(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
3 November 2005 (03.11.2005)

PCT

(10) International Publication Number
WO 2005/102971 A1

(51) **International Patent Classification**^{7}: **C07C 29/48**, 45/51

(21) **International Application Number:** PCT/CN2005/000540

(22) **International Filing Date:** 20 April 2005 (20.04.2005)

(25) **Filing Language:** English

(26) **Publication Language:** English

(30) **Priority Data:**
60/563,645 20 April 2004 (20.04.2004) US

(71) **Applicant** *(for all designated States except US)*: **THE UNIVERSITY OF HONGKONG** [CN/CN]; G18, Eliot Hall, Pokfulam Road, Hong Kong Special Administrative Region (CN).

(72) **Inventors: CHE, Chiming**; Flat 5, 5/F., Block A, Parkway Court, 4 Park Road, Hong Kong (CN). **YU, Wingyiu**; 989 King's Road, Sunway Garden, 14/F, D-5, Quarry Bay, Hong Kong (CN). **HO, Chiming**; Room 3202, Shing Hang House, Tin Shing Court, Tin Shui Wai, Hong Kong (CN).

(74) **Agent: CHINA PATENT AGENT (H.K.) LTD.**; 22/F, Great Eagle Centre, 23 Harbour Road, Wanchai, Hong Kong (CN).

(81) **Designated States** *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) **Designated States** *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
- *with international search report*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: SUPPORTED RUTHENIUM NANOPARTICLE CATALYST FOR *CIS*-DIHYDROXYLATION AND OXIDATIVE CLEAVAGE OF ALKENES

(57) **Abstract:** The present invention relates to the use of nanosized metal particles (e.g., ruthenium) grafted on inert solid support for oxidation of alkenes. The supported metal catalyst can effect *cis*-dihydroxylation and oxidative cleavage of alkenes to give the respective *cis*-diols and carbonyl products.

SUPPORTED RUTHENIUM NANOPARTICLE CATALYST FOR *CIS*-DIHYDROXYLATION AND OXIDATIVE CLEAVAGE OF ALKENES

FIELD OF THE INVENTION

The invention relates to the use of supported ruthenium nanoparticles as a catalyst for oxidation of alkenes, including *cis*-dihydroxylation and oxidative cleavage of alkenes.

BACKGROUND OF THE INVENTION

The addition of two hydroxy groups in a *cis* manner to the carbon-carbon double bond of an alkene, as shown in FIG. 1, is an important transformation in organic synthesis. The resulting *cis*-1,2-diol products are versatile building blocks for pharmaceutical products and fine chemicals.

Traditionally, *cis*-dihydroxylation can be performed using stoichiometric amounts of osmium tetroxide or potassium permanganate (see: Haines, A. H., in *Comprehensive Organic Synthesis*; Trost, B. M.; Fleming, I. (eds.) Pergamon: Oxford, 1991; Vol. 7, p. 437). However, an immediate drawback is that these processes produce a large amount of toxic effluent. Furthermore, osmium tetroxide is highly toxic and very expensive, which hampers its use in large-scale synthesis. For the use of permanganate as oxidant, the reaction usually produces undesired over-oxidized products, and yields are lower than with osmium tetroxide.

Catalytic systems for alkene *cis*-dihydroxylation have been extensively pursued. In particular, development of osmium-catalyzed alkene dihydroxylation and its asymmetric variants represents an important milestone in modern organic synthesis [see: (a) Johnson, R. A.; Sharpless, K. B. In *Catalytic Asymmetric Synthesis*; by Ojima, I. 2nd ed., VCH: New York, 2000. (b) Kolb, H. C.; Van Nieuwenhze, M. S.; Sharpless, K. B. *Chem. Rev.* 1994, 94, 2483]. Several secondary oxidants including metal chlorates (see: Hoffmann, K. A. *Chem.* 1912, 45, 3329), hydrogen peroxide (see: Milas, N. A.; Trepagnier, J.-H.; Nolan, J. T.; Iliopolus, J. Ji. *J. Am. Chem. Soc.* 1959, 81, 4730), *tert*-butyl hydroperoxide [see: (a) Sharpless, K. B.; Akashi, K. *J. Am. Chem. Soc.* 1976, 98, 1986. (b) Carlsen, P. H. J.; Katsuki, T.; Martin, V. S. ; Sharpless, K. B. *J. Org. Chem.* 1981, 46, 3936. (c) Webster, F. X.; Rivas-Enterrios, J.; Silverstein, R. M. *J. Org. Chem.* 1987, 52, 689. (d) Martin, V. S.; Nunez, M. T.; Tonn, C. E. *Tetrahedron Lett.* 1988, 29, 2701 (e) Caron, M.; Carlier, P. R.; Sharpless, K. B. *J. Org. Chem.* 1988, 53, 5185], *N*-methylmorpholine *N*-oxide (NMO, Upjohn process) [see: (a) Schneider, W. P.; McIntosh, A. V. US 2,769,824 (1956). (b) Van Rheenen, V.; Kelly, R. C.; Cha, D. Y. *Tetrahedron Lett.* 1976, 17, 1973] are known for effective catalytic *cis*-dihydroxylation reactions. For sterically hindered alkenes, the catalytic system employing trimethylammonia *N*-oxide as secondary oxidant has been reported to give improved product yields (see: Ray, R.; Matteson, D. S. *Tetrahedron Lett.* 1980, 21, 449).

To overcome problems of over-oxidation and inertness towards sterically hindered alkenes, catalytic system using hexacyanoferrate(III) as secondary oxidant has been developed (see: Minato, M.; Yamamoto, K.; Tsuji, J. *J. Org. Chem.* 1990, 55, 766). Consequently, an enantioselective version based on hexacyanoferrate(III) as oxidant was developed by Sharpless and co-workers (see: Ogino, Y.; Chen, H.; Kwong, H. L.; Sharpless, K. B. *Tetrahedron Lett.* 1991, 32, 3965). Currently, the "$K_2[OsO_2(OH)_4$ + $K_3[Fe(CN)_6]$" formulation is commercially available and branded as AD-mix.

The search for transition metal catalysts alternative to osmium for *cis*-dihydroxylation of alkene is receiving current attention. Earlier work by Shing and co-workers showed that $RuCl_3 \cdot xH_2O$ is an effective catalyst for *cis*-dihydroxylation of alkenes when using $NaIO_4$ as oxidant with a mixture of acetonitrile, ethyl acetate and water as solvent at reaction temperature = 0 °C [see: (a) Shing, T. K. M.; Tai, V. W.-F.; Tam, E. K. M. *Angew. Chem., Int. Ed. Engl.* 1994, 33, 2313. (b) Shing, T. K. M.; Tai, V. W. F.; Tam, E. K. M. Chung, I. H. F.; Jiang, Q. *Chem. Eur. J.* 1996, 2, 50. (c) Shing, T. K. M.; Tam, E. K. M. *Tetrahedron Lett.* 1999, 40, 2179]. Recently, Que and co-workers disclosed that alkene *cis*-dihydroxylation can be achieved with moderate selectivity using some iron complexes as catalyst and hydrogen peroxide as oxidant [see: (a) Chen, K.; Costas, M.; Kim, J.; Tipton, A. K.; Que, L. Jr. *J. Am. Chem. Soc.* 2002, 124, 3026. (b) Costas, M.; Tipton, A. K.; Chen, K.; Jo, D.-H.; Que, L. Jr. *J. Am. Chem. Soc.* 2001, 123, 6722. (c) Chen, K.; Que, L. Jr. *Angew. Chem. Int. Ed.* 1999, 38, 2227]. In addition, Jacobs and coworkers reported that some manganese cyclic triamine complexes could convert alkene to its corresponding *cis*-1,2-diol in low yield using hydrogen peroxide as secondary oxidant (see: De Vos, D. E.; de Wildeman, S.; Sels, B. F.; Grobet, P. J.; Jacobs, P. A. *Angew. Chem. Int. Ed.* 1999, *38*, 980).

At present, osmium-catalyzed alkene *cis*-dihydroxylation is still the system of choice because of its effectiveness and selectivity. However, recovery of the precious metal catalysts are difficult, and it may result in product contamination. This has restricted its use for large-scale reactions in industry. To this end, several research groups have already attempted to address the issues by heterogenization of the metal catalysts onto solid support [see: (a) Bolm, C.; Gerlach, A. *Eur. J. Chem.* 1998, 21, 1. (b) Salvadori, P.; Pini, D.; Petri, A. *Synlett.* 1999, 1181. (c) Gravert, D. J.; Janda, K. D. *Chem. Rev.* 1997, 97, 48]. However, limited success was achieved with respect to recovery and reuse of the metal catalysts. For example, Kobayashi and co-workers recently developed a highly recoverable and reusable polymer-supported osmium catalyst for alkene *cis*-dihydroxylations using a microencapsulation technique (see: Kobayashi, S.; Endo, M.; Nagayama, S. *J. Am. Chem. Soc.* 1999, 121, 11229). A recent work by Choudary and co-workers reported that immobilized OsO_4^{2-} on layered double hydroxides by ion-exchange technique was found to attain good recoverability and reusability for alkene *cis*-dihydroxylation (see: Choudary, B, M.; Chowdari, N. S.; Kantam, M. L.; Raghavan, K. V. *J. Am. Chem. Soc.* 2001, 123, 9220). Despite these advances, development of more easily handled metal catalysts with superior recyclability and catalytic activities is still highly desirable. A recent report by Park and co-workers showed that a 3-D networked osmium nanomaterial is an effective heterogeneous catalyst for dihydroxylation and oxidative cleavage of alkenes (see: Lee, K.; Kim, Y.-H.; Han, S. B.; Kang, H.; Park, S.; Seo, W. S.; Park, J. T.; Kim, B.; Chang, S. *J. Am. Chem. Soc.* 2003, 125, 6844).

Limited examples involving supporting transition metal catalysts other than osmium based complexes for alkene *cis*-dihydroxylation and alkene oxidative cleavage have been reported. Supported manganese cyclic triamine complexes converted alkenes to *cis*-diols when using hydrogen peroxide as oxidant, but poor yield and selectivity made this process impractical (De Vos, D. E.; de

Wildeman, S.; Sels, B. F.; Grobet, P. J.; Jacobs, P. A. *Angew. Chem. Int. Ed.* 1999, *38*, 980).

Application of nanosized metal particles as catalysts for organic transformations is receiving current attention [see: (a) Moreno-Mañas, M.; Pleixats, R. *Acc. Chem. Res.* 2003, 36, 638. (b) Roucoux, A.; Schulz, J.; Patin, H. *Chem. Rev.* 2002, 102, 3757. (c) Horn, D.; Rieger, J. *Angew. Chem. Int. Ed.* 2001, 40, 4330. (d) Bönnermann, H.; Richards, R. M. *Eur. J. Inorg. Chem.* 2001, 2455. (e) Rao, C. N. R.; Kulkarni, G. U.; Thomas, P. J.; Edwards, P. P. *Chem. Soc. Rev.* 2000, 29, 27. (f) Johnson, B. F. G. *Coord. Chem. Rev.* 1999, 190, 1269. (g) Bradley, J. S. In *Clusters and Colloids: from Theory to Application*; Ed.: Schmid, G. VCH: Weiheim, 1994; p. 459. (h) Lewis, L. N. *Chem. Rev.* 1993, 93, 2693. (i) Schmid, G. *Chem. Rev.* 1992, 92, 1709]. Due to its high surface area and the high density of active sites, nanosized metal particles exhibit superior catalytic activities versus the corresponding bulk materials.

Various synthetic methods for ruthenium nanoparticles have been reported in the literature. The reduction of ruthenium salts in polyol solution at evaluated temperature is promising and simple for ruthenium nanoparticles [see: (a) Viau, G.; Brayner, R.; Poul, L.; Chakroune, N.; Lacaze, E.; Fiévet-Vincent, F.; Fiévet, F. *Chem. Mater.* 2003, 15, 486. (b) Balint, I.; Mayzaki, A.; Aika, K.-I. *J. Catal.* 2002, 207, 66. (c) Miyazaki, A.; Balint, I.; Aika, K.-I.; Nakano, Y. *J. Catal.* 2001, 204, 364]. Besides, several research groups have developed some new preparation procedures for nanosized ruthenium particles. Chaudret and co-workers utilized the reaction of an organometallic ruthenium precursor under a hydrogen atmosphere in organic solvent to obtain a stable ruthenium colloid (see: Vidoni, O.; Philipport, K.; Amiens, C.; Chaudret, B.; Balmes, O.; Malm, J. O.;

Bovin, J. O. Senocq, F.; Casanove, J. *Angew. Chem. Int. Ed. Engl.* 1999, 38, 3736). Also, Che and coworkers demonstrated that the solvothermal reduction of ruthenium salts is a viable route to nanosized ruthenium particles (see: Gao, S.; Zhang, J.; Zhu, Y.-F.; Che, C. M. *New J. Chem.* 2000, 739). In addition, Alonso-Vante and co-workers disclosed that highly dispersed nanocrystalline ruthenium particles could be prepared under mild conditions in an organic solvent from the ruthenium carbonyl precursor (see: Vogel, W.; Le Rhun, V.; Garnier, E.; Alonso-Vante, N. *J. Phys. Chem. Chem. B* 2001, 105, 5238). Furthermore, Lee and coworkers reported that nanosized ruthenium particles could be prepared by the sodium borohydride reduction of ruthenium chloride and ruthenium hydroxide (see: Lee, D.-S.; Liu, T.-K. *Journal of Non-Crystalline Solids*, 2002, 311, 323).

The reports on the catalytic reactivity of these ruthenium particles are, however, sparse in the literature. Miyazaki and co-workers reported alumina-supported ruthenium nanoparticles have a high reactivity for ammonia synthesis [see: (a) Balint, I.; Mayzaki, A.; Aika, K.-I. *J. Catal.* 2002, 207, 66. (b) Miyazaki, A.; Balint, I.; Aika, K.-I.; Nakano, Y. *J. Catal.* 2001, 204, 364]. Wakatsuki and coworker disclosed that TiO_2-supported ruthenium nanosized metal particles exhibited the reduction of SO_2 and H_2 to give element sulfur (see: Ishiguro, A.; Nakajima, T.; Iwata, T.; Fujita, M.; Minato, T.; Kiyotaki, F.; Izumi, Y.; Aika, K.-I.; Uchida, M.; Kimoto, K.; Matsui, Y.; Wakatsuki, Y. *Chem. Eur. J.* 2002, 8, 3260). Schmid and co-workers revealed that ruthenium nanoparticles included in nanoporous alumina membranes catalyzed alkene hydrogenation (see: Pelzer, K.; Philippot, K.; Chaudret, B.; Meyer-Zaika, W.; Schmid, G. *Zeitschrift fur anorganische und allgemieine chemie*, 2003, 629, 1217). U.S. Patent No. 6,551,960 discloses the fabrication of supported nanosized ruthenium catalyst and its reactivity for methanol reformation. Chan and co-workers reported that Ru-Pt nanoparticles, prepared by water-in-oil reverse micro-emulsion, displaced high catalytic activity for methanol oxidation when supported on carbon electrode (see: Zhang, Z.; Chan, K.-Y. *Chem. Mater.* 2003, 15, 451). Recently, it was reported that zeolited-confined nanosized ruthenium dioxide can efficiently promote aerobic oxidation of alcohols (see: Zhan, B.-Z.; White, M. A.; Sham, T.-K.; Pincock, J. A.; Doucet, R. J.; Rao, K. V. R.; Roberson, K. N.; Cameron, T. S. *J. Am. Chem. Soc.* 2003, 125, 2195). However, the reactivities of ruthenium nanoparticles toward *cis*-dihydroxylation and oxidative cleavage of alkenes are hitherto unknown in the literature.

Ruthenium salts and complexes are known to be versatile catalysts for various oxidative transformations [see: (a) Murahashi, S.-I.; Komiya, N. In *Biomimetic Oxidations Catalyzed by Transition Metal Complexes*; Ed.: Meunier, B.; Imperial College Press, 2000; p. 563. (b) McLain, J. L.; Lee, J.; Groves, J. T. In *Biomimetic Oxidations Catalyzed by Transition Metal Complexes*; Ed.: Meunier, B.; Imperial College Press, 2000; p. 91. (c) Ley, S. V.; Norman, J.; Griffith, W. P.; Marsden, S. P. *Synthesis*, 1994, 639. (d) Griffith, W. P. *Chem. Soc. Rev.* 1992, 21, 179]. Here, we report that ruthenium nanoparticles immobilized on hydroxyapatite is a superior catalyst for *cis*-dihydroxylation and oxidative cleavage of alkenes. With ethyl *trans*-cinnamate as a substrate, the supported catalyst has been recycled for successive *cis*-dihydroxylation reactions without significant deterioration of catalytic activities.

BRIEF DESCRIPTION OF THE FIGURES AND TABLES

FIG. 1. illustrates the described *cis*-addition of two hydroxyl group to the carbon-carbon double bond.

FIG. 2. provides a typical transmission electron micrograph of hydroxyapatite supported ruthenium nanoparticles catalyst.

FIG. 3. provides an X-ray diffraction (XRD) spectrum of hydroxyapatite supported ruthenium nanoparticles catalyst and its parent hydroxyapatite as control.

TABLE 1. provides representative examples of *cis*-dihydroxylation of alkenes catalyzed by ruthenium nanoparticles.

TABLE 2. provides representative examples of oxidative cleavage of alkenes catalyzed by ruthenium nanoparticles.

TABLE 3. provides representative examples of oxidative cleavage of α,β-unsaturated alkenes catalyzed by ruthenium nanoparticles.

DETAILED DESCRIPTION OF THE INVENTION

The invention relates to the use of ruthenium colloids supported on an inert solid support (e.g., calcium hydroxyapatite) for oxidative transformations of alkenes. Stable ruthenium colloid was prepared by the reduction of $RuCl_3{\cdot}xH_2O$ (0.32 mmol) in 1,2 immobilization of ruthenium colloids onto calcium hydroxyapatite. Stable ruthenium colloid was prepared by the reduction of $RuCl_3{\cdot}xH_2O$ (0.325 mmol) in 1,2-propanediol (100 mL) in the presence of sodium acetate (1 mmol) at 150 °C by following a reported procedure (see: Viau, G.; Brayner, R.; Poul, L.; Chakroune, N.; Lacaze, E.; Fiévet-Vincent, F.; Fiévet, F. *Chem. Mater.* 2003, 15, 486).

In this work, we chose calcium hydroxyapatite as an example of solid support. Reported uses of hydroxyapatite include artificial bones and teeth, adsorbents, ion-exchangers, and catalysts [see: (a) Elliott, J. C. *Structure and Chemistry of the Apatite and Other Calcium Orthophosphates*; Elsevier, Amsterdam, 1994. (b) Sugiyama, S.; Minami, T.; Hayashi, H.; Tanaka, M.; Shigemoto, N.; Moffat, J. B. *J. Chem. Soc. Faraday Trans.* 1996, 92, 293]. Calcium hydroxyapatite was prepared according to a reported method (see: Hayek, E.; Newesely, H. *Inorg. Synth.* 1963, 7, 63). Successful immobilization of the ruthenium nanoparticles was achieved by treating the colloidal solution with calcium hydroxylapatite (0.4 g) and H_2O (50 mL) for 24 h. The hydroxyapatite-supported ruthenium nanoparticles (nano-RuHAP) were obtained as a dark grey solid after centrifugation, followed by washing with deionized water and dried under vacuum at 110 °C for overnight. On the basis of ICP analysis, the Ru content of nano-RuHAP was determined to be 5 wt% (0.5 mmol g^{-1}) and the measured Ca/P molar ratio being 1.66, which agrees with the reported value of 1.67, indicating no significant exchange of the constituent Ca^{2+} ions.

The X-ray powder diffraction (XRD) pattern of nano-RuHAP showed prominent peaks at $2\theta = 25.90°$, 31.85°, 32.25°, 32.95° and 49.55°, which are indexed to (002), (211), (112), (300) and (213) reflections of the hexagonal crystal system of the hydroxyapatite [JCPSD card no: 09-0432], respectively (FIG. 2). It should be noted that almost identical XRD pattern was observed for the free hydroxyapatite (i.e., without Ru particles). This result indicates that the crystallinity of hydroxyapatite was retained after immobilization of ruthenium nanoparticles. The transmission electron microscope (TEM) image of nano-RuHAP showed uniformly dispersed particles, and EDX analysis confirmed that the particles corresponded to ruthenium with an average diameter being ca. 4 nm (FIG. 3). There is a small increase in the surface area of nano-RuHAP (25 $m^2 g^{-1}$) compared to its parent hydroxyapatite (17 $m^2 g^{-1}$) as determined by the N_2 adsorption isotherms. This can be accounted for by the physical adsorption of the ruthenium nanoparticles on the solid support.

EXAMPLE 1

cis-Dihydroxylation of Alkenes Catalyzed by nano-RuHAP

The invention relates to a direct method of synthesis of *cis*-1,2-diol using nano-RuHAP as a general and effective catalyst for the direct *cis*-dihydroxylation of alkenes. Generally, to a dilute sulfuric acid solution (0.4 N, 2 mL) was added $NaIO_4$ (642 mg, 3 mmol) with stirring to form a clear solution. Upon cooling to 0 °C using an ice-water bath, nano-RuHAP (40 mg) was added and the mixture was stirred for 3 min, followed by addition of an EtOAc-MeCN mixture (1 : 1 (v/v); 12 mL). The combined mixture was stirred at 0 °C for an additional 5 min. Alkene (2 mmol) was added in one portion and the reaction mixture was stirred until all the starting alkene was consumed as monitored by TLC. Excess acid and $NaIO_4$ were quenched using a saturated $NaHCO_3$ solution (10 mL) and a saturated $Na_2S_2O_3$ solution (10 mL). The catalyst was separated from the reaction mixture by centrifugation. The recovered catalyst was washed with water and then dried in vacuum before recycle. The supernatant liquid was extracted with ethyl acetate (3 × 15 mL), and the organic extracts were dried over $MgSO_4$. Pure *cis*-1,2-diols were obtained by flash chromatography on silica gel (230-400 mesh) and were characterized by IR, MS and NMR spectroscopies. Following a series of control experiments, 20 mol % of H_2SO_4 gave the maximum yield; further increase of H_2SO_4 did not improve the yield. Using $NaIO_4$ as oxidant was shown the best among hypochlorate, hydrogen peroxide and *tert*-butyl hydroperoxide.

Using the nano-RuHAP catalyzed protocol, alkenes were selectively converted into corresponding *cis*-1,2-diol with moderate to good yields (see TABLE 1). *α,β*-unsaturated alkenes such as ethyl *trans*-cinnamate, ethyl crotonate, dimethyl fumarate, dimethyl maleate and isophorone can be transformed to their corresponding *cis*-1,2-diols in 70, 65, 53, 50 and 64 % isolated yields, respectively (entries 1–5). Under the Ru-catalyzed conditions, effective oxidations of styrene and 1-dodecene gave styrene glycol (85%) and dodecene glycol (75%) in good yields (entries 6 and 7). Likewise, dihydroxylation of 1,2-disubstituted alkenes including 1,4-diacetoxy-*cis*-but-2-ene and phenanthrene has been achieved to afford the corresponding *cis*-1,2-diols in 61 and 60% yields (entries 8 and 9). Using 1-acetoxy cyclohex-2-ene as substrate, the Ru-catalyzed dihydroxylation furnished 1-acetoxy-2,3-dihydroxycyclohexane in 75% yield (entry 10) with the *anti*-isomer being the major product (*anti* : *syn* = 9 : 1). Yet, the catalytic dihydroxylation of trisubstituted alkenes such as (3-benzloxy)-1-methylbut-1-ene appeared to be less effective, and the corresponding *cis*-1,2-diol was obtained in only 45% yield (entry 11).

The organic products of the catalytic dihydroxylation were identified by their spectral and physical data with the reported data (see: Shing, T. K.-M.; Tai, V. W. F.; Tam, E. K.-M.; Chung, I. H.-F.; Jiang, Q. *Chem. Eur. J.* 1996, 2, 50).

EXAMPLE 2

Recycling refers to the return to an original catalyst so that reaction can begin again. This is particularly important to save the valuable catalyst and minimize product contamination. The nano-RuHAP catalyst was recovered by centrifugation and was used for the second, third and fourth runs under identical reaction conditions. With ethyl *trans*-cinnamate as substrate, no apparent loss of catalyst activity was observed, and the product *cis*-1,2-diol was isolated in 80, 82 and 66% yields, respectively. A total product turnover = 298 was attained over four consecutive runs. For each cycle of catalyst recovery, ICP-MS analysis of the supernatent solution revealed the residual Ru content was below 5 ppm. It is noteworthy that zero-valent Ru metal powder is completely ineffective catalyst for the dihydroxylation reaction.

Turnover refers to the relative number of molecules of products per number of molecules of catalyst prior to the exhaustion of a given reaction and shows a very important aspect of catalyst efficiency. It should be noted that the turnover number of $RuCl_3$ catalyst do not exceed 168 for methyl *trans*-cinnamate, a derivative of *trans*-cinnamate ester (see: Plietker, B.; Niggemann, M. *Org. Lett.* 2003, 5, 3353). The nano-RuHAP- catalyzed protocol is equally effective when operating at a larger-scale. For example, the reaction of ethyl *trans*-cinnamate (10 mmol) in the presence of nano-RuHAP (0.2 mol%) gave the corresponding *cis*-1,2-diol in 67% isolated yield (product turnover = 330).

EXAMPLE 3

Oxidative Cleavage of Alkenes catalyzed by nano-RuHAP using $NaIO_4$ as Oxidant (see: Yang, D.; Zhang, C. *J. Org. Chem.* 2001, 66, 4814).

The invention relates to a direct method of synthesis of aldehydes and ketones using nano-RuHAP as a general and effective catalyst for the oxidative cleavage of alkenes. To a mixture of 1,2-dichloroethane (5 mL) and distilled water (1 mL) containing alkene (90 mg, 0.5 mmol) and nano-RuHAP (40 mg) was added $NaIO_4$ (214 mg, 1 mmol) by portions over a period of 10 min at room temperature. After complete reaction based on TLC monitoring, excess $NaIO_4$ was quenched by a saturated $Na_2S_2O_3$ solution. The catalyst was separated from the reaction mixture by centrifugation, and the recovered catalyst was washed with water and dried in vacuum before reuses. The supernatant liquid was extracted with CH_2Cl_2 (3 × 10 mL) and the combined organic extracts were dried over anhydrous Na_2SO_4. The reaction products were identified and quantified by capillary GC analysis using 1,4-dichlorobenzene as internal standard.

With nano-RuHAP as catalyst, alkenes were cleaved to corresponding aldehydes or ketones in excess yields upon treatment with $NaIO_4$ (1 mmol) in a 1,2-dichloroethane-H_2O (5 : 1 v/v) at room temperature for 2-3 hours (TABLE 2).. Oxidative cleavage of other stilbene derivatives such as *cis*-stilbene and 1-methyl-1,2-diphenylethylene under the nano-RuHAP catalyzed conditions produced the carbonyl products in excellent yields (>85%) (entries 2–3). As expected, styrene, α-methylstyrene and *trans*-β-methylstyrene were found to undergo oxidative cleavage using the "nano-RuHAP + $NaIO_4$" protocol, and benzaldehyde was obtained in 66 – 92% yields (entries 4-6). When cyclic aromatic alkenes such as dihydronaphthalene was used as substrate, the corresponding dicarbonyl product was isolated in 86% yield with 76% substrate conversion (entry 7). Likewise, cyclic aliphatic alkenes such as norbornene and cyclooctene were found to undergo effective C=C bond cleavage to afford the corresponding dicarbonyl products in 72 – 87% yields (entries 8-9).

EXAMPLE 4

Oxidative Cleavage of Alkenes catalyzed by nano-RuHAP using Oxone as Oxidant.

The invention relates to a direct method of synthesis of aldehydes and ketones using nano-RuHAP as a general and effective catalyst for the oxidative cleavage of α,β-unsaturated alkenes. To a mixture of CH_3CN (7.5 mL) and distilled water (5 mL) containing alkene (104 mg, 0.5 mmol) and nano-RuHAP (40 mg) was added a mixture Oxone (770 mg, 1.25 mmol) and $NaHCO_3$ (330 mg, 2.3 mmol) over a period of 10 min at room temperature. Upon complete reaction based on TLC analysis, excess $NaIO_4$ was quenched by a saturated $Na_2S_2O_3$ solution. The catalyst was separated from the reaction mixture by centrifugation, and the recovered catalyst was washed with water and dried in vacuum before reuse. The supernatant liquid was extracted with CH_2Cl_2 (3 × 10 mL) and the combined organic extracts were dried over anhydrous Na_2SO_4. The reaction products were purified by flash chromatography and were characterized by IR, MS and NMR spectroscopies. "nano-RuHAP + Oxone" protocol would also effect oxidative cleavage of *α,β*-unsaturated alkenes. When chalcone (0.5 mmol) was treated with Oxone (1.25 mmol) and nano-RuHAP (4 mol %) in a $NaHCO_3$

buffered MeCN-H_2O (1.5 : 1 v/v) at room temperature for 3 h, benzaldehyde and benzoic acid were produced (entry 1). Similar oxidative cleavage products were found in isophorone and (+)-pulegone (entry 2,3). Notably, facile oxidative cleavage of C≡C bonds was also observed. For example, subjecting alkynes such as 1-phenyl-1-propyne to the Ru-catalyzed conditions produced benzoic acid in 82% yield (entry 4).

What is claimed is:

1. A method for synthesizing a *cis*-1,2-diol from an alkene comprising the step of reacting an oxidant and an acid with the alkene in the presence of a catalytic amount of a solid supported ruthenium nanoparticle as catalyst.

2. The method for synthesizing a *cis*-1,2-diol from an alkene, an oxidant, and an acid described in claim 1, wherein the alkene has the structure $R_1R_2C=CR_3R_4$, and

   where R_1 to R_4 can be H, alkyl, CN, COOH, COO-alkyl, COO-aryl, CO-alkyl, CO-aryl, O-alkyl, O-aryl, O-CO-alkyl, O-CO-aryl, OCOO-alkyl, OCOO-aryl, N-alkyl$_2$, N-aryl$_2$, NH-alkyl, NH-aryl, NO, NO_2, NOH, aryl, fluoro, chloro, iodo, CHO, SO_3H, SO_3-alkyl, SO_2-alkyl, SO-alkyl, CF_3, alkyl is a 1 to 18 carbon-atom hydrocarbon, aryl is an aromatic ring.

3. A method for synthesizing a *cis*-1,2-diol from an alkene, an oxidant, and an acid as set forth in claim 1, wherein the organic and inorganic oxidants includes a hypervalent iodine compound, a hypervalent chlorine compound, hydrogen peroxide or a derivative thereof, a peracid compound, or a derivative thereof.

4. A method for synthesizing a *cis*-1,2-diol from an alkene, an oxidant, and an acid as set forth in claim 1, wherein the solvent is a mixture of water and an organic solvent that includes acetonitrile, ethyl acetate, dichloremethane, chloroform, 1,2-dichloroethane, hexane, benzene, toluene, methanol, ethanol, isopropanol, *tert*-butanol, or mixtures thereof.

5. A method for synthesizing a *cis*-1,2-diol from an alkene, an oxidant, and acid as set forth in claim 1, wherein reaction temperature is between –78 to 40 °C.

6. A method for synthesizing a *cis*-1,2-diol from an alkene ester, an oxidant, and an acid as set forth in claim 1, wherein the organic and inorganic acids include sulfuric acid, nitric acid, hydrochloric acid, and acetic acid.

7. A method for synthesizing a *cis*-1,2-diol from an alkene and an oxidant and base as set forth in claim 1, wherein ruthenium nanoparticles range in size from 1 to 100 nm, and are supported on hydroxyapatite.

8. A catalyst as set forth in claim 1, wherein the metal nanoparticles includes a transition metal.

9. A catalyst as set forth in claim 7, wherein the metal nanoparticle includes ruthenium, manganese, iron or mixtures thereof.

10. A catalyst as set forth in claim 7 can be separated by filtration or centrifugation and reused.

11. A method for synthesizing an aldehyde or a ketone from an alkene comprising reacting an oxidant with the alkene in the presence of a catalytic amount of a solid supported ruthenium nanoparticle.

12. A method for synthesizing an aldehyde or a ketone from an alkene as set forth in claim 11, wherein the alkene has the structure $R_1R_2C=CR_3R_4$, and

where R_1 to R_4 can be H, alkyl, CN, COOH, COO-alkyl, COO-aryl, CO-alkyl, CO-aryl, O-alkyl, O-aryl, O-CO-alkyl, O-CO-aryl, OCOO-alkyl, OCOO-aryl, N-alkyl$_2$, N-aryl$_2$, NH-alkyl, NH-aryl, NO, NO_2, NOH, aryl, fluoro, chloro, iodo, CHO, SO_3H, SO_3-alkyl, SO_2-alkyl, SO-alkyl, CF_3, alkyl is a 1 to 18 carbon-atom hydrocarbon, aryl is an aromatic ring.

13. A method for synthesizing an aldehyde or a ketone from an alkene and an oxidant as described in claim 12, wherein the organic and inorganic oxidant includes a hypervalent iodine compound, a hypervalent chlorine compound, hydrogen peroxide or its derivatives, a peracid compound, or its derivatives.

14. A method as set forth in claim 12, wherein the method is carried out in a solvent which is a mixture of water and acetonitrile, ethyl acetate, dichloremethane, chloroform, 1,2-dichloroethane, hexane, benzene, toluene, methanol, ethanol, isopropanol, *tert*-butanol, or mixtures thereof.

15. A method as set forth in claim 12, wherein metal nanoparticles are of the size from 1 to 100 nm.

16. A catalyst of claim 15, wherein the metal nanoparticles comprise a transition metal.

17. A catalyst as set forth in claim 16, wherein the metal nanoparticle is comprised of ruthenium, manganese or iron, or mixtures thereof.

18. A method for synthesizing an aldehyde, a ketone or a carboxylic acid from an alkene comprising reacting an oxidant, in the presence of a buffer, with an alkene using a catalytic amount of a solid supported ruthenium nanoparticle.

19. A method as set forth in claim 18, wherein the alkene has the structure $R_1R_2C{=}CR_3R_4$, and

where R_1 to R_4 can be H, alkyl, CN, COOH, COO-alkyl, COO-aryl, CO-alkyl, CO-aryl, O-alkyl, O-aryl, O-CO-alkyl, O-CO-aryl, OCOO-alkyl, OCOO-aryl, N-alkyl$_2$, N-aryl$_2$, NH-alkyl, NH-aryl, NO, NO_2, NOH, aryl, fluoro, chloro, iodo, CHO, SO_3H, SO_3-alkyl, SO_2-alkyl, SO-alkyl, CF_3, alkyl is a 1 to 18 carbon-atom hydrocarbon, aryl is an aromatic ring.

20. A method as set forth in claim 19, wherein the organic and inorganic oxidant includes a hypervalent iodine compound, a hypervalent chlorine compound, a hydrogen peroxide or a derivative thereof, a peracid or a derivative thereof.

21. A method as set forth in claim 19, wherein the buffer includes $NaHCO_3$.

22. A method as set forth in claim 19, wherein the method is carried out in the presence of acetonitrile, ethyl acetate, dichloremethane, chloroform, 1,2-dichloroethane, hexane, benzene, toluene, methanol, ethanol, isopropanol, *tert*-butanol, water or mixtures thereof.

23. A method as set forth in claim 19, wherein the ruthenium nanoparticles range in size from 1 to 100 nm.

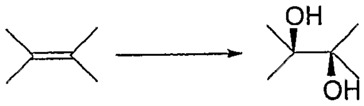

OH
OH

FIG. 1

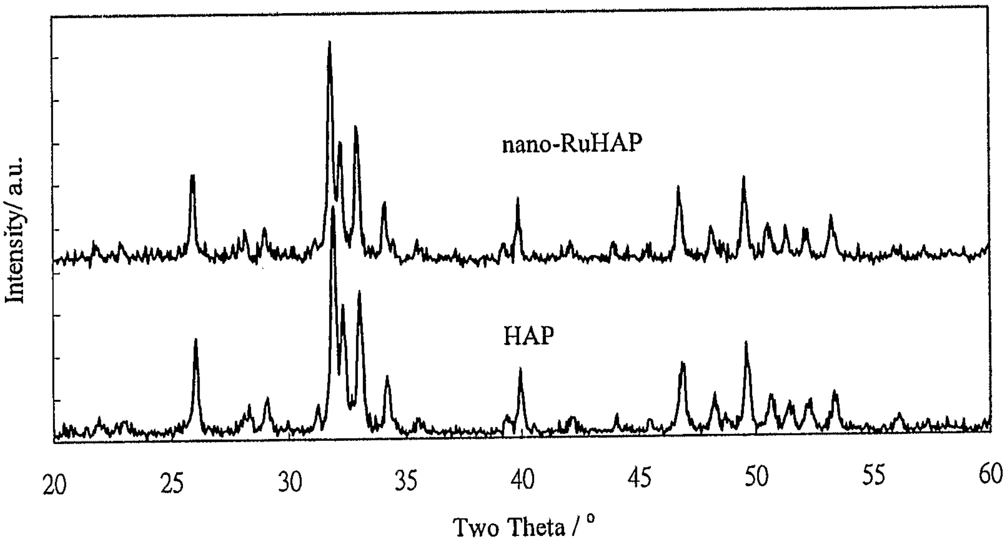

nano-RuHAP
HAP
Intensity/ a.u.
20
25
30
35
40
45
50
55
60
Two Theta / °

FIG. 2

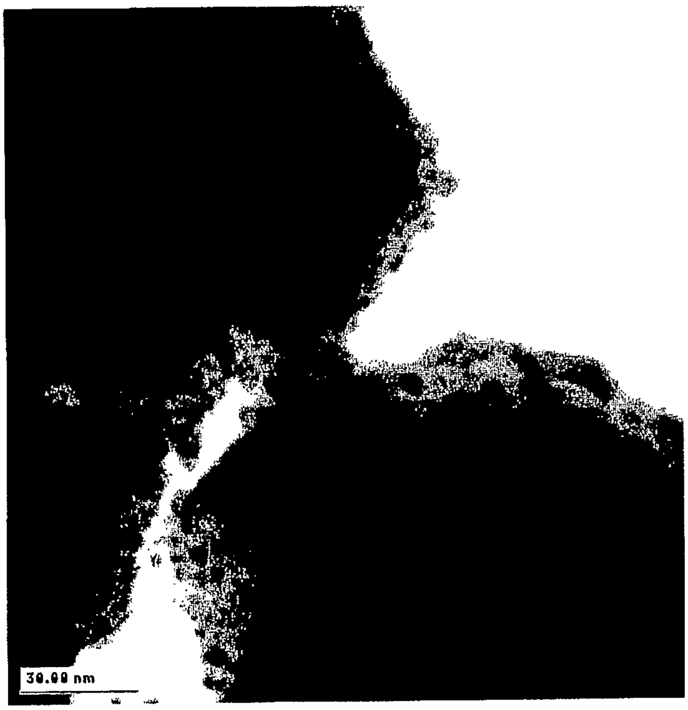
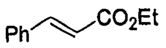
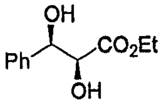
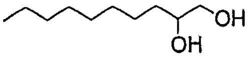
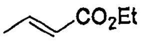
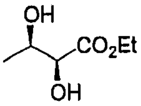
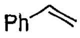
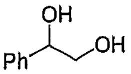
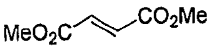
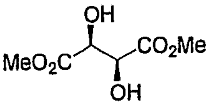
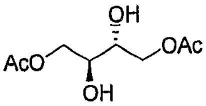
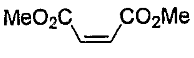
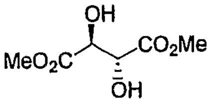
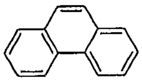
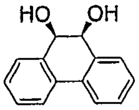
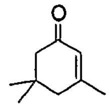
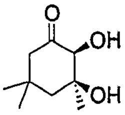
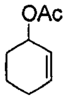
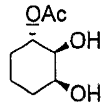
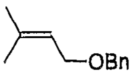
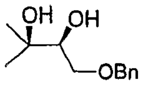


FIG. 3

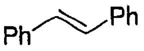
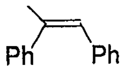
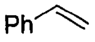
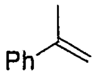
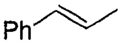
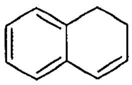
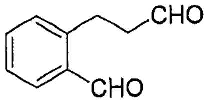
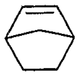
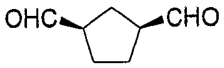
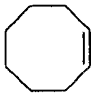
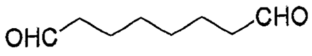
Nano-RuHAP Catalyzed *cis*-Dihydroxylation of Alkenes [a]

entry	alkene	product	yield (%)[b]	entry	alkene	product	yield (%)[b]
1			70	6			75
2			65	7			85
3			53	8			61
4[c]			50	9[d]			60
5			64	10			75 (*anti* : *syn* = 9 : 1)
				11			45

[a] Reaction conditions: alkene (2 mmol), nano-RuHAP (40 mg), $NaIO_4$ (1.5 equiv) and H_2SO_4 (20 mol %) in EtOAc-MeCN-H_2O (3:3:1 v/v) at 0 °C, reaction time = 30 min. [b] Isolated yield. [c] Reaction time = 10 min. [d] Reaction time = 40 min.

TABLE 1

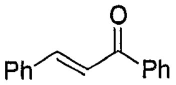
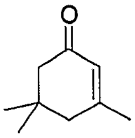
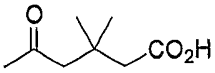
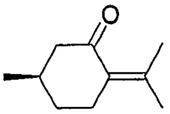
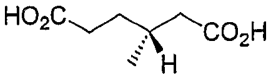
Nano-RuHAP Catalyzed Oxidative Cleavage of Alkenes [a]

entry	alkene	time(h)	product	yield (%)
1		2	PhCHO	81[b]
2		2	PhCHO	85[b]
3		3	PhCHO PhCOMe	85 89
4		2	PhCHO	66
5		3	PhCOMe	92
6		3	PhCHO	90
7[d]		3		86[c]
8		3		72[c]
9		3		87[c]

[a] Reaction conditions: alkene (0.5 mmol), nano-RuHAP (40 mg), $NaIO_4$ (1 mmol), in $ClCH_2CH_2Cl\text{-}H_2O$ (5:1v/v) at room temperature, and the products were identified and qunatified by GC analysis. [b] Percentage yield was calculated based on 2 equiv of benzaldehyde formed.[c] Isolated yield. [d] 76 % conversion.

TABLE 2

Nano-RuHAP Catalyzed Oxidative Cleavage of α,β-Unsaturated Alkenes [a]

entry	alkene	time(h)	product	yield (%)[b]
1		4	PhCHO $PhCO_2H$	67 72
2		7		85
3		3		84
4[c]	$Ph-C\equiv C-CH_3$	2	$PhCO_2H$	82

[a] Reaction conditions: alkene (0.5 mmol), nano-RuHAP (40 mg), Oxone (2.5 equiv) and $NaHCO_3$ (7.7 equiv) in MeCN-H_2O 1.5:1 at rt. [b] Isolated yield. [c] Oxone (4 equiv) and $NaHCO_3$ (12 equiv).

TABLE 3

INTERNATIONAL SEARCH REPORT

International application No.
PCT/CN2005/000540

A. CLASSIFICATION OF SUBJECT MATTER

IPC^7 C07C29/48, C07C45/51

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)

IPC^7 C07C29/48, 29/00, C07C45/51,45/00

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

IPC^7 C07C, B01J

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

WPI, EPODOC, PAJ, CPRS, CA

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	Zhan,Bi-Zeng et al:“Zeolite-Confined Nano-RuO$_2$:A Green,Selective, and Efficient Catalyst for Aerobic Alcohol Oxidation” Journal of the American Chemical Society,125(8), 2003, pages 2195-2199	1-23
A	DE19920038A1 (BAYER AG) 26,Oct 2000(26-10-2000) the whole document	1-23
A	US4393253A (EXXON RES & ENG CO) 12,Jul 1983(12-07-1983) the whole document	1-23

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

* Special categories of cited documents:

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

“E” earlier application or patent but published on or after the international filing date

“L” document which may throw doubts on priority claim (S) or which is cited to establish the publication date of another citation or other special reason (as specified)

“O” document referring to an oral disclosure, use, exhibition or other means

“P” document published prior to the international filing date but later than the priority date claimed

“T” later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

“X” document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

“Y” document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

“&”document member of the same patent family

Date of the actual completion of the international search 26 Jul 2005	Date of mailing of the international search report 18 · AUG 2005 (1 8 · 0 8 · 2 0 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 吕青印 Lv qing Telephone No. 86-10-62085607

Form PCT/ISA /210 (second sheet) (April 2005)

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/CN2005/000540

Patent Documents referred in the Report	Publication Date	Patent Family	Publication Date
DE19920038A1	26-10-2000	JP2002543051T	17-12-2002
		WO0064848 A1	02-11-2000
		AU200045520 A	10-11-2000
		EP1175382 A1	30-01- 2002
US4393253A	12-07- 1983	EP0053023 A	02-06-1982
		NO8103897 A	21-06-1982
		BR8107610 A	17-08-1982
		JP57131732 A	14-08-1982
		CA1181098 A	15-01-1985
		EP0053023 B	17-04-1985
		DE3170031G	23-05-1985