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(54) Title: ORGANOMETALLIC RUTHENIUM COMPLEXES AND RELATED METHODS FOR THE PREPARATION OF TETRA-SUBSTITUTED AND OTHER HINDERED OLEFINS

(57) Abstract: The invention relates to ruthenium alkylidene complexes having an N-heterocyclic carbene ligand comprising a 5-membered heterocyclic ring having a carbenic carbon atom and at least one nitrogen atom contained within the 5-membered heterocyclic ring, wherein the nitrogen atom is directly attached to the carbenic carbon atom and is substituted by a phenyl ring, and wherein the phenyl ring has a hydrogen at either or both ortho positions and is substituted and at least one orthq or meta position. The invention also relates to an olefin metathesis reactions and particularly to the preparation of tetra-substituted cyclic olefins via a ring-closing metathesis.

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ORGANOMETALLIC RUTHENIUM COMPLEXES AND RELATED METHODS FOR THE PREPARATION OF TETRA-SUBSTITUTED AND OTHER HINDERED OLEFINS

Technical Field

[0001] This invention relates generally to olefin metathesis. More particularly, the invention relates to organometallic ruthenium complexes and olefin metathesis methods using them to produce hindered olefins. The catalysts and methods of the invention have utility in the fields of catalysis, organic synthesis, and industrial chemistry.

Background of the Invention

[0002] Olefin metathesis catalysis is a powerful technology, which in recent years has received tremendous attention as a versatile method for the formation of carbon-carbon bonds and has numerous applications in organic synthesis and polymer chemistry. R.H. Grubbs, *Handbook of Metathesis*, Vol. 2 and 3; Wiley VCH, Weinheim, 2003. The family of olefin metathesis reactions includes, but is not limited to, ring-closing metathesis (RCM), cross metathesis (CM), ring-opening metathesis polymerization (ROMP), and acyclic diene metathesis polymerization (ADMET). The success of olefin metathesis stems from the development of several well-defined transition metal complexes, such as the Schrock molybdenum catalysts and the Grubbs ruthenium catalysts. R.H. Grubbs, *Handbook of Metathesis*, Vol. 1; Wiley VCH, Weinheim, 2003. The molybdenum catalysts are generally highly active but are also highly sensitive to air, moisture, and to certain functional groups present in the olefinic substrate, the reaction solvent, or impurities. The ruthenium catalysts are much more robust than the molybdenum catalysts.

[0003] The original first-generation ruthenium catalysts were primarily bisphosphine complexes of the general formula $(PR_3)_2(X)_2Ru{=}CHR^a$ wherein X represents a halogen (e.g., Cl, Br, or I), R represents an alkyl, cycloalkyl, or aryl group (e.g., butyl, cyclohexyl, or phenyl), and R^a represents an alkyl, alkenyl, or aryl group (e.g., methyl, $CH{=}CMe_2$, phenyl, etc.). Examples of these types of catalysts are described in US Patent Nos. 5,312,940, 5,969,170 and 6,111,121, which are incorporated herein by reference. While they catalyze a considerable number of olefin metathesis transformations, these bisphosphine complexes can exhibit lower activity than desired.

[0004] Second-generation metathesis catalysts with greatly increased activity have now been prepared by replacing one of the phosphine ligands with an N-heterocyclic carbene (NHC) ligand to give complexes of the general formula $(L)(PR_3)(X)_2Ru{=}CHR^a$ wherein L represents an NHC ligand such as 1,3-dimesitylimidazole-2-ylidene (IMES) and 1,3-dimesityl-4,5-dihydroimidazol-2-ylidene (sIMES), X represents a halogen (e.g., Cl, Br, or I), R represents an alkyl, cycloalkyl, or aryl group (e.g., butyl, cyclohexyl, or phenyl), and R^a represents an alkyl, alkenyl, or aryl group (e.g., methyl, $CH{=}CMe_2$, phenyl, etc.). Examples of these types of NHC ligands and catalysts are described in PCT publications WO 99/51344 and WO 00/71554, which are incorporated herein by reference. Further examples of the synthesis and reactivity of some of these active ruthenium complexes are reported by A. Fürstner, L. Ackermann, B. Gabor, R. Goddard, C.W. Lehmann, R. Mynott, F. Stelzer, and O.R. Thiel, *Chem. Eur. J.*, ***2001***, 7, No. 15, 3236-3253; Blackwell H.E., O'Leary D.J., Chatterjee A.K., Washenfelder R.A., Bussmann D.A., Grubbs R.H. *J. Am. Chem. Soc.* **2000**, 122, 58-71; Chatterjee A.K., Morgan J.P., Scholl M., Grubbs R.H. *J. Am. Chem. Soc.* **2000**, 122, 3783-3784; Chatterjee A.K., Grubbs R.H. *Angew. Chem. Int. Ed.* **2002**, 41, 3171-3174; Chatterjee A.K., Choi T.L., Sanders D.P., Grubbs R.H. *J. Am. Chem. Soc.* **2003**, 125, 11360-11370. The disclosure of these articles are incorporated herein by reference.

[0005] Despite such advances in the development of olefin metathesis catalysts, the metathesis of hindered olefins remains difficult and certain metathesis reactions to form tetra-substituted olefins proceed slowly and in low to moderate yields. A need exists, therefore, for metathesis catalysts capable of efficiently and effectively carrying out metathesis reactions with hindered olefins. The ruthenium catalysts of this invention answer that need.

Brief Description of the Drawings

[0006] Further features and advantages of the organometallic complexes, methods and reaction systems herein disclosed will become apparent from the following detailed description, taken in combination with the appended drawings, in which:

[0007] Fig. 1 shows a reaction scheme illustrating an exemplary embodiment of the method for preparing a cyclic tetra-substituted olefin via ring-closing metathesis herein disclosed.

[0008] Fig. 2 shows a diagram illustrating the results of a ring-closing metathesis of **1** with catalysts **6a**, **6b**, **6c** and **A** (referred to as C848 in graph), reported in Example 3 and in particular in Tables 3 to 6.

[0009] Fig. 3 shows a diagram illustrating the results of a ring-closing metathesis of **1** with catalysts **7a**, **7b**, **7c**, reported in Example 3 and in particular in Tables 9 to 11.

[0010] Fig. 4 depicts the single crystal X-ray structure was obtained for catalyst **12** described in Example 7.

[0011] Fig. 5 is a graph of the conversion over time for the ring-closing metathesis of **1** with catalyst **12**, described in Example 8.

[0012] Fig. 6 is a graph of the conversion over time for the ring-closing metathesis of **1** with catalyst **12** in C_6D_6, described in Example 8.

[0013] Fig. 7 is a graph of the conversion over time for the ring-closing metathesis of **13** with catalyst **12** described in Example 9.

[0014] Fig. 8 is a graph of the conversion over time for the ring-closing metathesis of **15** with catalyst **12** described in Example 9.

[0015] Fig. 9 shows the graph of conversion over time for the ring-closing metathesis of **1** with catalyst **24** described in Example 19.

[0016] Fig. 10 is a graph of conversion over time for the ring-closing metathesis of **1** with catalyst **24** in C_6D_6, described in Example 19.

[0017] Fig. 11 is a graph of conversion over time for the ring-closing metathesis of **13** with catalyst **24** described in Example 20.

[0018] Fig. 12 is a graph of the conversion over time for the ring-closing metathesis of **15** with catalyst **24** described in Example 20.

[0019] Fig. 13 is a graph of conversion over time for the ring-closing metathesis of **1** with catalyst **25** described in Example 21.

[0020] Fig. 14 is a graph of the conversion over time for the ring-closing metathesis of **1** with catalyst **25** in C_6D_6 described in Example 21.

[0021] Fig. 15 is a graph of the conversion over time for the ring-closing metathesis of **13** with catalyst **25** described in Example 22.

[0022] Fig. 16 is a graph of conversion over time for the ring-closing metathesis of **15** with catalyst **25** described in Example 22.

[0023] Fig. 17 is a graph of the conversion over time for the ring-closing metathesis of **1** with catalyst **26** described in Example 23.

[0024] Fig. 18 shows the conversion over time for the ring-closing metathesis of **1** with catalyst **6a**, **6c**, **27a** and **27c** described in Example 24.

[0025] Fig. 19 shows the conversion over time for the ring-closing metathesis of **1** with catalyst **6a and 7a** in toluene described in Example 25.

[0026] Fig. 20 is a graph of the conversion over time for the RCM reaction of **15** in Example 29 for catalyst **6a**.

[0027] Fig. 21 is a graph of the conversion over time for the RCM reaction of **13** in Example 29 for catalyst **6a**.

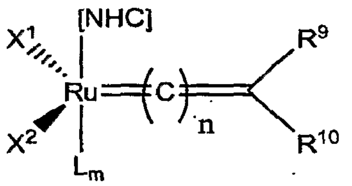
[0028] Fig. 22 is a graph of the conversion over time for the RCM reaction of **15** in Example 29 for catalyst **7a**.

[0029] Fig. 23 is a graph of the conversion over time for the RCM reaction of **13** in Example 29 for catalyst **7a**.

Summary of the Invention

[0030] The invention relates to ruthenium alkylidene complexes having an *N*-heterocyclic carbene ligand comprising a 5-membered heterocyclic ring having a carbenic carbon atom and at least one nitrogen atom contained within the 5-membered heterocyclic ring, wherein the nitrogen atom is directly attached to the carbenic carbon atom and is substituted by a phenyl ring, and wherein the phenyl ring has a hydrogen at either or both ortho positions and is substituted at at least one ortho-; or meta-position.

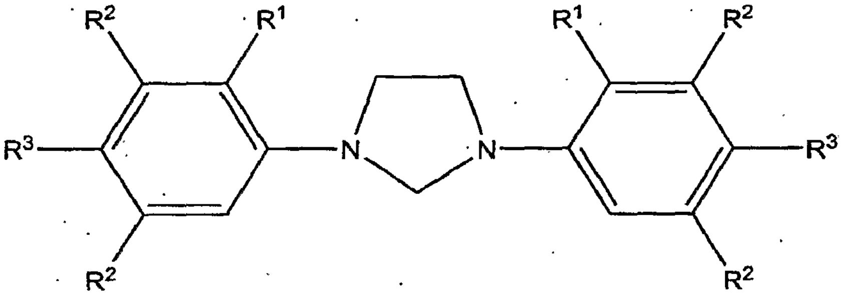
[0031] In a preferred embodiment, the invention relates to *N*-heterocyclic carbene (NHC) ruthenium olefin metathesis catalyst of formula (I):



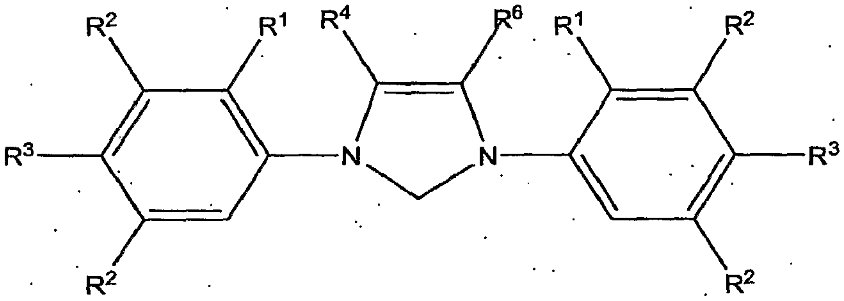
(I).

[0032] The catalysts of formula (I) contain the NHC ligand as well as the other ligands shown. In formula (I), X^1 and X^2 are independently anionic ligands; "n" is 0, 1, or 2; R^9 and R^{10} are each independently hydrogen or a substituted or unsubstituted substituent selected from the group consisting of C_1-C_{20} alkyl, C_2-C_{20} alkenyl, C_2-C_{20} alkynyl, aryl, C_1-C_{20} carboxylate, C_1-C_{20} alkoxy, C_2-C_{20} alkenyloxy, C_2-C_{20} alkynyloxy, aryloxy, C_2-C_{20} alkoxycarbonyl, C_1-C_{20} alkylthio, C_1-C_{20} alkylsulfonyl and C_1-C_{20} alkylsulfinyl; L is a neutral 2-electron donor ligand; and "m" is 1 or 2. R^9 and R^{10} may optionally be linked together to form a cyclic structure via one of the substituents mentioned above. L may optionally be linked to R^{10} to form a chelating carbene ligand, however, the formation of the chelating carbene ligand only occurs when n is 0. When "m" is a heteroarene ligand. Preferably, the heteroarene ligand 2, L is pyridine or substituted pyridine, which forms a (bis)pyridine catalyst. See Example 28, depicting a (bis)pyridine catalyst.

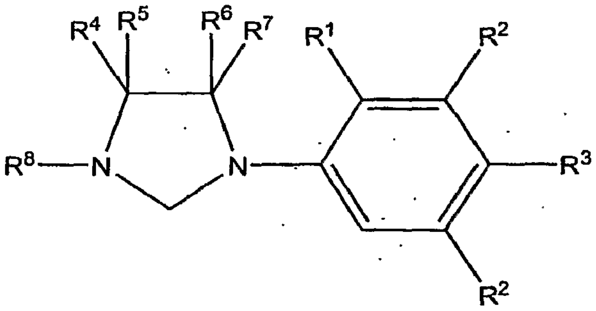
[0033] Preferred NHC ligands for the ruthenium catalysts of the invention are those of formulas (II)-(V):



(II)



(III)



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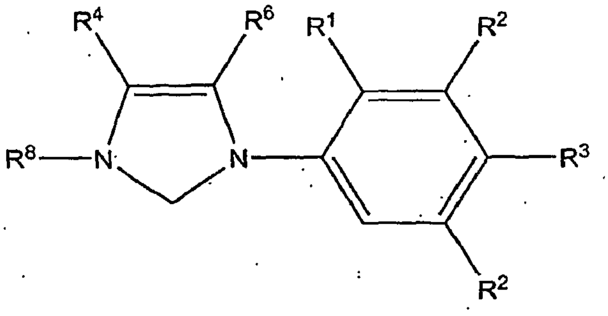


(V)

In formulas (II)-(V), R^1, R^2, and R^3 are either:

a) each R^1 is independently a primary or secondary C_1-C_4 alkyl group; each R^2 is independently H, a substituted or unsubstituted C_1-C_{10} alkyl group, substituted or unsubstituted phenyl, substituted or unsubstituted naphthyl, or substituted or unsubstituted anthracenyl; and each R^3 is independently H, a substituted or unsubstituted C_1-C_8 alkyl group, substituted or unsubstituted phenyl, substituted or unsubstituted naphthyl, or substituted or unsubstituted anthracenyl, or a functional group selected from the group consisting of halo, hydroxyl, sulfhydryl, cyano, cyanato, thiocyanato, amino, nitro, nitroso, sulfo, sulfonato, boryl, borono, phosphono, phosphonato, phosphinato, phospho, phosphino, and silyloxy; or

b) R^1 is H; each R^2 is independently H, a substituted or unsubstituted C_1-C_8 alkyl group, substituted or unsubstituted phenyl, substituted or unsubstituted naphthyl, or substituted or unsubstituted anthracenyl; and R^3 is independently H, a substituted or unsubstituted C_1-C_8 alkyl group, substituted or unsubstituted phenyl, substituted or unsubstituted naphthyl, or substituted or unsubstituted anthracenyl or a functional group selected from the group consisting of halo, hydroxyl, sulfhydryl, cyano, cyanato, thiocyanato, amino, nitro, nitroso, sulfo, sulfonato, boryl, borono, phosphono, phosphonato, phosphinato, phospho, phosphino, and silyloxy; with the provisos that both R^2 substituents on the same phenyl ring are not H.

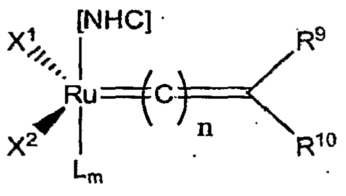
R^4 and R^6 are each independently H, a substituted or unsubstituted C_1-C_8 alkyl group, substituted or unsubstituted aryl, or in formulas (III) and (V) together with the carbons carrying them form a substituted or unsubstituted, fused 4-8 membered carbocylic ring or a substituted or unsubstituted, fused aromatic ring, preferably a fused phenyl ring. R^5 and R^7 are independently H, a substituted or unsubstituted C_1-C_8 alkyl group. R^8 is a C_1-C_{12} alkyl or a C_3-C_{12} cycloalkyl.

[0034] Another embodiment of the invention relates to an olefin metathesis reaction which contacts an olefin with an *N*-heterocyclic carbene (NHC) ruthenium olefin metathesis catalyst of the invention under metathesis conditions. The catalysts of the invention may be used in, for example, ring-closing metathesis (RCM), cross metathesis (CM), ring-opening metathesis polymerization (ROMP), and acyclic diene metathesis polymerization (ADMET).

[0035] A further embodiment of the invention relates to the preparation of tetra-substituted cyclic olefins via a ring-closing metathesis. In this embodiment, the invention provides a ring-closing metathesis method to prepare a tetra-substituted cyclic olefin. In the method, an olefinic compound having at least two terminal olefins which are substituted at the beta-carbon of each terminal olefin is contacted with an *N*-heterocyclic carbene (NHC) ruthenium olefin metathesis catalyst of the invention under metathesis conditions to form a cyclic tetra-substituted olefin.

Detailed Description of the Invention

[0036] The invention relates to *N*-heterocyclic carbene (NHC) ruthenium olefin metathesis catalysts. Advantageously, the catalysts of the invention display greater efficiency/activity than current olefin metathesis catalysts for catalyzing ring-closing metathesis (RCM) reactions to form tetra-substituted cyclic olefins. The catalysts also perform the other known metathesis reactions in the family of metathesis reactions discussed above. The catalysts are also particularly useful in cross-metathesis to prepare tri-substituted olefins, and di-substituted olefins that are further substituted at the allylic carbon. The *N*-heterocyclic carbene (NHC) ruthenium olefin metathesis catalysts of the invention have the following general formula (I):



(I)

[0037] In the catalysts of formula (I), X^1 and X^2 are independently anionic ligands. Preferably, X^1 and X^2 are halide, or one of the following groups: C_1-C_{20} alkyl, aryl, C_1-C_{20} alkoxide, aryloxide, C_3-C_{20} alkyldiketonate, aryldiketonate, C_1-C_{20} carboxylate, arylsulfonate, C_1-C_{20} alkylsulfonate, C_1-C_{20} alkylthio, C_1-C_{20} alkylsulfonyl, or C_1-C_{20} alkylsulfinyl. Optionally, X^1 and X^2 may be substituted with one or more moieties selected from the group consisting of C_1-C_{10} alkyl, C_1-C_{10} alkoxy, and aryl which in turn may each be further substituted with one or more groups selected from halogen, C_1-C_5 alkyl, C_1-C_5 alkoxy, and phenyl. In more preferred embodiments, X^1 and X^2 are halide, benzoate, C_1-C_5 carboxylate, C_1-C_5 alkyl, phenoxy, C_1-C_5 alkoxy, C_1-C_5 alkylthio, aryl, and C_1-C_5 alkyl sulfonate. As discussed below, the other ligands in a catalyst of the invention, when substituted, may also contain such substituents. In even more preferred embodiments, X^1 and X^2 are each halide, CF_3 CO_2, CH_3,CO_2, CFH_2 CO_2, $(CH_3)_3$ CO, $(CF_3)_2$ $(CH_3)CO$, $(CF_3)(CH_3)_2CO$, PhO, MeO, EtO, tosylate, mesylate, or trifluoromethanesulfonate. In the most preferred embodiments, X^1 and X^2 are each chloride.

[0038] The variable “n” defines the number of successive double bounds in the alkylidene substituted by R^9 and R^{10}. The variable “n” is 0, 1 or 2. Preferably, “n” is 0.

[0039] R^9 and R^{10} are each independently hydrogen or a substituted or unsubstituted group selected from the group consisting of C_1-C_{20} alkyl, C_2-C_{20} alkenyl, C_2-C_{20} alkynyl, aryl, C_1-C_{20} carboxylate, C_1-C_{20} alkoxy, C_2-C_{20} alkenyloxy, C_2-C_{20} alkynyloxy, aryloxy, C_2-C_{20} alkoxycarbonyl, C_1-C_{20} alkylthio, C_1-C_{20} 20 alkylsulfonyl and C_1-C_{20} alkylsulfinyl. Optionally, each of the R^9 or R^{10} substituent group may be substituted with one or more moieties selected from the group consisting of C_1-C_{10} alkyl, C_1-C_{10} alkoxy, and aryl which in turn may each be further substituted with one or more groups selected from a halogen, a C_1-C_5 alkyl, C_1-C_{15} alkoxy, and phenyl. Moreover, R^9 and R^{10}, as well as any other of the catalyst ligands, may further include one or more functional groups as long as they do not defeat the activity of the catalyst. Examples of suitable functional groups include but are not limited to: hydroxyl, thiol, thioether, ketone, aldehyde, ester, ether, amine, imine, amide, nitro, carboxylic acid, disulfide, carbonate, isocyanate, carbodiimide, carboalkoxy, carbamate, and halogen. R^9 and R^{10} may optionally be linked together to form a cyclic structure via one of the substituents mentioned above.

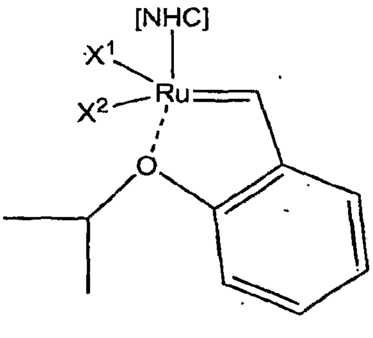
[0040] In preferred embodiments of these catalysts, the R^9 substituent is hydrogen, C_1-C_5 alkyl or aryl and the R^{10} substituent is selected from the group consisting of C_1-C_{20} alkyl, C_2-C_{20} alkenyl, and aryl. In even more preferred embodiments, the R^{10} substituent is phenyl or vinyl, optionally substituted with one or more moieties selected from the group consisting of C_1-C_5 alkyl, C_1-C_5 alkoxy, phenyl, and a functional group. In especially preferred embodiments, R^{10} is phenyl or vinyl substituted with one or more moieties selected from the group consisting of chloride, bromide, iodide, fluoride, $-NO_2$, $-NMe_2$, methyl, methoxy and phenyl. In the most preferred embodiments, the R^{10} substituent is phenyl or $-C{=}C(CH_3)_2$.

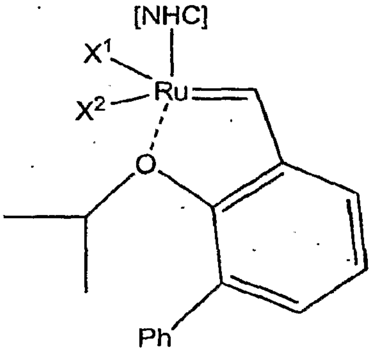
[0041] L may be any neutral 2-electron donor ligand known in the art. The variable “m” defines the number of neutral donor ligands, L. The variable “m” is 1 or 2 and preferably 1.

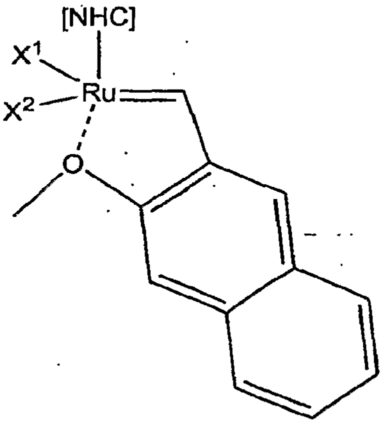
When "m" is 1, L is any neutral 2-electron donor ligand. L may be linked to R^{10} forming a chelating carbene ligand when "n" is zero. When "m" is 2, L is a heteroarene ligand such as pyridine or substituted pyridine. See U.S. Patent Nos. 6,759,537 and 6,818,586, herein incorporated by reference in their entirety; for examples of suitable heteroarene ligands. Preferably, the heteroarene ligand is pyridine or substituted pyridine.

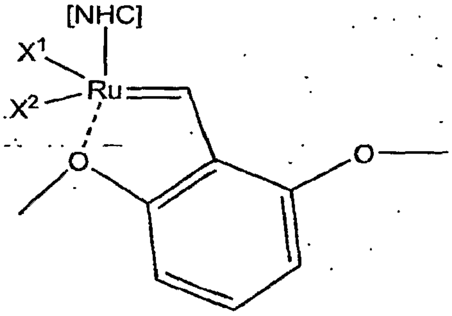
[0042] In a preferred embodiment, L is selected from the group consisting of phosphine, sulfonated phosphine, phosphite, phosphinite, phosphonite, arsine, stibine, ether, amine, amide, imine, sulfoxide, carboxyl, nitrosyl, pyridine, and thioether. In more preferred embodiments, L is a phosphine of the formula PR'R''R''', where R', R'', and R''' are each independently aryl; C_1-C_{10} alkyl (in particular, a primary or secondary alkyl); or C_3-C_6 cycloalkyl. In the most preferred embodiments, L is selected from the group consisting of $P(cyclohexyl)_3$, $P(cyclopentyl)_3$, $P(isopropyl)_3$, and $P(phenyl)_3$.

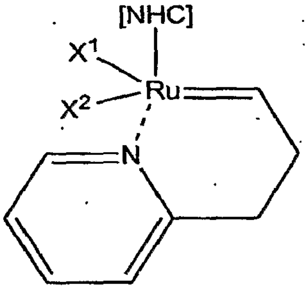
[0043] In a preferred embodiment, L may be linked to R^{10} forming a chelating carbene ligand. When forming a chelating carbene ligand, n is zero. The L portion of the chelating carbene ligand is still a 2-electron donor ligand when linked to R^{10}. L may or may not be linked to R^{10} through a spacer moiety. U.S. Patent 6,921,735 describes chelating carbene ligands and is incorporated herein by reference for examples of how the ligand and R substituent on the carbene can be linked through various spacer moieties. The spacer moiety may be substituted or unsubstituted. Preferred catalysts of the invention where L and R^{10} are linked include the following:

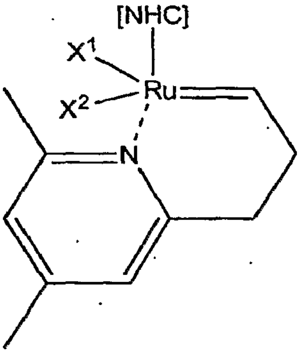


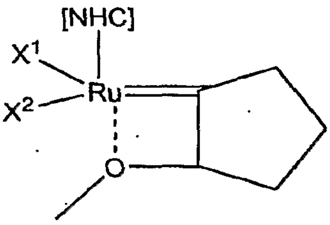








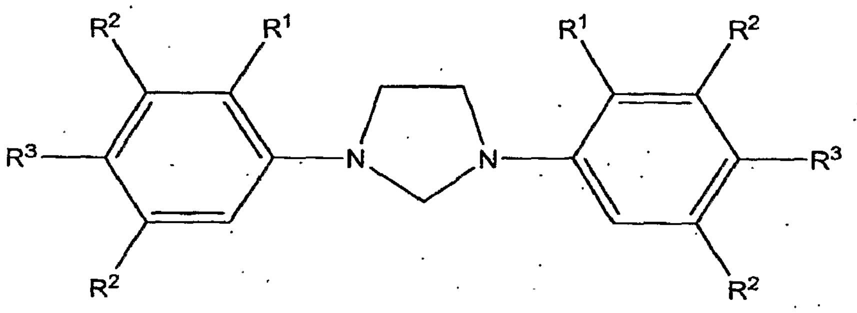




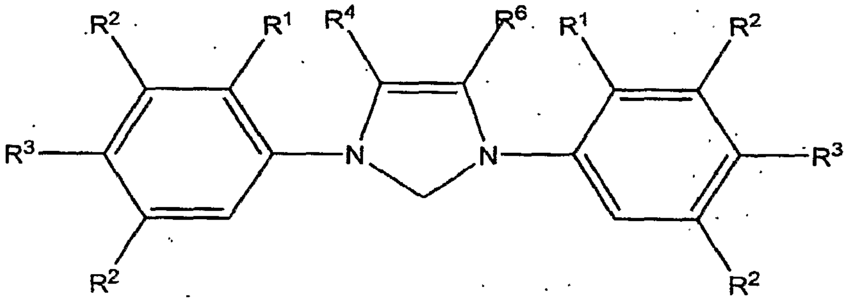
[0044] Examples of ruthenium complexes with chelating carbene ligands, ligands linking the L ligand and the R^{10} substitutent, are also described in Kingsbury, J. S.; Harrity, J. P. A.; Bonitatebus, P. J., Jr.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1999**, *121*, 791 and Garber, S. B.; Kingsbury, J. S.; Gray, B. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2000**, *122*, 8168. Preferably, R^{10} is linked to L via spacer group being 2-5 atoms in length between L and R^{10}, for example via an alkyl group, a cycoloalkyl group, or an aryl group. A preferred spacer group is a substituted or unsubstituted phenyl group.

[0045] In the catalysts of the invention there is an *N*-heterocyclic carbene (NHC) ligand which is a ligand comprising a 5-membered NHC ring, i.e., a carbene where the carbenic carbon atom is contained within a 5-membered cyclic structure. The 5-membered cyclic structure that contains the carbenic carbon atom also contains at least one nitrogen atom directly attached to the carbenic carbon atom and that nitrogen atom is substituted by a phenyl ring. The phenyl ring itself has a hydrogen (i.e. is unsubstituted) at either or both ortho positions but substituted at at least one ortho-; or meta-position.

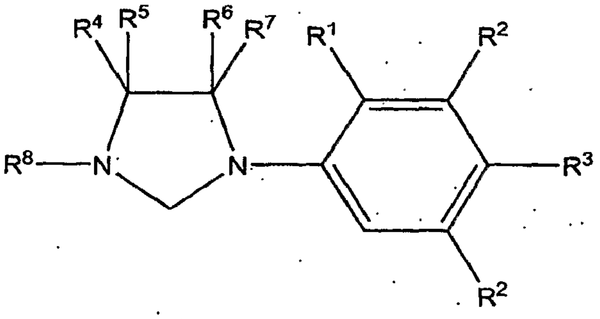
[0046] As described in the preferred embodiments below, the 5-membered NHC ring may, in some circumstances, be part of a polycyclic group and the phenyl ring may be part of a polycyclic aryl group. Preferred NHC ligands are those of those of formulas (II)-(V):



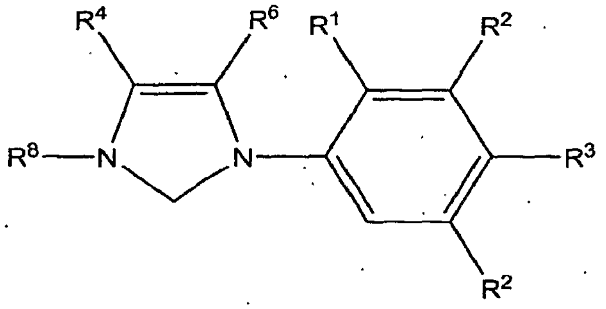
(II)



(III)



(IV)



(V)

In the preferred NHC ligands of formulas (II) - (V) there are two preferred combinations of R^1, R^2, and R^3 which define the substitution pattern on the phenyl ring bound to the nitrogen atom bound to the carbene carbon. Note that in the NHC ligands used in the complexes of the invention, at least one ortho position on the phenyl ring is a hydrogen. In other words, the phenyl ring is always unsubstitued at least one ortho position. In certain preferred combinations of R^1, R^2, and R^3 both ortho positions are hydrogen and, therefore, unsubstituted. The preferred combinations of R^1, R^2, and R^3 are:

> a) each R^1 is independently a primary or secondary C_1-C_4 alkyl group; each R^2 is independently H, a substituted or unsubstituted C_1-C_{10} alkyl group, substituted or unsubstituted phenyl, substituted or unsubstituted naphthyl, or substituted or unsubstituted anthracenyl; and each R^3 is independently H, a substituted or unsubstituted C_1-C_8 alkyl group, substituted or unsubstituted phenyl, substituted or unsubstituted naphthyl, or substituted or unsubstituted anthracenyl, or a functional group selected from the group consisting of halo, hydroxyl, sulfhydryl, cyano, cyanato, thiocyanato, amino, nitro, nitroso, sulfo, sulfonato, boryl, borono, phosphono, phosphonato, phosphinato, phospho, phosphino, and silyloxy; or
>
> b) R^1 is H; each R^2 is independently H, a substituted or unsubstituted C_1-C_8 alkyl group, substituted or unsubstituted phenyl, substituted or unsubstituted naphthyl, or substituted or unsubstituted anthracenyl; and R^3 is independently H, a substituted or unsubstituted C_1-C_8 alkyl group, substituted or unsubstituted phenyl, substituted or unsubstituted naphthyl, or substituted or unsubstituted anthracenyl or a functional group selected from the group consisting of halo, hydroxyl, sulfhydryl, cyano, cyanato, thiocyanato, amino, nitro, nitroso, sulfo, sulfonato, boryl, borono, phosphono, phosphonato, phosphinato, phospho, phosphino, and silyloxy; with the proviso that both R^2 substituents on the same phenyl ring are not H.

[0047] In combination a), R^1 is preferably methyl, ethyl, or iso-propyl. Each separate R^2 is preferably H, iso-butyl, tert-butyl, neopentyl, neohexyl, or phenyl and is most preferably H.

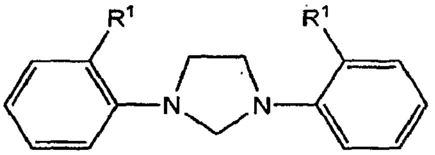
Each R^3 is preferably H, iso-butyl, tert-butyl, neopentyl, neohexyl, or phenyl and is most preferably H.

[0048] In combination b), when R^1 and R^3 are H and R^2 is one of the listed substituents, the phenyl group of the NHC ligand is bis-meta substituted; and when R^1 and R^3 and R^2 are each one of the listed substituents, the phenyl group of the NHC ligand is bis-meta and para-substituted. Because R^1 is H, the proviso within combination b), that both R^2's on the same phenyl ring are H, exclude those NHC ligands having an unsubstituted phenyl or a, para-substituted phenyl. R^2 is preferably a secondary or tertiary C_3-C_{10} alkyl or aryl; more preferably, iso-butyl, tert-butyl, neopentyl, neohexyl, or phenyl and most preferably tert-butyl. R^3 is preferably H, iso-butyl, tert-butyl, neopentyl, neohexyl, or phenyl and is most preferably H.

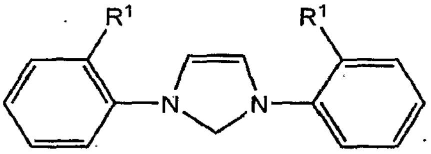
[0049] In the NHC ligands used in the complexes of the invention, R^4 and R^6 are each independently H, a substituted or unsubstituted C_1-C_8 alkyl group, substituted or unsubstituted aryl, or in formulas (III) and (V), together with the carbons carrying them, form a substituted or unsubstituted, fused 4-8 membered carbocylic ring or a substituted or unsubstituted, fused aromatic ring. Preferably R^4 and R^6 are H, C_1-C_4 alkyl, or fused cycolhexyl or phenyl (in formulas (III) and (V)). R^5 and R^7 are independently H, a substituted or unsubstituted C_1-C_8 alkyl group and preferably H or C_1-C_4 alkyl.

[0050] In the NHC ligands of formulas (IV) and (V), R^8 is a C_1-C_{12} alkyl or a C_3-C_{12} cycloalkyl. Preferably R^8 is methyl, ethyl, or iso-propyl and most preferably is methyl.

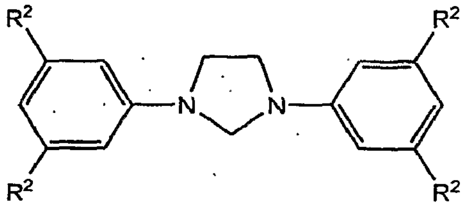
[0051] Examples of preferred NHC ligands for catalysts of the invention are shown below:



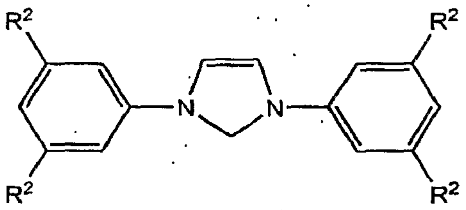
where R^1 = methyl, ethyl, propyl, isopropyl



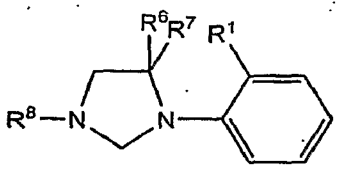
where R^1 = methyl, ethyl, propyl, isopropyl



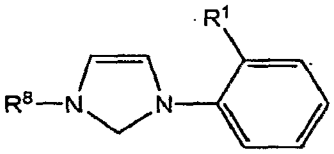
where R^2 = tert-butyl



where R^2 = tert-butyl



where R^1 = methyl, ethyl, propyl, isopropyl; $R^6 = R^7$ = hydrogen or methyl; and R^8 = methyl.



where R^1 = methyl, ethyl, propyl, isopropyl; and R^8 = methyl.

Synthesis of NHC ligands

[0052] The NHC ligands of formulas (II) and (III) used to form the catalysts of the invention may be prepared from aniline derivatives using known procedures used to prepare other known NHC ligands, such as the second generation metathesis catalysts discussed above. The aniline derivative used bears the desired substituents and substitution pattern. Typically, two equivalents of the aniline derivative are reacted with glyoxal to begin the synthesis. Use of the two equivalents of the same aniline gives a symmetric NHC ligand. Asymmetric NHC ligands can be prepared by using two different aniline derivatives. For asymmetric NHC ligands, the aniline derivatives are preferably reacted with the glyoxal in two separate steps to avoid a mixture of products.

[0053] Alternatively, NHC ligands of formulas (II) and (III) maybe prepared by reacting two equivalents of the same aniline with oxalyl chloride. Subsequent reduction of the product bisamide yields a diamine that can be transformed by techniques known in the art to a salt, which is a direct NHC ligand precursor. For differentially substituted NHC ligands, typically, one aniline is reacted with ethyl chlorooxoacetate and the product of that reaction is reacted with the second aniline. Again, reduction of the product bisamide yields a diamine that can be transformed by techniques known in the art to a salt, which is a direct NHC ligand precursor. Examples of the preparation of NHC ligands of formulas (II) and (III) are shown below in Examples 1, 6, 12, 13, and 17.

[0054] Salt precursors of NHC ligands of formulas (IV) and (V) can be prepared by a procedure similar to that described by Blechert and coworkers in *Organometallics* **2006**, *25*, 25-28: first a diamine $R^8NH-(CH_2)_2-NH_2$ is arylated under Buchwald-Hartwig conditions to give $R^8NH-(CH_2)_2-NH[C_6HR^1(R^2)_2R^3]$, which is then reacted with triethylorthoformate in the presence of NH_4BF_4 to give the HBF_4 salt precursor of NHC ligands of formula (IV). Salt precursors of NHC ligands of formula (V) can be prepared by reacting N-(substituted phenyl)imidazole (where substituted phenyl is $C_6HR^1(R^2)_2R^3$) with an alkyl halide (where alkyl is R^8) according to the procedure described by Fürstner and coworkers in *Organometallics* **2004**, *23*, 280-287. The NHC ligands of formulas (IV) and (V) may be prepared by deprotonation of their corresponding NHC salts.

Synthesis of catalysts

[0055] The ruthenium catalysts of the invention may be prepared using methods known in the art. In general, the catalysts of the present invention are prepared via a ligand exchange reaction, for example, by substituting an NHC ligand for one of the neutral electron donor ligands in a first generation ruthenium carbene complexes (discussed above). For example, a catalyst of the invention can be prepared by replacing a phosphine ligand in a complex of the general formula $(PR_3)_2(X)_2Ru=CHR$ with an NHC ligand described above. As discussed in the Background of the Invention, these synthetic procedures are known in the art. Examples 2, 7, 11, 12, 14, and 15 illustrate preparation of ruthenium catalysts of the invention by this method.

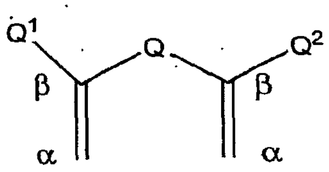
Metathesis Reactions

[0056] The ruthenium catalysts of the invention are particularly efficient olefin metathesis catalysts. Accordingly, one embodiment of the invention is an olefin metathesis reaction which contacts an olefin with an *N*-heterocyclic carbene (NHC) ruthenium olefin metathesis catalyst of the invention under metathesis conditions. The catalysts of the invention may be used in, for example, ring-closing metathesis (RCM), cross metathesis (CM), self metathesis (which is a type of cross metathesis), ring-opening metathesis polymerization (ROMP), and acyclic diene metathesis polymerization (ADMET).

[0057] The metathesis conditions for the catalysts of the invention are the same as those used in other olefin metathesis reactions and with other known olefin metathesis catalysts. Generally speaking, the olefin metathesis reactions are run at a temperature ranging from about 10 °C to about 70 °C and for a time period ranging from about 5 minutes to about 24 hours. The catalysts of the invention may be used in the same amounts as know for other olefin metathesis catalysts. Typically, about 1 to about 10 mol% of the catalyst is used and more often about 5 mol%.

[0058] The ruthenium catalysts of the invention are particularly useful in metathesis reactions for the production of tetra-substituted cyclic olefins. The catalysts of the invention have significantly increased efficiency/activity for the preparation of tetra-substituted cyclic olefins via olefin metathesis. To answer the need for more efficient preparation of such olefins another embodiment of the invention is a ring-closing metathesis method to prepare a tetra-substituted cyclic olefin. The method contacts an olefinic compound having at least two terminal olefins which are substituted at the beta-carbon of each terminal olefin with an *N*-heterocyclic carbene (NHC) ruthenium olefin metathesis catalyst of the invention under metathesis conditions to form a cyclic tetra-substituted olefin.

[0059] A preferred group of olefinic compounds are those which have a structure according to formula (VI):



(VI).

In formula (VI), Q is selected from hydrocarbylene, substituted hydrocarbylene, heteroatom-containing hydrocarbylene, and substituted heteroatom-containing hydrocarbylene. Q^1 and Q^2 are independently selected from hydrogen, hydrocarbyl, substituted hydrocarbyl, heteroatom-containing hydrocarbyl, substituted heteroatom-containing hydrocarbyl, and other groups such as halide, hydroxyl, sulfhydryl, cyano, cyanato, thiocyanato, amino, nitro, nitroso, sulfo, sulfonato, boryl, borono, phosphono, phosphonato, phosphinato, phospho, phosphino, and silyloxy. In the preparation of hindered cyclic olefins, both Q^1 and Q^2 cannot both be hydrogen and, more preferably, are both not hydrogen.

[0060] The catalysts are useful in cross-metathesis to prepare tri-substituted olefins, and di-substituted olefins which are further substituted at the allylic carbon. Accordingly, an embodiment of the invention relates to a cross-metathesis reaction in which an *N*-heterocyclic carbene (NHC) ruthenium olefin metathesis catalyst of the invention contacts two olefins under metathesis conditions. The first olefin is monosubstituted at the β-carbon and either unsubstituted or monosubstituted at the α-carbon. The second olefin is either disubstituted at the β-carbon or monosubstituted at the β-carbon but also has further substitution at the allylic carbon. Both olefins are either monosubstituted or unsubstituted at the α-carbon.

[0061] Examples of tri-substituted olefins are those having the formula $Q^1Q^2C{=}CHQ^3$. Q^1, Q^2 , and Q^3 are independently selected from hydrocarbyl, substituted hydrocarbyl, heteroatom-containing hydrocarbyl, substituted heteroatom-containing hydrocarbyl, and other groups such as halide, hydroxyl, sulfhydryl, cyano, cyanato, thiocyanato, amino, nitro, nitroso, sulfo, sulfonato, boryl, borono, phosphono, phosphonato, phosphinato, phospho, phosphino, and silyloxy. Any number of Q^1, Q^2 , and Q^3 may also be linked as part of a cyclic olefin.

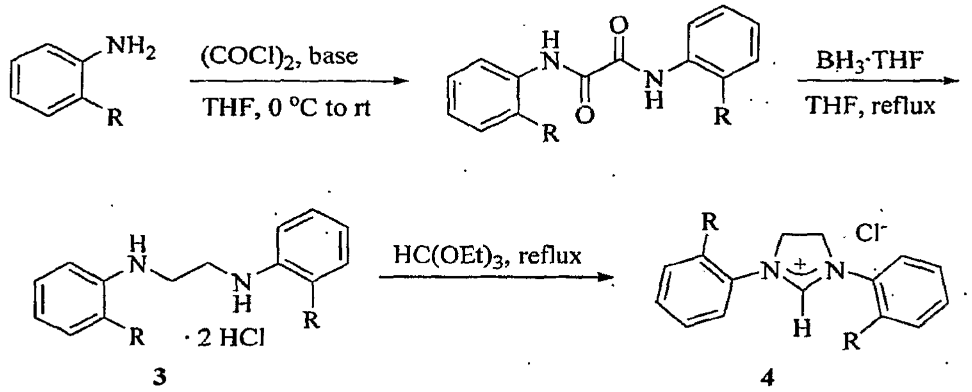
[0062] Di-substituted olefins are represented, for example, by the formula $Q^1Q^2C{=}CH_2$ or $Q^1HC{=}CHQ^2$. Q^1 and Q^2 are independently selected from hydrocarbyl, substituted hydrocarbyl, heteroatom-containing hydrocarbyl, substituted heteroatom-containing hydrocarbyl, and other groups such as halide, hydroxyl, sulfhydryl, cyano, cyanato, thiocyanato, amino, nitro, nitroso, sulfo, sulfonato, boryl, borono, phosphono, phosphonato, phosphinato, phospho, phosphino, and silyloxy. Q^1 and Q^2 may also be linked in the case of cyclic olefins.

[0063] The formula $Q^1HC{=}CHCQ^2Q^3Q^4$ is representative of exemplary di-substituted olefins having further substitution at the allylic carbon. In this formula Q^1, Q^2 , Q^3, and Q^4 are independently selected from hydrogen, hydrocarbyl, substituted hydrocarbyl, heteroatom-containing hydrocarbyl, substituted heteroatom-containing hydrocarbyl, and other groups such as halide, hydroxyl, sulfhydryl, cyano, cyanato, thiocyanato, amino, nitro, nitroso, sulfo, sulfonato, boryl, borono, phosphono, phosphonato, phosphinato, phospho, phosphino, and silyloxy, provided that at least two of Q^2, Q^3 and Q^4 are different from hydrogen. Q^1, Q^2 , Q^3, and Q^4 can be linked when the olefin is a cyclic olefin.

[0064] The term "hydrocarbyl" refers to univalent hydrocarbyl radicals containing 1 to about 30 carbon atoms, preferably 1 to about 24 carbon atoms, most preferably 1 to about 12 carbon atoms, including linear, branched, cyclic, saturated and unsaturated species, such as alkyl groups, alkenyl groups, aryl groups, and the like. The term "lower hydrocarbyl" intends a hydrocarbyl group of 1 to 6 carbon atoms, preferably 1 to 4 carbon atoms, and the term "hydrocarbylene" intends a divalent hydrocarbyl moiety containing 1 to about 30 carbon atoms, preferably 1 to about 24 carbon atoms, most preferably 1 to about 12 carbon atoms, including linear, branched, cyclic, saturated and unsaturated species. The term "lower hydrocarbylene" intends a hydrocarbylene group of 1 to 6 carbon atoms. "Substituted hydrocarbyl" refers to hydrocarbyl substituted with one or more substituent groups such as discussed above, and the terms "heteroatom-containing hydrocarbyl" and "heterohydrocarbyl" refer to hydrocarbyl in which at least one carbon atom is replaced with a heteroatom. Similarly, "substituted hydrocarbylene" refers to hydrocarbylene substituted with one or more substituent groups discussed above, and the terms "heteroatom-containing hydrocarbylene" and heterohydrocarbylene" refer to hydrocarbylene in which at least one carbon atom is replaced with a heteroatom. Unless otherwise indicated, the term "hydrocarbyl" and "hydrocarbylene" are to be interpreted as including substituted and/or heteroatom-containing hydrocarbyl and hydrocarbylene moieties, respectively.

Examples

Example 1: Ortho substituted NHC Ligand synthesis



[0065] **General procedure for the preparation of *N,N'*-Diaryl oxamides.** Oxalyl chloride (4.36 mL, 50 mmol) was added dropwise to a stirred solution of aniline $C_6H_4RNH_2$ (100 mmol, 2 equiv) and base (100 mmol, 2 equiv) in THF (200 mL) at 0 °C. Triethylamine or aq. NaOH may be used as bases for this reaction. Upon addition, the reaction was allowed to warm up to room temperature (r.t.) and stirred for 1 h. The reaction mixture was then concentrated *in vacuo* and diluted with water (100 mL). The white precipitate was collected by filtration, washed with dilute HCl (100 mL), water (2x100 mL), and dried *in vacuo*. The following *N,N'*-diaryl oxamides were prepared by this procedure:

[0066] ***N,N'*-Bis(*o*-tolyl) oxamide.** Obtained in a 98 % yield as a white solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.38 (s, 2H), 8.09 (d, $^3J_{HH}$ = 7.8 Hz , 2H), 7.31-7.12 (m, 6H), 2.39 (s, 6H).

[0067] ***N,N'*-Bis(2-ethylphenyl) oxamide.** Obtained in a 71 % yield as a white solid.

[0068] ***N,N'*-Bis(2-isopropylphenyl) oxamide.** Obtained in a 60 % yield as a white solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.52 (s, 2H), 8.05 (d, $^3J_{HH}$ = 6.9 Hz, 2H), 7.36-7.21 (m, 6H), 3.16 (m, 2H), 1.32 (d, $^3J_{HH}$ = 6.6. Hz, 12H), 0.98 (d, $^3J_{HH}$ = 6.9 Hz, 12H).

[0069] **General procedure for the preparation of *N,N'*-Diarylethylenediamine hydrochloride 3.** Borane-tetrahydrofuran complex (1M solution in THF, 125 mL, 6.25 equiv) was added dropwise with stirring to oxamide (20 mmol) at r.t. The reaction mixture was refluxed overnight, allowed to cool to r.t. and excess borane was quenched by careful, dropwise addition of water until no more gas evolutiom was observed. The reaction mixture was concentrated *in vacuo*, extracted with ether and the organic extracts were dried over Na_2SO_4. 2M HCl in ether (30 mL, 3 equiv) was then added to the dry organic extracts and the resulting white precipitate was collected by filtration, washed with a small amount of ethanol and dried *in vacuo*. The following *N,N'*-diarylethylenediamine hydrochlorides were prepared by this procedure:

[0070] ***N,N'*-Bis(*o*-tolyl)ethylenediamine hydrochloride 3a** (i.e. compound **3** wherein R = methyl). Obtained in a 89 % yield as a white solid. ^{1}H NMR (300 MHz, D_2O): δ 7.30-7.10 (m, 8H), 3.67 (s, 4H), 2.45 (s, 6H).

[0071] ***N,N'*-Bis(2-ethylphenyl)ethylenediamine hydrochloride 3b** (i.e. compound 3 wherein R = ethyl). Obtained in a 74 % yield as a white solid.

[0072] ***N,N'*-Bis(2-isopropylphenyl)ethylenediamine hydrochloride 3c** (i.e. compound 3 wherein R = isopropyl). Obtained in a 91 % yield as a white solid. ^{1}H NMR (300 MHz, D_2O): δ 7.33 (d, $^3J_{HH}$ = 6.9 Hz, 2H), 7.15 (m, 4H), 6.98 (d, $^3J_{HH}$ = 6.9 Hz, 2H), 3.51 (s, 4H), 2.74 (m, 2H), 0.98 (d, $^3J_{HH}$ = 6.9 Hz, 12H).

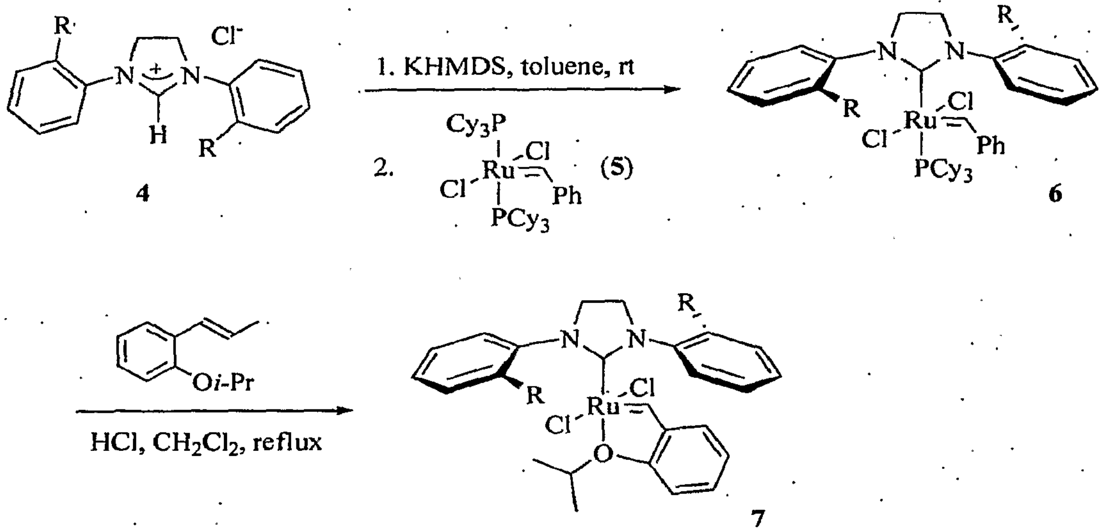
[0073] **General procedure for the preparation of NHC ligand precursor 4 or Dihydroimidazolium salt 4.** Triethyl orthoformate (150 mL) was added to the diamine hydrochloride 3 in a 250-mL r.b. flask. The flask was equipped with a distillation head and heated for about 1 h, during which ethanol distilled over at 78-80 °C, followed by about 70 mL of triethyl orthoformate at 135-140 °C. The reaction mixture was then allowed to cool to r.t., diluted with hexanes and the white precipitate was collected by filtration, washed with hexanes and ether and dried *in vacuo*. The following dihydroimidazolium salts were prepared by this procedure:

[0074] **1,3-Bis(*o*-tolyl)-4,5-dihydroimidazolium chloride 4a** (i.e. compound 4 wherein R = methyl). Obtained in a 93 % yield as a white solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.83 (s, 1H), 7.78-7.21 (d, 8H), 4.64 (s, 4H), 2.43 (s, 6H).

[0075] **1,3-Bis(2-ethylphenyl)-4,5-dihydroimidazolium chloride 4b** (i.e. compound 4 wherein R = ethyl). Obtained in a 74 % yield as a white solid. ^{1}H NMR (300 MHz, CD_2Cl_2) δ 9.04 (1H, s); 7.92 (2H, d, J = 7.5 Hz), 7.47-7.30 (6H, m), 4.64 (4H, s), 2.78 (4H, q, J = 7.8 Hz), 1.31 (6H, t, J = 7.8 Hz).

[0076] **1,3-Bis(2-isopropylphenyl)-4,5-dihydroimidazolium chloride 4c** (i.e. compound 4 wherein R = isopropyl). Obtained in an 84% yield as a white solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.22 (d, $^3J_{HH}$ = 7.2 Hz, 2H), 8.04 (s, 1H), 7.34 (m, 6H), 4.73 (s, 4H), 3.06 (m, 2H), 1.29 (d, $^3J_{HH}$ = 6.0 Hz, 12H).

[0077] **Example 2:** Catalyst synthesis



[0078] **General procedure for the preparation of ortho-substituted catalyst 6.** Potassium bis(trimethylsilyl)amide (1.4 g, 7.0 mmol, 1.23 equiv) was added to a suspension of dihydroimidazolium salt **4** (compound 4 of reaction scheme 3) (2.3 g, 6.7 mmol, 1.15 equiv) in toluene (57 mL) under argon. The reaction mixture was stirred at r.t. for 30 min, then compound **5** (4.7 g, 5.7 mmol) was added and stirring was continued for 1.5 h at r.t. The reaction mixture was then concentrated and catalyst **6** was isolated by column chromatography and dried *in vacuo*. The ortho-substituted catalysts were prepared by this procedure:

[0079] **Catalyst 6a** (i.e. compound 6 wherein R = methyl). Obtained in a 66 % yield after column chromatography on silica gel (unreacted **5** was first eluted with 1:9 EtOAc-hexanes, then **6a** was eluted with 1:3 EtOAc-hexanes). Brown crystalline solid. ^{1}H NMR (300 MHz, C_6D_6): δ 19.61 (s), 8.70 (br), 7.64 (br), 7.31-6.76 (m), 6.59 (m), 6.34 (br), 3.53-3.01 (m), 2.62 (s), 2.20-2.04 (br), 1.67-1.06 (m). ^{31}P NMR (121 MHz, C_6D_6): δ 27.87 (s), 25.15 (s).

[0080] **Catalyst 6b** (i.e., compound 6 wherein R = ethyl) Obtained in a 60 % yield after column chromatography on silica gel (unreacted **5** was first eluted with 1:9 EtOAc-hexanes, then **6a** was eluted with 1:3 EtOAc-hexanes). Brown crystalline solid. ^{1}H NMR (300 MHz, C_6D_6): δ 19.59 (s), 8.74-8.62 (m), 8.25 (br), 7.71 (br), 7.34-6.85 (m), 6.67 (br), 6.44 (br), 3.55-3.07 (m), 2.79-2.19 (m), 1.69-0.91 (m), 1.67-1.06 (m). ^{31}P NMR (121 MHz, C_6D_6): δ 25.75 (s), 25.04 (s).

[0081] **Catalyst 6c** (i.e. compound 6 wherein R = isopropyl). Obtained in a 68 % yield after column chromatography on silica gel (unreacted **5** was first eluted with 1:10 EtOAc-hexanes, then **6c** was eluted with 1:3 EtOAc-hexanes). Brown crystalline solid. ^{1}H NMR (300 MHz, C_6D_6): δ 19.68 (s), 19.49 (s), 8.93-8.87 (m), 8.30 (b), 7.60 (d), 7.34-7.12 (m), 6.97 (t), 6.80 (d), 6.70-6.44 (m), 3.85-3.08 (m), 2.22-2.12 (q), 2.02-1.91 (q), 1.66-0.97 (m). ^{31}P NMR (121 MHz, C_6D_6): δ 26.33 (s), 23.92 (s).

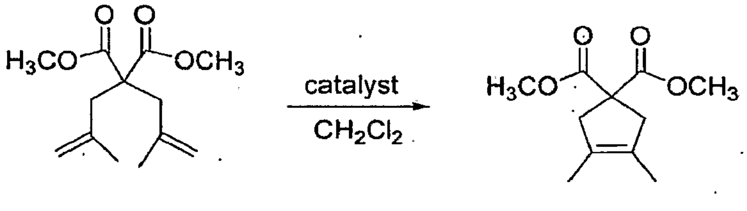
[0082] **General procedure for the preparation of ortho-substituted Catalyst 7.** 2-Isopropoxy-β-methylstyrene (0.89 g, 5.1 mmol, 2 equiv) was added to a solution of catalyst **6** (2.1 g, 2.5 mmol) in CH_2Cl_2 (25 mL). The reaction mixture was refluxed for 1 h, then 2N HCl in methanol (1.8 mL, 3.6 mmol, 1.5 equiv) was added and the mixture was refluxed for another 1 h, then evaporated to dryness *in vacuo*. The residue was dissolved in a minimal amount of CH_2Cl_2 and catalyst **7** was precipitated by addition of pentane. It was collected by filtration and dried *in vacuo*. The following ortho-substituted catalysts were prepared by this procedure:

[0083] **Catalyst 7a** (i.e., compound 7 wherein R = methyl). Obtained in a 71 % yield after column chromatography on silica gel (eluted with 1:5 EtOAc-hexanes). Green crystalline solid. ^{1}H NMR (300 MHz, CD_2Cl_2): δ 16.47 (s, 1H), 8.59 (s, 1H), 7.43 (br, 8H), 6.91 (d, $^3J_{HH}$ = 5.1 Hz, 3H), 4.97 (m, 1H), 4.38 (s, 2H), 4.10 (s, 2H), 2.53 (s, 6H), 1.34 (br, 6H).

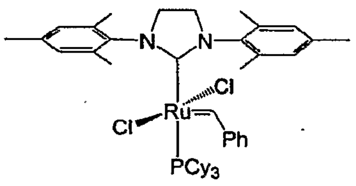
[0084] **Catalyst 7b** (i.e. compound 7 wherein R = ethyl). Obtained in a 68 % yield after column chromatography on silica gel (eluted with 1:5 EtOAc-hexanes). Green crystalline solid ^{1}H NMR (300 MHz, CD_2Cl_2): δ 16.48 (s, 1H), 8.56 (br, 1H), 7.53 (m, 8H), 6.89 (d, $^3J_{HH}$ = 6.6 Hz, 3H), 4.95 (m, 1H), 4.42 (s, 2H), 4.10 (s, 2H), 2.93 (br, 4H), 1.37 (br, 12H).

[0085] **Catalyst 7c** (i.e. compound 7 wherein R = isopropyl). Obtained in a 77 % yield as a green crystalline solid. ^{1}H NMR (300 MHz, C_6D_6): δ 16.65 (s), 16.46 (s), 9.18 (m), 7.90 (d), 7.40-6.93 (m), 6.59 (t), 6.34 (d, $^3J_{HH}$ = 7.5 Hz), 4.47 (m), 3.80-3.32 (m), 2.66 (br), 1.95-1.12 (m).

[0086] **Example 3:** Catalyst performance in RCM



[0087] **Ring-closing metathesis of dimethyl 2,2-di(2-methylallyl)malonate.** Catalyst was added to a 0.1 M solution of dimethyl 2,2-di(2-methylallyl)malonate in CH_2Cl_2 in a round bottom (r.b.) flask. The flask was equipped with a reflux condenser and a bubbler outlet. The reaction mixture was sparged with argon for 5 min, then heated to desired temperature. Reaction progress was monitored by GC analysis of aliquots after removing the catalyst by treating the aliquot with 1M solution of THMP in IPA, heating the quenched mixture at 60 °C for 1 h, diluting it with water and extraction with EtOAc. The activity of catalysts of the invention were compared with the olefin metathesis catalyst (**A**) shown below:



A.

Table 3: RCM of dimethyl 2,2-di(2-methylallyl)malonate with 5 mol % of **A** at 40 °C		
Time (min)	**Starting Material (GC%)**	**Product (GC%)**
30	91.9	3.0
60	92.4	4.2
180	84.3	15.7
1080	49.7	44.7
1440	42.4	49.8
2520	38.1	54.5

Table 4: RCM of dimethyl 2,2-di(2-methylallyl)malonate with 5 mol % of **6a** at 40 °C

Time (min)	**Starting Material (GC%)**	**Product (GC%)**
15	16.2	80.9
30	12.1	83.7
45	11.2	85.4
60	11.1	86.4
90	11.0	87.5
120	10.9	86.7
240	10.9	86.8

Table 5: RCM of dimethyl 2,2-di(2-methylallyl)malonate with 5 mol % of **6b** at 40 °C

Time (min)	**Starting Material (GC%)**	**Product (GC%)**
15	34.0	61.5
30	30.1	69.9
45	28.7	70.7
60	28.0	70.9
120	27.1	70.6
240	27.7	72.3
480	27.2	72.8

Table 6: RCM of dimethyl 2,2-di(2-methylallyl)malonate with 5 mol % of **6c** at 40 °C

Time(min)	**Starting Material (GC%)**	**Product (GC%)**
15	25.2	71.5
30	23.0	73.0
45	22.1	73.1
60	21.9	74.3
90	21.2	75.0
120	20.8	75.5
240	19.2	75.1

Table 7: RCM of dimethyl 2,2-di(2-methylallyl)malonate with 5 mol % of **6c** at 30 °C

Time (min)	**Starting Material (GC%)**	**Product (GC%)**
15	37.9	54.0
30	27.9	65.5
45	25.7	67.2
60	25.8	69.8
240	22.7	69.8
1140	20.7	69.5

Table 8: RCM of dimethyl 2,2-di(2-methylallyl)malonate with 1 mol % of **6c** at 30 °C

Time (min)	**Starting Material (GC%)**	**Products (GC%)**
15	50.9	46.3
30	47.6	49.4
45	46.6	51.0
60	45.5	51.6
90	44.2	52.8
120	44.0	53.7
360	41.2	54.9

Table 9: RCM of dimethyl 2,2-di(2-methylallyl)malonate with 5 mol % of **7a** at 40 °C

Time (h)	**Starting Material (GC%)**	**Product (GC%)**
0.5	65.8	30.6
1	52.3	44.7
3	31.5	65.1
18	28.4	69.9
24	28.3	70.0
42	27.5	68.8

Table 10: RCM of dimethyl 2,2-di(2-methylallyl)malonate with 5 mol % of **7b** at 40 °C

Time (h)	**Starting material (GC%)**	**Product (GC%)**
0.25	96.7	0.7
0.50	89.3	3.3
0.75	81.8	11.8
1	71.1	21.5
2	57.7	34.7
4	51.4	42.9
8	38.9	55.9
24	36.4	58.6

Table 11: RCM of dimethyl 2,2-di(2-methylallyl)malonate with 5 mol % of **7c** at 40 °C

Time (h)	**Starting Material (GC%)**	**Product (GC%)**
0.25	97.2	0.7
0.50	93.8	2.9
0.75	87.2	9.3
1	81.7	15.6
1.5	71.9	24.2
2	69.7	27.5
6	63.4	32.0
24	63.4	32.5

[0088] The results of the RCM performed with second generation catalysts and second generation catalysts with chelating carbene ligands reported above are further illustrated in the charts shown in Fig. 2 and Fig. 3. Fig. 2 shows that catalysts **6a**, **6b** and **6c** perform much better than catalyst **A** in the RCM of compound **1**. Indeed, the reactions catalyzed by **6a**, **6b** and **6c** reach much higher conversions (between about 70 % and about 90 % conversion) compared to the reactions catalyzed by **A** (about 20 % conversion). Additionally, the data represented on Fig. 2 demonstrate that catalysts **6a**, **6b** and **6c** require short reaction times and mild temperatures to reach high conversions. For example, catalyst **6a** gives a high conversion (i.e., greater than 80 %) within only 15 minutes at 40 °C, compared to 7 hours at

60 °C for catalyst **12**. Fig. 3 shows that catalysts **7a**, **7b** and **7c** are also more active than **A** in the RCM of compound **1**, but are less active than catalysts **6a**, **6b** and **6c**.

[0089] **Example 4:** Cross Metathesis Studies

[0090] Catalyst performance in cross-metatheses involving hindered olefins
Inside the glovebox, a 4-mL vials was charged with approximately 1 mL of the appropriate hindered olefin solution (2M in CH_2Cl_2) followed by one equivalent of 5-hexene. The appropriate amount of the tested catalyst was added to the vial, after which it was sealed and heated to desired temperature. Reaction progress was monitored by GC analysis of aliquots after removing the catalyst by treating the aliquot with 1M solution of THMP in IPA, heating the quenched mixture at 60 °C for 1 h, diluting it with water and extraction with EtOAc. An identical cross-metathesis reaction was run with **A** for comparison.

[0091] Cross metathesis (CM) of 5-decene ($5C_{10}$) and 2,5-dimethyl-3-hexene using 1 mol % of **6a** and **A** at 40 °C

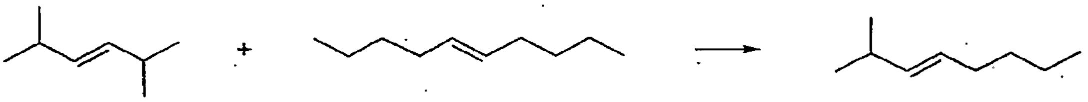


Table 12: Results of CM of $5C_{10}$ and 2,5-dimethyl-3-hexene using 1 mol % of **6a** and **A** at 40 °C			
	Product (GC %)		
	0.5 h	1 h	40 h
6a	20.0	23.9	29.9
A	11.8	15.3	7.8

[0092] Cross metathesis of 5-decene, $5C_{10}$, and 2-methyl-1-nonene using 1 mol % of **6b**, **6c**, **6a** and **A** at 40 °C

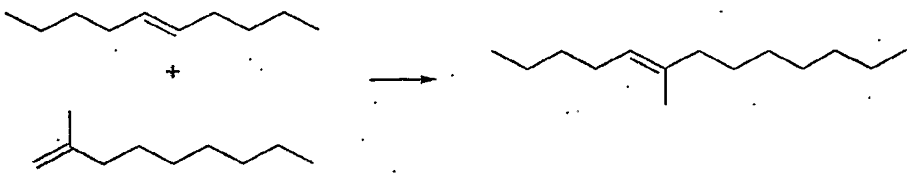


Table 13: Results of CM of $5C_{10}$ and 2-methyl-1-nonene using 1 mol % of **6b**, **6c**, **6a** and **A** at 40 °C

	Product (GC %)		
	1 h	3 h	6 h
6b	27.4	28.4	29.0
6c	22.2	23.5	24.0
6a	20.1	19.5	20.0
A	15.2	21.7	25.6

[0093] **Example 5:** Catalyst performance in self-metathesis of methyl oleate

Inside the glovebox, a 4-mL vial was charged with approximately 10 g of methyl oleate. The appropriate amount of a stock solution of 6a in benzene was added to the vial, after which it was sealed and heated to 40 °C. Reaction progress was monitored by GC analysis of aliquots after removing the catalyst by treating the aliquot with 1M solution of THMP in IPA, heating the quenched mixture at 60 °C for 1 h, diluting it with water and extraction with EtOAc.

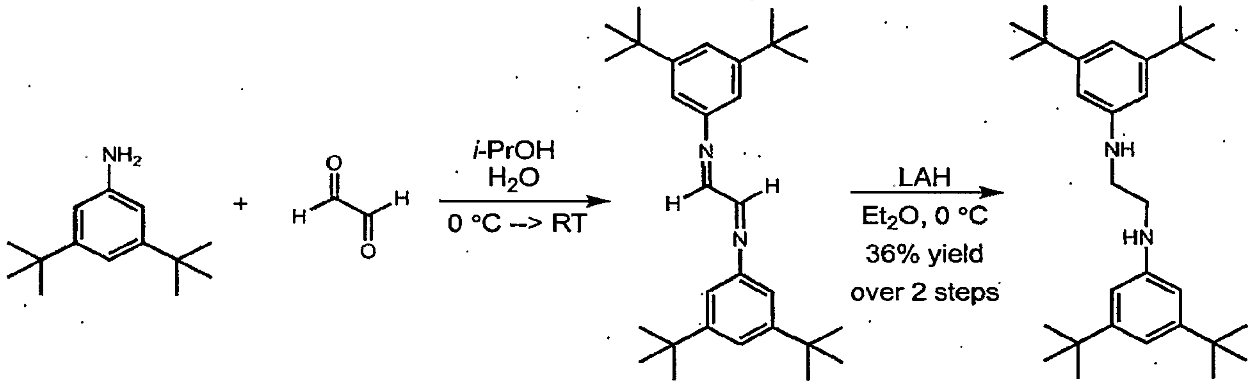
[0094] Self metathesis (SM) of neat methyl oleate using 2, 5 and 20 ppm of **6a** and **A** at 40 °C

Table 14: results of SM of neat methyl oleate using 2, 5 and 20 ppm of **6a** and **A** at 40 °C

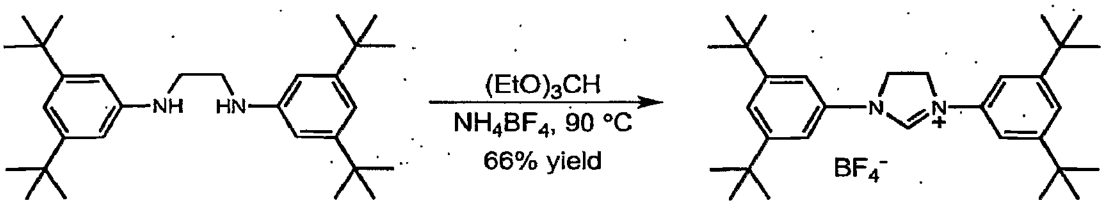
	Maximum conversion[a] reached at, min		
	2 ppm	5 ppm	20 ppm
6a	30	10	5
A	30	10	<10

[a] Maximum conversion in this reaction corresponds to a mixture containing 50 mol % of the starting material and 25 mol % of each of the products (25 mol % 9-octadecene and 25 mol % 1,18-dimethyl-octadecenoate)

[0095] **Example 6:** Preparation of salt **10.**



8 **9**



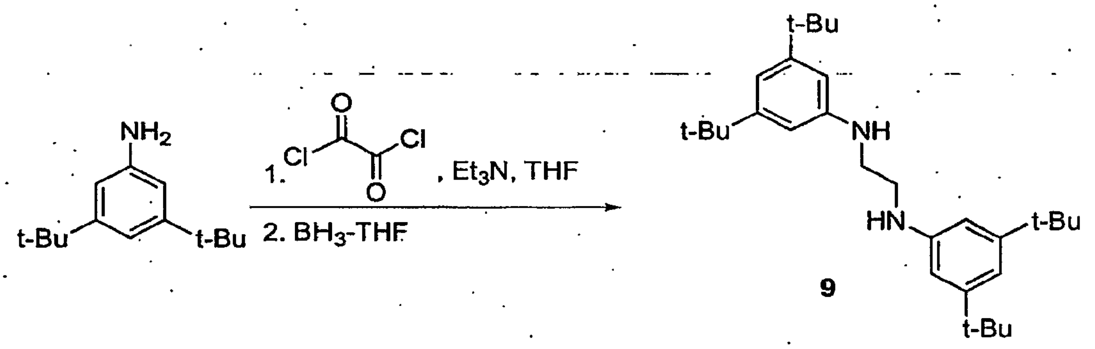
9 **10**

[0096] **Preparation of Diamine 9.** This is a two step procedure. In the first step, a 40% solution of glyoxal in water (465 µl, 4.1 mmol) was added to 3,5-di-*tert*-butylaniline (1.83 g, 8.9 mmol) in isopropanol (16 ml) and water (16 ml) at 0 °C. The reaction stirred for 7 hours and during this time it warmed to room temperature. The reaction mixture was filtered through a glass frit; the filtrate was dissolved in CH_2Cl_2, dried over $MgSO_4$, filtered through another glass frit and concentrated. This crude reaction product was then dissolved in Et_2O (50 ml) and added to LAH (570 mg, 15 mmol) in Et_2O (50 ml) at 0 °C. The reaction stirred for 36 hours and warmed to room temperature. The reaction was quenched with H_2O (570 µl), 15% $NaOH/H_2O$ (570 µl), H_2O (2 ml), filtered through a glass frit dried over $MgSO_4$, filtered through another glass frit and concentrated. The reaction mixture was then purified by flash column chromatography (30% EtOAc/Hexanes) to yield 9 (786 mg, 36% over two steps) as an oil. ^1H NMR (300 MHz, $CDCl_3$) δ 6.85 (2H, t, J = 1.5 Hz), 6.55 (4H, d, J = 1.8

Hz), 5.31 (2H, s), 3.45 (4H, s), 1.31 (36H, s); ^{13}C (75 MHz, $CDCl_3$) δ 152.1, 147.8, 112.8, 107.9, 44.1, 35.1, 31.7; HRMS (EI+) calc for $C_{30}H_{49}N_2$, 437.3896. Found 437.3902.

[0097] **Preparation of NHC ligand precursor 10.** To diamine **9** (786 mg, 1.8 mmol), was added $(EtO)_3CH$ (3 ml, 18 mmol), NH_4BF_4 (189 mg, 1.8 mmol) and formic acid (2 drops). The reactions stirred at 90 °C for 48 hours. Et_2O was added to precipitate the salt. The reaction mixture was then filtered and the solids were washed with Et_2O and collected to yield **8** (633 mg, 66%) as a white solid. ^1H NMR (300 MHz, $CDCl_3$) δ 8.57 (1H, s), 7.42 (2H, t, J = 1.5 Hz), 7.23 (4H, d, J = 1.8 Hz), 4.69 (4H, s), 1.32 (36H, s); ^{13}C (75 MHz, $CDCl_3$) δ 153.6, 151.4, 135.4, 123.1, 114.9, 50.5, 35.4, 31.5.

[0098] **Alternate preparation of diamine 9:**

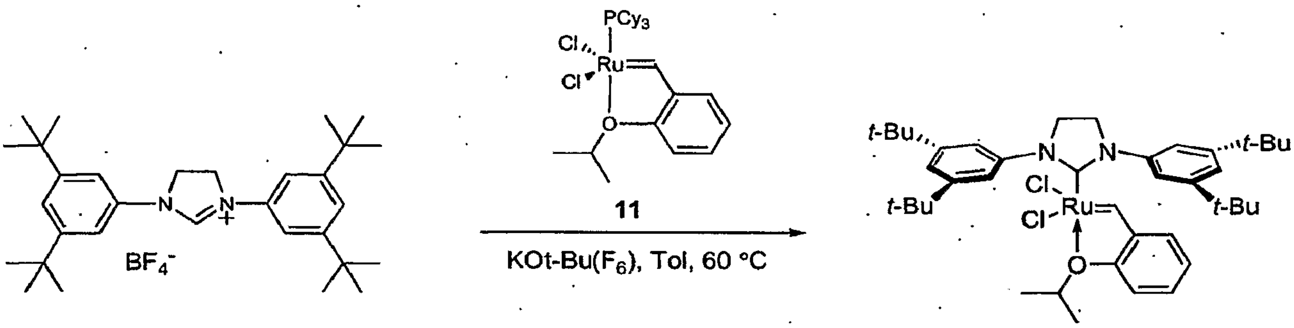


[0100] ***N,N'*-Bis(3,5-di-t-butylphenyl) oxamide.** Oxalyl chloride (2.16 mL, 25 mmol) was added dropwise to a stirred solution of 3,5-di-t-butylaniline (10.28 g, 50 mmol) and triethylamine (7.0 mL, 50 mmol) in THF (200 mL) at 0 °C. Upon addition, the reaction was allowed to warm up to r.t. and stirred for 1 h. The reaction mixture was then concentrated *in vacuo* and diluted with water (100 mL). The white precipitate was collected by filtration, washed with dilute HCl (100 mL), water (2x100 mL), and dried *in vacuo*. Obtained 9.07 g (78%) of *N,N'*-Bis(3,5-di-t-butylphenyl) oxamide as a white solid.

[0101] ***N,N'*-Bis(3,5-di-t-butylphenyl)ethylenediamine (9).** A 1M solution of BH_3-THF in THF (125 mL, 125 mmol) was added dropwise with stirring to the solid oxamide (9.06 g, 19.52 mmol) at r.t. The resulting homogeneous mixture was then refluxed for 15 h, allowed to cool down to r.t. and carefully quenched by adding water. The mixture was then concentrated and extracted with ether. Column chromatography (2:1 hexanes – dichloromethane, silica gel) afforded 6.51 g (76%) of pure **9** as a colorless oil and 1.27 g of impure **9** (contaminated with 3,5-di-t-butylaniline) which was subjected to a second chromatographic purification. The combined yield of **9** was 86%. ^1H NMR (300 MHz,

$CDCl_3$) δ 6.85 (2H, t, J = 1.5 Hz), 6.55 (4H, d, J = 1.8 Hz), 5.31 (2H, s), 3.45 (4H, s), 1.31 (36H, s); ^{13}C (75 MHz, $CDCl_3$) δ 152.1, 147.8, 112.8, 107.9, 44.1, 35.1, 31.7; HRMS (EI+) calc for $C_{30}H_{49}N_2$, 437.3896. Found 437.3902.

[0102] **Example 7:** Preparation of catalyst **12**.



10

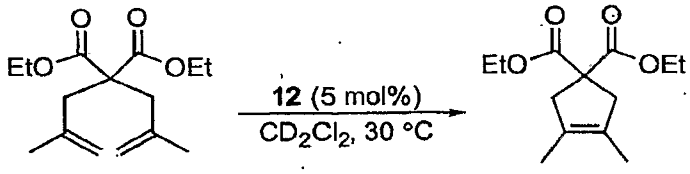
12

[0103] **Preparation of Catalyst 12. NHC ligand precursor 10** (156 mg, .3 mmol), KO*t*-Bu(F_6) (66 mg, .3 mmol), and ruthenium complex **11** (132 mg, .22 mmol) were all combined in toluene in a glove box. The flask was removed and stirred at 60 °C for 18 hours in a fume hood. The reaction mixture was then directly purified by flash column chromatography (5% Et_2O/Hexanes, run 2 times) to yield catalyst **12** (34 mg, 20%) as a green oil. The catalyst was then lyophilized from benzene to give a pale green solid. It should be noted that by ^1H NMR the conversion to **12** is 50%. ^1H NMR (300 MHz, $CDCl_3$) δ 16.91 (1H, s), 8.14-8.13 (2H, m), 7.73 (2H, m), 7.64 (1H, m), 7.52 (1H, m), 7.06-6.92 (2H, m), 6.62 (1H, t, J = 7.5 Hz), 6.31 (1H, d, J = 8.4 Hz), 4.47 (1H, quint, J = 6 Hz), 3.51 (4H, s), 1.51 (18H, s), 1.35 (6H, d, J = 6 Hz), 1.24 (18H, s); HRMS (EI+) calc for $C_{41}H_{58}N_2OCl_2Ru$ 766.2970. Found 766.3007. Fig. 4 depicts the single crystal X-ray structure was obtained for catalyst **12**.

[0104] **Example 8:** Catalyst activity studies.

[0105] **Preparation of stock solutions.** Catalyst **12** (14 mg) was placed in a 2ml volumetric flask and taken into a glove box. In the glove box, 2ml of CD_2Cl_2 was added to make stock solution **Z.** 0.44 ml of **Z** was then transferred to another 2ml volumetric flask and diluted to 2ml with CD_2Cl_2 to make stock solution **Y.**

Reaction scheme 10.

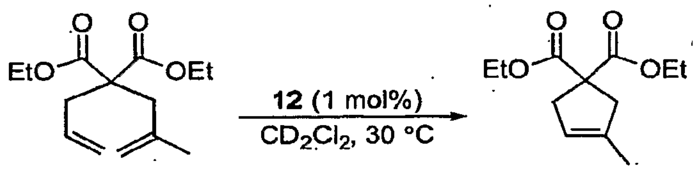


1 **2**

[0106] In a glove box, 0.44 ml of stock solution **Z** (3.1 mg of **12**, 0.004 mmol) was transferred to a screw cap NMR tube. CD_2Cl_2 (.36 ml) was added and then **1** (21.5 µl, 0.08 mmol). The NMR tube was sealed, removed from the glove box and heated to 30 °C. Fig. 5 is a graph of the conversion over time, demonstrating the dramatically improved reactivity **12** shows for ring-closing metathesis (RCM) to form tetrasubstituted olefins.

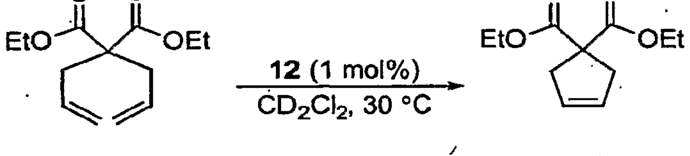
[0107] This study was repeated in C_6D_6 at 60 °C to examine the impact of temperature. Catalyst **12** (3.1 mg, 0.004 mmol) and C_6D_6 (.8 ml) were combined in a screw cap NMR tube and **1** (21.5 µl, 0.08 mmol) was added. The NMR tube was sealed, removed from the glove box and heated to 60 °C. A graph of conversion over time is shown in Fig. 6. As can be seen, after 24 hours 88% conversion has been achieved, and 83% conversion is achieved in only 7 hours.

[0108] **Example 9:** RCM studies with less hindered olefins.



13 **14**

[0109] In a glove box, 0.4 ml of stock solution **Y** (0.6 mg of **12**, 0.0008 mmol) was transferred to a screw cap NMR tube. CD_2Cl_2 (.4 ml) was added and the NMR tube was sealed and transferred to a 500 MHz NMR which was warmed to 30 °C. The NMR tube was then ejected, **13** (20.5 µl, 0.08 mmol) was added and the tube was injected for data collection. A graph of conversion over time is shown in Fig. 7.



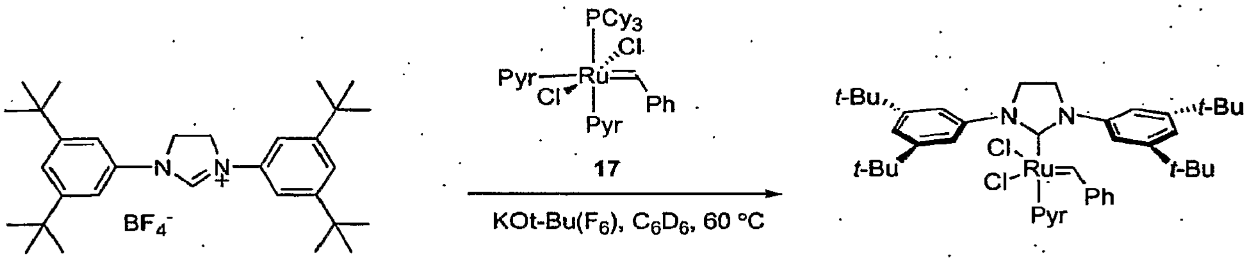
15 **16**

[0110] In a glove box, 0.4 ml of stock solution **Y** (0.6 mg of **12**, 0.0008 mmol) was transferred to a screw cap NMR tube.. CD_2Cl_2 (.4 ml) was added and the NMR tube was sealed and transferred to a 500 MHz NMR which was warmed to 30 °C. The NMR tube was then ejected, **15** (19.5 μl, 0.08 mmol) was added and the tube was injected for data collection. Fig. 8 shows a graph of the conversion over time.

[0111] **Example 10:** Stability studies.

[0112] A striking feature of catalyst **12** is its stability. In solution (CH_2Cl_2 or Benzene), in the absence of substrate, it is stable for at least 4 weeks. As a solid, **12** is stable in air for at least 5 weeks. Finally, during the catalytic reactions described above, for the reactions performed at 30 °C the only time point the original catalyst was not observed by ^1H NMR was 162 hours. For the reaction performed at 60 °C, none of the original catalyst was observed by ^1H NMR at 24.8 hours. Overall, catalyst **12** is highly stable.

[0113] **Example 11:** Preparation of catalyst -**18.**

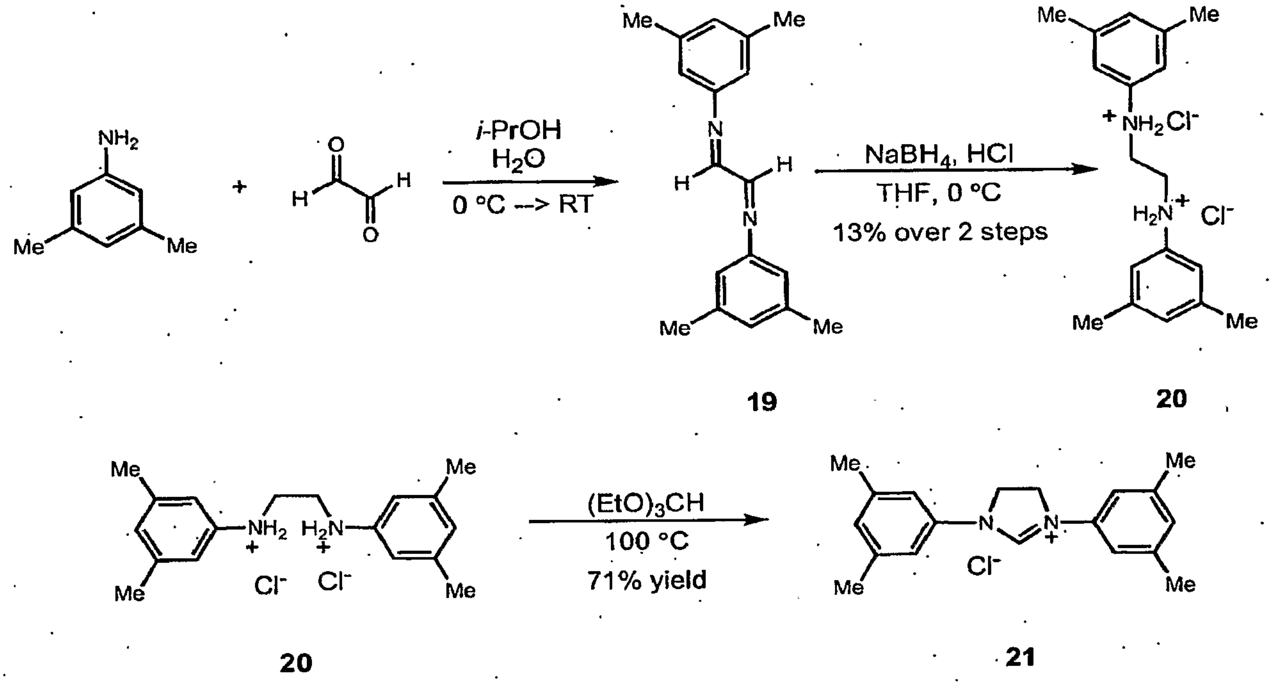


10 **18**

[0114] **Catalyst-18. NHC ligand precursor 10** (14 mg, .03 mmol), KO*t*-Bu(F_6) (6 mg, .03 mmol), and ruthenium complex **17** (14 mg, .02 mmol) were all combined in C_6D_6 in a screw cap NMR tube in a glove box. The NMR tube was removed and heated at 60 °C for 1 hour in a fume hood. Conversion to catalyst **18** was determined to be 52% by proton NMR. ^1H NMR (300 MHz, $CDCl_3$) δ 19.43 (1H, s).

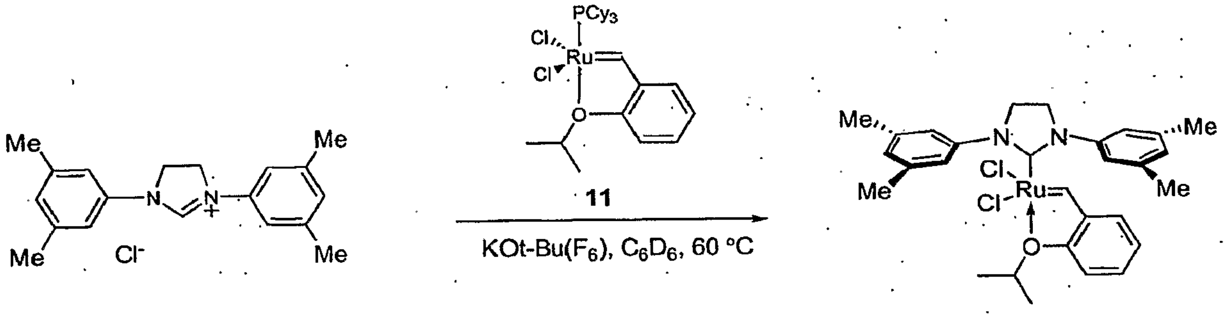
[0115] It should be noted that complex **18** is relatively unstable. The phosphine analogue in which the pyridine ligand is replaced by PCy_3 is also unstable. It is believed that the tert-butyl groups on the NHC are so large that they actively dissosciate the pyridine and phosphine respectively. The transient stability makes these complexes less suitable for catalysis.

[0116] **Example 12** Preparation of an NHC with smaller bis-meta substitution.



[0117] **Diamine salt 20.** This is a two step procedure. In the first step, a 40% solution of glyoxal in water (1.15 ml, 10 mmol) was added to 3,5-di-methylaniline (2.5 ml, 20 mmol) in isopropanol (40 ml) and water (40 ml) at 0 °C. The reaction stirred for 7 hours and during this time it warmed to room temperature. The reaction mixture was filtered through a glass frit; the filtrate was dissolved in CH_2Cl_2, dried over $MgSO_4$, filtered through another glass frit and concentrated. This crude reaction product was then dissolved in THF (37 ml) and to this at 0 °C was added $NaBH_4$ (1.5 g, 40 mmol). Concentrated HCl (1.6 ml) was added dropwise over 25 min. The reaction was stirred for 1 hour and then 4N HCl (75 ml) was added. The reaction was stirred for 1 hour and then filtered. The filtrate was wash extensively with Et_2O to give diamine salt **20** (438 mg, 13% over 2 steps) as an off white solid. ^1H NMR (300 MHz, $CDCl_3$) δ 6.84 (4H, s), 6.76 (2H, s), 3.62 (4H, s), 2.25 (12H, s).

[0118] **NHC ligand precursor 21.** $HC(OEt)_3$ (10 ml) was added to diamine salt **20** and the reaction was stirred at 90 °C for 14 hours. The reaction mixture was filtered and washed with Et_2O to give NHC ligand precursor **21** (290 mg, 71%) as an off white solid. ^1H NMR (300 MHz, DMSO(D_6) δ 9.89 (1H, s), 7.29 (4H, s), 7.02 (2H, s), 4.54 (4H, s), 2.51-2.49 (12H, m). HRMS (EI+) calc for $C_{19}H_{23}N_2$ 279.18613. Found 279.18572.



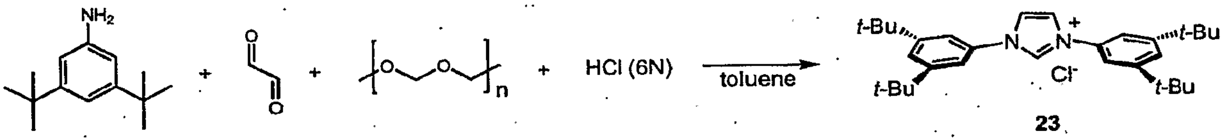
21

22

[0119] **Catalyst 22.** NHC ligand precursor **21** (9 mg, .03 mmol), KO*t*-Bu(F_6) (6 mg, .03 mmol), and ruthenium complex **911** (13 mg, .02 mmol) were all combined in C_6D_6 in a screw cap NMR tube in a glove box. The NMR tube was removed and heated at 60 °C for 2.5 hour in a fume hood. Conversion to catalyst 22 was determined to be 14% by proton NMR. ^{1}H NMR (300 MHz, $CDCl_3$) δ 17.19 (1H, s).

[0120] It should be noted that complex **22** is relatively unstable. It seems that the meta-methyl groups are not large enough and the complex is difficult to handle without decomposition. For this reason, this complex is unattractive for catalysis.

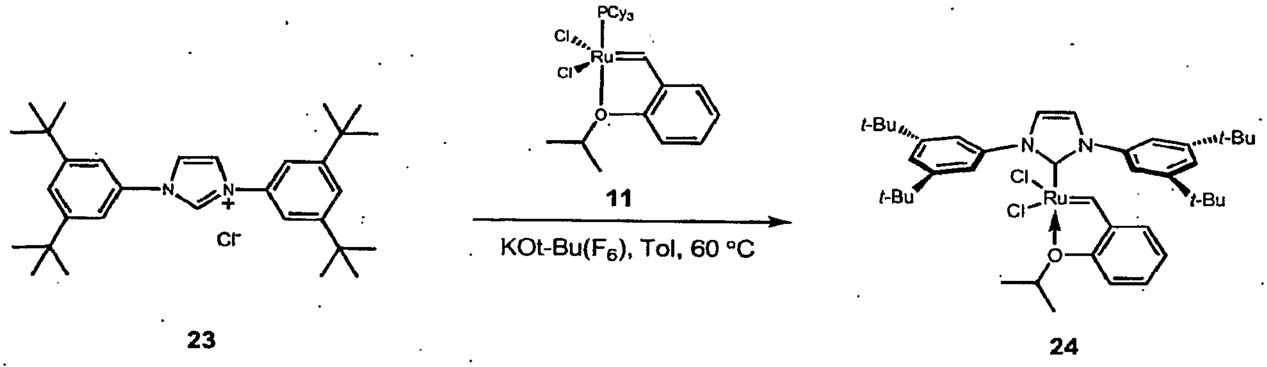
[0121] **Example 13:** Preparation of unsaturated meta-substituted NHC ligands.



23

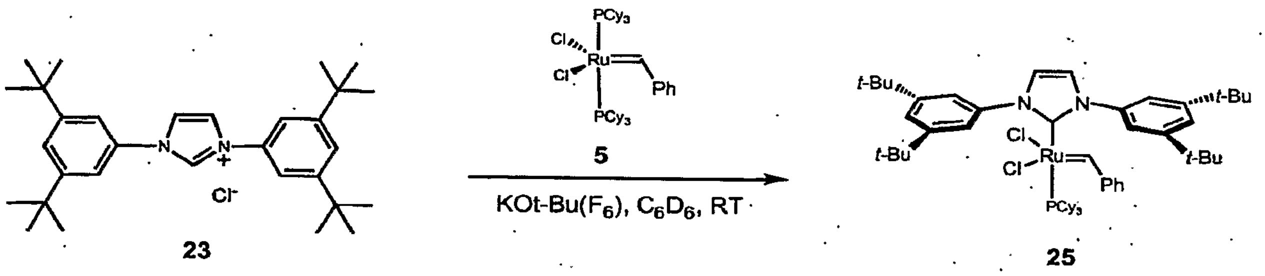
[0122] **NHC ligand precursor 23.** A solution of 3,5-ditertbutylaniline (3 g, 14.6 mmol) in toluene (5 ml) was added to a solution of paraformaldehyde (220 mg, 7.3 mmol) in toluene (5 ml). The reaction was then stirred at 100 °C for 1.5 hours. The reaction was cooled to 40 °C and 6N HCl (1.2 ml, 7.3 mmol) was added. The reaction was stirred for 5 minutes, glyoxal (837 μl, 7.3 mmol) was added and the reaction was stirred another 5 minutes. The reaction was stirred at 100 °C for 14 hours, cooled to RT and purified by column chromatography (5% MeOH/CH_2Cl_2) to yield a brown foam. This foam was washed with Et_2O to yield 806 mg (23%) of **23** as a white solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.89 (br, 1H), 7.78-7.76 (m, 6H), 7.59 (s, 2H), 1.42 (s, 36H); ^{13}C (75 MHz, $CDCl_3$) δ; HRMS (EI+) calc for $C_{31}H_{45}N_2$, 445.3583. Found 445.3561.

[0123] **Example 14:** Preparation of catalyst **24**.



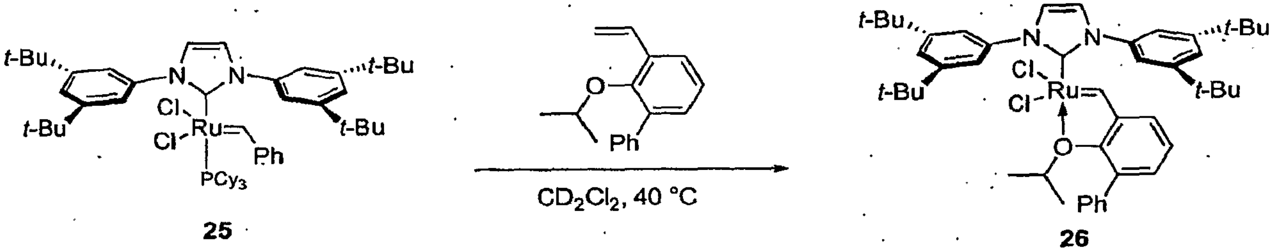
[0124] **Ruthenium Catalyst 24.** In a glove box, NHC ligand precursor **23** (63 mg, .13 mmol), ruthenium precursor **11** (78 mg, .13 mmol) and KO*t*-Bu(F_6) (29 mg, .13 mmol) were combined in toluene. The flask was sealed, removed from the glove box and stirred at 60 °C for 18 hours. The reaction was concentrated and purified by flash column chromatography (5% --> 20% Et_2O/Pent). There were 3 bands that could be isolated from this column, first 2 brown bands and then one green band. The second brown band was the desired product; however, it was not completely pure after one column. Recolumning in 10% Et_2O/Pentane gave a brown oil product completely pure by ^1H NMR (9 mg, 9%) and another fraction still slightly impure (18 mg, 18%). The products were lyophilized from benzene to give solids. ^1H NMR (300 MHz, $CDCl_3$) δ 16.78 (s, 1H), 8.13 (br, 2H), 7.74-7.62 (m, 4H), 7.07-7.04 (m, 1H), 6.97 (dd, J = 3, 1.5 Hz, 1H), 6.66 (t, J = 7.5 Hz, 3H), 6.34 (d, J = 8.4 Hz, 1H), 4.49 (sept, J = 6 Hz, 1H), 1..44 (d, J = 6 Hz, 6H), 1.44 (br, 18H), 1.18 (br, 18H); ^{13}C (75 MHz, $CDCl_3$) δ; HRMS (EI+) calc for $C_{41}H_{56}Cl_2N_2ORu$, 764.2814. Found 764.2842.

[0125] **Example 15:** Preparation of catalyst **25**.



[0126] **Ruthenium Catalyst 25.** In a glove box, NHC ligand precursor **23** (162 mg, .34 mmol), ruthenium precursor **5** (150 mg, .27 mmol) and KO*t*-Bu(F_6) (74 mg, .34 mmol) were combined in C_6D_6 and stirred at RT for 2.5 hours. The flask was sealed, removed from the glove box and the reaction was concentrated and purified by flash column chromatography (2.5% --> 5% Et_2O/Pent) to yield a brown oil. The brown oil was lyophilized from benzene to give 25 as a brown solid (66 mg, 25%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 20.07 (d, J = 10.5 Hz, 1H), 8.03 (br, 2H), 7.60 (t, 1.8 Hz, 1H), 6.86-6.81 (m, 2H), 6.51 - 6.47 (m, 1H), 1.81 - 1.07 (m).

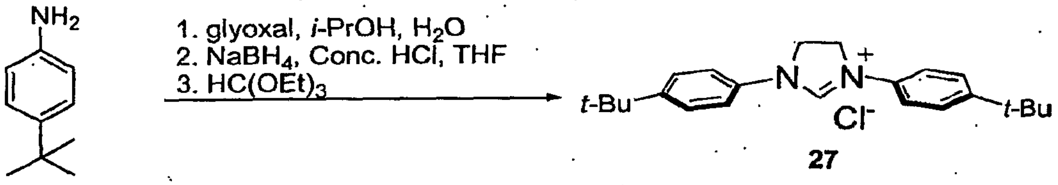
[0127] **Example 16:** Preparation of catalyst **26**.



[0128] **Ruthenium Catalyst 26.** In a screw cap NMR tube, ruthenium compound **25** (10 mg, .01 mmol), 2-isopropoxy-3-vinylbiphenyl (5 mg, .02 mmol) and CuCl (1 mg, .01 mmol) were combined in CD_2Cl_2 (1 ml) in the glove box. The reaction was heated at 40 °C for 29 hours, concentrated and purified by column chromatography (10% --> 25% Et_2O/Pentange) to yield a grayish green oil. This oil was lyophilized from benzene to yield **26** as a solid (2 mg, 25%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 16.77 (s, 1H), 7.89 (s, 1H), 7.66 - 7.59 (m, 6H), 7.50 - 7.38 (m, 7H), 7.02 (t, J = 4.5 Hz, 1H), 6.72 (dd, J = 3.6, 1.2 Hz, 1H), 4.45 (sept, J = 3.6 Hz, 1H), 1.47 (s, 18H), 1.30 (s, 18H), 0.95 (d, J = 3.6 Hz, 6H).

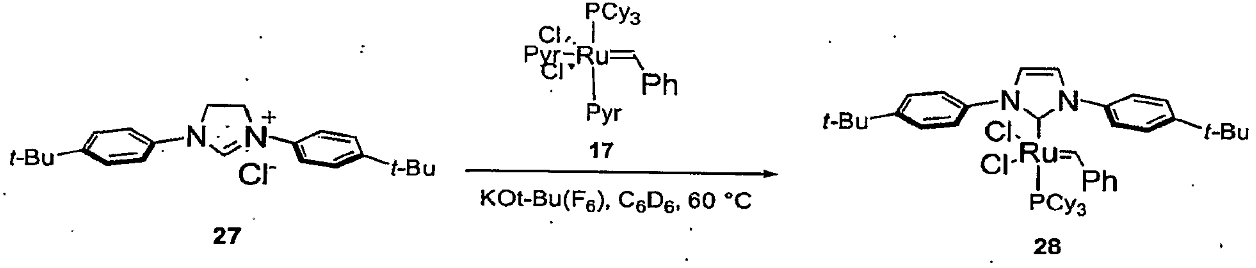
[0129] **Example 17:** Preparation of para-substituted NHC ligand

Reaction scheme 21



[0130] **NHC ligand precursor 27.** Glyoxal (1.92 ml, 16.8 mmol) was added to a solution of 4-tertbutylaniline (5.87 ml, 37 mmol), *i*-PrOH (60 ml) and water (60 ml). The reaction was stirred for 1 hour and then the liquids were decanted off. The remaining sticky solid was washed with *i*-PrOH and then any remaining solvent was removed under vacuum. THF (62 ml) was then added to the flask and it was cooled to 0 °C. $NaBH_4$ (2.57 g, 68 mmol) was added to the solution. Concentrated HCl (2.7 ml) was added dropwise over 0.5 hours, and the reaction was stirred for 2 hours. 4N HCl (150 ml) was added slowly and the reaction was stirred for 0.5 hours, filtered and the filtrate was washed with Et_2O to give a white solid. To this filtrate was added $HC(OEt)_3$ (20 ml) and the reaction was stirred at 100 °C for 18 hours. The reaction was filtered. The filtrate was washed with Et_2O to give **27** as a white solid (80 mg, 1%). ^{1}H NMR (300 MHz, CDCl$_3$) δ 11.35 (br, 1H), 7.89 (br, 4H), 7.38 (br, 4H), 4.44 (br, 4H), 1.15 (s, 18H); ^{13}C (75 MHz, CDCl$_3$) δ 151.1, 150.9, 133.0, 127.3, 118.6, 48.7, 34.8, 31.3; HRMS (EI+) calc for $C_{23}H_{31}N_2$ 335.2487. Found 335.2476.

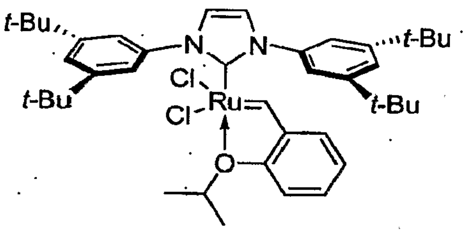
[0131] **Example 18:** Preparation of catalyst **28**



[0132] **Ruthenium Compound 928 (Comparative).** In a glove box, **NHC ligand precursor 27** (5 mg, .014 mmol), ruthenium precursor **17** (10 mg, .014 mmol) and KO*t*-Bu(F$_6$) (3 mg, .014 mmol) were combined in C$_6$D$_6$ in a screw cap NMR tube. The tube was removed from the box and immersed in a 60 °C oil bath. The solution immediately turned brown and a new species (**28**) was transiently observed. ^{1}H NMR (300 MHz, CDCl$_3$) δ 19.46 (d, J = 6 Hz).

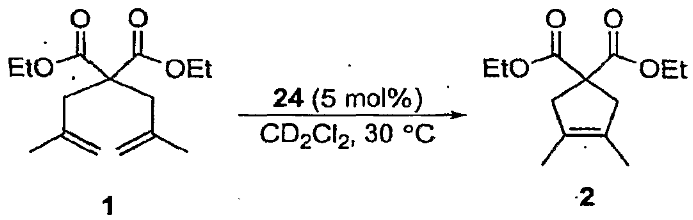
[0133] **Example 19:** Catalyst activity

[0134] Standard activity tests were used to determined the utility of the new catalysts of the invention.



Catalyst 24. **24**

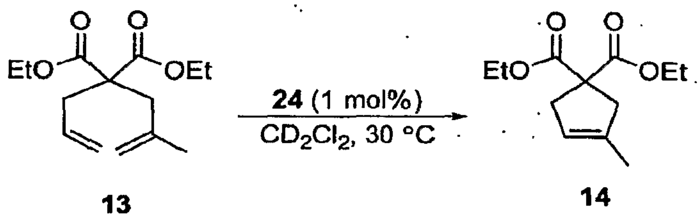
[0135] Preparation of stock solutions. Catalyst **24** (9 mg) was placed in a 2ml volumetric flask and taken into a glove box. In the glove box, 2ml of CD$_2$Cl$_2$ was added to make stock solution **X**. 0.33 ml of **X** was then transferred to another 2ml volumetric flask and diluted to 2ml with CD$_2$Cl$_2$ to make stock solution **W**.



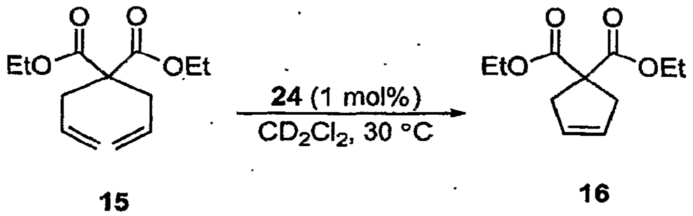
[0136] In a glove box, 0.67 ml of stock solution X (3 mg of **24**, 0.004 mmol) was transferred to a screw cap NMR tube. CD_2Cl_2 (.13 ml) was added and then **1** (21.5 µl, 0.08 mmol). The NMR tube was sealed, removed from the glove box and heated to 30 °C. Fig. 9 shows the graph of conversion over time.

[0137] This experiment was repeated in C_6D_6 at 60 °C to examine the impact of temperature. Catalyst **24** (3 mg, 0.004 mmol) and C_6D_6 (.8 ml) were combined in a screw cap NMR tube and **1** (21.5 µl, 0.08 mmol) was added. The NMR tube was sealed, removed from the glove box and heated to 60 °C. Fig. 10 is a graph of conversion over time in C_6D_6.

[0138] **Example 20:** RCM activity with less hindered olefins.



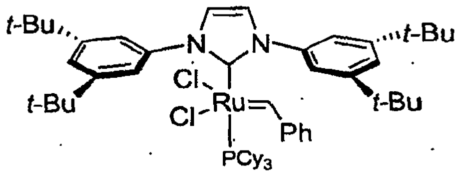
[0139] In a glove box, 0.8 ml of stock solution W (0.6 mg of **24**, 0.0008 mmol) was transferred to a screw cap NMR tube. The NMR tube was sealed and transferred to a 500 MHz NMR which was warmed to 30 °C. The NMR tube was then ejected, **13** (20.5 µl, 0.08 mmol) was added and the tube was injected for data collection. Fig. 11 is a graph of the conversion over time.



[0140] In a glove box, 0.8 ml of stock solution W (0.6 mg of **24**, 0.0008 mmol) was transferred to a screw cap NMR tube. The NMR tube was sealed and transferred to a 500 MHz NMR which was warmed to 30 °C. The NMR tube was then ejected, **15** (19.5 µl, 0.08

mmol) was added and the tube was injected for data collection. Fig. 12 is a graph of the conversion over time.

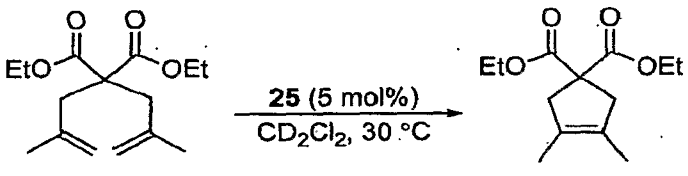
[0141] **Example 21:** Activity studies



Catalyst **25**. **25**

[0142] **Preparation** of stock solutions. Catalyst **25** (11 mg) was placed in a 2ml volumetric flask and taken into a glove box. In the glove box, 2ml of CD_2Cl_2 was added to make stock solution **V**. 0.4 ml of **V** was then transferred to another 2ml volumetric flask and diluted to 2ml with CD_2Cl_2 to make stock solution **U**.

Reaction scheme 25

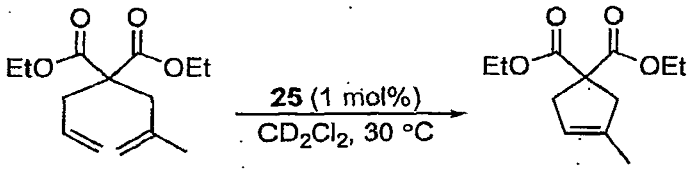


1 **2**

[0143] In a glove box, 0.55 ml of stock solution **V** (3 mg of **25**, 0.003 mmol) was transferred to a screw cap NMR tube. CD_2Cl_2 (.25 ml) was added and then **1** (21.5 µl, 0.08 mmol). The NMR tube was sealed, removed from the glove box and heated to 30 °C. A graph of conversion over time is shown in Fig. 13. No further conversion is observed after 2 hours.

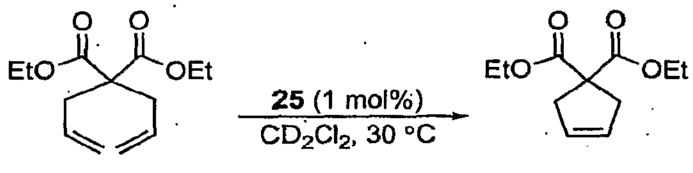
[0144] This experiment was repeated in C_6D_6 at 60 °C to examine the impact of temperature. Catalyst **25** (3 mg, 0.003 mmol) and C_6D_6 (.8 ml) were combined in a screw cap NMR tube and **10** (21.5 µl, 0.08 mmol) was added. The NMR tube was sealed and transferred to a 500 MHz NMR which was warmed to 60 °C. The NMR tube was then ejected, **1** (21.5 µl, 0.08 mmol) was added and the tube was injected for data collection. Fig. 14 is a graph of the conversion over time.

[0145] **Example 22:** Activity studies with less hindered olefins.



13 **14**

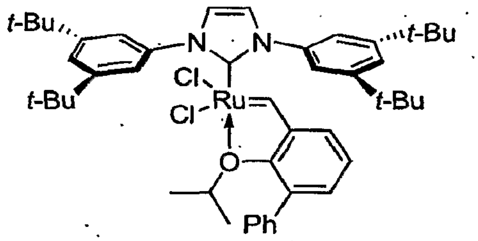
[0146] In a glove box, 0.55 ml of stock solution **U** (0.6 mg of **25**, 0.0008 mmol) was transferred to a screw cap NMR tube and 0.25 ml of CD_2Cl_2 was added. The NMR tube was sealed and transferred to a 500 MHz NMR which was warmed to 30 °C. The NMR tube was then ejected, **13** (20.5 μl, 0.08 mmol) was added and the tube was injected for data collection. Fig. 15 is a graph of the conversion over time.



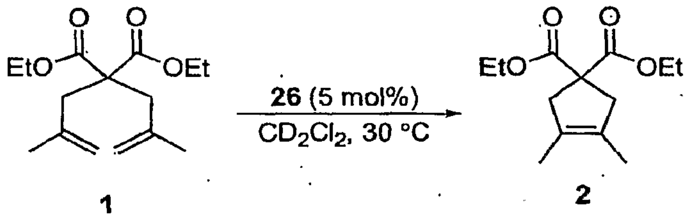
15 **16**

[0147] In a glove box, 0.55 ml of stock solution **U** (0.6 mg of **25**, 0.0008 mmol) was transferred to a screw cap NMR tube and 0.25 ml of CD_2Cl_2 was added. The NMR tube was sealed and transferred to a 500 MHz NMR which was warmed to 30 °C. The NMR tube was then ejected, **15** (19.5 μl, 0.08 mmol) was added and the tube was injected for data collection. Fig. 16 is a graph of the conversion over time.

[0148] **Example 23:** Activity study.

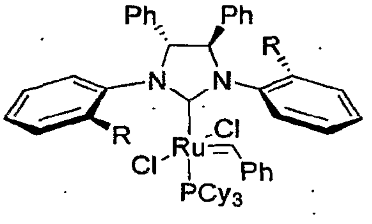


Catalyst **26**. **26**



[0149] In a glove box, catalyst **26** (2 mg, .002 mmol) was combined with CD_2Cl_2 (.4 ml) in a screw cap NMR tube. The NMR tube was sealed and transferred to a 500 MHz NMR which was warmed to 30 °C. The NMR tube was then ejected, **1** (11 μl, 0.04 mmol) was added and the tube was injected for data collection. Fig. 17 is a graph of the conversion over time that illustrates the dramtic decrease in reaction time necessary, relative to catalyst **12**, for catalyst **26** to give 90% conversion of **1** to **2**.

[0150] **Example 24:** Activity of catalysts **6a**, **6c**, **27a** and **27c** in the ring-closing metathesis of dimethyl 2,2-di(2-methylallyl)malonate:



27a (R = Me)
27c (R = i-Pr)

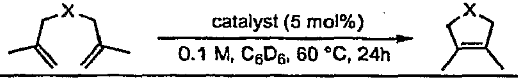
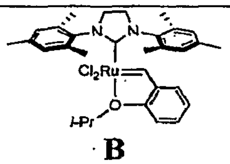
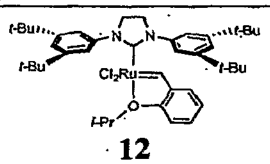
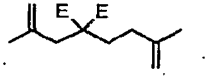
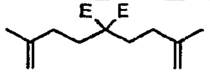
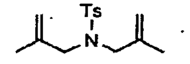
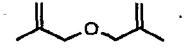
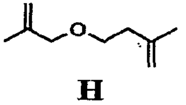
[0151] The procedure used was the same as that described in **Example 3** using catalysts **27a** and **27c**. The results for **6a**, **6c**, **27a** and **27c** are shown in Fig. 18. The results shown in Fig. 18 demonstrate that catalysts **6a** and **6c** perform better than **27a** and **27c** in the ring-closing metathesis of dimethyl 2,2-di(2-methylallyl)malonate. These results indicate that a catalyst based on an NHC ligand that has an unsubstituted bridge between the nitrogen atoms performs better than a catalyst that has phenyl substitutents on each carbons of that same bridge..

[0152] **Example 25:** Ring-closing metathesis of dimethyl 2,2-di(2-methylallyl)malonate using 5 mol % of catalysts **6a** and **7a** in toluene at 40 °C and 60 °C:

[0153] A procedure analogous to that described in **Example 3** was used, except that methylene chloride was replaced with toluene. The results are shown in Figure 19.

[0154] **Example 26:** Catalyst **12** and catalyst **B** were compared under identical reaction conditions for the production of tetrasubstituted olefins by RCM. The reactions were performed with 0.08 mmol of substrate, 0.004 mmol of catalyst, 0.8 ml of C_6D_6 at 60 °C. A comparison table follows.

Table 15. RCM to form tetrasubstituted olefins. NR = no reaction.

		
Substrate (E =CO_2Et)	**Conversions (isolated yields) with catalysts**	
	 **B**	 **12**
 **C**	30	93 (86)
 **D**	>95	>95 (99)
 **E**	50	51 (47)
 **F**	85	>95 (99)
 **G**	>95	>95
 **H**	43[1]	78[2]

[1] 75% consumption of **H**.

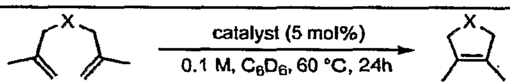
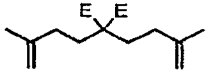
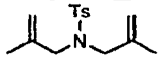
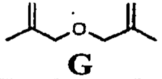
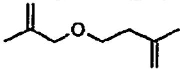
[2] 10% 2,6-dichlorobenzoquinone added. Without 2,6-dichlorobenzoquinone: 60% conversion to product, 95% consumption of **H**.

[0155] Two of these substrates, **D** and **G**, were completely converted to product with both catalysts. Catalyst **12** gave improved conversion relative to catalyst **B** for every other substrate except **E**. Substrate **H** warrants further discussion. Use of catalyst **B** gave a mixture of three compounds, with 43% conversion to product, 32% conversion to a rearranged byproduct and 25% remaining starting material (**H**). Use of catalyst **12** resulted in complete consumption of **H**, but with only 60% conversion to product and 40% conversion to the byproduct. Interestingly, catalyst **10** gave 43% conversion to the product and no byproduct formation. Ruthenium hydride species formed from the decomposition of ruthenium olefin metathesis catalysts are known to catalyze the migration of olefins at 40 °C in CD_2Cl_2. Hong, S. H.; Day, M. W.; Grubbs, R. H. *J. Am. Chem. Soc.* **2004**, *126*, 7414. Repeating the reactions using **B** and **12** with 10% 2,6-dichloroquinone added to consume any hydride formed, (Hong, S. H.; Sanders, D. P.; Lee, C. W.; Grubbs, R. H. *J. Am. Chem. Soc.* **2005**, *127*, 17160) catalyst **B** gave very poor conversion, but catalyst **12** gave 78% conversion to product with no byproduct formation. Overall, catalyst **12** performed as well as or better than **B** for all of the substrates.

[0156] **Example 26:** Comparison of catalysts **A, 12** and **7a** in different ring-closing metathesis reactions to form tetrasubstituted olefins.

[0157] A procedure similar to that described in **Example 8** was used to set up the ring-closing metathesis reactions and to follow their progress. The results are summarized in Table 16.

Table 16. RCM to form tetrasubstituted olefins (E = CO_2Et; Ts = tosyl). NR = no reaction.

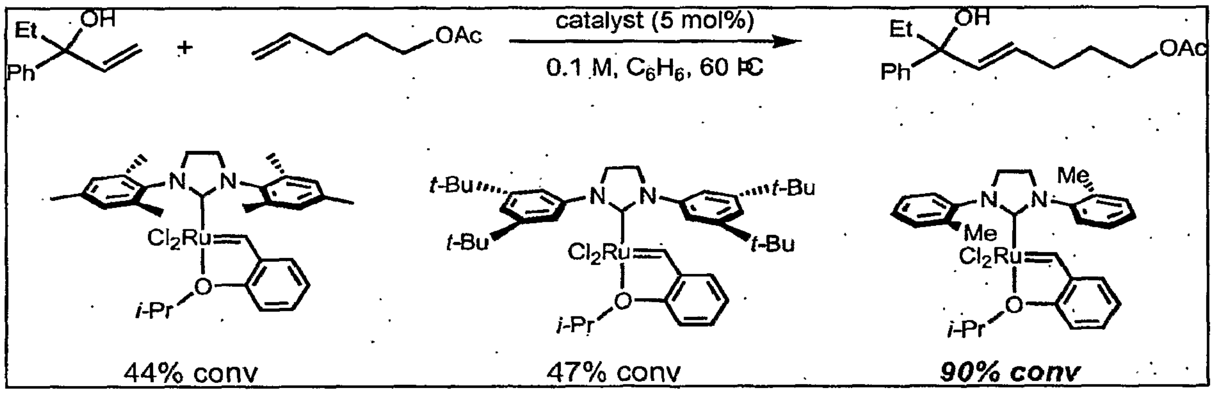
			
	Conversions (isolated yields) [%] with catalysts C848, 12, and 7a		
Substrate	**A**	**12**	**7a**
 **C**	30	93 (86)	> 95
 **D**	>95	>95 (99)	> 95
 **E**	50	51 (47)	62
 **F**	85	>95 (99)	> 95
 **G**	>95	>95	> 95
 **H**	43^{a}	78^{b}	88

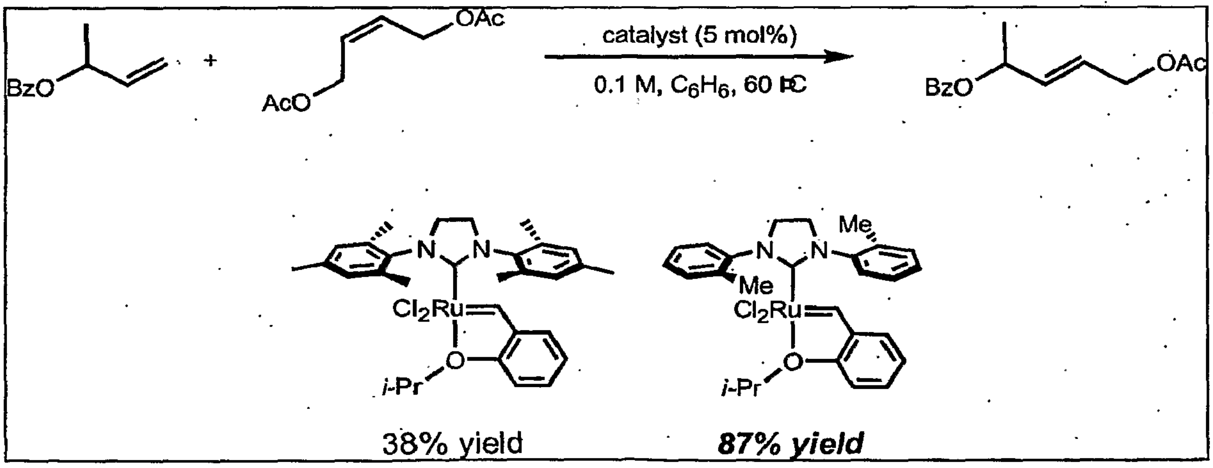
[a] 75% consumption of **17**.

[b]10% 2,6-dichlorobenzoquinone added. Without 2,6-dichlorobenzoquinone: 60% conversion to product, 95% consumption of **17**.

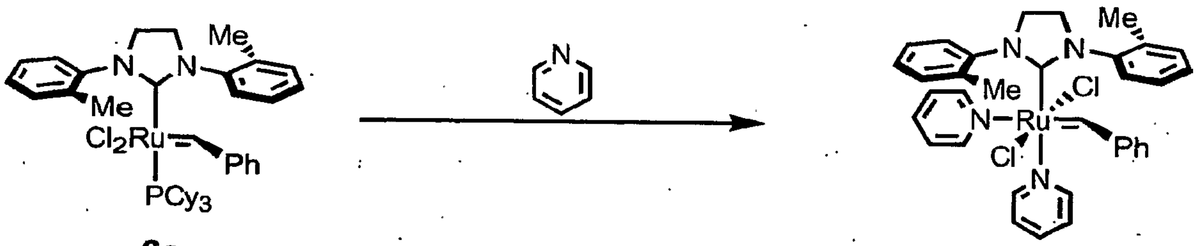
[0158] **Example 27:** Cross Metathesis (CM) Results with Catalyst **7a**

[0159] **General procedure for CM reactions.** A reflux condenser was attached to a flame-dried 10 mL 2-neck round bottom flask and the apparatus was flushed with argon. The flask was charged with solid catalyst and a stir bar. The second neck was closed with a septum, and dry, degassed C_6H_6 (2.5 mL) was added via syringe. The reagents were then added simultaneously via syringe. The solution was heated to 60 °C using an oil bath, and was stirred under argon for 18 h. The solution was then cooled to room temperature and concentrated. Conversions were measured by ^{1}H NMR of this crude reaction mixture, and yields determined by isolating the desired products by silica gel column chromatography.





[0160] **Example 28:** Preparation of bis(pyridine) catalyst **28**.



6a

[0161] In a nitrogen-filled glove box, pyridine (3.0 mL) was added to catalyst **6a** (0.1 g, 0.126 mmol) and the solution was stirred until all of **6a** had dissolved. The desired product was isolated by precipitation with pentane (0.070 g, 0.104 mmol, 83 % yield). Green crystalline solid. ^{1}H NMR (300 MHz, C_6D_6): δ 19.30 (s), 9.51 (d), 8.53 (m), 7.92 (d), 7.25-7.05 (m), 7.00-6.77 (m), 6.64 (m), 6.51 (t), 6.22 (t), 3.08-3.64 (m), 2.49 (s), 2.31 (s).

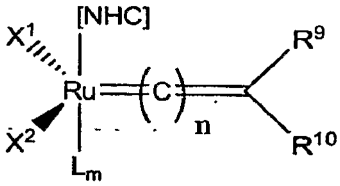
[0162] **Example 29: Ring-closing metathesis reactions using catalysts 6a and 7a.**

[0163] The ring-closing reactions described in Example 22 were repeated using catalysts 6a and 7a with of substrates **13** and **15** to form the corresponding di- and tri-substituted olefins. The results are shown in Figs. 20 -23. Fig. 20 is a graph of the conversion of **15** over time for the RCM reaction for catalyst **6a**. Fig. 21 is a graph of the conversion of **13** over time for the RCM reaction for catalyst **6a**. Fig. 22 is a graph of the conversion of **15** over time for the RCM reaction for catalyst **7a**. Fig. 23 is a graph of the conversion of **13** over time for the RCM reaction for catalyst **7a**.

The claimed invention is:

1. A ruthenium alkylidene complex having an *N*-heterocyclic carbene ligand comprising a 5-membered heterocyclic ring having a carbenic carbon atom and at least one nitrogen atom contained within the 5-membered heterocyclic ring, wherein the nitrogen atom is directly attached to the carbenic carbon atom and is substituted by a phenyl ring, and wherein the phenyl ring has a hydrogen at either or both ortho positions and is substituted at at least one ortho or meta position.

2. An *N*-heterocyclic carbene (NHC) ruthenium olefin metathesis catalyst of formula (I):



(I)

wherein:

X^1 and X^2 are independently anionic ligands;.

n is 0, 1 or 2;

R^9 and R^{10} are each independently hydrogen or a substituted or unsubstituted substituent selected from the group consisting of C_1-C_{20} alkyl, C_2-C_{20} alkenyl, C_2-C_{20} alkynyl, aryl, C_1-C_{20} carboxylate, C_1-C_{20} alkoxy, C_2-C_{20} alkenyloxy, C_2-C_{20} alkynyloxy, aryloxy, C_2-C_{20} alkoxycarbonyl, C_1-C_{20} alkylthio, C_1-C_{20} 20 alkylsulfonyl and C_1-C_{20} alkylsulfinyl; or R^9 and R^{10} may optionally be linked together to form a cyclic structure via one of the listed substituents;

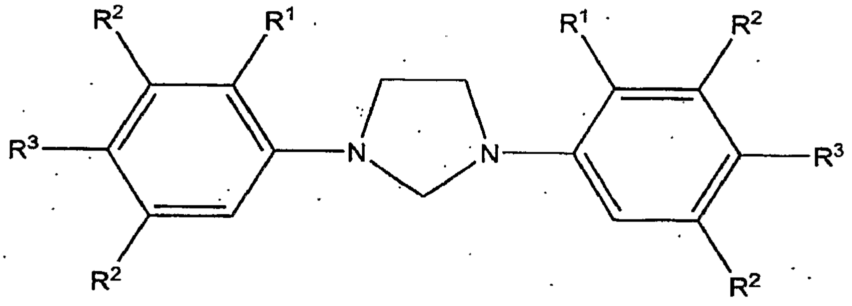
m is 1 or 2;

when m is 1, L is a neutral 2-electron donor ligand and may optionally be linked to R^{10} forming a chelating carbene ligand when n is zero;

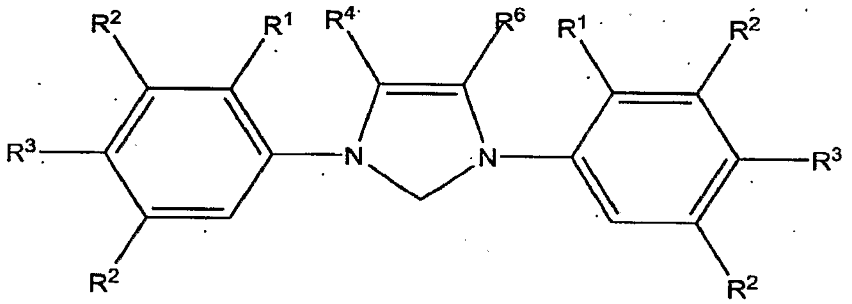
when m is 2, L is a heteroarene ligand; and

NHC is an *N*-heterocyclic carbene ligand comprising a 5-membered heterocyclic ring having a carbenic carbon atom and at least one nitrogen atom contained within the 5-membered heterocyclic ring, wherein the nitrogen atom is directly attached to the carbenic carbon atom and is substituted by a phenyl ring, and wherein the phenyl ring has a hydrogen at either or both ortho positions and is substituted at at least one ortho or meta position.

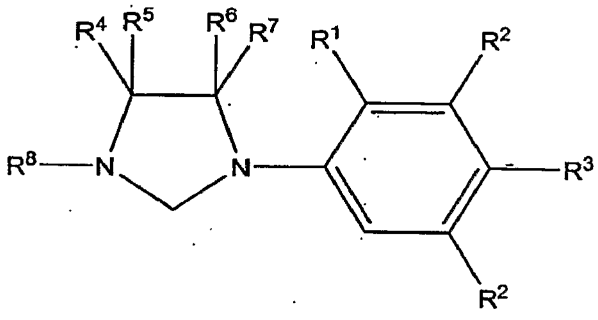
3. An *N*-heterocyclic carbene (NHC) ruthenium olefin metathesis catalyst according to claim 2, wherein the NHC ligand is selected from a ligand of formula of formulas (II)-(V):



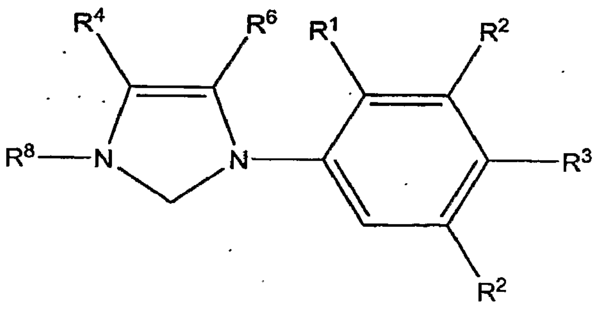
(II)



(III)



(IV)



(V)

wherein

R^1, R^2, and R^3 are either:

a) each R^1 is independently a primary or secondary C_1-C_4 alkyl group; each R^2 is independently H, a substituted or unsubstituted C_1-C_{10} alkyl group, substituted or unsubstituted phenyl, substituted or unsubstituted naphthyl, or substituted or unsubstituted anthracenyl; and each R^3 is independently H, a substituted or unsubstituted C_1-C_8 alkyl group, substituted or unsubstituted phenyl, substituted or unsubstituted naphthyl, or substituted or unsubstituted anthracenyl, or a functional group selected from the group consisting of halo, hydroxyl, sulfhydryl, cyano, cyanato, thiocyanato, amino, nitro, nitroso, sulfo, sulfonato, boryl, borono, phosphono, phosphonato, phosphinato, phospho, phosphino, and silyloxy; or

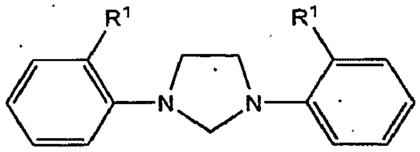
b) R^1 is H; each R^2 is independently H, a substituted or unsubstituted C_1-C_8 alkyl group, substituted or unsubstituted phenyl, substituted or unsubstituted naphthyl, or substituted or unsubstituted anthracenyl; and each R^3 is independently H, a substituted or unsubstituted C_1-C_8 alkyl group, substituted or unsubstituted phenyl, substituted or unsubstituted naphthyl, or substituted or unsubstituted anthracenyl or a functional group selected from the group consisting of halo, hydroxyl, sulfhydryl, cyano, cyanato, thiocyanato, amino, nitro, nitroso, sulfo, sulfonato, boryl, borono, phosphono, phosphonato, phosphinato, phospho, phosphino, and silyloxy; with the provisos that both R^2 substituents on the same phenyl ring are not H.

R^4 and R^6 are each independently H, a substituted or unsubstituted C_1-C_8 alkyl group, substituted or unsubstituted aryl, or in formulas (III) and (V) together with the carbons carrying them form a substituted or unsubstituted, fused 4-8 membered carbocylic ring or a substituted or unsubstituted, fused aromatic ring;

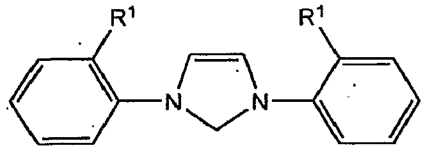
R^5 and R^7 are independently H, a substituted or unsubstituted C_1-C_8 alkyl group; and

R^8 is a C_1-C_{12} alkyl or a C_3-C_{12} cycloalkyl.

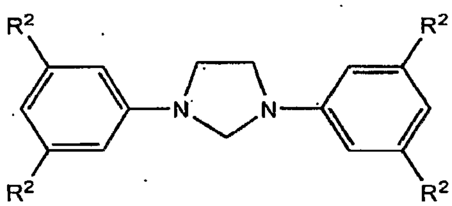
4. An *N*-heterocyclic carbene (NHC) ruthenium olefin metathesis catalyst according to claim 3, wherein the NHC ligand is selected from the group consisting of



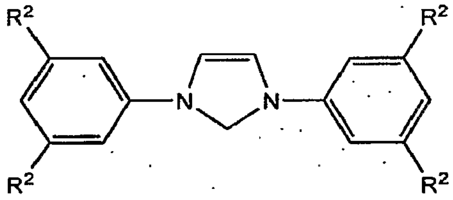
where $R^1$is methyl, ethyl, propyl, or isopropyl;



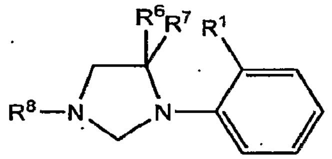
where R^1 ismethyl, ethyl, propyl, or isopropyl;



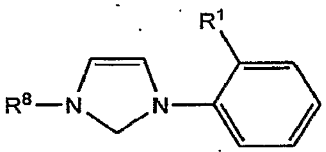
where R^2 is tert-butyl;



where R^2 is tert-butyl;



and



where R^1 is methyl, ethyl, propyl,or isopropyl; R^6 and R^7 are hydrogen or methyl; and R^8 is methyl;

where R^1 is methyl, ethyl, propyl, or isopropyl; and R^8 is methyl.

5. An *N*-heterocyclic carbene (NHC) ruthenium olefin metathesis catalyst according to claim 2, 3, or 4, wherein:

X^1 and X^2 are halide, or a substituted or unsubstituted group selected from the group consisting of benzoate, C_1-C_5 carboxylate, C_1-C_5 alkyl, phenoxy, C_1-C_5 alkoxy, C_1-C_5 alkylthio, aryl, and C_1-C_5 alkyl sulfonate;

n is 0 or 1;

R^9 is hydrogen, C_1-C_5 alkyl or aryl;

R^{10} is a substituted or unsubstituted group selected from the group consisting of C_1-C_{20} alkyl, C_2-C_{20} alkenyl, and aryl;

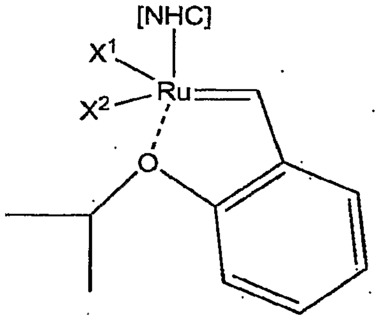
m is 1; and

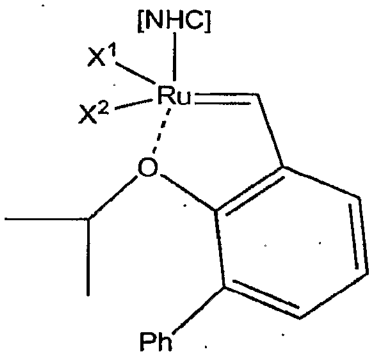
L is selected from the group consisting of phosphine, sulfonated phosphine, phosphite, phosphinite, phosphonite, arsine, stibine, ether, amine, amide, imine, sulfoxide, carboxyl, nitrosyl, pyridine, and thioether, or is linked to R^{10} forming a chelating carbene ligand when n is 0.

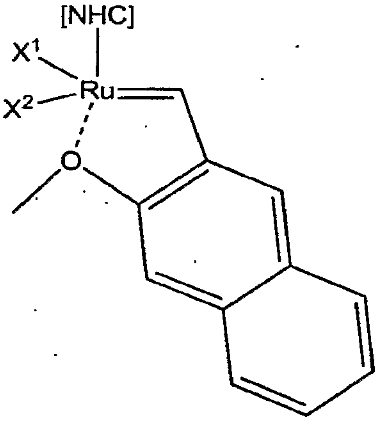
6. An *N*-heterocyclic carbene (NHC) ruthenium olefin metathesis catalyst according to claim 5, wherein:
X^1 and X^2 are each halide, CF_3CO_2, CH_3,CO_2, CFH_2CO_2, $(CH_3)_3CO$, $(CF_3)_2(CH_3)CO$, $(CF_3)(CH_3)_2CO$, PhO, MeO, EtO, tosylate, mesylate, or trifluoromethanesulfonate;
n is 0 or 1;
R^9 is hydrogen, C_1-C_5 alkyl or aryl;
R^{10} is a substituted or unsubstituted group selected from the group consisting of C_1-C_{20} alkyl, C_2-C_{20} alkenyl, and aryl;
m is 1; and
L is a phosphine of the formula PR'R''R''', where R', R'', and R''' are each independently aryl, C_1-C_{10} alkyl, or C_3-C_6 cycloalkyl, or is linked to R^{10} forming a chelating carbene ligand when n is 0.

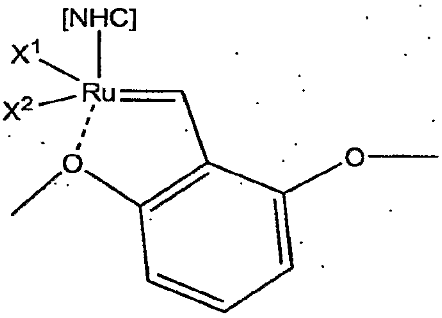
7. An *N*-heterocyclic carbene (NHC) ruthenium olefin metathesis catalyst according to claim 6, wherein:
X^1 and X^2 are each chloride,
n is 0;
R^9 is hydrogen;
R^{10} is phenyl, vinyl or $-C=C(CH_3)_2$;
m is 1; and
L is selected from the group consisting of $P(cyclohexyl)_3$, $P(cyclopentyl)_3$, $P(isopropyl)_3$, and $P(phenyl)_3$, or is linked to R^{10} forming a chelating carbene ligand.

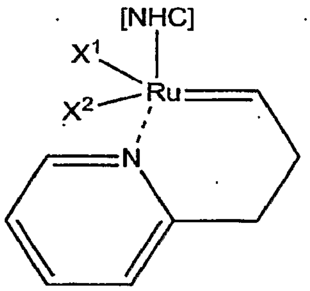
8. An *N*-heterocyclic carbene (NHC) ruthenium olefin metathesis catalyst according to claim 7, wherein the catalyst of formula (I) is selected from the group consisting of:

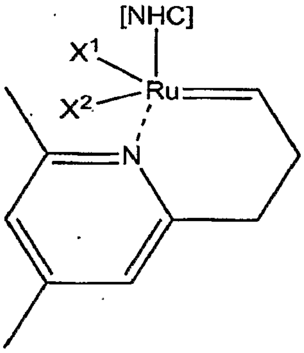












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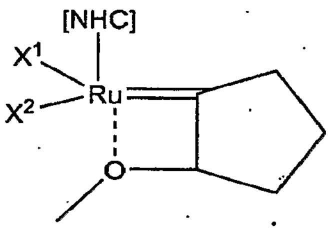
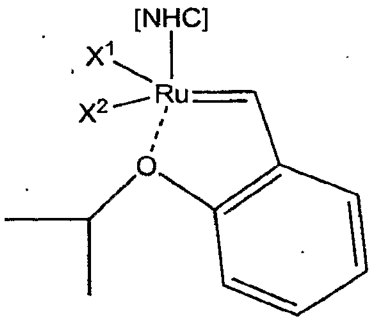
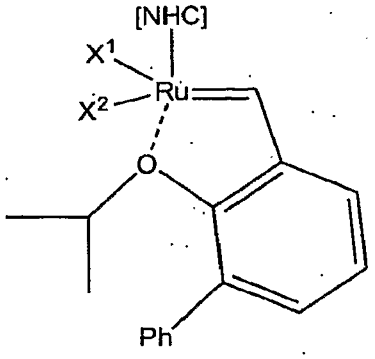
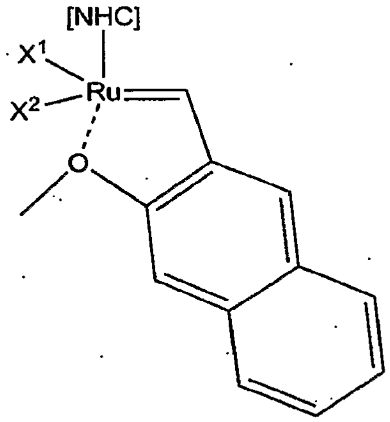
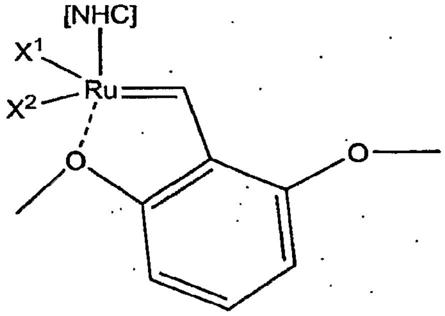


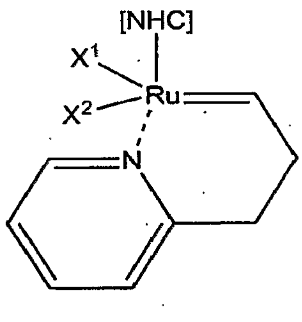
9. An *N*-heterocyclic carbene (NHC) ruthenium olefin metathesis catalyst according to claim 5, wherein the catalyst of formula (I) is selected from the group consisting of:

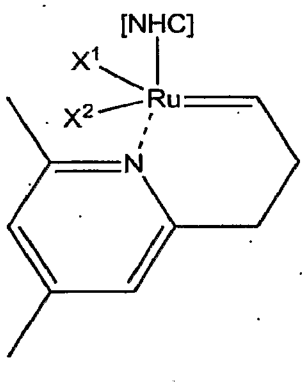












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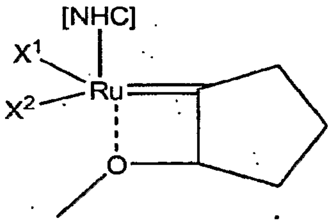


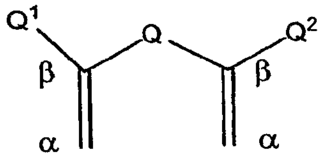
10. An *N*-heterocyclic carbene (NHC) ruthenium olefin metathesis catalyst according to claim 7, wherein L is selected from the group consisting of P(cyclohexyl)$_3$, P(cyclopentyl)$_3$, P(isopropyl)$_3$, and P(phenyl)$_3$.

11. An *N*-heterocyclic carbene (NHC) ruthenium olefin metathesis catalyst according to claim 5, wherein L is selected from the group consisting of P(cyclohexyl)$_3$, P(cyclopentyl)$_3$, P(isopropyl)$_3$, and P(phenyl)$_3$.

12. A ring-closing metathesis method for preparing a tetrasubstituted cyclic olefin comprising the step of:

contacting an olefinic compound having at least two terminal olefins which are substituted at the beta-carbon of each terminal olefin with an *N*-heterocyclic carbene (NHC) ruthenium olefin metathesis catalyst of claims 1, 2, 3, or 4 under metathesis conditions to form a cyclic tetra-substituted olefin.

13. A ring-closing metathesis reaction of claim 12 wherein the olefinic compound is a compound of formula (VI):



(VI).

wherein

Q is selected from the group consisting of hydrocarbylene, substituted hydrocarbylene, heteroatom-containing hydrocarbylene, and substituted heteroatom-containing hydrocarbylene; and

Q^1 and Q^2 are independently selected from the group consisting of hydrocarbyl, substituted hydrocarbyl, heteroatom-containing hydrocarbyl, substituted heteroatom-containing hydrocarbyl, halide, hydroxyl, sulfhydryl, cyano, cyanato, thiocyanato, amino, nitro, nitroso, sulfo, sulfonato, boryl, borono, phosphono, phosphonato, phosphinato, phospho, phosphino, and silyloxy, wherein the substituted hydrocarbyl and substituted heteroatom-containing hydrocarbyl are substituted with at least one member selected from the group consisting of alkyl, aryl, halide, hydroxyl, sulfhydryl, cyano, cyanato, thiocyanato, amino, nitro, nitroso, sulfo, sulfonato, boryl, borono, phosphono, phosphonato, phosphinato, phospho, phosphino, and silyloxy.

14. The method of claim 12 wherein the catalyst is present in an amount ranging from about 1 to about 10 mol%.

15. An olefin metathesis reaction comprising the step of:

contacting an olefin with an *N*-heterocyclic carbene (NHC) ruthenium olefin metathesis catalyst according to claim 1, 2, 3, or 4 under metathesis conditions.

16. A cross-metathesis reaction comprising the step of contacting an olefin and a tri-substituted olefin or a di-substituted olefin having further substitution at the allylic carbon with an *N*-heterocyclic carbene (NHC) ruthenium olefin metathesis catalyst according to claim which claims 1, 2, 3, or 4 under metathesis conditions.

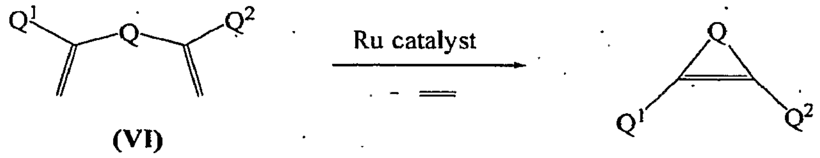


Figure 1

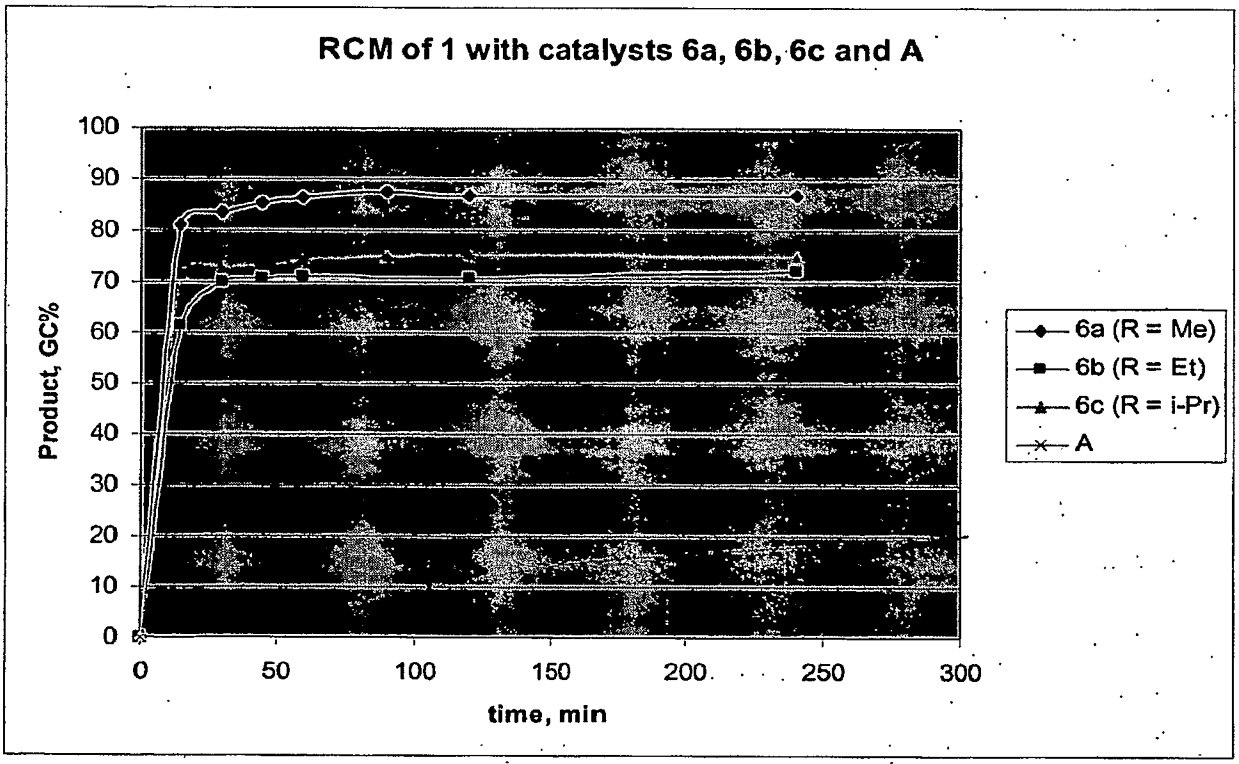


Figure 2

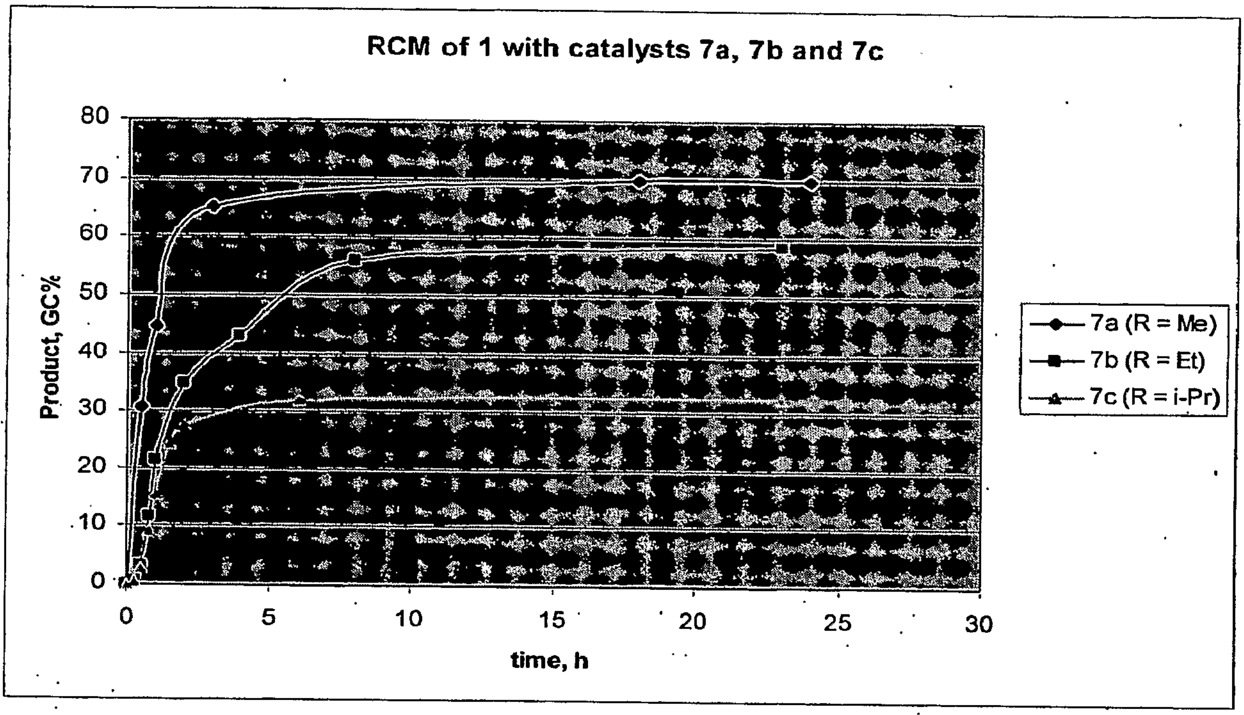


Figure 3

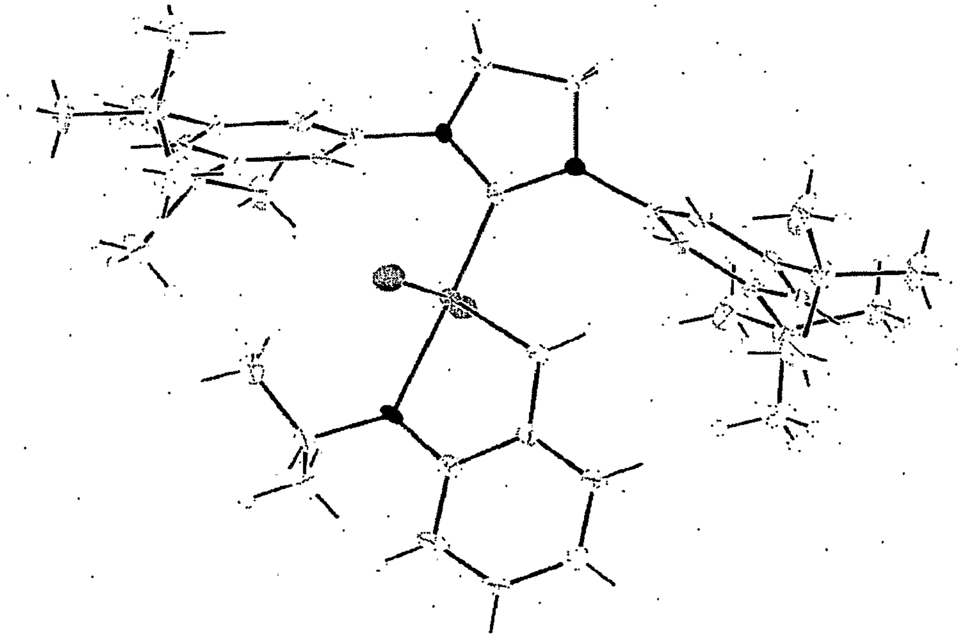


Figure 4

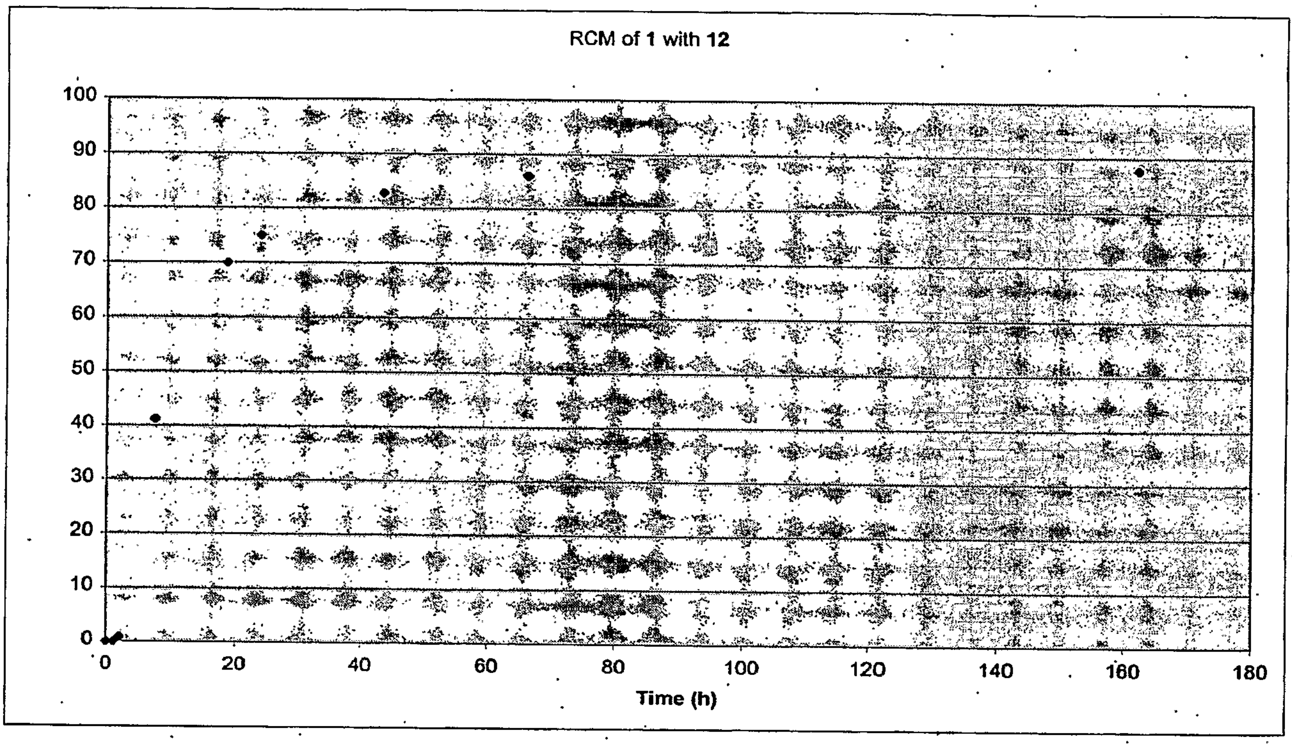


Figure 5

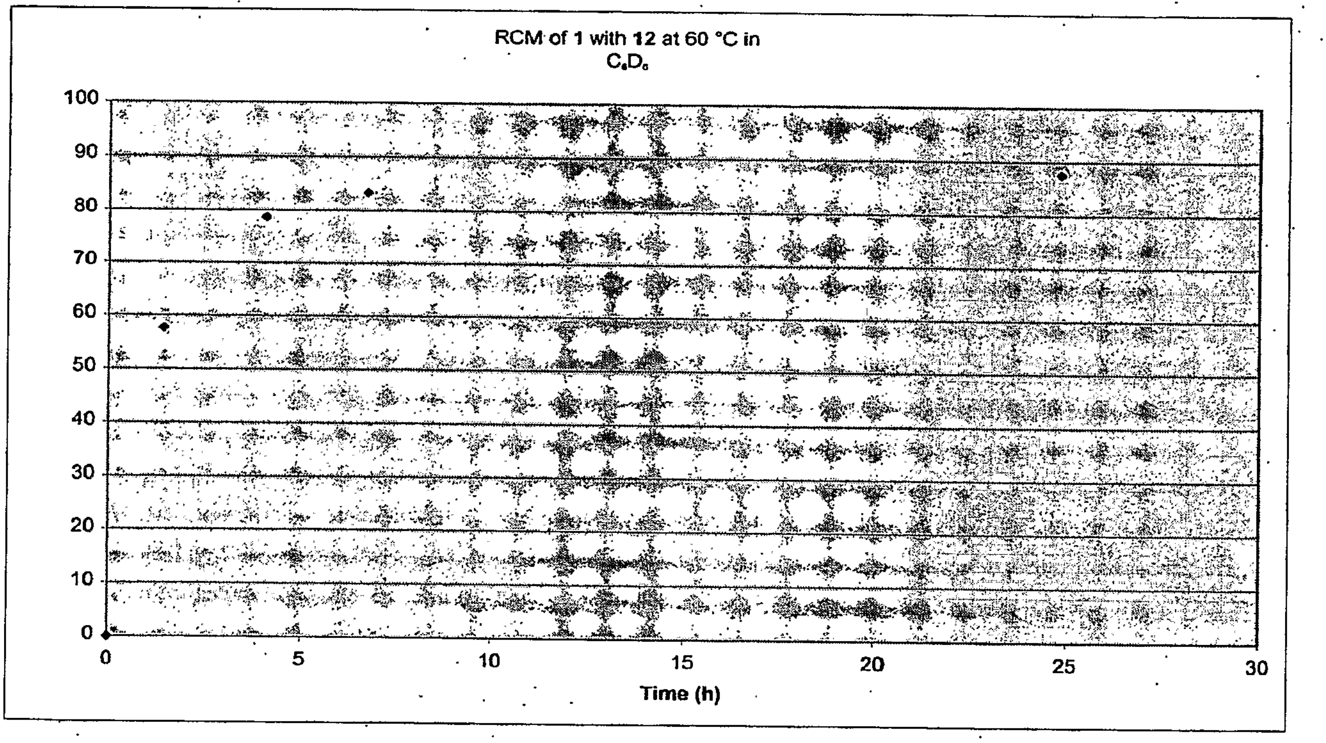


Figure 6

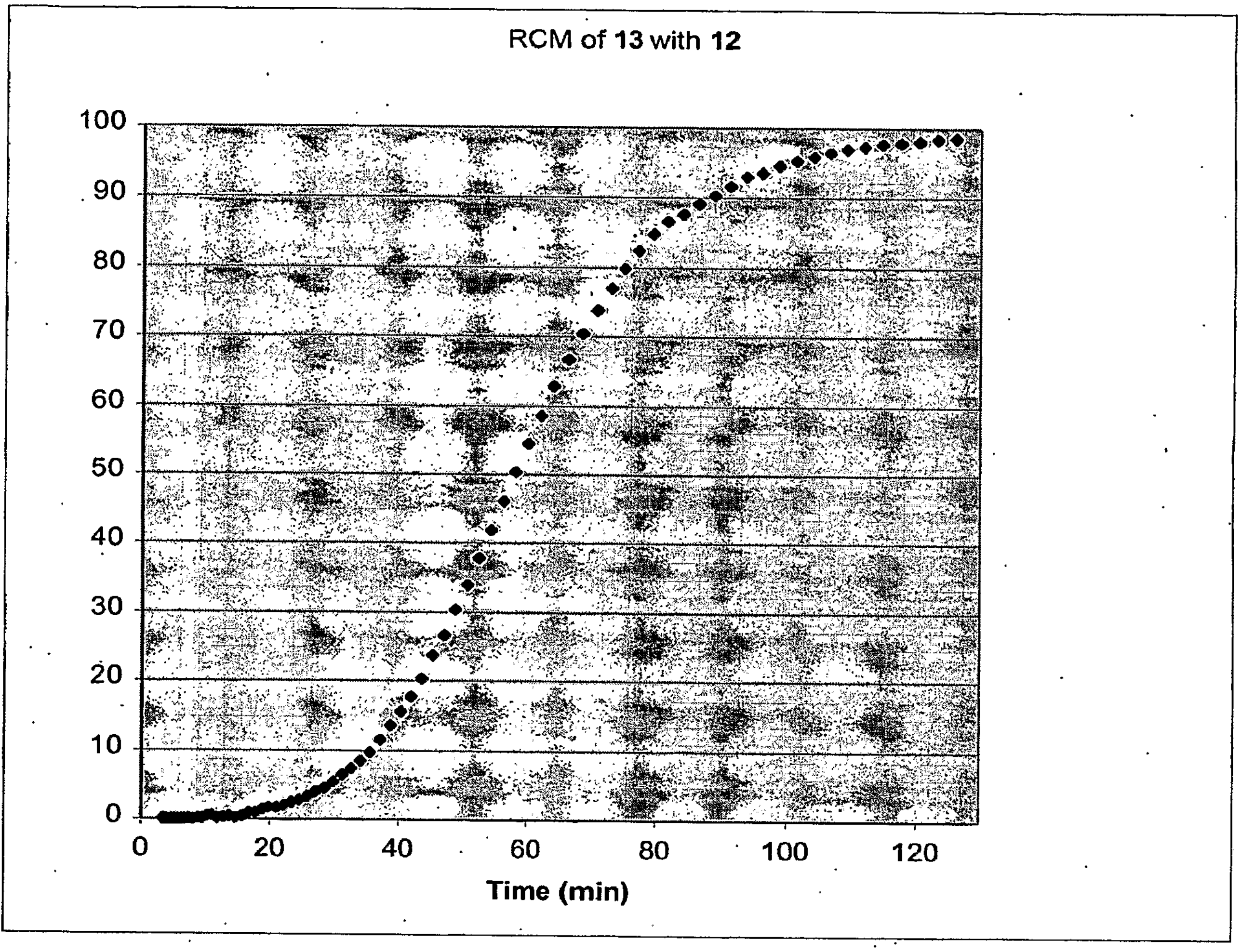

RCM of **13** with **12**
100
90
80
70
60
50
40
30
20
10
0
0
20
40
60
80
100
120
Time (min)

Figure 7

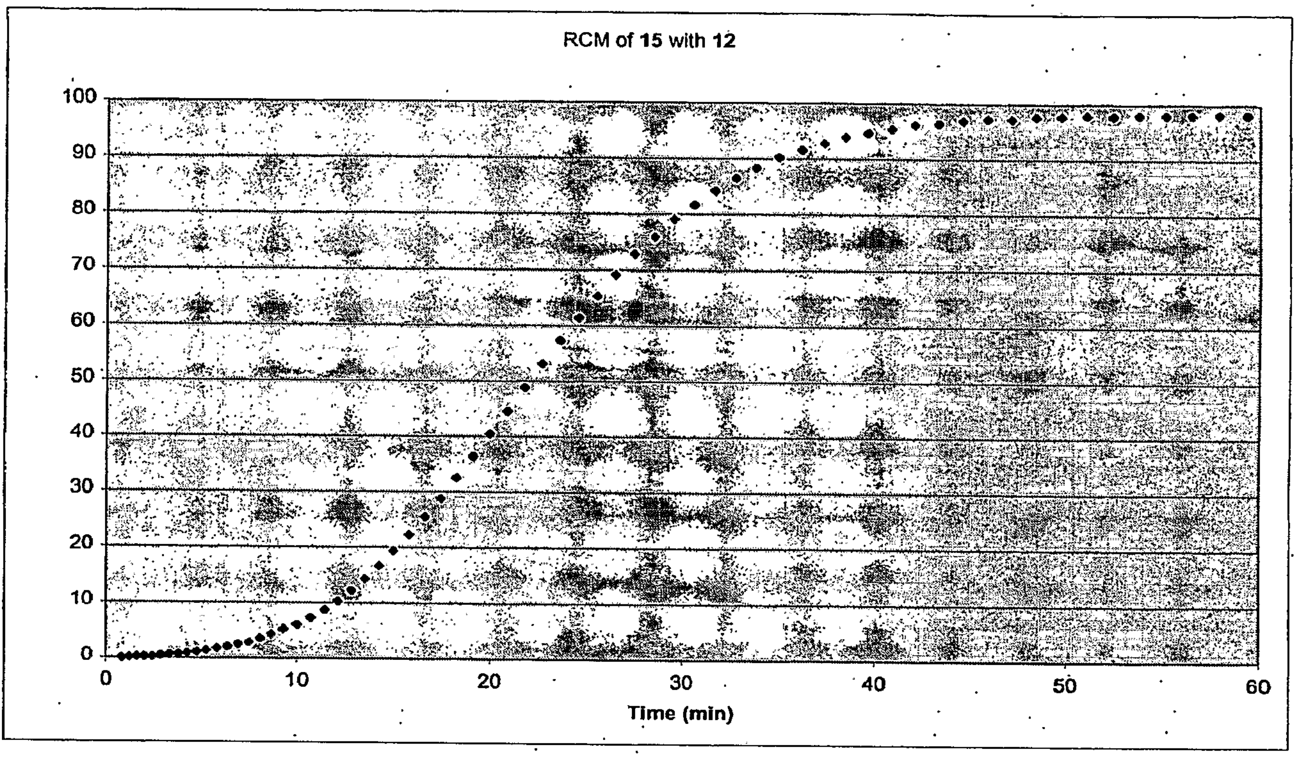


Figure 8

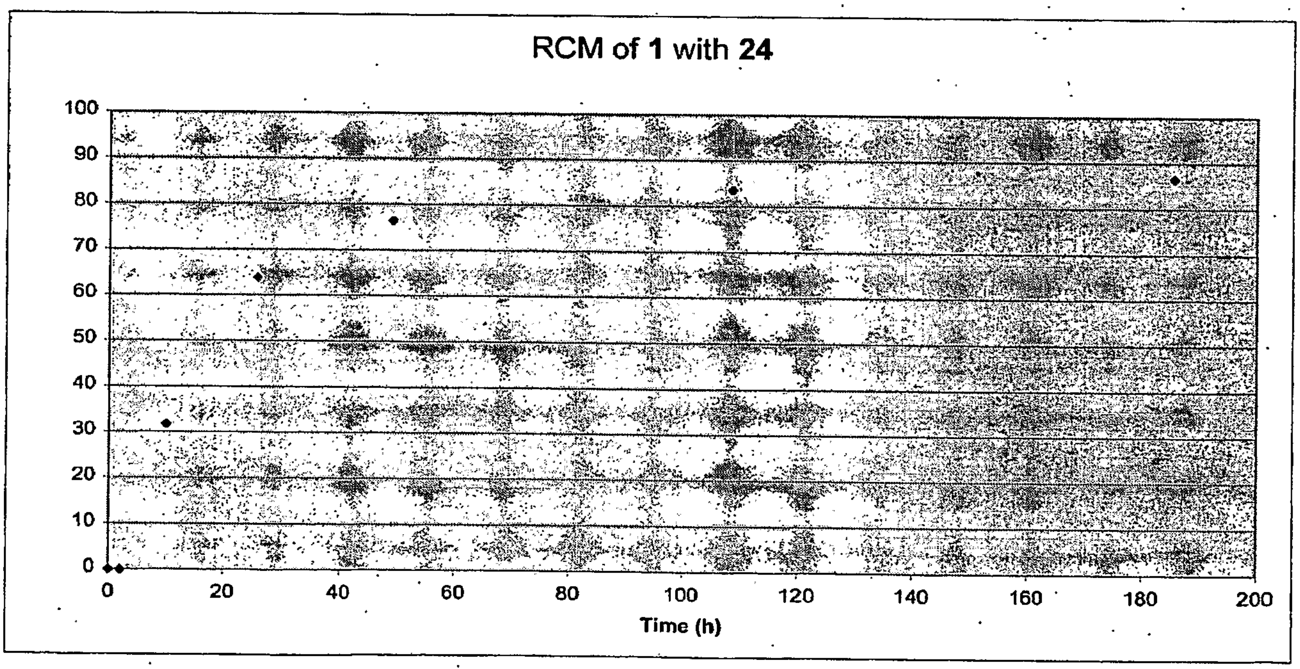
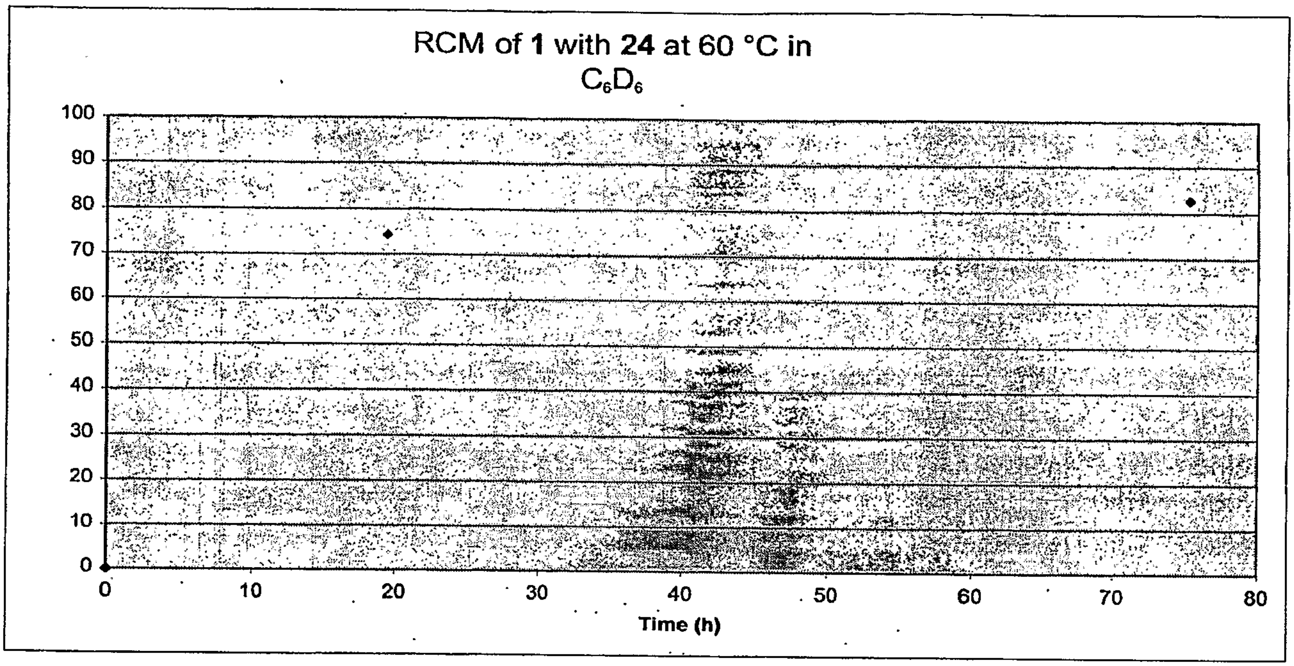


Figure 9



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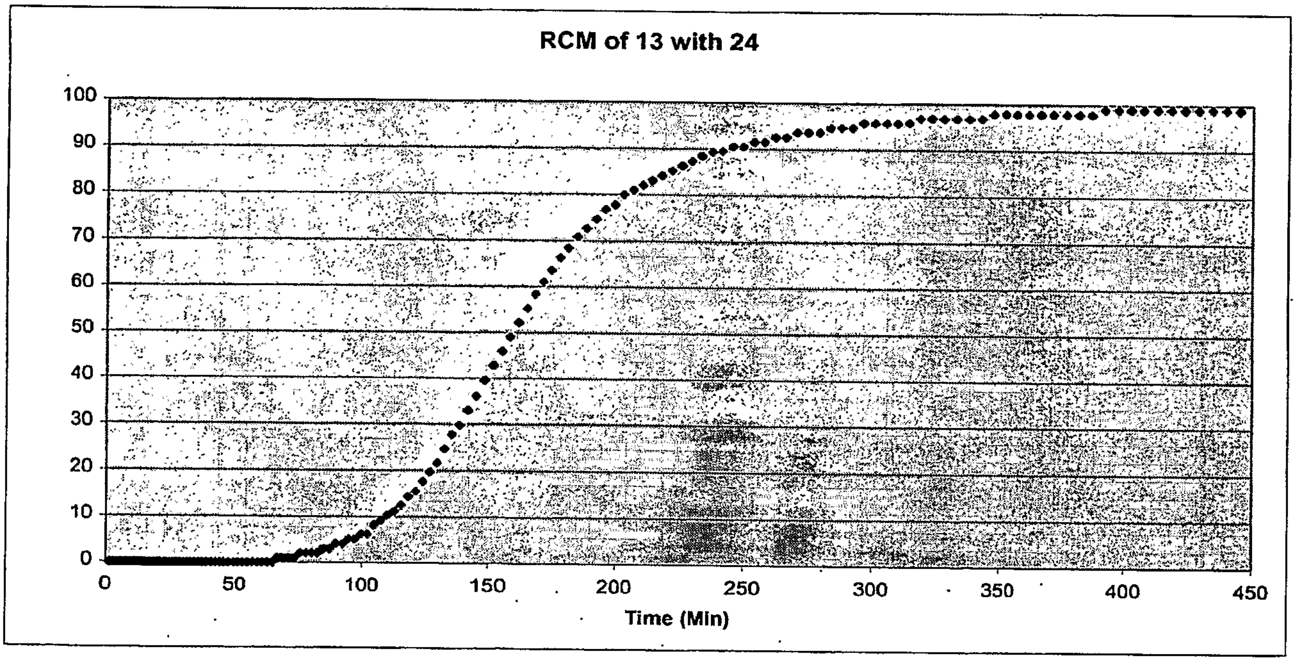

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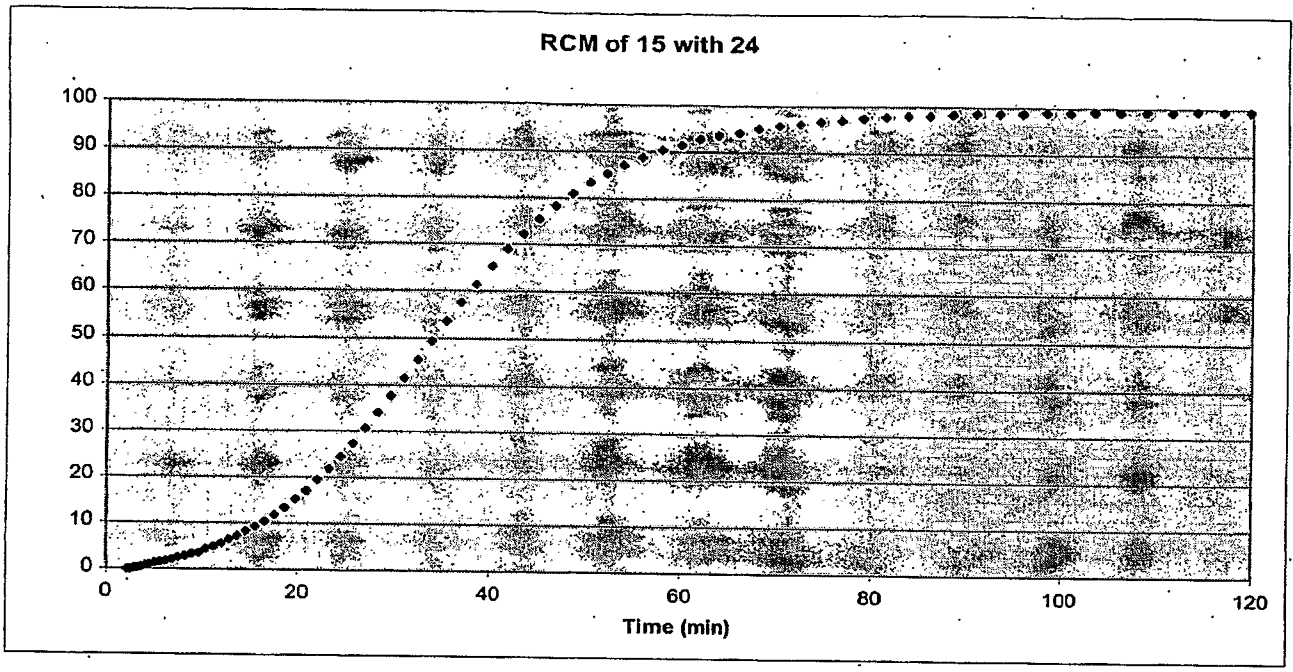

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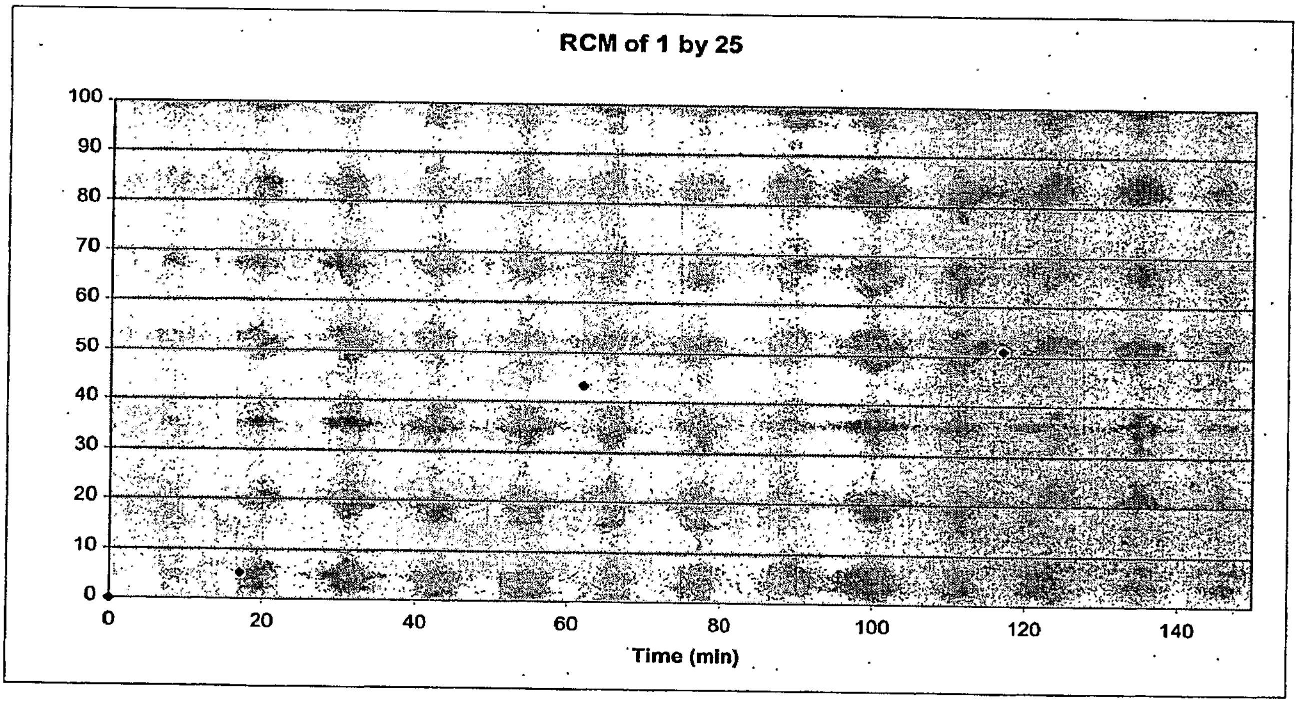
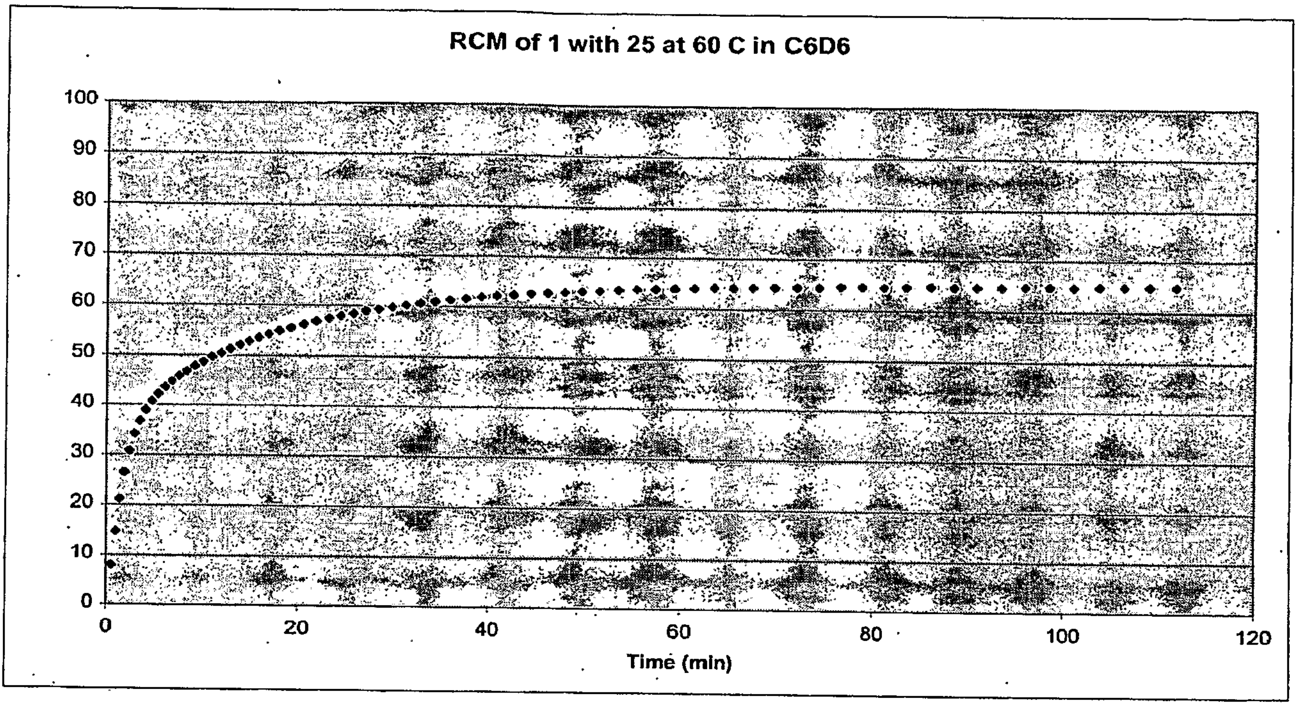


Figure 13



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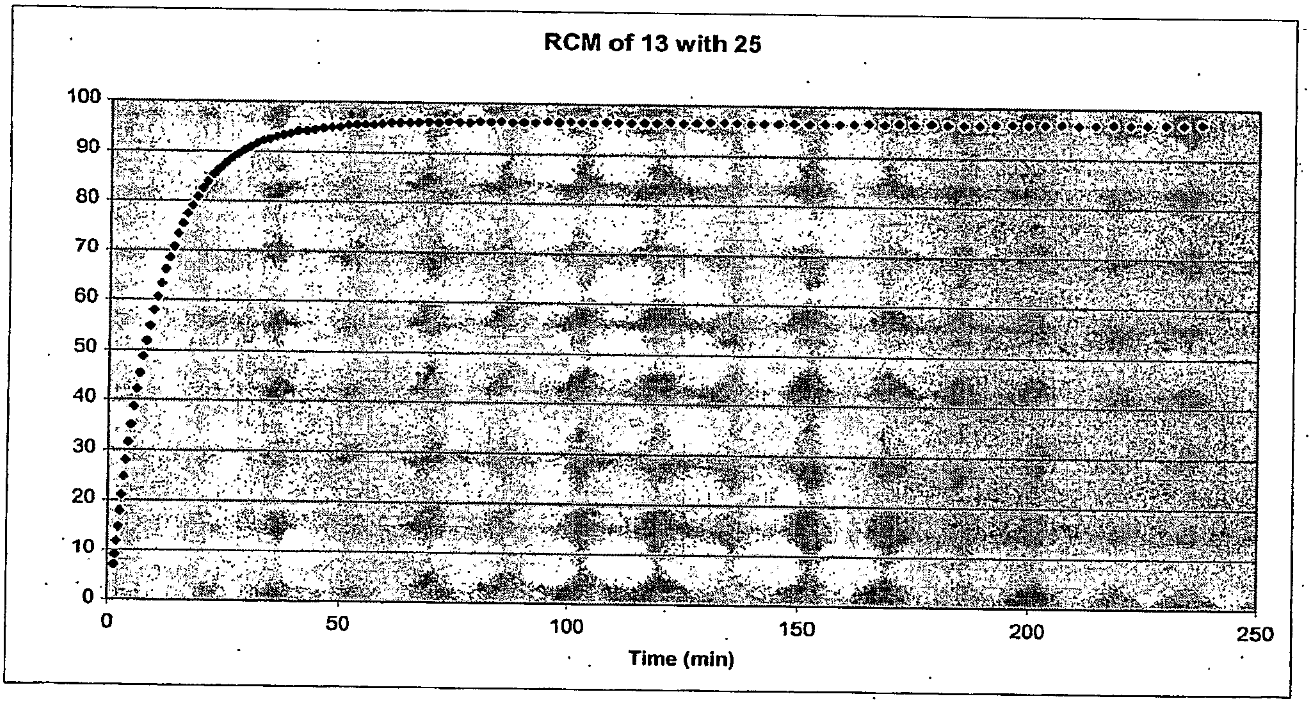

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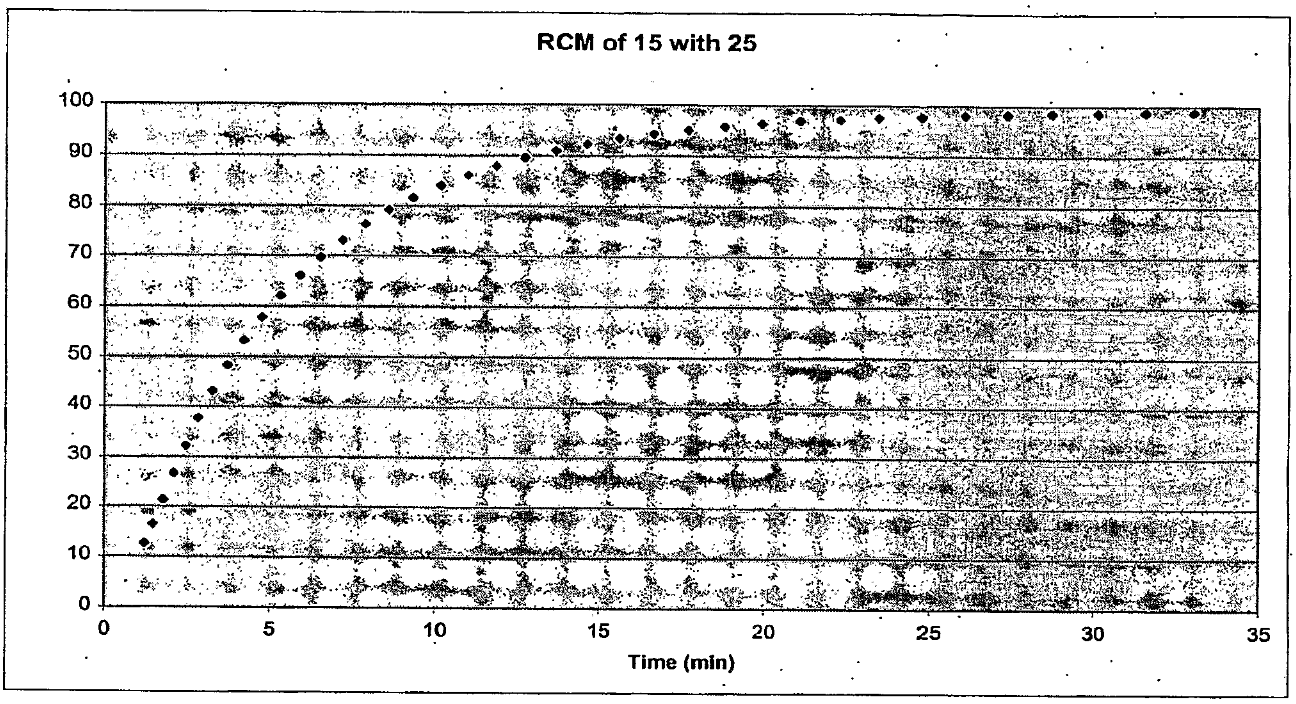


Figure 16

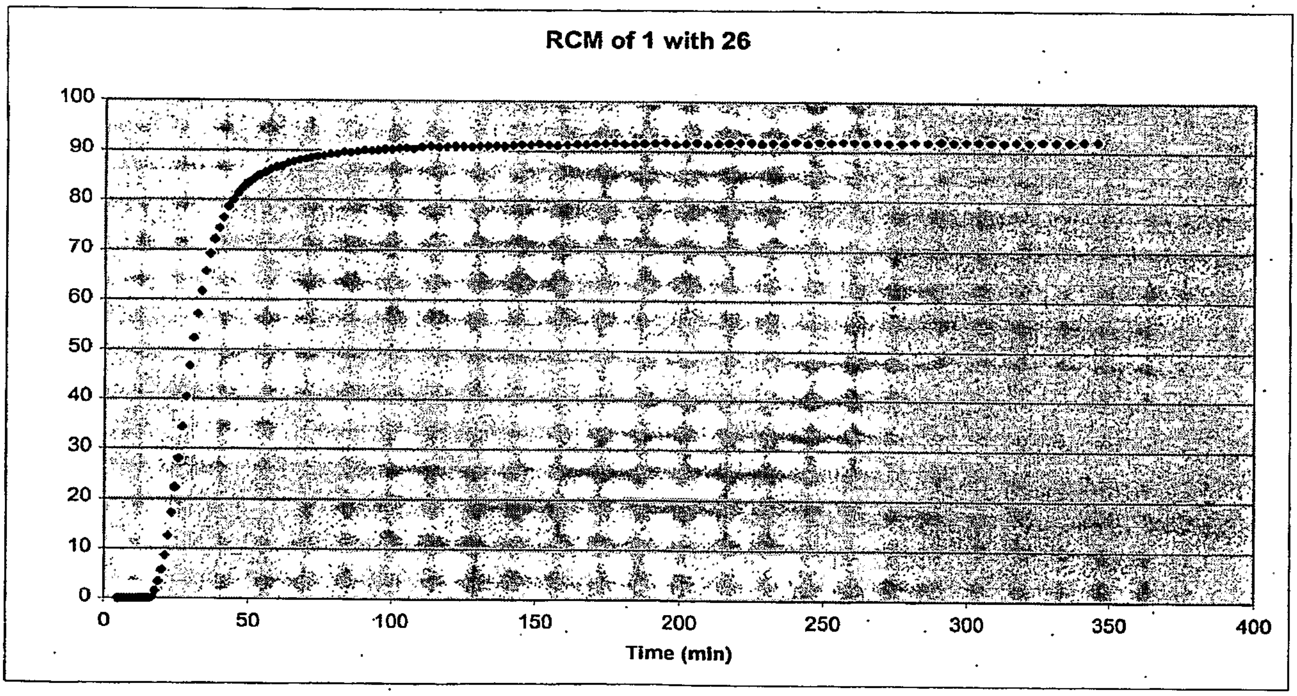
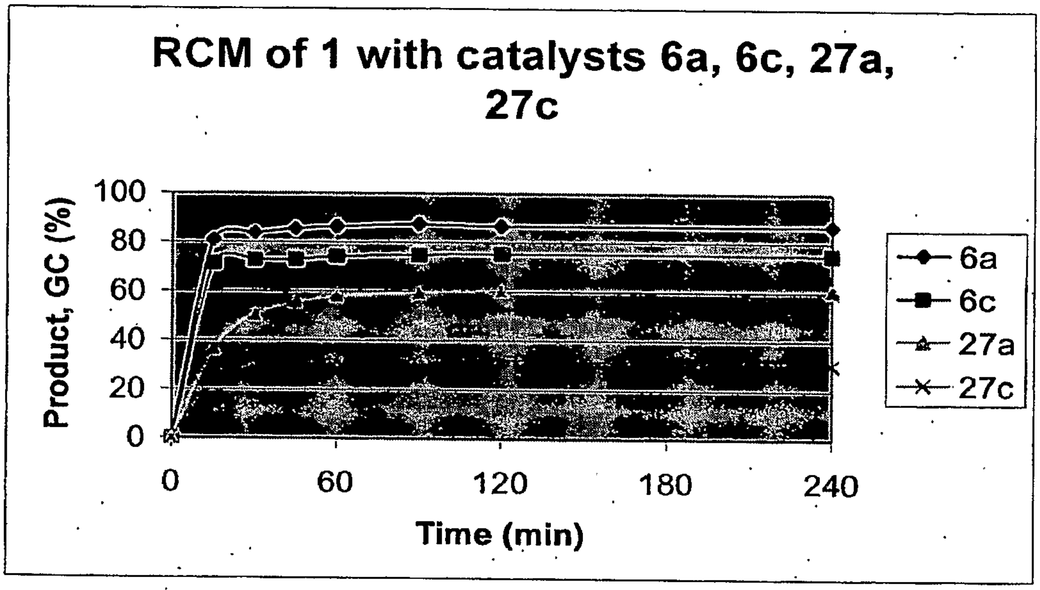


Figure 17



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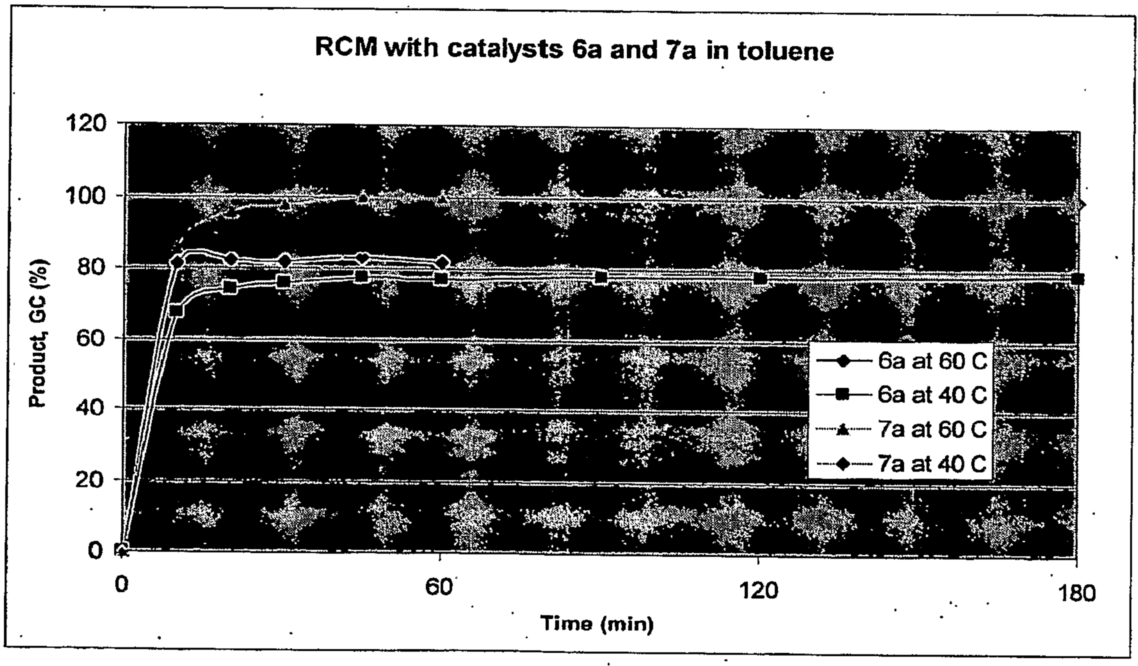

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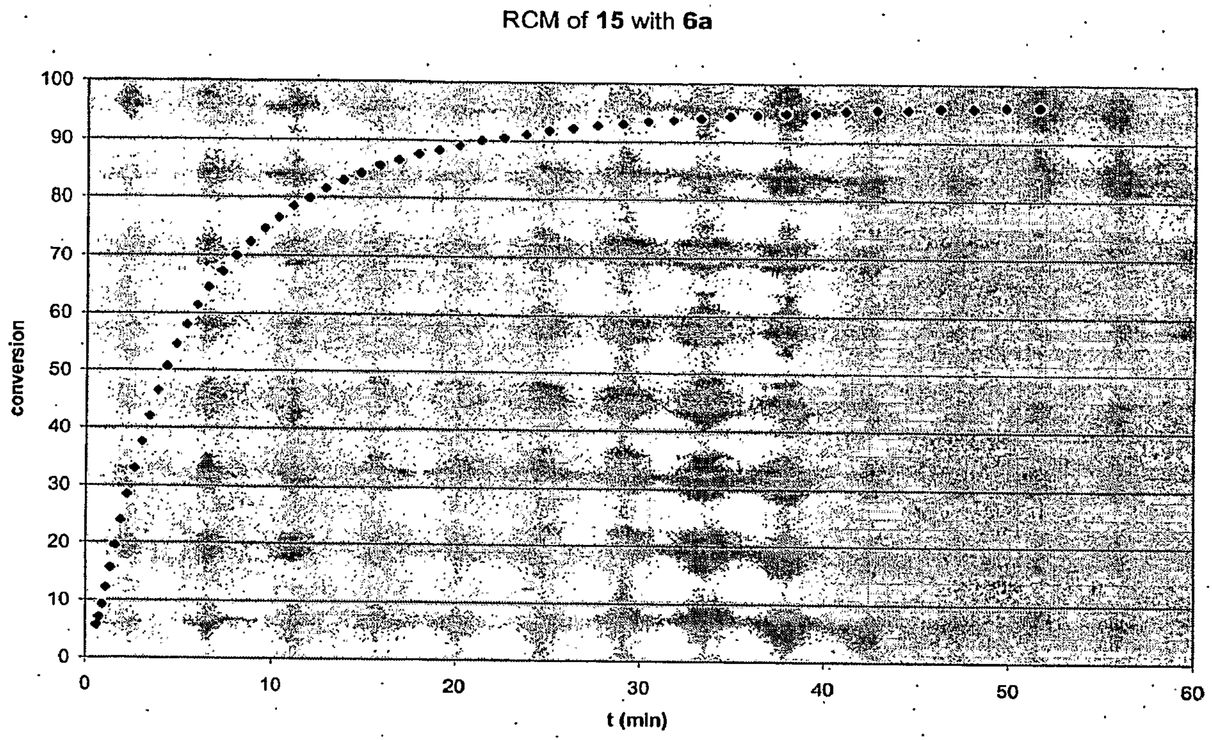

Figure 20

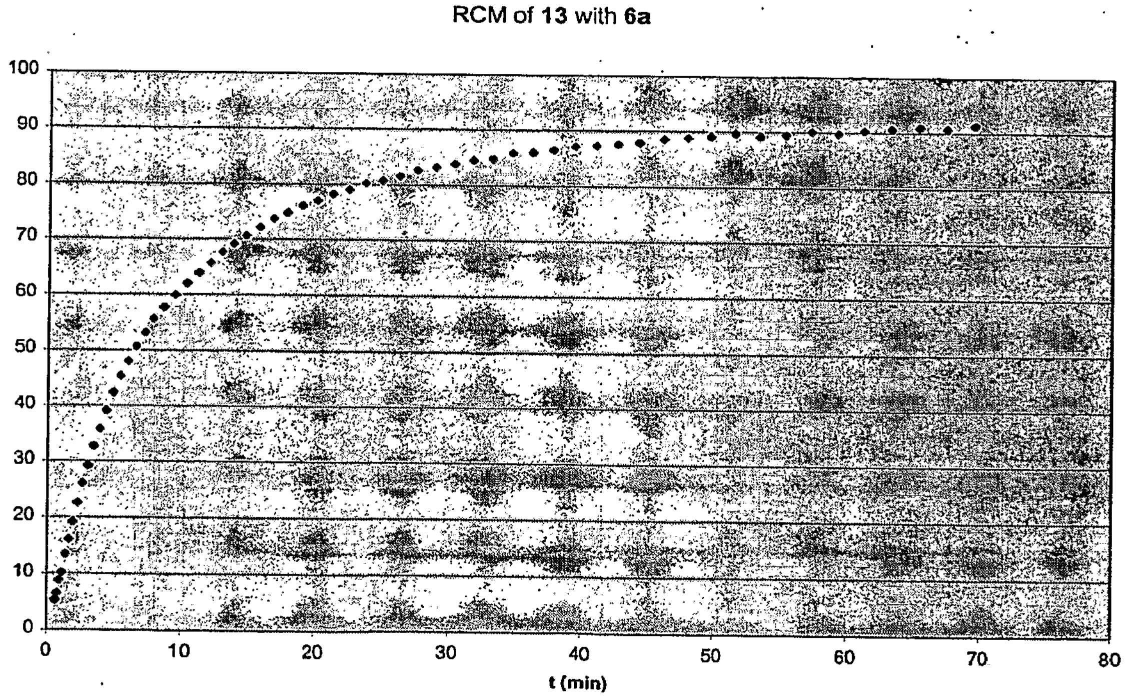

Figure 21

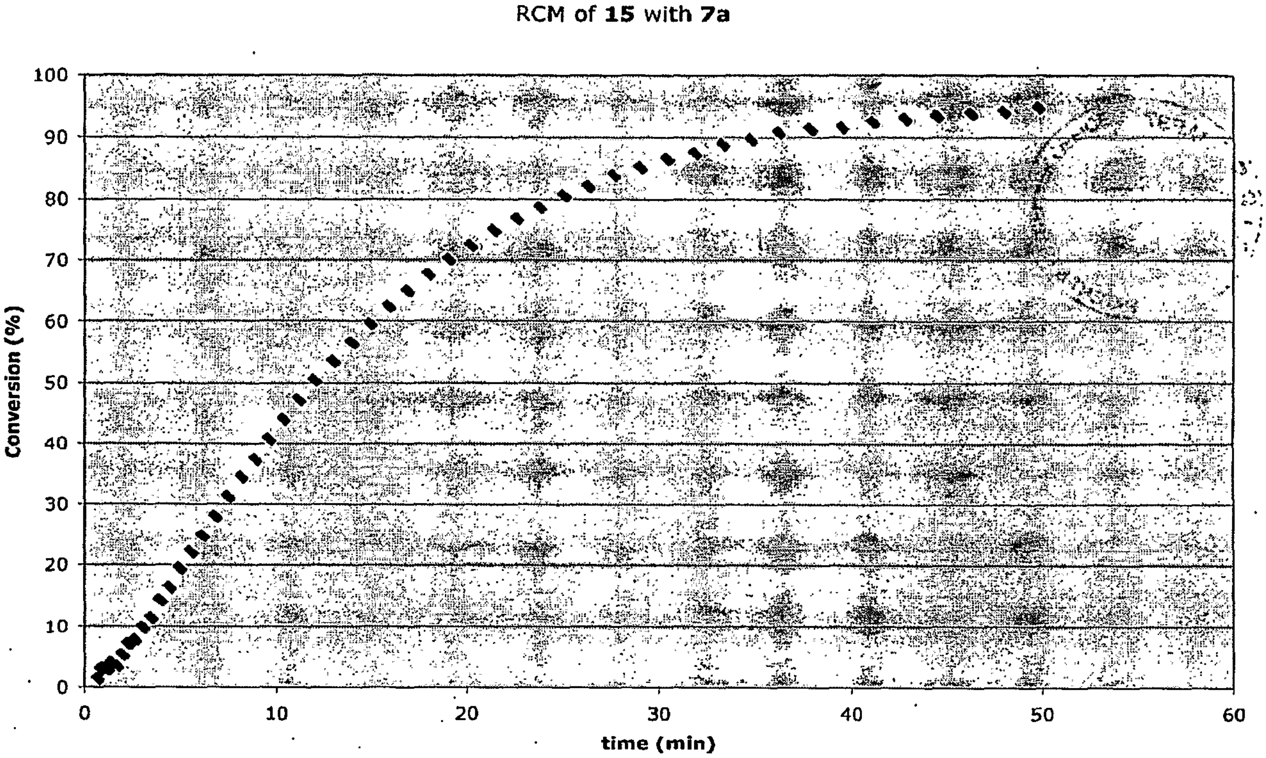

Figure 22

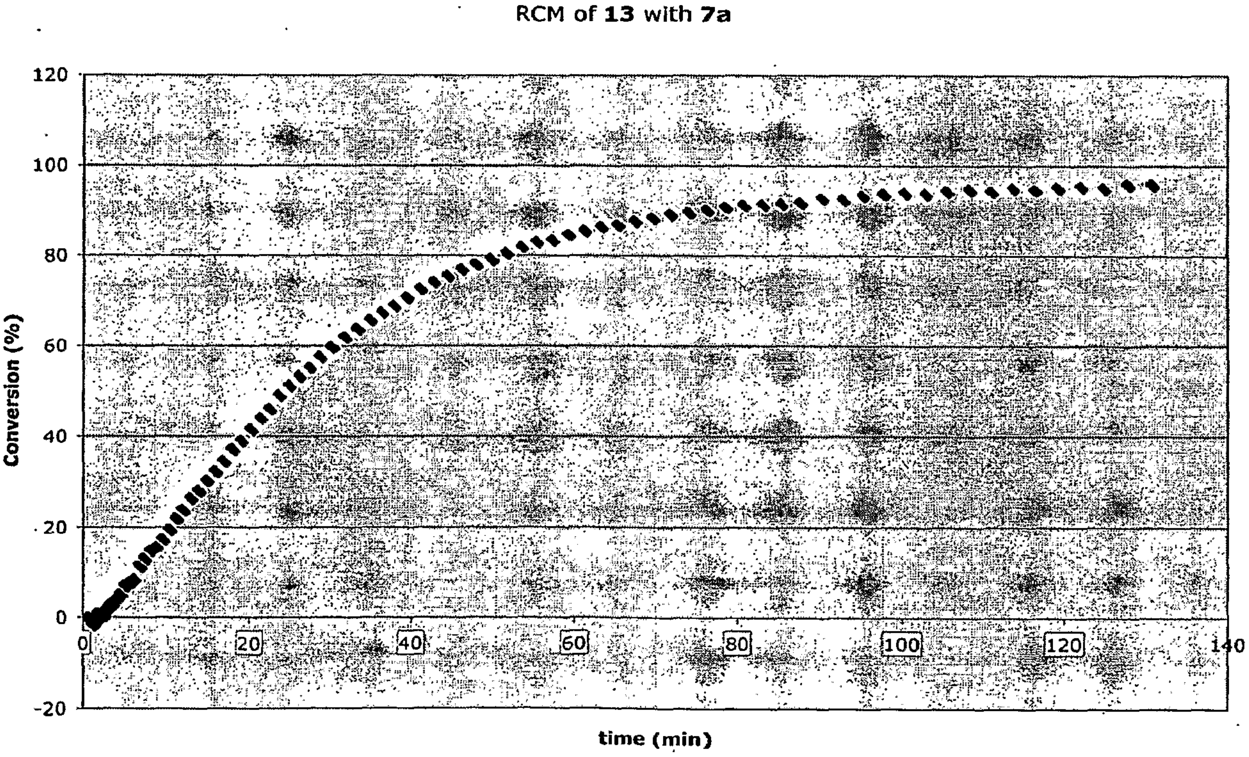

Figure 23

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2006/047934

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07F15/00 B01J31/22 C08G61/08

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)
C07F B01J C08G

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 practical, search terms used)

EPO-Internal, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	SEIDERS, T. JON ET AL: "Enantioselective ruthenium-catalyzed ring-closing metathesis" ORGANIC LETTERS , 3(20), 3225-3228 CODEN: ORLEF7; ISSN: 1523-7060, 2001, XP002431916 the whole document	1-16
Y	WO 02/083742 A (CALIFORNIA INST OF TECHN [US]; GRUBBS ROBERT H [US]; WARD DONALD W [US) 24 October 2002 (2002-10-24) the whole document	1-16
Y	WO 00/71554 A (CALIFORNIA INST OF TECHN [US]; GRUBBS ROBERT H [US]; SCHOLL MATTHIAS [) 30 November 2000 (2000-11-30) cited in the application the whole document	1-16

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☒ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

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"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

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"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.

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Date of the actual completion of the international search 3 May 2007	Date of mailing of the international search report 14/05/2007
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Authorized officer Rinkel, Bert

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	OCCHIPINTI, GIOVANNI ET AL: "Quantitative Structure-Activity Relationships of Ruthenium Catalysts for Olefin Metathesis" JOURNAL OF THE AMERICAN CHEMICAL SOCIETY , 128(21), 6952-6964 CODEN: JACSAT; ISSN: 0002-7863, 2006, XP002431917 the whole document	1-16
P,X	FUNK, TIMOTHY W. ET AL: "Highly Active Chiral Ruthenium Catalysts for Asymmetric Ring-Closing Olefin Metathesis" JOURNAL OF THE AMERICAN CHEMICAL SOCIETY , 128(6), 1840-1846 CODEN: JACSAT; ISSN: 0002-7863, 2006, XP002431918 the whole document	1-16
P,X	BERLIN, JACOB M. ET AL: "Highly active chiral ruthenium catalysts for asymmetric cross- and ring-opening cross-metathesis" ANGEWANDTE CHEMIE, INTERNATIONAL EDITION , 45(45), 7591-7595 CODEN: ACIEF5; ISSN: 1433-7851, 2006, XP002431919 the whole document	1-16
T	STEWART, I.C. ET AL: "Highly efficient ruthenium catalysts for the formation of tetrasubstituted olefins via ring-closing metathesis" ORGANIC LETTERS , 9(8), 1589-1592 CODEN: ORLEF7; ISSN: 1523-7060, 2007, XP002431920 the whole document	1-16

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2006/047934

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