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(54) Title: METHOD FOR CONVERTION OF TERMINAL ALKENES TO ALDEHYDES USING RUTHENIUM(IV) PORPHRIN CATALYSTS

(57) Abstract: Aldehydes were obtained in excellent yields from ruthenium-porphyrin-catalyzed oxidation of various terminal alkenes with 2,6-dichloropyridine N-oxide under mild conditions. The aldehydes generated from these ruthenium-catalyzed alkene oxidation reactions can be used in-situ for olefination reactions with ethyl diazoacetate in the presence of PPh_3, leading to one-pot diazoacetate olefination starting from alkenes.

METHOD FOR CONVERSION OF TERMINAL ALKENES TO ALDEHYDES USING RUTHENIUM(IV) PORPHYRIN CATALYSTS

Background of the Invention

Wacker-type alkene oxidation to carbonyl compounds is one of the most important oxidation reactions in synthetic chemistry and pharmaceutical industry (Smidt et al. Angew. Chem. (1959), Vol. 71, page 176; Smidt et al. Angew. Chem. Int. Ed. Engl. (1962), Vol. 1, page 80; Tsuji, Synthesis (1984), page 369; Tsuji, (1998) Palladium Reagents and Catalysts Innovation in Organic Synthesis; John Wiley & Sons, New York). Conversion of alkenes $RCH=CH_2$ to acetaldehyde (R = H) or methyl ketones (R $\neq$ H) through Wacker process (FIG 1a) has been well documented by Smidt and Tsuji; however, highly selective formation of aldehydes from catalytic oxidation of $RCH=CH_2$ (R $\neq$ H) without C=C bond cleavage (FIG 1b) remains a challenge. Previous work by Feringa (Feringa, Chem. Commun. (1986), page 909), Murahashi (Murahashi et al., Chem. Commun., (1991), page 1559), and Wenzel (Wenzel et al. Chem. Commun. (1993), page 862) showed that oxidation of aliphatic alkenes (such as oct-1-ene and dec-1-ene), N-allyl amides/lactams, and allyl esters with O_2 or air in the presence of certain palladium or palladium/copper catalysts affords a mixture of aldehyde and methyl ketone products. Recently, Ho and co-workers reported palladium/copper-catalyzed oxidation of a few 1,5-aliphatic dienes with O_2 to form aldehydes in 60–99% yields (Ho et al. Tetrahedron Lett. (2003), Vol. 44, page 6955).

In efforts to develop new oxidation technology based on ruthenium porphyrin catalysts, we found that the oxidation of a wide variety of terminal alkenes with 2,6-dichloropyridine N-oxide (Cl_2pyNO) in the presence of dichlororuthenium(IV) porphyrin catalysts [$Ru^{IV}(por)Cl_2$] (por = tdcpp 1, tmp 2, where H_2tdcpp = meso-tetrkis(2,6-dichlorophenyl)porphyrin and H_2tmp = meso-tetramesitylporphyrin) produced aldehydes in up to 99% yields with 100% substrate conversion without C=C bond cleavage. The present invention describes the first ruthenium-catalyzed "Wacker-type oxidation" of terminal alkenes (Hirobe et al., Heterocycles (1995), Vol. 40, page 867; Groves et al., J. Am. Chem. Soc. (1996), Vol. 118, page 8961; Berkessel et al., J. Chem. Soc. Perkin Trans. 1 (1997), page 2265; Che et al., Chem.

Commun. (1998), page 1583; Che *et al., J. Org. Chem.* (1998), Vol. *63*, page 7364; Gross *et al. Org. Lett.* (1999), Vol. *1*, page 2077; Gross *et al., Inorg. Chem.* (1999), Vol. *38*, page 1446; Che *et al., J. Am. Chem. Soc.* (2000), Vol. *122*, page 5337; Che *et al., J. Org. Chem.* (2001), Vol. *66*, page 8145; Che *et al., Chem. Eur. J.* (2002),

5   Vol. *8*, page 1554; Che *et al., Org. Lett.* (2002), Vol. *4*, page 1911; Che *et al., Chem. Commun.* (2002), page 2906; Berkessel *et al., Chem. Eur. J.* (2003), Vol. *9*, page 4746; Simonneaux *et al., J. Mol. Catal. A* (2003), Vol. *206*, page 95; Gray *et al., Inorg. Chim. Acta* (1998), Vol. *270*, page 433), which apparently proceeded by a different mechanism from those proposed for the palladium- or palladium/copper-

10   catalyzed reactions reported by the respective groups of Feringa, Murahashi, Wenzel and Ho. The realization of a one-pot diazoacetate olefination directly from aldehyde substrates generated in-situ from this ruthenium-porphyrin-catalyzed alkene oxidation reaction is also reported herein.

Summary of the Invention

The invention provides a mild and practical protocol using [Ru^{IV}(tdcpp)Cl$_2$] as a catalyst for highly regioselective formation of aldehydes from terminal alkenes without C=C bond cleavage. This protocol is a supplement to the Wacker process for oxidation of terminal alkenes to ketones or aldehydes. The catalytic reactions reported herein can be conducted in air at room temperature, affording a series of isolable β,γ-unsaturated aldehydes in good-to-excellent yields. The present work provides a new, practical, and convenient method for preparing multi functional compounds.

Brief Description of the Figures

FIG 1. illustrates the conversion of alkenes $RCH=CH_2$ to acetaldehyde (R = H) or methyl ketones (R ≠ H) through oxidation process.

FIG 2. provides examples of metalloporphyrin catalysts capable of catalyzing the highly selective conversion of terminal alkenes to aldehydes via a subsequent epoxidation/isomerization route.

FIG 3. illustrates the described method which involves the highly selective conversion of terminal alkenes to aldehydes via a subsequent epoxidation/isomerization route using metalloporphyrins as general and efficient catalysts.

FIG 4. provides representative examples of oxidation of 1-phenyl-1,3-butadiene (3) with various amounts of Cl_2pyNO catalyzed by a dichlororuthenium(IV) porphyrin to give the corresponding aldehyde (4) or epoxide (5) in good to excellent yields and excellent regioselectivity.

FIG 5. provides representative examples of conversion of terminal 1,3-dienes using a dichlororuthenium(IV) porphyrin catalyst to give the corresponding aldehydes in good to excellent yields and excellent regioselectivity.

FIG 6. provides representative examples of conversion of variously substituted alkenes using a dichlororuthenium(IV) porphyrin catalyst to give the corresponding aldehydes in good to excellent yields.
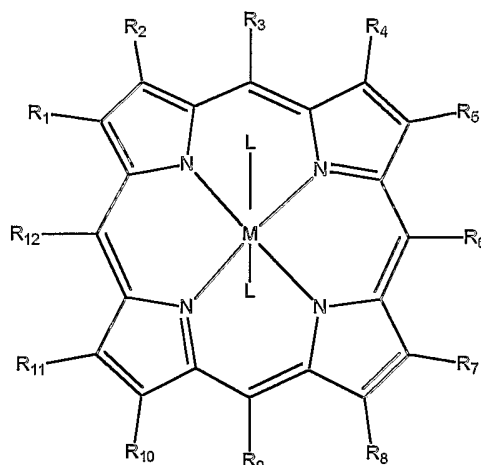
FIG 7. provides representative examples of conversion of alkenes using a dichlororuthenium(IV) porphyrin catalyst and subsequent in-situ olefination of the aldehyde products obtained with ethyl diazoacetate in the presence of PPh_3, leading to one-pot diazoacetate olefination starting from alkenes in good to excellent yields over two steps.

FIG 8. illustrates the utility of the metalloporphyrin catalyzed oxidation reaction for organic synthesis through the preparation of representative examples of synthetically useful compounds afforded from dichlororuthenium(IV) porphyrin catalyzed oxidative epoxidation/isomerization reaction of silyl enol ethers.

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Detailed Description of the Invention

The present invention provides a practical and mild process for highly selective conversion of terminal alkenes to aldehydes via a subsequent epoxidation/isomerization route using using non-chiral metalloporphyrin catalysts represented by structural formula:

wherein

each R_1-R_{12} is independently H, optionally substituted hydroxyl, optionally substituted amino, halogen, -CN, -NO$_2$, optionally substituted C_{1-20} alkyl, optionally substituted phenyl; optionally substituted naphthyl; optionally substituted anthracenyl, -SR^{13}, -SO$_2$R^{13}, -CO$_2$R^{13}, and optionally substituted heteroatom-containing aromatic ring, in which the optional substitutents are independently selected from the foregoing alkyl, phenyl, naphthyl, anthracenyl and heteroatom-containing aromatic groups; R^{13} is independently selected from the same groups as R^1 other than –SR^{13} and –SO$_2$R^{13}; and L is a halogen molecule, solvent molecule, CO or R^1. The various R groups may be optically pure or can be stereo and regio isomers.

In an embodiment of this invention, the metalloporphyrin is a transition metal porphyrin, such as ruthenium, manganese, iron, osmium, copper or cobalt porphyrin. In an embodiment of this invention, the porphyrin ligand is a tetraphenylporphyrin and the phenyl rings are attached at the *meso*-positions of the porphyrin. In an embodiment of the present invention, the catalysts are capable of exhibiting regioselectivity. Two of the preferred catalysts are shown in Fig. 2. In an embodiment of the present invention, the catalysts are capable of selectively catalyzing oxidation

of C=C bonds without C-C bond cleavage. In an embodiment of this invention, the regioselectivity is the oxidation of terminal C=C bonds.

Additionally, the present invention provides a method for the preparation of carbonyl compounds with the catalysts from alkenes as starting materials. Further, the present invention provides a method for producing primary aldehydes with the catalyst. The present invention also provides a method for producing regioselective carbonyl compounds with the catalyst. Preferably, the method involves the use of an oxidant which selectively alters the oxidation state of the substrate, preferably in the presence of a solvent. The solvent can be CH_3OH, CH_3CN, N,N-dimethylformaldehyde (DMF), $C_4H_4Cl_2$, CH_2Cl_2 and benzene. A typical oxidant is Cl_2pyNO. In an embodiment of this invention, the substrate is an alkene derivative, or a hydrocarbon containing a C=C functional group. As shown in the figures, carbon to which the alkene moiety is attached can be a part of a cyclic or non-cyclic moiety, which in turn can be substituted with a functional group such as CO_2Me or by an aromatic or cycloaliphatic group.

As used herein, the term "regioselective" refers to selection of terminal C=C bonds over internal C=C bond that undergo reaction. The term "conversion" refers to the relative number of molecules of substrate that is consumed under the applied reaction conditions.

Examples

Example 1
Regioselective Conversion of Terminal Alkenes to Aldehydes via a Subsequent Epoxidation/Isomerization Route Catalyzed by either Dichlororuthenium(IV) Porphyrins **1** or **2**

The invention relates to a practical and mild method for the synthesis of aldehydes using either dichlororuthenium(IV) porphyrins **1** or **2** (prepared according to Leung *et al. J. Chem. Soc. Dalton Trans* (1997), page 237) as general and effective catalysts for the oxidation of terminal alkenes.

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Typical conditions employ 0.1 mmol of alkene substrate, Cl_2pyNO (1.03 equiv), and 1 (0.5–2.0 mol%) dissolved in $CDCl_3$ (0.5–1.0 mL) in a NMR tube at room temperature or 60 °C. The progress of the reaction was monitored by ^1H NMR. After determination of the product yield by ^1H NMR spectroscopy, the reaction mixture was separated by flash chromatography on silica gel. For the large-scale reaction, 0.65 mmol of alkene substrate, Cl_2pyNO (1.03 equiv), and 1.0 mol% of 1 in 10 mL of $CHCl_3$ were used and reaction was carried out at room temperature for 30 min.

With 0.5 mol% catalyst loading, a solution of 1-phenyl-1,3-butadiene (3) and 1.03 equiv Cl_2pyNO, in $CDCl_3$ was stirred for 30 min at room temperature, affording the β,γ-unsaturated aldehyde 4-phenyl-but-3-enal (4, styrylacetaldehyde) in 99% yield (FIG. 4). No ketone products were detected in the reaction mixture. The reaction gave similar results with $CHCl_3$ and CH_2Cl_2 as solvents. Other solvents, such as benzene, toluene, acetone, ether, and methanol, were inferior to $CHCl_3$ and CH_2Cl_2 for this catalytic process.

The 1,3-diene 3 was first oxidized by Cl_2pyNO to form epoxide 5 in the presence of catalyst 1. The same catalyst, or its derivative, induced subsequent isomerization of the epoxide to β,γ-unsaturated aldehyde (Alper *et al. J. Org. Chem.* (1976), Vol. *41*, page 3611; Sankararaman *et al. J. Org. Chem.* (1996), Vol. *61*, page 1877; Kulawiec *et al. J. Org. Chem.* (1997), Vol. *62*, page 6547; Ranu *et al. J. Org. Chem.* (1998), Vol. *63*, page 8212; Suda *et al. Tetrahedron Lett.* (1999), Vol. *40*, page 7243; Llama *et al. J. Chem. Soc. Perkin Trans. 1* (2000), page 1749). We abbreviate the epoxidation of terminal alkenes followed by isomerization of the epoxide products as E-I reactions.

To provide support for the above mechanism, we examined the effect of Cl_2pyNO on the catalysis (FIG. 4). With Cl_2pyNO in excess, the yield of aldehyde 4 significantly decreased from 99% to 51%, and epoxide 5 was obtained in 49% yield. This could be rationalized by the coordination of epoxide to the active ruthenium porphyrin species for the isomerization reactions. Excess Cl_2pyNO would compete with the epoxide for coordination to ruthenium, thus decreasing the aldehyde yield. We found that the use of 1.01–1.03 equiv Cl_2pyNO could give the best results in terms of

reaction completion time (30 min) and aldehyde yield (99%). Changing the temperature from room temperature to 10 °C or 40 °C did not appreciably affect the reaction.

5   The E-I reaction of 3 with Cl_2pyNO could be equally efficiently catalyzed by 2 but less efficiently catalyzed by $[Ru^{VI}(tdcpp)O_2]$. Oxidation of 3 with Cl_2pyNO catalyzed by $[Ru^{VI}(tdcpp)O_2]$ under similar conditions to those for catalyst 1 (1.03 equiv Cl_2pyNO, 1.7 mol% catalyst loading) afforded 4 in 41% yield within 5 h. However, complex $[Ru^{II}(tdcpp)(CO)]$ was a relatively inactive catalyst toward the E-I reaction.

10

A series of other 1,3-dienes were treated with 1.01–1.03 equiv Cl_2pyNO and 0.5–1.0 mol% 1 at room temperature (FIG. 5). For dienes 6–10, the corresponding β,γ-unsaturated aldehydes 13–17 were obtained in 81–99% yields and were stable enough to be purified by flash chromatography on silica gel. However, the aldehyde

15 product 18a (formed in 90% yield) in the oxidation of diene 11 was converted to 18b upon flash chromatography on silica gel. Non-terminal alkene 12 was oxidized more slowly, affording the β,γ-unsaturated ketone 19 in 99% yield after the reaction proceeded at 60 °C for 6 h.

20 When styrene (20) was treated with 1.03 equiv Cl_2pyNO and 1.0 mol% 1 in refluxing CH_2Cl_2 for 5 h, a mixture of styrene oxide and phenylacetaldehyde (27) was obtained in 90% and 10% yield, respectively (Collman *et al. J. Am. Chem. Soc.* (1986), Vol. *108*, page 2588; Burrows *et al. J. Am. Chem. Soc.* (1988), Vol. *110*, page 6124; Minisci *et al. J. Am. Chem. Soc.* (1995), Vol. *117*, page 226; Gross *et al. Angew.*

25 *Chem. Int. Ed.* (2000), Vol. *39*, page 4045; Gray *et al. Angew. Chem. Int. Ed.* (2001), Vol. *40*, page 2132). To our surprise, adding more catalyst 1 and allowing the reaction to proceed for a longer time resulted in complete conversion of styrene oxide to aldehyde 27. For example, reaction of styrene with 1.03 equiv Cl_2pyNO in the presence of 2.0 mol% 1 in $CHCl_3$ at 60 °C for 12 h afforded 27 in 99% yield; no

30 benzaldehyde was observed (Gray *et al. Inorg. Chim. Acta* (1998), Vol. *270*, page 433). Other styrene derivatives 21–25 could also be converted to the corresponding arylacetaldehydes 28–32 in excellent yields (FIG. 6). However, for the non-aromatic alkene 26, only the epoxide product was obtained.

All the target aldehydes were characterized by ^{1}H, ^{13}C NMR and IR spectroscopy, and LRMS, HRMS spectrometry. The spectral data of 5 (*Org. Synth., Coll. Vol. 4*, (1963), page 424), 13 (Frejd *et al. J. Org. Chem.* (1998), Vol. *63*, page 3595), 19 (Brookhart *et al. J. Am. Chem. Soc.* (1994), Vol. *116*, page 1869) and 27-33 (Palecek *et al. Collect. Czech. Chem. Commun.* (1988), Vol. *53*, page 822; Paris *et al. Synth. Commun.* (1991), Vol. *21*, page 819; Chikashita *et al. Synth. Commun.* (1987), Vol. *17*, page 677; Kulawiec *et al. J. Org. Chem.* (1997), Vol. *62*, page 6547; Stratakis *et al. J. Org. Chem.* (2002), Vol. *67*, page 8758) are identical with those reported in the literature. 4 ^{1}H NMR (300 MHz, CDCl$_3$): δ9.76 (t, 1H, *J* = 1.8 Hz), 7.23–7.40 (m, 5H), 6.54 (d, 1H, *J* = 16.2 Hz), 6.29 (dt, 1H, *J* = 16.2, 6.9 Hz), 3.36 (ddd, 2H, *J* = 6.9, 1.8, 1.2 Hz); ^{13}C NMR(75 MHz, CDCl$_3$): δ199.4, 136.5, 134.9, 128.5, 127.7, 126.2, 119.2, 47.3; IR: 1724, 1599, 1496, 967, 748, 694 cm^{-1}; MS (EI) *m/z* (rel intensity) 146 (31) [*M*]$^+$; HRMS: calcd for C$_{10}$H$_{10}$O 146.0732, found 146.0731.

14 ^{1}H NMR (300 MHz, CDCl$_3$): δ 9.57 (d, 1H, *J* = 7.8 Hz), 8.22 (d, 2H, *J* = 9.0 Hz), 7.38 (d, 2H, *J* = 9.0 Hz), 6.95 (dt, 1H, *J* = 15.3, 6.9 Hz), 6.13 (ddt, 1H, *J* = 15.3, 7.8, 1.5 Hz), 3.78 (d, 2H, *J* = 6.9 Hz), IR: 1689, 1598, 1517, 1347, 980, 856, 736 cm^{-1}; MS (EI): *m/z* 191 (8) [*M*]$^+$. 15 ^{1}H NMR (300 MHz, CDCl$_3$): δ9.77 (t, 1H, *J* = 1.8 Hz), 7.30 (d, 2H, *J* = 8.1 Hz), 7.15 (d, 2H, *J* = 8.4 Hz), 6.53 (d, 1H, *J* = 15.6 Hz), 6.25(dt, 1H, *J* = 7.2, 16.5 Hz), 3.34–3.37 (m, 2H); 2.36 (s, 3H); ^{13}C NMR(75 MHz, CDCl$_3$): δ 199.8, 137.7, 135.1, 133.9, 129.3, 126.2, 118.1, 47.6, 21.3; IR: 1721, 1513, 974, 799, 505 cm^{-1}; MS (EI): *m/z* 160 (27) [*M*]$^+$; HRMS: calcd for C$_{11}$H$_{12}$O + H 161.0966, found 161.0959. 16 ^{1}H NMR (300 MHz, CDCl$_3$): δ9.75 (t, 1H, *J* = 2.1 Hz), 7.43 (dd, 1H, *J* = 7.5, 1.5 Hz), 7.23 (td, 1H, *J* = 7.5, 2.1 Hz), 6.83–6.95 (m, 3H), 6.28 (dt, 1H, *J* = 16.2, 7.2 Hz), 3.84 (s, 3H), 3.35 (dt, 2H, *J* = 7.2, 1.5, 2.1 Hz); ^{13}C NMR (75 MHz, CDCl$_3$): δ 199.7, 156.6, 130.1, 128.8, 126.9, 125.8, 120.7, 119.8, 110.9, 55.5, 48.0; IR: 1721, 1598, 1490, 1245, 1028, 975, 752 cm^{-1}; MS (EI): *m/z* (rel intensity) 176 (6) [*M*]$^+$; HRMS: calcd for C$_{11}$H$_{12}$O$_2$ 176.0837, found 176.0829. 17 ^{1}H NMR (300 MHz, CDCl$_3$): δ9.68 (t, 1H, *J* = 1.8 Hz), 7.22 (t, 1H, *J* = 8.4 Hz), 6.56 (d, 2H, *J* = 8.4 Hz), 6.50 (d, 1H, *J* = 11.1 Hz), 6.02 (dt, 1H, *J* = 11.1, 7.5 Hz), 3.77 (s, 6H), 3.04 (ddd, 2H, *J* = 7.5, 1.5, 1.5 Hz); ^{13}C NMR (75 MHz, CDCl$_3$): δ201.1, 157.6, 129.0, 125.2, 123.5, 113.6, 103.7, 55.6, 44.9; IR: 1724, 1593, 1585, 1471, 1253, 1113, 748 cm^{-1}; MS (EI) *m/z* (rel intensity); 206 (51) [*M*]$^+$; HRMS: calcd for C$_{12}$H$_{14}$O$_3$

206.0943, found 206.0960.18b ^{1}H NMR (300 MHz, CDCl$_3$): δ 9.47 (s, 1H), 8.20 (d, 2H, J = 8.7 Hz), 7.38 (d, 2H, J = 9.0 Hz), 6.61 (t, 1H, J = 7.2 Hz), 3.82 (d, 2H, J = 7.2 Hz), 1.89 (s, 3H); ^{13}C NMR (75 MHz, CDCl$_3$): δ 194.6, 149.2, 146.9, 145.8, 140.8, 129.4, 124.1, 34.8, 29.7; IR: 1681, 1145, 1606, 1594, 1511, 851, 750, 700 cm^{-1}; MS

5   (EI) m/z (rel intensity) 205 (42) [M]$^+$; HRMS: calcd for C$_{11}$H$_{11}$NO$_3$ + H 206.0817, found 206.0802.

Example 2

Regioselective Conversion of Terminal Alkenes to Aldehydes via a Subsequent

10 Epoxidation/Isomerization Route Catalyzed by either Dichlororuthenium(IV) Porphyrins 1 and in-situ Olefination with Ethyl Diazoacetate in the Presence of PPh$_3$, Leading to One-pot Diazoacetate Olefination Starting from Alkenes

Recently, Woo (Woo *et al. J. Am. Chem. Soc.* (2002), Vol. *124*, page 176), Aggarwal

15 (Aggarwal *et al. J. Am. Chem. Soc.* (2003), Vol. *125*, page 6034), and Zhang (Zhang *et al. J. Org. Chem.* (2003), Vol. *68*, page 3714) reported that iron or ruthenium *meso*-tetraaryl porphyrins [Fe^{II}(ttp)], [Fe^{III}(tpp)Cl], or [Ru^{II}(tpp)(CO)] can catalyze the olefination of certain classes of aldehydes with ethyl diazoacetate (EDA) in the presence of PPh$_3$. We observed that both 1 and [Ru^{II}(tdcpp)(CO)] could also catalyze

20 such olefination reactions. Recognizing that the aldehyde products in the 1-catalyzed E-I reactions could be in-situ used as the substrates for olefination reactions, we were interested in developing a practical one-pot E-I-olefination reaction, i.e. one-pot diazoacetate olefination directly starting from alkenes rather than from aldehydes.

25 Typical conditions involve using the "1 + Cl$_2$pyNO" protocol, 0.1 mmol 3 was converted to aldehyde 4 in CHCl$_3$ within 30 min (the reaction conditions are exactly the same as that stated for EXAMPLE 1). Removal of the solvent, followed by addition of 1.2 equiv Ph$_3$P, 1 mL toluene, and 1.2 equiv EDA, the olefination product 34 was obtained in 99% yield after the reaction mixture was heated at 80 °C for 2 h,

30 cooled to room temperature and separated by flash chromatography on silica gel with petroleum ether/ethyl acetate (3:1) as eluent. Similarly, through a one-pot E-I-olefination reaction of 35, we isolated the olefination product 40 in 55% yield (FIG. 7).

The target olefination products were characterized by ^{1}H, ^{13}C NMR and IR spectroscopy, and LRMS, HRMS spectrometry. **34** ^{1}H NMR (300 MHz, CDCl$_3$): δ 7.22–7.37 (m, 5H), 7.04 (dt, 1H, J = 15.3, 6.3 Hz), 6.45 (d, 1H, J = 16.2 Hz), 6.19 (dt, 1H, J = 15.9, 6.9 Hz), 5.90 (td, 1H, J = 1.5, 15.3 Hz), 4.20 (q, 2H, J = 6.9 Hz), 3.08–3.13 (m, 2H), 1.29 (t, 3H, J = 6.9 Hz); IR: 1720, 1653, 1267, 1160, 1043, 967, 745, 693 cm^{-1}; MS (EI) m/z (rel intensity) 216 (67) [M]$^+$. **40** ^{1}H NMR (300 MHz, CDCl$_3$): δ 7.91 (d, 2H, J = 7.8 Hz), 7.66 (t, 1H, J = 7.5 Hz), 7.53 (t, 2H, J = 7.5 Hz), 6.94 (dt, 1H, J = 7.8, 15.9 Hz), 5.83 (d, 1H, J = 15.9 Hz), 5.19–5.15 (m, 1H), 4.18 (q, 2H, J = 6.9 Hz), 3.84 (d, 1H, J = 6.6 Hz), 2.76–2.84 (m, 1H), 2.41–2.51 (m, 1H), 1.28 (t, 3H, J = 6.9 Hz); ^{13}C NMR (75 MHz, CDCl$_3$): δ200.5, 165.9, 142.6, 134.4, 133.2, 129.1, 128.6, 124.6, 71.9, 60.4, 38.5, 14.3; IR: 3467, 1716, 1684, 1657, 1598, 1581, 1450, 1271, 1167, 979, 695 cm^{-1}; MS (EI) m/z (rel intensity) 248 (0.1) [M]$^+$; HRMS ([M + Na]$^+$): calcd for C$_{14}$H$_{16}$O$_4$Na 271.0941, found 271.0919.

Example 3

Preparation of Synthetically Organic Compounds by Application of the Dichlororuthenium(IV) Porphyrin Catalyzed Oxidation of Silyl Enol Ethers

4-Oxoarylbutanal derivatives are useful compounds for organic synthesis. For example, the preparation and application of 4-oxo-4-phenylbutanal (**39**) have been extensively studied in the literature. (Kruse *et al. Heterocycles* (1987), Vol. *26*, page 3141; Molander *et al. Tetrahedron Lett.* 1989, Vol. *30*, page 2351; Molander *et al. J. Org. Chem.* (1991), Vol. *56*, page 2617; Molander *et al. J. Am. Chem. Soc.* 1993, Vol. *115*, page 830; Savoia *et al. Tetrahedron Lett.* (1994), Vol. *35*, page 2775; Utimoto *et al. Tetrahedron Lett.* (1995), Vol. *36*, page 8067). In this work, we found that **39** could be prepared in 52% NMR yield (isolated yield: 41%) from the E-I reaction of silyl enol ether **35** (FIG. 8). The same reaction also afforded hydroxyl ketoaldehyde **37** in 23% yield. When 2.06 equiv Cl$_2$pyNO were used, **37** could be obtained in 88% yield (determined by ^{1}H NMR).

Typical conditions involve dropwise addition of a solution of **1** (0.02 mmol) in CHCl$_3$ (50 mL) over 30 min to a well-stirred solution of **35** (2.0 mmol) and Cl$_2$pyNO (2.2
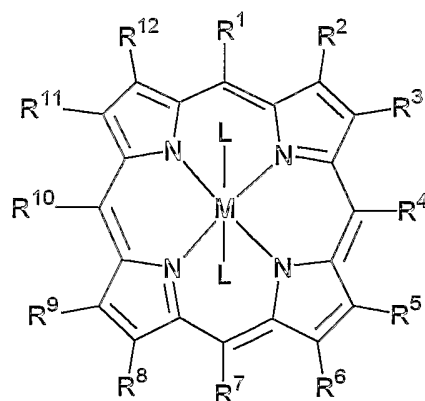
13

mmol) in $CHCl_3$ (100 mL) in a 25-mL flask. A drop of 12 N HCl was then added. The resulting mixture was stirred for 5 min. The product was purified by flash chromatography on silica gel.

5   The spectral data of 38 (Chong *et al. Tetrahedron* 1999, Vol. *55*, page 14233) and 39 (Molander *et al. J. Am. Chem. Soc.* 1993, Vol. *115*, page 830) are identical with those reported in the literature.

What is claimed is:

1.   A method for producing an aldehyde from an unsaturated compound having one or more C=C functional groups, which comprises catalyzing the reaction of an oxidant with the compound with a catalytic amount of metalloporphyrin, thereby producing the aldehyde.

2.   The method according to claim 1, wherein the compound comprises a terminal alkene.

3.   The method according to claim 1, wherein the oxidant comprises 2,6-dichloropyridine N-oxide (Cl$_2$pyNO).

4.   The method according to claim 1, wherein the reaction is carried out using CDCl$_3$, CHCl$_3$, CH$_2$Cl$_2$, diethyl ether, acetone, CH$_3$OH, toluene or benzene as a solvent.

5.   The method according to claim 1, wherein the metalloporphyrin is a transition metal metalloporphyrin.

6.   The method according to claim 5, wherein the transition metal metalloporphyrin is ruthenium, manganese, iron, cobalt, copper or osmium metalloporphyrin.

7.   The method according to claim 6, wherein the metalloporphyrin is ruthenium porphyrin.

8.   The method of claim 3, wherein the metalloporphyrin is a transition metal metalloporphyrin, and the method is carried out using CDCl$_3$, CHCl$_3$, CH$_2$Cl$_2$, diethyl ether, acetone, CH$_3$OH, toluene or benzene as a solvent.

9.   The method of claim 8, wherein the metalloporphyrin exhibits regioselectivity and provides yields of at least 52 percent.

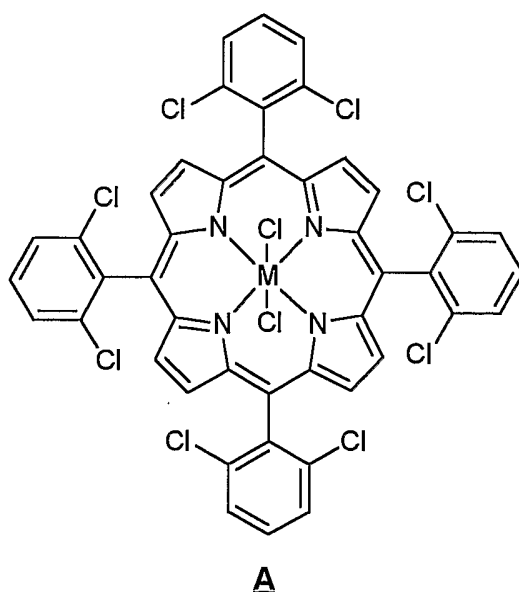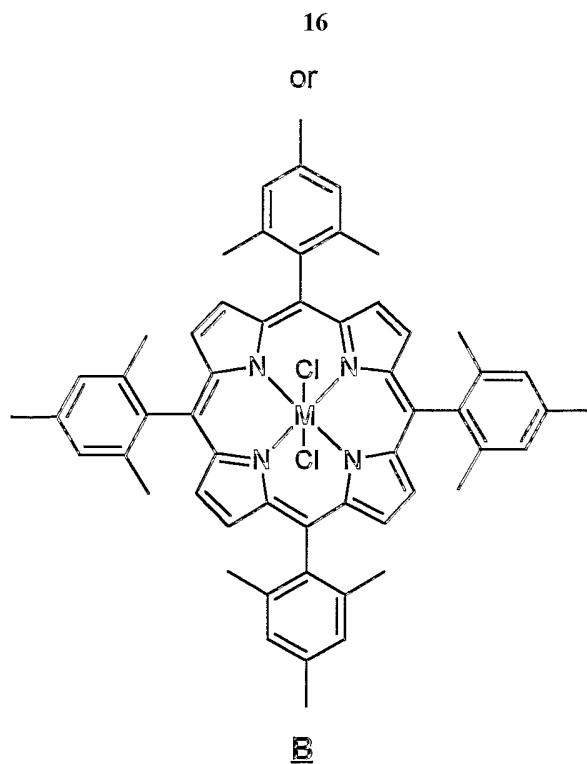10.   The method according to claim 1, wherein the metalloporphyrin has the structure:

wherein M is a transition metal;

wherein each R_1-R_{12} is independently H, optionally substituted hydroxyl, optionally substituted amino, halogen, -CN, -NO$_2$, optionally substituted C$_{1-20}$ alkyl, optionally substituted phenyl; optionally substituted naphthyl; optionally substituted anthracenyl, -SR^{13}, -SO$_2$R^{13}, -CO$_2$R^{13}, and optionally substituted heteroatom-containing aromatic ring, in which the optional substitutents are independently selected from the foregoing alkyl, phenyl, naphthyl, anthracenyl and heteroatom-containing aromatic groups; R^{13} is independently selected from the same groups as R^1 other than –SR^{13} and –SO$_2$R^{13}; and

wherein L is a halogen molecule, solvent molecule, CO or R^1.

11. The method according to claim 10, wherein the metalloporphyrin has the structure A or B:

A

or

B

wherein M represents a metal.

12. The method according to claim 11, wherein M is a transition metal.

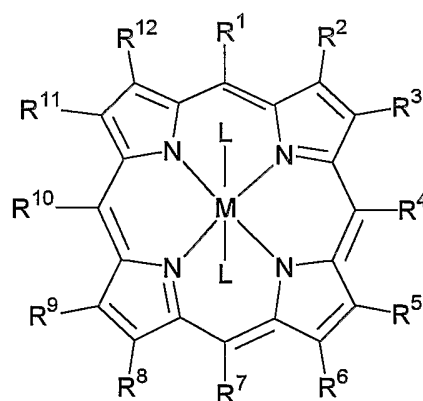13. The method according to claim 12, wherein the metalloporphyrin has structure A or B:

A

or

B.
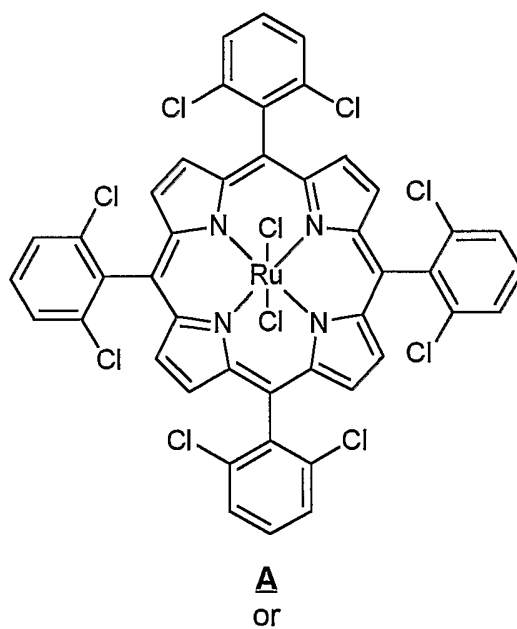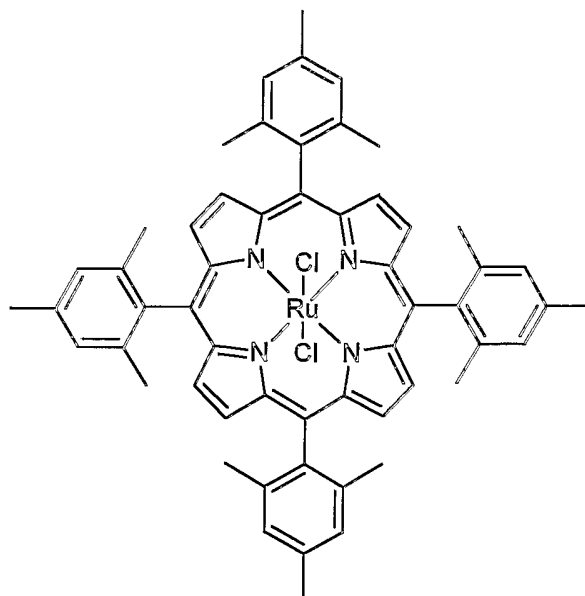
14.   A method for producing diazoacetate olefination from an unsaturated compound having one or more C=C functional groups, which comprises catalyzing the reaction of an oxidant with the unsaturated compound in the presence of a catalytic amount of metalloporphyrin and adding a Lewis base and a diazo compound to the reaction, thereby producing an α,β-unsaturated ester of the diazoacetate olefination.

15.   The method according to claim 14, wherein the compound comprises a terminal alkene.

16.   The method according to claim 14, wherein the oxidant comprises 2,6-dichloropyridine N-oxide (Cl_2pyNO).

17.   The method according to claim 14, wherein the Lewis base comprises PPh_3.

18.   The method according to claim 14, wherein the diazo compound comprises ethyl diazoacetate (EDA).

19.   The method according to claim 14, wherein the reaction in carried out with $CDCl_3$, $CHCl_3$, CH_2Cl_2, diethyl ether, acetone, CH_3OH, toluene or benzene as a solvent.

18

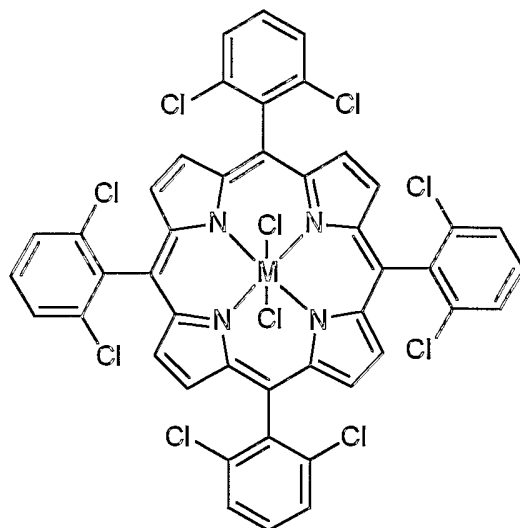20.   The method according to claim 14, wherein the metalloporphyrin is a transition metal metalloporphyrin.

21.   The method according to claim 20, wherein the transition metal metalloporphyrin is ruthenium, manganese, iron, cobalt, copper or osmium metalloporphyrin.

22.   The method according to claim 21, wherein the metalloporphyrin is ruthenium porphyrin.

23.   The method of claim 16, wherein the metalloporphyrin is a transition metal metalloporphyrin, the Lewis base is PPh_3, the diazo compound is ethyl diazoacetate, and the reaction is carried out using $CDCl_3$, $CHCl_3$, CH_2Cl_2, diethyl ether, acetone, CH_3OH, toluene or benzene as a solvent.

24.   The method according to claim 14, wherein the metalloporphyrin has the structure:

wherein M is a transition metal;

wherein each R_1-R_{12} is independently H, optionally substituted hydroxyl, optionally substituted amino, halogen, -CN, $-NO_2$, optionally substituted C_{1-20} alkyl, optionally substituted phenyl; optionally substituted naphthyl; optionally substituted anthracenyl, $-SR^{13}$, $-SO_2R^{13}$, $-CO_2R^{13}$, and optionally substituted heteroatom-containing aromatic ring, in which the optional substitutents are independently selected from the foregoing alkyl, phenyl, naphthyl, anthracenyl and heteroatom-containing aromatic groups; R^{13} is independently selected from the same groups as R^1 other than $-SR^{13}$ and $-SO_2R^{13}$; and

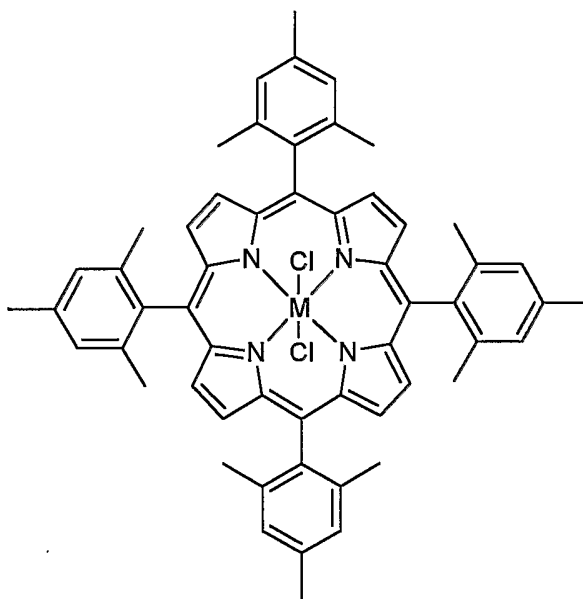wherein L is a halogen molecule, solvent molecule, CO or R^1.

25. The method according to claim 24, wherein the metalloporphyrin has the structure A or B:
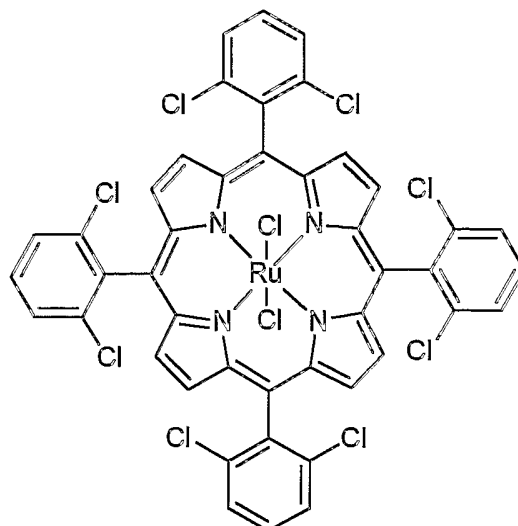

A

or

B

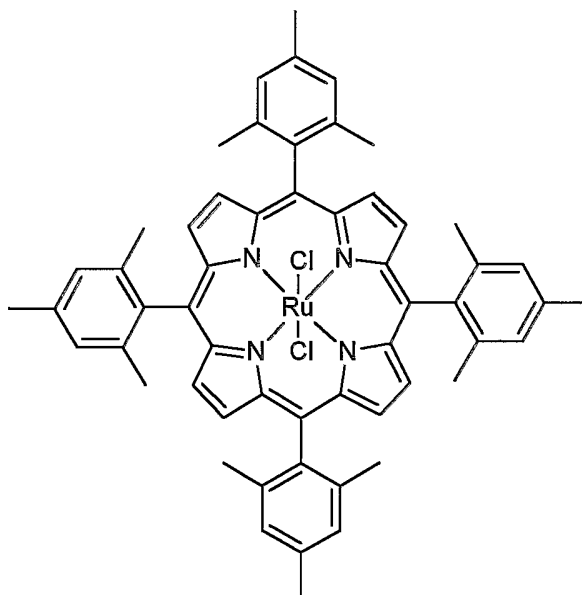wherein M represents a metal.

26. The method according to claim 25, wherein M is a transition metal.

27. The method according to claim 26, wherein the catalyst is a compound having the structure A or B:
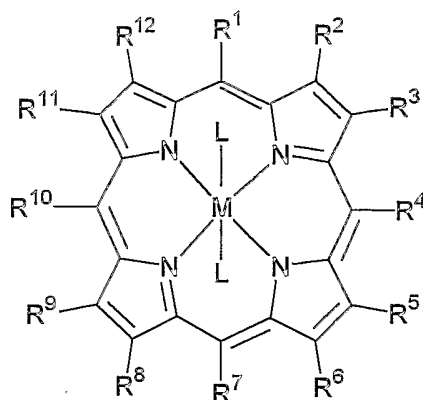
A

or

B.

28. The method of claim 23 wherein the metalloporphyrin exhibits regioselectivity.

29. The method of claim 28, wherein the catalyst exhibits *trans*-selectivity and yields a *trans-α,β*-unsaturated ester.

30. A compound having the structure:

wherein M is a transition metal;

wherein each R_1-R_{12} is independently H, optionally substituted hydroxyl, optionally substituted amino, halogen, -CN, -NO$_2$, optionally substituted $C_{1\text{-}20}$ alkyl, optionally substituted phenyl; optionally substituted naphthyl; optionally substituted anthracenyl, -SR^{13}, -SO$_2$R^{13}, -CO$_2$R^{13}, and optionally substituted heteroatom-containing aromatic ring, in which the optional substitutents are independently selected from the foregoing alkyl, phenyl, naphthyl, anthracenyl and heteroatom-containing aromatic groups; R^{13} is independently selected from the same groups as R^1 other than –SR^{13} and –SO$_2$R^{13}; and

wherein L is a halogen molecule, solvent molecule, CO or R^1.

31. The compound of claim 30 having the following structure
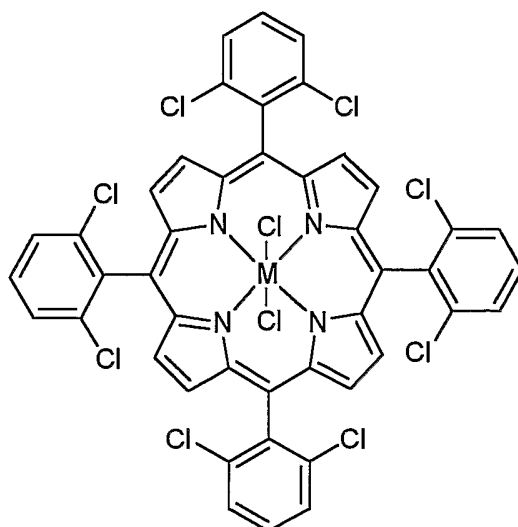
32. The compound of claim 31, wherein M comprises a transition metal.

33. The compound of claim 31, wherein the transition metal is ruthenium, manganese, cobalt, iron, copper or osmium.

5   34. The compound of claim 33, wherein the transition metal is ruthenium.
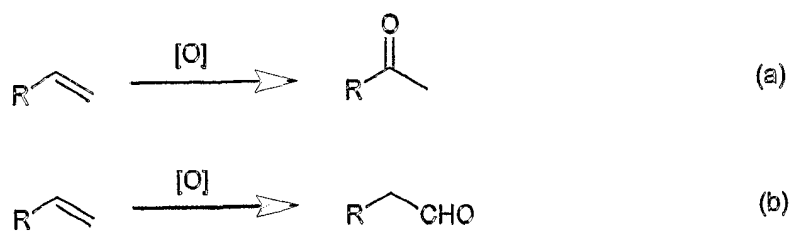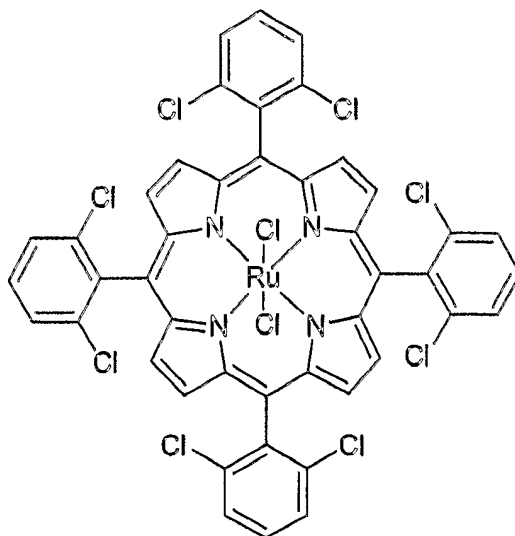
$$R\diagup\!\!\!\diagdown\ \xrightarrow{\text{[O]}}\ R\overset{\text{O}}{\underset{}{\diagup}}\!\!\!\diagdown\ \text{(a)}$$

$$R\diagup\!\!\!\diagdown\ \xrightarrow{\text{[O]}}\ R\diagup\!\!\!\diagdown\text{CHO}\ \text{(b)}$$

FIG. 1

[Ru^{IV}(tdcpp)Cl$_2$] (1)

[Ru^{IV}(tmp)Cl$_2$] (2)

FIG. 2

(a)

(b)
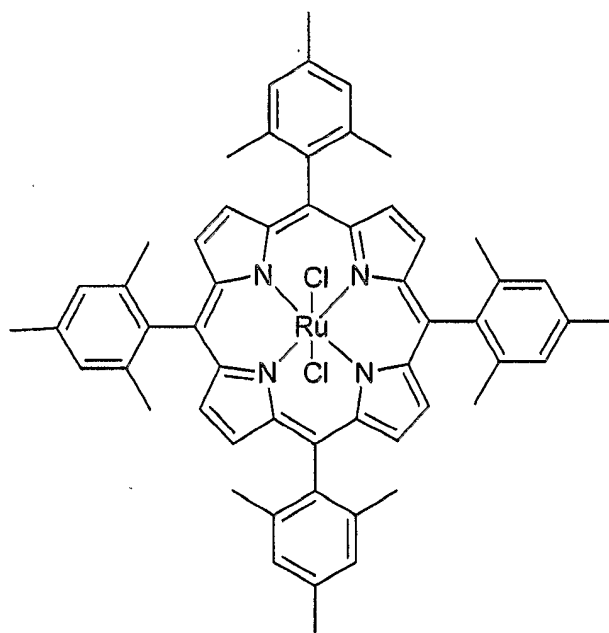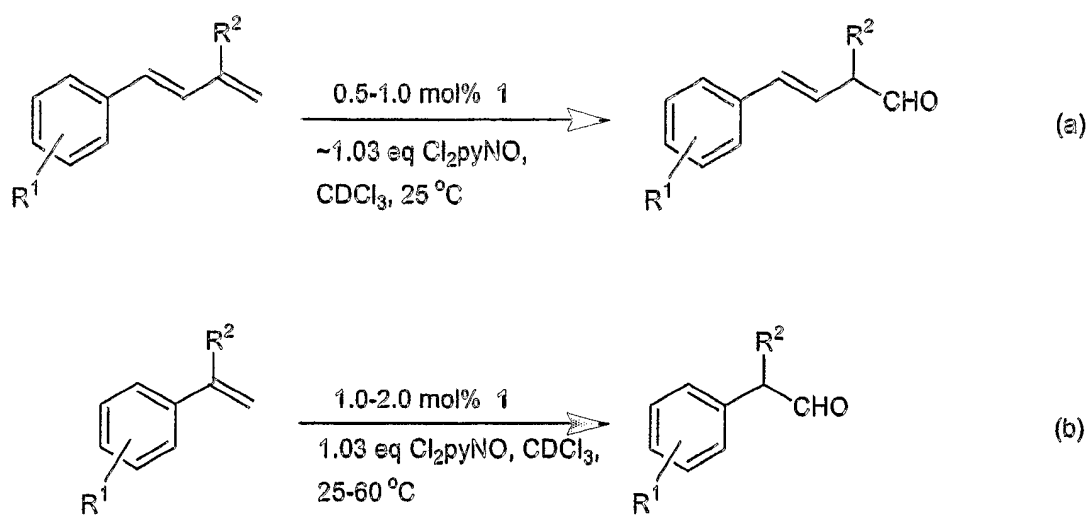
FIG. 3

Oxidation of **3** with various amounts of Cl$_2$pyNO catalyzed by **1**.
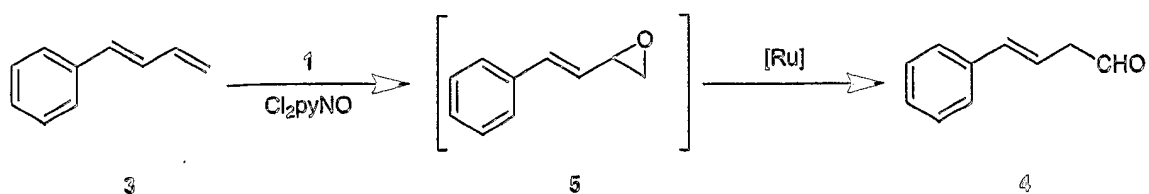
Entry[a]	Cl$_2$pyNO	Conversion of 3 (%)	Yield (%)[b]	
			5	4
1	2.0	100	49	51
2	1.03	100	0	99
3	0.9	90	0	>99

[a]Reaction conditions: **3**: 0.1 mmol, **1**: 0.5 mol%, CDCl$_3$: 0.5 mL; 25 °C, open to air.
[b]Determined by ^{1}H NMR (based on consumed substrate).

FIG. 4

Oxidation of 1,3-dienes 6–12 with Cl₂pyNO catalyzed by 1

R = OMe: 6
NO₂: 7
Me: 8

R = H: 9
OMe: 10

11

12

R = OMe: 13
NO₂: 14
Me: 15

R = H: 16
OMe: 17

18a

18b

19
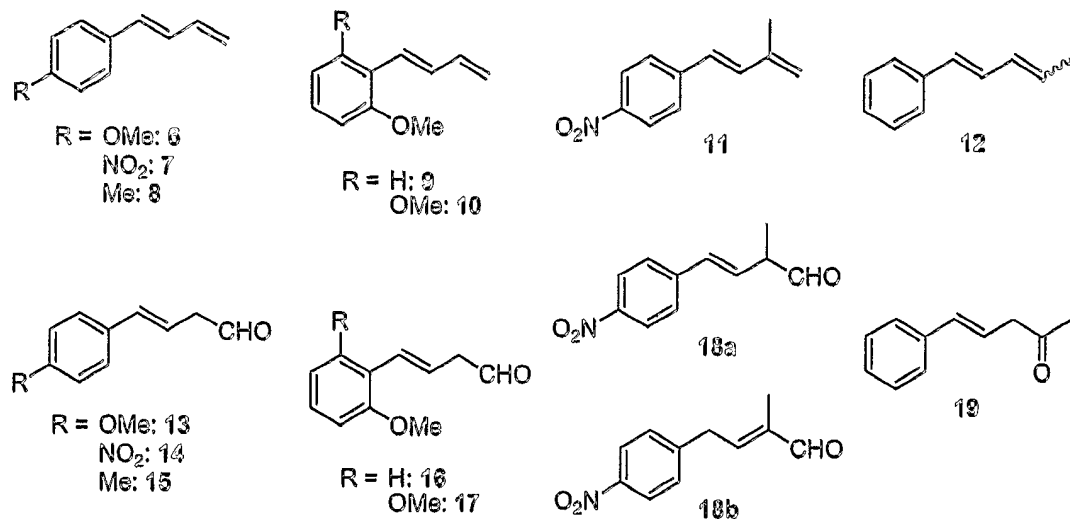
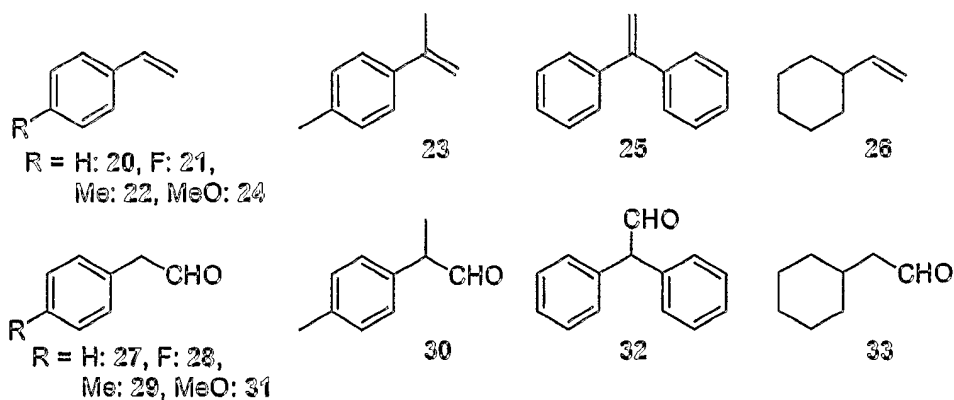| Entry[a]	Substrate	Temperature (°C)	Time (h)	Product	Yield[b] (%)
1	6	25	0.5	13	83
2	7	25	1	14	99
3	8	25	0.5	15	88
4	9	25	0.5	16	81
5[c]	10	25	0.5	17	91[d]
6	11	25	0.5	18a	90
7	12	60	6	19	99

[a]Reaction conditions: diene: 0.1 mmol, Cl₂pyNO: 1.03 equiv, 1: 0.5–1.0 mol%, CDCl₃: 0.5–1.0 mL; open to air. [b]Determined by GC or ^{1}H NMR. [c]Reaction conditions: diene: 0.65 mmol, Cl₂pyNO: 1.03 equiv, 1: 1.0 mol%, CHCl₃: 10 mL; open to air. [d]Isolated yield.

FIG. 5

Oxidation of terminal alkenes 20–26 with Cl₂pyNO catalyzed by 1

R = H: 20, F: 21,
    Me: 22, MeO: 24

23

25

26

R = H: 27, F: 28,
    Me: 29, MeO: 31

30

32

33

Entry[a]	Substrate	Temperature (°C)	Time (h)	Product	Yield[b] (%)
1	20	60	12	27	99
2	21	60	12	28	99
3	22	60	2	29	96
3	22	25	60	29	99
4	23	25	0.5	30	91
5	24	25	0.5	31	99
6	25	25	0.5	32	92
7	26	60	24	33	0[c]

[a]Reaction conditions: alkene: 0.1 mmol, Cl₂pyNO: 1.03 equiv, 1: 1.0–2.0 mol%, CDCl₃: 0.5–2.0 mL; open to air. [b]Determined by GC or ^{1}H NMR. [c]The corresponding epoxide was produced in 99% yield (determined by ^{1}H NMR).
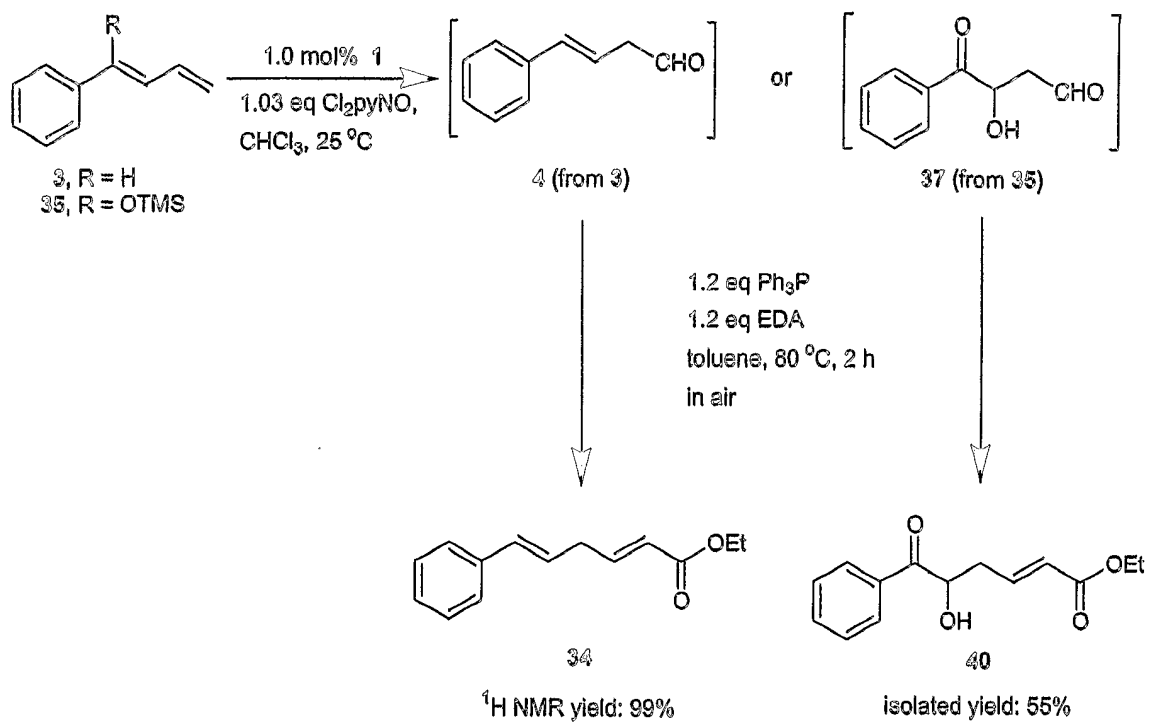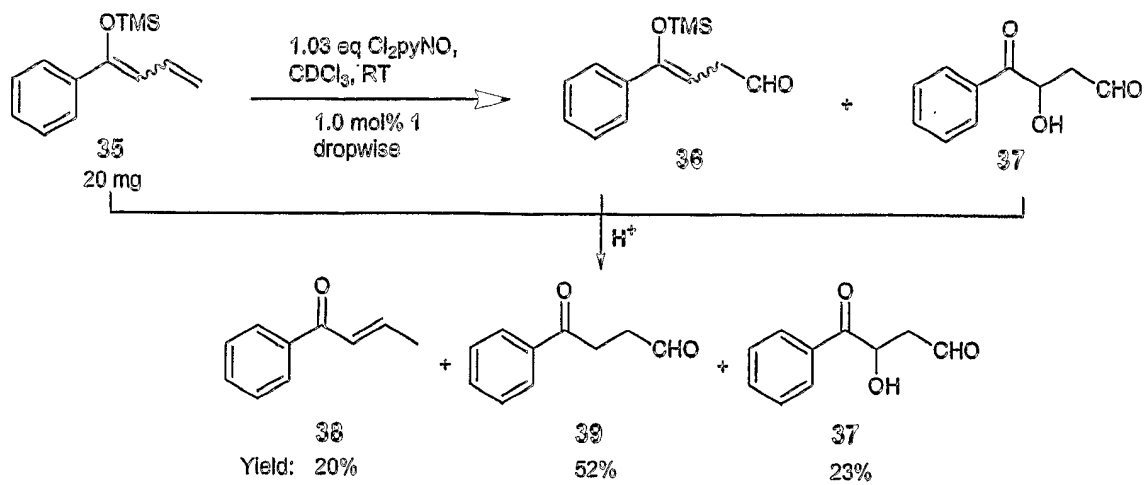
FIG. 6

FIG. 7

FIG. 8

A. CLASSIFICATION OF SUBJECT MATTER

Int.Cl[7] C07C47/232,C07C47/228,C07C49/217,C07C49/86,C07C45/50,C07C69/738,C07C69/618,C07C67/44,C07D487/22

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)

Int.Cl[7] C07C, C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

CAPLUS (STN) , REGISTRY (STN)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	Angewandte Chemie, International Edition(01.2004), 43(37), 4950-4954, Jian Chen et al., "A practical and mild method for the highly selective conversion of terminal alkenes into aldehydes through epoxidation-isomerization with ruthenium(IV)-porphyrin catalyst"	1-34
P,X	Journal of the American Chemical Society (26.01.2005), 127(3), 834-835, Rina Ito et al., " Unique Oxidation Reaction of Amides with Pyridine-N-oxide Catalyzed by Ruthenium Porphyrin: Direct Oxidative Conversion of N-Acyl-L-proline to N-Acyl-L-glutamate", ee page 834, left column	30
X	Chemical Communications (Cambridge) (1998), (10), 1105-1106, Zeev Gross et al., "Halogen to metal π-donation in metalloporphyrins" see page 1105, Scheme 1	30

☒ Further documents are listed in the continuation of Box C.   ☐ See patent family annex.

* Special categories of cited documents:	"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
"A" document defining the general state of the art which is not considered to be of particular relevance	
"E" earlier application or patent but published on or after the international filing date	"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
"L" document which may throw doubts on priority claim (S) or which is cited to establish the publication date of another citation or other special reason (as specified)	"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
"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	"&"document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
28 Sep 2005 (28.09.2005)	20 OCT 2005 (2 0 · 1 0 · 20 0 5)
Name and mailing address of the ISA/CN The State Intellectual Property Office, the P.R.China 6 Xitucheng Rd., Jimen Bridge, Haidian District, Beijing, China 100088 Facsimile No. 86-10-62019451	Authorized officer Wang Jing Telephone No. 86-10-62085581

C (Continuation).   DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Inorganic Chemistry (1997), 36(16), 3503-3511, Lilia Kaustov et al., " Spin Transition in a Manganese(III) Porphyrin Cation Radical, Its ransformation to a Dichloromanganese(IV) Porphyrin, and Chlorination of Hdrocarbons by the Latter" see page 3508-3510	30
X	Inorganic Chemistry (1996), 35(25), 7260-7263, Gross, Zeev et al., " One-Pot Synthesis of Dihalo(porphyrinato)osmium(IV) Complexes. Evidence or Monohalo(carbonyl)osmium(III) Intermediates", see page 7261 right column to page 7263	30
X,	Journal of the American Chemical Society (1992), 114(26), 10660-2, Hiro Ohtake et al., " Highly efficient oxidation of alkanes and alkyl alcohols with heteroaromatic N-oxides catalyzed by ruthenium porphyrins", see page 10661,right column; page 10662 right column, the last paragraph	30
A		1-29,31-34

Box No. II	Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
   because they relate to subject matter not required to be searched by this Authority, namely:

2. ☒ Claims Nos.: 1-10,14-24,28-30 (all partially)
   because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
   Present claims 1-10,14-24,28-30 relate to an extremely large number of possible preparation methods or metalloporphyrin compounds. Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the preparation methods or metalloporphyrin compounds claimed. In the present case, these claims are so large and so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to the methods or compounds wherein the metalloporphyrin has the structure A or B.
   It is stressed that the initial phase of the search revealed a very large number of documents destroying the subject-matter of claims 1-10,14-24,28-30; only a few of them have been cited in search report. Therefore a meaningful search over the whole of the claimed scope is impossible. Consequently the seach has been limited as defined above.

3. ☐ Claims Nos.:
   because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III	Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on protest   ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.