 1.69-1.99 (m, 6H), 1.53-1.58 (m, 2H);

¹³C NMR (CDCl₃, 100 MHz): δ = 177.4, 51.6, 28.5, 28.1, 25.1.

1-(4-Pyridinylmethyl)-2,5-pyrroUdinedione (5l) (Pal, B, et al., Synthesis (2003) 1549)

[0078] Colorless oil, isolated yield: 57%.

15 ¹H NMR (CDCl₃, 300 MHz): δ = 3.87-3.97 (m, 1H), 2.59 (s, 4H), 2.03-2.16 (m, 2H), 1.69-1.79 (m, 2H), 1.50-1.62 (m, 3H), 1.20-1.33 (m, 3H);

¹³C NMR (CDCl₃, 100 MHz): δ = 177.4, 51.7, 28.7, 28.1, 25.9, 25.0

1-(1-Phenylethyl)-2,5-pyrrolidinedione (5m) (Far, AR, & Tidwell, TT, J. Org. Chem. (1998) 63, 8636)

[0079] Colorless oil, isolated yield: 36%.

20 ¹H NMR (CDCl₃, 300 MHz): δ = 7.23-7.44 (m, 5H), 5.39 (m, 1H), 2.61 (s, 4H), 1.78 (d, *J* = 7.5 Hz, 3H);

¹³C NMR (CDCl₃, 100 MHz): δ = 177.0, 139.6, 128.4, 127.8, 127.6, 50.3, 28.1, 16.5.

HR-MS (ESI) calcd. for C₁₀H₁₀N₂O₂: 191.0821. Found: 190.0824 [MH⁺].

1-[(4-Methoxyphenyl)methyl]-3-phenyl-2,5-pyrrolidinedione (5n)

25 [0080] Colorless oil, isolated yield: 78%.

¹H NMR (CDCl₃, 300 MHz): δ = 7.23-7.34 (m, 5H), 7.10-7.13 (m, 2H), 6.81 (d, *J* = 8.7 Hz, 2H), 4.65 (d, *J* = 13.8 Hz, 1H), 4.58 (d, *J* = 13.8 Hz, 1H), 3.95 (dd, *J* = 4.8 Hz, *J* = 6.6 Hz,

1H), 3.75 (s, 3H), 3.14 (dd, $J = 18.6$ Hz, $J = 6.6$ Hz, 1H), 2.75 (dd, $J = 18.6$ Hz, $J = 4.8$ Hz, 1H);

^{13}C NMR (CDCl_3 , 100MHz): $\delta = 177.5, 175.8, 159.4, 137.2, 130.4, 129.2, 128.1, 127.9, 127.4, 114.0, 55.3, 45.9, 42.2, 37.2$.

5 HR-MS (ESI) calcd. for $\text{C}_{18}\text{H}_{17}\text{NO}_3$: 296.1287. Found: 296.1284 [MH^+].

1-[(4-Methoxyphenyl)methyl]-3-methyl-3-phenyl-2,5-pyrrolidinedione (5o)

[0081] Colorless oil, isolated yield: 55%. CDCl_3 δ . HRMS (ESI) calcd for $\text{C}_{19}\text{H}_{19}\text{NO}_3$: 310.1443. Found: 310.1443 [MH^+]

10 ^1H NMR (CDCl_3 , 300 MHz): $\delta = 7.19\text{--}7.40$ (m, 7H), 6.84–6.87 (m, 2H), 4.68 (s, 2H), 3.80 (s, 3H), 3.10 (d, $J = 18$ Hz, 1H), 2.85 (d, $J = 18$ Hz, 2H), 1.70 (s, 3H);

^{13}C NMR (CDCl_3 , 100MHz): $\delta = 180.7, 175.2, 159.3, 141.9, 130.1, 129.0, 128.9, 128.1, 127.5, 125.6, 125.2, 114.0, 55.3, 47.8, 45.3, 42.1, 42.0, 25.5$.

HR-MS (ESI) calcd. for $\text{C}_{19}\text{H}_{19}\text{NO}_3$: 310.1443. Found: 310.1443 [MH^+].

2-[(4-Methoxyphenyl)methyl]-cis-hexahydro-1H-isoindole-1,3(2H)-dione (5p)

15 [0082] Colorless oil, isolated yield: 80%.

^1H NMR (CDCl_3 , 300 MHz): $\delta = 7.25$ (d, $J = 8.7$ Hz, 2H), 6.78 (d, $J = 8.7$ Hz, 2H), 4.52 (s, 2H), 3.73 (s, 3H), 2.7 (m, 2H), 1.75 (m, 2H), 1.65 (m, 2H), 1.35 (m, 4H)

^{13}C NMR (CDCl_3 , 100MHz): $\delta = 179.4, 159.2, 130.1, 128.4, 113.9, 55.2, 41.5, 39.8, 23.6, 21.5$.

20 HR-MS (ESI) calcd. for $\text{C}_{16}\text{H}_{19}\text{NO}_3$: 274.1443. Found: 274.1443 [MH^+].

2-[(4-Methoxyphenyl)methyl]-1H-isoindole-1,3(2H)-dione (5q) (Worlikar, SA, & Larock, RC, J. Org. Chem. (2008) 73, 7175)

[0083] White solid, isolated yield: 74%.

25 ^1H NMR (CDCl_3 , 300 MHz): $\delta = 7.80$ (m, 2H), 7.65 (m, 2H), 7.36 (d, $J = 8.7$ Hz, 2H), 6.78 (d, $J = 8.7$ Hz, 2H), 4.75 (s, 2H), 3.73 (s, 3H);

^{13}C NMR (CDCl_3 , 100MHz): $\delta = 168.1, 159.2, 133.9, 132.2, 130.2, 128.7, 123.3, 114.0, 55.3, 41.1$.

HR-MS (ESI) calcd. for $\text{C}_{16}\text{H}_{13}\text{NO}_3$: 268.0974. Found: 268.0977 [MH^+].

2-(3-Phenylpropyl)-1H-isoindole-1,3(2H)-dione (5r) (Martin, B, et al., Org. Lett. (2003) 5, 1851)

[0084] Colorless oil, isolated yield: 67%.

¹H NMR (CDCl₃, 300 MHz): δ = 7.65-7.81 (m, 4H), 7.08-7.24 (m, 5H), 3.72 (t, *J* = 7.2 Hz, 2H), 2.66 (t, *J* = 7.5 Hz, 2H), 1.96-2.06 (m, 2H);

¹³C NMR (CDCl₃, 100MHz): δ = 168.4, 141.0, 133.9, 132.1, 128.4, 128.3, 125.9, 123.2, 37.8, 33.2, 29.9.

HR-MS (ESI) calcd. for C₁₇H₁₅N₂O₂: 266.1181. Found: 266.1180 [MH⁺].

2-Pentyl-1H-isoindole-1,3(2H)-dione (5s) [Griesbeck, AG, et al., Helv. Chim. Acta (1997) 80, 912]

[0085] Colorless oil, isolated yield: 61%. ¹H NMR (CDCl₃) δ ¹³C NMR (CDCl₃) δ HRMS (ESI) calcd for C₁₃H₁₅N₂O₂: 218.1181. Found: 218.1180 [MH⁺].

¹H NMR (CDCl₃, 300 MHz): δ = 7.62-7.80 (m, 4H), 3.62 (t, *J* = 7.5 Hz, 2H), 1.57-1.67 (m, 2H), 1.24-1.33 (m, 4H), 0.83 (t, *J* = 6.6 Hz, 3H);

¹³C NMR (CDCl₃, 100MHz): δ = 168.4, 133.8, 132.2, 123.1, 38.0, 29.0, 28.3, 22.3, 13.9.

HR-MS (ESI) calcd. for C₁₃H₁₅N₂O₂: 218.1181. Found: 218.1180 [MH⁺].

2-(3-Pyridinylmethyl)-1H-isoindole-1,3(2H)-dione (5t) (Thorp-Greenwood, FL, et al., L Organomet. Chem. (2009) 694, 1400)

[0086] Colorless oil, isolated yield: 51%.

¹H NMR (CDCl₃, 300 MHz): δ = 8.67 (d, *J* = 2.1 Hz, 1H), 8.49 (dd, *J* = 1.5 Hz, *J* = 4.8 Hz, 1H), 7.67-7.84 (m, 5H), 7.19-7.22 (m, 2H), 4.82 (s, 2H);

¹³C NMR (CDCl₃, 100MHz): δ = 167.8, 150.1, 149.3, 136.4, 134.2, 132.0, 123.6, 123.5, 39.1.

1-[(4-Methoxyphenyl)methyl]-2,6-piperidinedione (5u) (Sattler et al., 1975, supra)

[0087] Colorless oil, isolated yield: 51%.

¹H NMR (CDCl₃, 300 MHz): δ = 7.31 (d, *J* = 8.7 Hz, 2H), 6.78 (d, *J* = 8.7 Hz, 2H), 4.85 (s, 2H), 3.74 (s, 3H), 2.62 (t, *J* = 5.4 Hz, 4H), 1.88 (m, 2H);

¹³C NMR (CDCl₃, 100MHz): δ = 172.4, 158.9, 130.5, 129.6, 113.7, 55.2, 42.1, 32.9, 17.1.

HR-MS (ESI) calcd. for C₁₃H₁₅N₂O₃: 234.1130. Found: 234.1134 [MH⁺].

1-(Phenylmethyl)-2,6-piperidinedione (5v) [Reddy et al., 1997, supra]

[0088] Colorless oil, isolated yield: 48%.

¹H NMR (CDCl₃, 300 MHz): δ = 7.17-7.34 (m, 5H), 4.92 (s, 2H), 2.63(t, J = 6.6Hz, 4H), 1.85-1.94 (m, 2H);

5 ¹³C NMR (CDCl₃, 100MHz): δ = 172.4, 137.3, 128.8, 128.4, 127.4, 42.7, 32.9, 17.1.

1-Methyl-3-phenyl-2,5-pyrrolidinedione (5w) (Shigemitsu, Y, & Tominaga, Y, Heterocycles (2001) 55, 2257)

[0089] Colorless oil, isolated yield: 63%.

10 ¹H NMR (CDCl₃, 300 MHz): δ = 7.18-7.36 (m, 5H), 4.00 (dd, J = 3.6 Hz, J = 6.9 Hz, 1H), 3.17 (dd, J = 7.2 Hz, J = 13.8 Hz, 1H), 3.04 (s, 3H), 2.79 (dd, J = 3.6 Hz, J = 13.8 Hz, 1H);

¹³C NMR (CDCl₃, 100MHz): δ = 177.8, 176.3, 137.1, 129.2, 128.0, 127.4, 46.0, 37.1, 25.2.

[0090] The listing or discussion of a previously published document in this specification should not necessarily be taken as an acknowledgement that the document is part of the state of the art or is common general knowledge.

15 [0091] The invention has been described broadly and generically herein. Each of the narrower species and subgeneric groupings falling within the generic disclosure also form part of the invention. This includes the generic description of the invention with a proviso or negative limitation removing any subject matter from the genus, regardless of whether or not the excised material is specifically recited herein.

20 [0092] One skilled in the art would readily appreciate that the present invention is well adapted to carry out the objects and obtain the ends and advantages mentioned, as well as those inherent therein. Further, it will be readily apparent to one skilled in the art that varying substitutions and modifications may be made to the invention disclosed herein without departing from the scope and spirit of the invention. The molecular complexes and the
25 methods, procedures, treatments, molecules, specific compounds described herein are presently representative of preferred embodiments are exemplary and are not intended as limitations on the scope of the invention. Changes therein and other uses will occur to those skilled in the art which are encompassed within the spirit of the invention are defined by the scope of the claims.

[0093] The invention illustratively described herein suitably may be practiced in the absence of any element or elements, limitation or limitations which is not specifically disclosed herein. Thus, for example, in each instance herein any of the terms "comprising", "consisting essentially of" and "consisting of" etc. shall be read expansively and without
5 limitation, and are not limited to only the listed components they directly reference, but include also other non-specified components or elements. As such they may be exchanged with each other. Additionally, the terms and expressions which have been employed are used as terms of description and not of limitation, and there is no intention that in the use of such terms and expressions of excluding any equivalents of the features shown and described or
10 portions thereof, but it is recognized that various modifications are possible within the scope of the invention claimed.

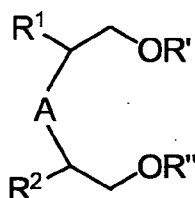
[0094] Other embodiments are within the following claims. In addition, where features or aspects of the invention are described in terms of Markush groups, those skilled in the art will recognize that the invention is also thereby described in terms of any individual member or
15 subgroup of members of the Markush group.

Claims

What is claimed is:

1. A process of forming a cyclic imide, the process comprising providing a Ruthenium (II) complex, wherein the Ruthenium (II) complex comprises at least one of an alicyclic ligand, an aromatic ligand, an arylalicyclic ligand, an arylaliphatic ligand and a phosphine ligand, and contacting in the presence of the Ruthenium (II) complex a primary amine and a diol compound.

2. The process of claim 1, wherein the diol compound is of the formula



wherein A is one of S, Se, O, N-R™, an aliphatic, an alicyclic, an aromatic, an arylaliphatic and an arylalicyclic bridge, R™ in N-R™ being one of H, a silyl group, an aliphatic group, an alicyclic group, an aromatic group, an arylaliphatic group and an arylalicyclic group,

R' and R'' are H or a suitable protecting group, and

R¹ and R² are one of H, halogen, a silyl group, an aliphatic, an alicyclic, an aromatic, an arylaliphatic and an arylalicyclic group.

3. The process of claims 1 or 2, wherein providing the Ruthenium (II) complex comprises providing an N-heterocyclic carbene.

4. The process of claim 3, wherein the N-heterocyclic carbene is provided as a complex with a metal halogenide.

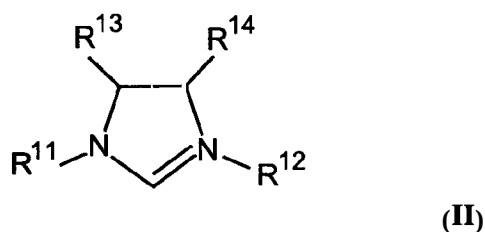
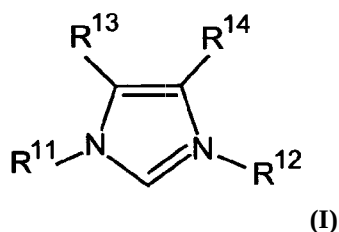
5. The process of claims 3 or 4, wherein providing the Ruthenium (II) complex comprises contacting the N-heterocyclic carbene and a Ruthenium (II) precatalyst complex.

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6. The process of claim 5, wherein the Ruthenium (II) precatalyst complex is a $[\text{Ru}(\text{A})\text{Cl}_2]_2$ precatalyst complex,

wherein A in $[\text{Ru}(\text{A})\text{Cl}_2]_2$ is a benzene based moiety, the benzene based moiety being benzene, optionally substituted with one or more groups selected from an aliphatic, an alicyclic, an aromatic, an arylaliphatic, an arylalicyclic group and a functional group.

7. The process of any one of claims 3 - 6, wherein the N-heterocyclic carbene is formed from an imidazole or an imidazoline compound and a base, wherein the imidazole compound is of general formula (I) and the imidazoline compound is of general formula (II):



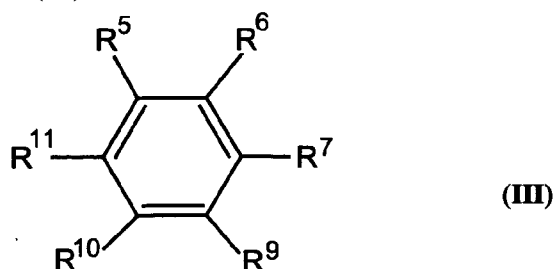
wherein R^{11} - R^{14} are independently selected from the group consisting of a H, an aliphatic, an alicyclic, an aromatic, an arylaliphatic, and an arylalicyclic group, comprising 0 to about 3 heteroatoms selected from the group N, O, S, Se and Si.

8. The process of claim 7, wherein at least one equivalent of the base is used relative to the imidazole or imidazoline compound.

9. The process of claims 7 or 8, wherein the base is a metal hydride or an alkoxide.

10. The process of any one of claims 6 - 10, wherein the Ruthenium complex is formed *in situ* from the N-heterocyclic carbene and the $[\text{Ru}(\text{A})\text{Cl}_2]_2$ precatalyst complex in the presence of the base.

11. The process of any one of claims 1 - 10, wherein A in $[\text{Ru}(\text{A})\text{Cl}_2]_2$ is a benzene moiety of the general formula (III)



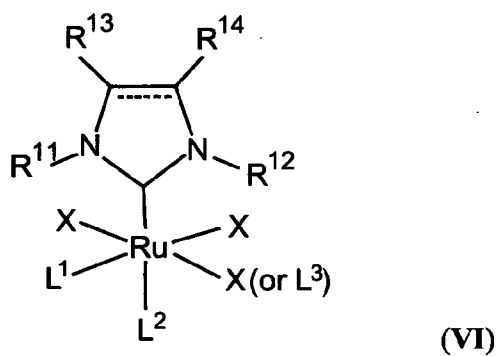
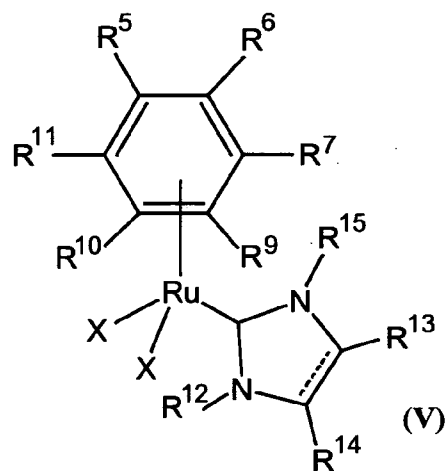
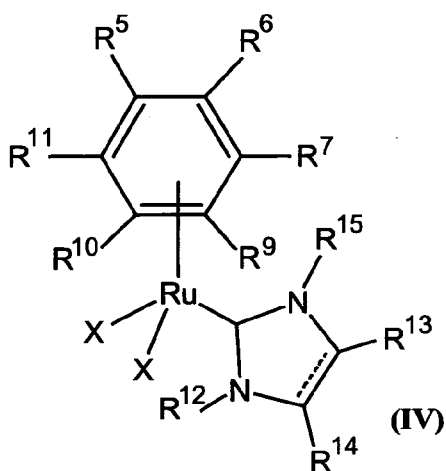
wherein $R^5 - R^7$ and $R^9 - R^{11}$ are independently selected from the group consisting of a H, an aliphatic, an alicyclic, an aromatic, an arylaliphatic, and an arylalicyclic group, comprising 0 to about 3 heteroatoms selected from the group N, O, S, Se and Si.

12. The process of any one of claims 6-11, wherein A in $[Ru(A)Cl_2]_2$ is unsubstituted benzene or cymene.

13. The process of any one of claims 1 - 12, wherein providing the Ruthenium complex further comprises providing a nitrogen containing L-type ligand.

14. The process of claim 13, wherein the nitrogen containing L-type ligand is acetonitrile or pyridine.

15. The process of any one of claims 1-14, wherein providing the Ruthenium (II) complex comprises forming one or more Ruthenium (II) complexes of formulae (IV), (V) and (VI)



wherein 7777 represents one of a single and a double bond,

in formulae (IV) and (V) $R^5 - R^7$, R^9 , R^{10} , R^{15} and in formulae (IV) - (VI) $R^{11} - R^{14}$ are independently selected from the group consisting of a H, an aliphatic, alicyclic, aromatic, arylaliphatic, and arylalicyclic group, comprising 0 to about 3 heteroatoms selected from the group N, O, S, Se and Si,

X is halogen or $-OR^{16}$, wherein R^{16} is one of H, an aliphatic group, an alicyclic group, an aromatic group, an arylaliphatic group, and an arylalicyclic group, comprising 0 to about 3 heteroatoms selected from the group N, O, S, Se and Si,

and L^1 , L^2 and L^3 are independently selected from a solvent molecule, pyridine, acetonitrile and the N-heterocyclic carbene.

16. The process of any one of claims 1-15, wherein by contacting the primary amine and the diol compound in the presence of the Ruthenium complex a reaction mixture is formed, and wherein the process further comprises exposing the reaction mixture to a temperature above ambient temperature.

17. The process of claim 16, wherein the temperature is selected in the range from about 30 °C to about 180 °C.

18. The process of any one of claims 1 - 17, being carried out under inert gas atmosphere.

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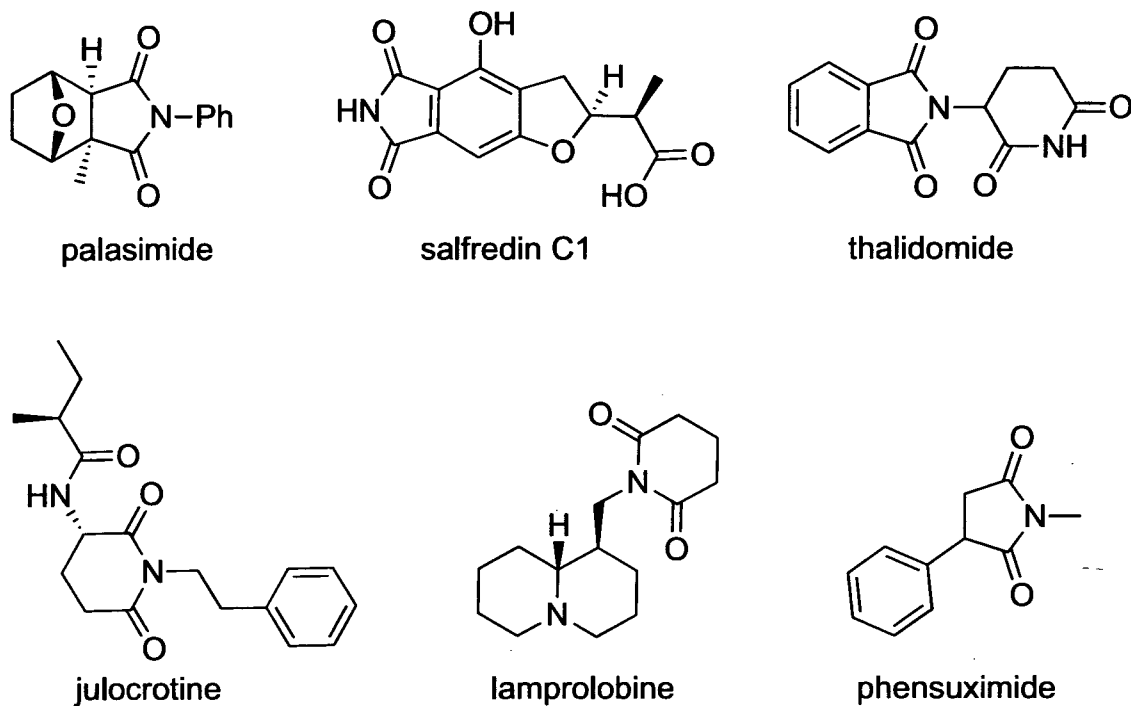


Fig. 1

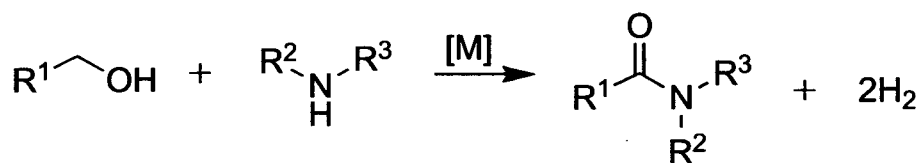
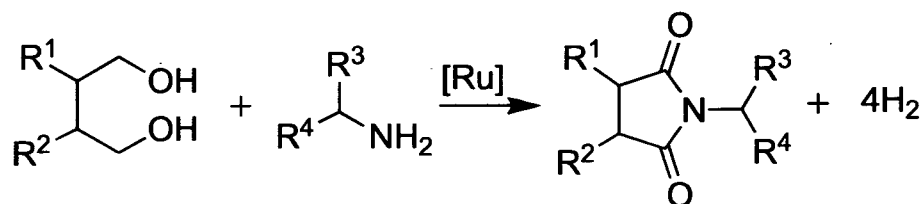
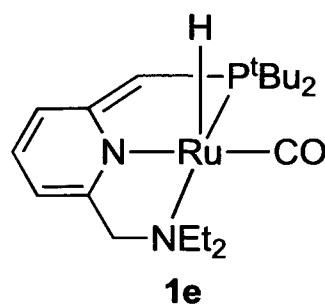
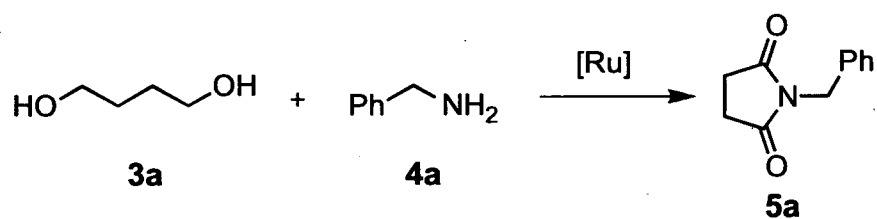
prior art*this invention*

Fig. 2

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 $[\text{Ru}(\text{benzene})\text{Cl}_2]_2$ **1a** $[\text{Ru}(p\text{-cymene})\text{Cl}_2]_2$ **1b** $\text{RuH}_2(\text{PPh}_3)_4$ **1c** $\text{Ru}(\text{COD})\text{Cl}_2$ **1d****Fig. 3****Fig. 4**

Entry	Catalyst	Ligand	Yield [%] ^[b]
1	1a	2 , CH ₃ CN	14 ^[c]
2	1b	2 , pyridine	24 ^[d]
3	1b	dppb	0 ^[e]
4	1c		0 ^[f]
5	1c	2 , CH ₃ CN	70 ^[g]
6	1d	2 , PCy ₃	41 ^[h]
7	1e		52 ^[i]

Entry	Amine	Amide	Yield [%] ^[b]
1	 4b	 5b	81
2	 4c	 5c	76

Fig. 5 (cont. on next page)

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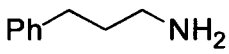
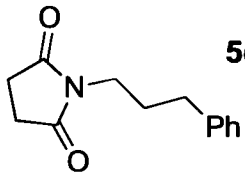
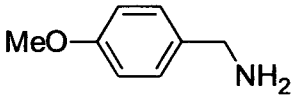
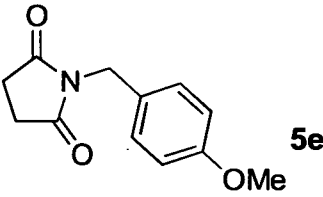
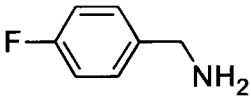
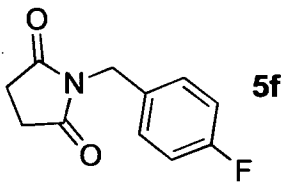
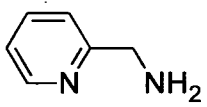
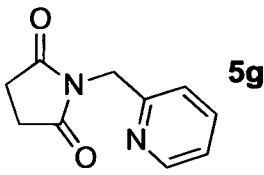
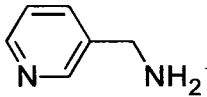
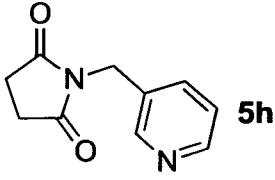
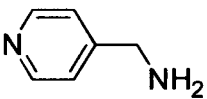
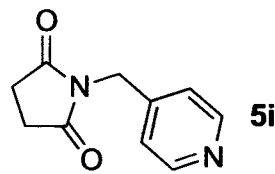
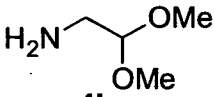
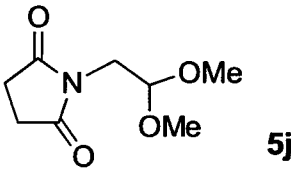
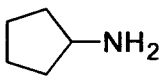
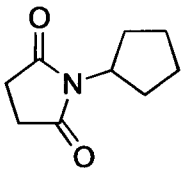
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3	 4d	 5d	88
4	 4e	 5e	87
5	 4f	 5f	61
6	 4g	 5g	44
7	 4h	 5h	73
8	 4i	 5i	59
9	 4j	 5j	73
10	 4k	 5k	68

Fig. 5 (cont. on next page)

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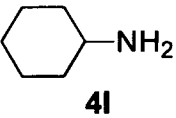
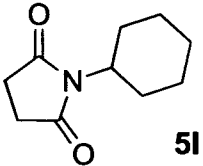
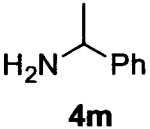
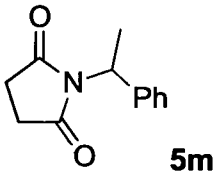
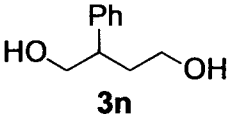
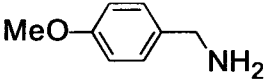
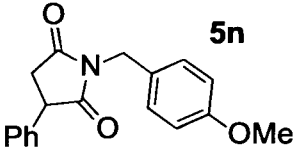
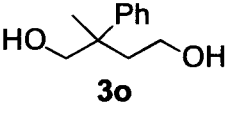
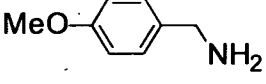
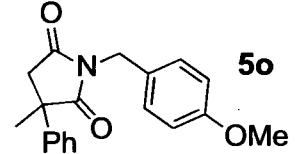
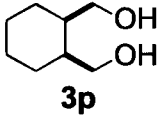
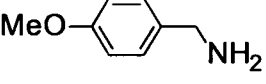
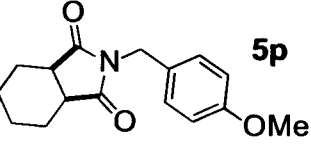
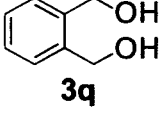
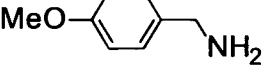
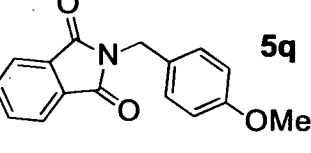
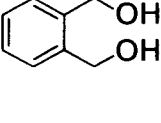
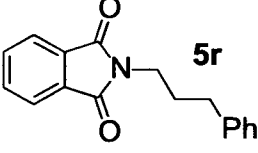
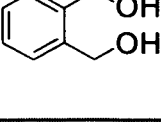
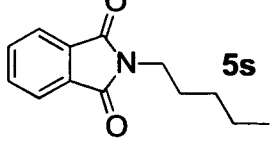
Entry	Amine	Amide	Yield [%] ^[b]
11	 4l	 5l	57
12	 4m	 5m	36

Fig. 5 (cont. from prev. page)

Fig. 6 (cont. on next page)

Entry	Diol	Amine	Cyclic Imide	Yield [%] ^[b]
1	 3n		 5n	78
2	 3o		 5o	55
3	 3p		 5p	80
4	 3q		 5q	74
5	 3q		 5r	67
6	 3q		 5s	61

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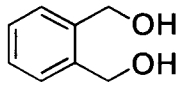
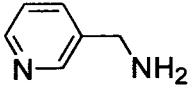
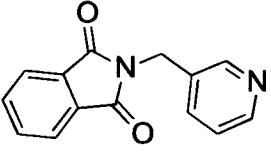
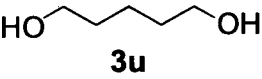
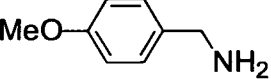
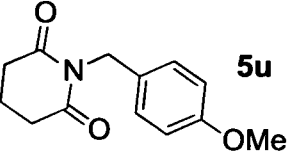
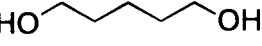
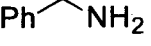
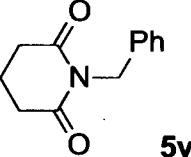
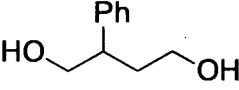
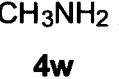
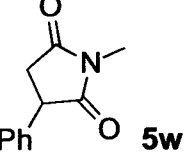
Entry	Diol	Amine	Cyclic Imide	Yield [%] ^[b]
7			 5t	51
8	 3u		 5u	51
9			 5v	48
10		 4w	 5w	63

Fig. 6 (cont. from prev. page)

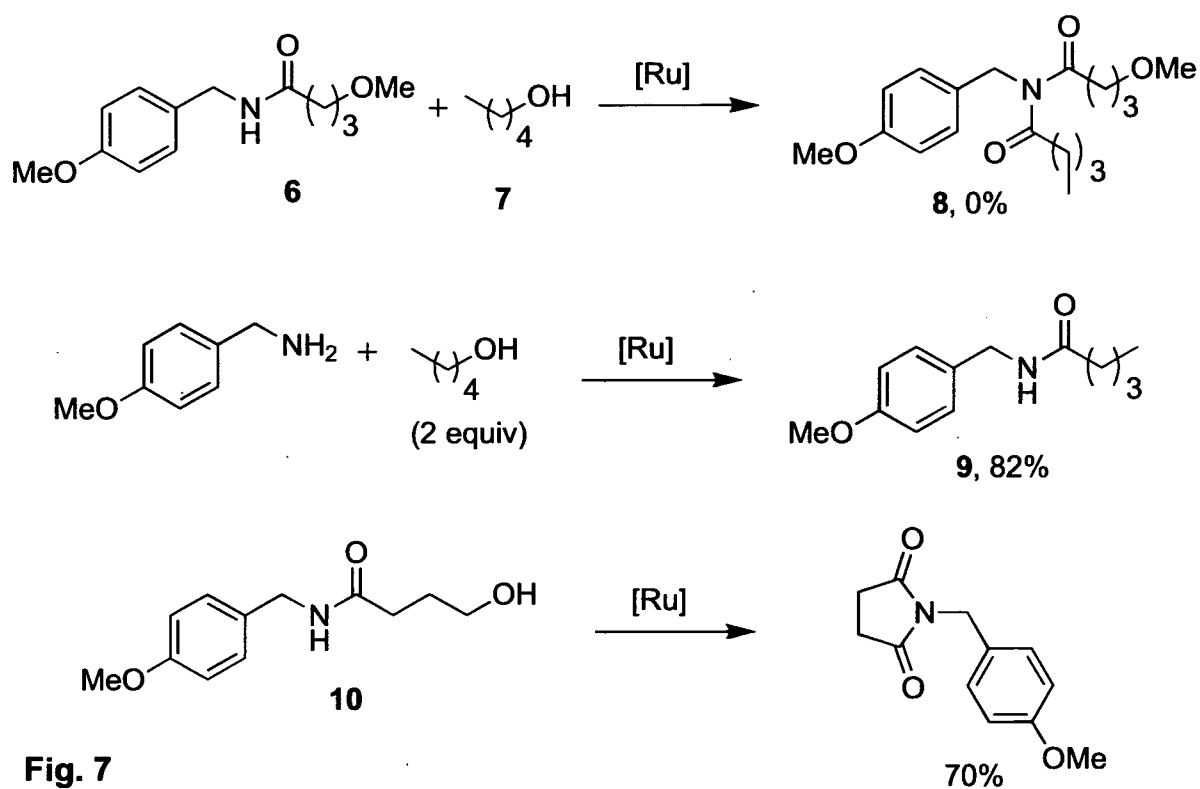


Fig. 7

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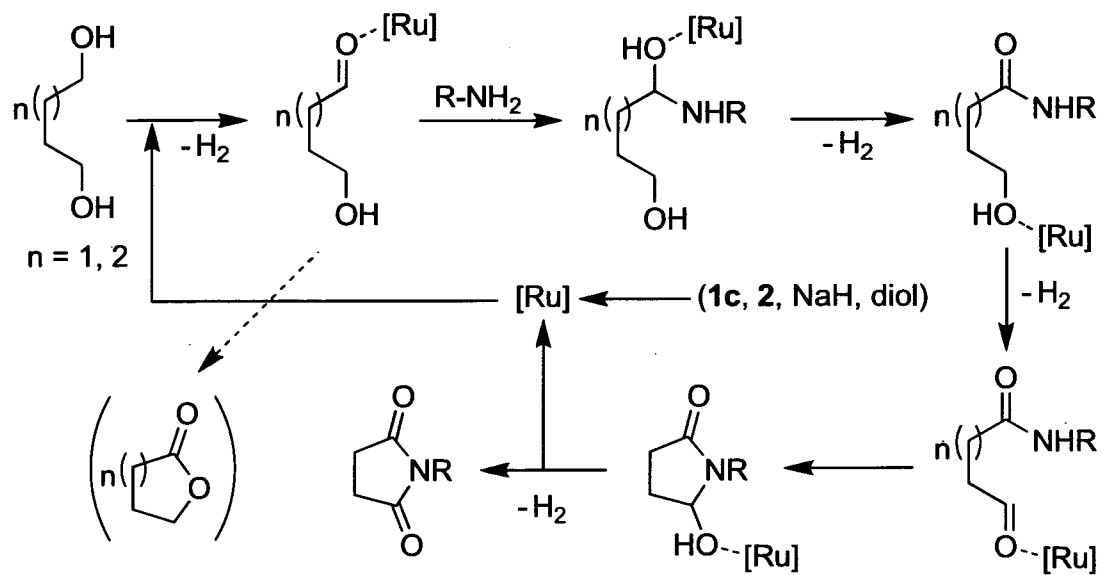


Fig. 8

INTERNATIONAL SEARCH REPORT

International application No.

PCT/SG20 11/000233

A. CLASSIFICATION OF SUBJECT MATTER Int. Cl. C07D 207/404 (2006.01) C07D 209/48 (2006.01) C07D 211/88 (2006.01) C07D 211/02 (2006.01) C07D 401/06 (2006.01) C07B 43/06 (2006.01) According to International Patent Classification (IPC) or to both national classification and IPC					
B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) CASReact: functional group reaction search based on alcohol starting material and imide group formation Registry and CPlus: substructure search for an imide, combined with keyword search (preparation, cyclization catalysts, amines, glycols) CPlus: keyword search (imides, amides, preparation amines, glycols, ruthenium catalyst)					
C. DOCUMENTS CONSIDERED TO BE RELEVANT					
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.			
<u>X</u> Y	GHOSH, S. C. & HONG, S. H. "Simple RuCl ₃ -Catalyzed Amide Synthesis from Alcohols and Amines" <i>Eur. J. Org. Chem.</i> 2010 , 4266-4270; published online 14 June 2010. See abstract; pp 4266-9; footnote 10.	<u>1-18</u> 1-5, 7-9, 13, 14, 16-18			
Y	NORDSTROM, L. U. et al. "Amide Synthesis from Alcohols and Amines by the Extrusion of Dihydrogen" <i>J. Am. Chem. Soc.</i> 2008 , 130, 17672-1 7673 See whole document, in particular table 1.	1-5, 7-9, 13, 16-18			
☒ Further documents are listed in the continuation of Box C ☒ See patent family annex					
<table style="width: 100%; border: none;"> <tr> <td style="width: 33%; vertical-align: top;"> * Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier application or patent but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed </td> <td style="width: 33%; vertical-align: top;"> "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "&" document member of the same patent family </td> <td style="width: 33%;"></td> </tr> </table>			* Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier application or patent but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "&" document member of the same patent family	
* Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier application or patent but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "&" document member of the same patent family				
Date of the actual completion of the international search 24 August 2011		Date of mailing of the international search report 29.08.2011			
Name and mailing address of the ISA/AU AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustralia.gov.au Facsimile No. +61 2 6283 7999		Authorized officer ALICA DALY AUSTRALIAN PATENT OFFICE (ISO 9001 Quality Certified Service) Telephone No : +61 3 9935 9606			

INTERNATIONAL SEARCH REPORT

International application No.

PCT/SG20 11/000233

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	MUTHAIAH, S. et al. "Direct Amide Synthesis from Either Alcohols or Aldehydes with Amines: Activity of Ru(II) Hydride and Ru(0) Complexes" <i>J. Org. Chem.</i> 2010 , 75, 3002-3006 See whole document, in particular table 1.	1-5, 7-9, 13, 14, 16-18
Y	US 2009/01 12005 A1 (MILSTEIN et al.) 30 April 2009 See whole document, in particular figure 1.	1, 2, 13, 16-18
P,X	ZHANG, J. et al. "Synthesis of Cyclic Imides from Simple Diols" <i>Angew. Chem. Int. Ed.</i> 2010 , 49(36), 6391-6395; published online 26 July 2010 See whole document.	1-18
P,X	MUTHAIAH, S. & HONG, S. H. "Atom-Economical Synthesis of Cyclic Imides" <i>Synlett</i> 2011 , No. 11, 1481-1485 See whole document.	1-18
P,A	ZENG, H. & GUAN, Z. "Direct Synthesis of Polyamides via Catalytic Dehydrogenation of Diols and Diamines" <i>J. Am. Chem. Soc.</i> 2011 , 133(5), 1159-1161 See whole document.	

INTERNATIONAL SEARCH REPORT**Information on patent family members****International application No.****PCT/SG2011/000233**

This Annex lists the known "A" publication level patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent Document Cited in Search Report		Patent Family Member
US	2009112005	NONE
Due to data integration issues this family listing may not include 10 digit Australian applications filed since May 2001.		
END OF ANNEX		