J|A|C|S COMMUNICATIONS

Published on Web 08/23/2010

Cp* Iridium Complexes Give Catalytic Alkane Hydroxylation with Retention of Stereochemistry

Meng Zhou, Nathan D. Schley, and Robert H. Crabtree*

Chemistry Department, Yale University, P.O. Box 208107, New Haven, Connecticut 06520

Received July 1, 2010; E-mail: robert.crabtree@yale.edu

Abstract: A series of Cp*Ir complexes can catalyze C−H oxidation, with ceric ammonium nitrate as the terminal oxidant and water as the source of oxygen. Remarkably the hydroxylation of *cis*-decalin and 1,4-dimethylcyclohexane proceeds with retention of stereochemistry. With H_2O^{18}, *cis*-decalin oxidation gave ^{18}O incorporation into the product *cis*-decalol.

Selective alkane oxidation holds promise for converting methane into a transportable fuel, methanol,[1] utilizing alkanes as raw materials for chemical feedstock production[1,2] and facilitating the synthesis of biologically active oxygenates.[3] Metal oxo complexes can carry out alkane oxidation[4] and are thought to be intermediates in the enzymes, CYP450, MMO and PSII, where they are responsible for such oxidation reactions as alkane hydroxylation, desaturation,[5] and water splitting.[6] A high valent oxotrimesityliridium(V) has been reported,[7] but it was only shown to oxidize triphenylphosphine.[8] $Cp^*Ir(PMe_3)(H)_2$ is well-known to perform C−H activation under irradiation.[9] Recently $[Cp^*Ir(N-C)H_2O]PF_6$ (N−C shown in **1**−**2**) was found to catalyze styrene epoxidation with iodosobenzene.[10] $[Ru^{II}(tpa)(H_2O)_2](PF_6)_2$ (tpa = 2,2′,2″-tripyridyl-amine) catalyzes deep oxidation of alkenes and C−H oxidation of sodium 4-sulfonate-1-ethylbenzene with aq. CAN (CAN = ceric ammonium nitrate).[11]

We previously described the robust and highly active water oxidation catalyst **1** (Figure 1) that uses Ce(IV) as the primary oxidant.[12] We proposed that the active species is $[Cp^*Ir^{V}(O)(N-C)]^+$ (**2**). Studies on water oxidation showed that the Cp* series gave excellent activity.

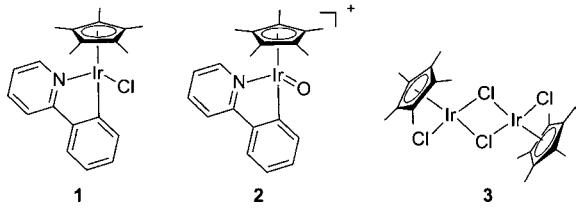
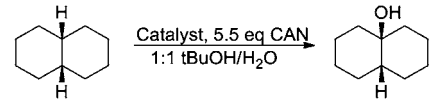


Figure 1. Cp*Ir complexes for C−H hydroxylation.

In view of the high activity of **1**, we looked for C−H hydroxylation with typical substrates using CAN as the terminal oxidant and water as the source of oxygen. Indeed, we now find hydroxylation of alkanes and related substrates when **1** in 1:1 *t*BuOH/H_2O is treated with CAN (Scheme 1). Remarkably, the reaction proceeds with retention of stereochemistry; for example *cis*-decalin (cis/trans ratio = 1200:1, 0.33 mmol in 5 mL of solvent, 66 mM) gives 9% 9-decalol with a cis/trans ratio of 160:1. In addition, the more active catalyst, **3**, gives 23% 9-decalol with a cis/trans ratio of 300:1 (decalin: 0.33 mmol in 4 mL of solvent, 83 mM). When the reaction catalyzed by **3** was run under air, the yield dropped to 12%. Hydroxylation of *cis*-1,4-dimethylcyclohexane with **3** (cis/trans ratio = 210:1) also gives 27% yield of hydroxylated product, again with retention of stereochemistry (cis/trans ratio 1:110) (Scheme 2). Most of the starting material remained unconverted, however. In 1:1 *t*BuOH/$H_2{}^{18}O$ as the solvent for *cis*-decalin hydroxylation, ^{18}O was essentially quantitatively incorporated into the product *cis*-9-decalol, but the very small amount of *trans*-9-decalol also formed contained predominantly ^{16}O, presumably from the air.

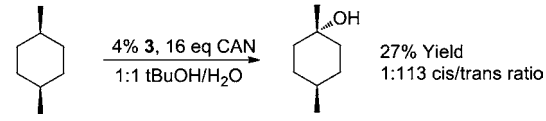
Scheme 1. *cis*-Decalin Hydroxylation by **1** and **3**



Catalyst, loading	Yield[a]	Product cis/trans ratio[b]
1, 4%	9% (79%)	163:1
3, 2%[c]	23% (91%)	300:1

[a] Isolated yield based on total starting material, 12 h at room temperature under nitrogen, yield based on converted starting material in parentheses. [b] Measured by GC-MS. [c] Per dimer.

Scheme 2. *cis*-1,4-Dimethylcyclohexane Hydroxylation by **3**



Without the catalyst the much slower hydroxylation of *cis*-decalin with Ce(IV) alone gave only a very low yield (<1%) and a cis/trans ratio of 1.5:1. IrO_2 25 nm nanoparticles[13] (2% Ir loading) and IrO_2 (4%) powder were ineffective as catalysts. In the dark the yield of epoxidation was not different from that in the regular lab setting.

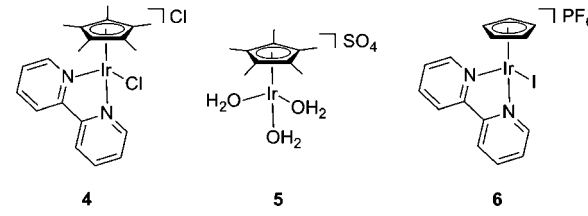
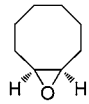
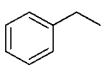
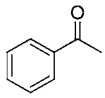
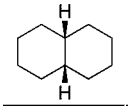
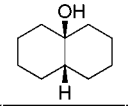


Figure 2. Additional complexes.

Other substrates and complexes (Figure 2) were tested (Table 1). Cp*Ir complexes catalyzed epoxidation (entries 1−2) and benzylic C−H oxidation (entries 4−7). Without the catalyst the reaction did not occur or was less efficient (entries 3, 8, and 13). **6** gave a lower yield than the uncatalyzed reaction (entry 7). **5**, a chloride-free version of **3**, did not give improved yield (entry 9).

10.1021/ja1058247

Table 1. Substrates in Reactions with Cp*Ir Catalysts[g]

Substrate[a]	Product	Entry	Catalyst	CAN eq	Time	Yield[b]
		1	**3**, 2%	8	3h	47%
		2	**5**, 2%	8	5h	72%[f] (72%)
		3	none	8	3h	0%
		4	**1**, 3%	18	20h	55% (56%)
		5	**3**, 1%	9	20h	29%
		6	**4**, 11%	18	24h	26%
		7	**6**, 3%	4.5	24h	0%
		8	none	18	24h	10%
		9	**5**, 6%	5.5	21h	17%[c] (95%)
		10	**1**, 2%	3	2h	48%[d]
		11	**5**, 0.5%	6	50min	55%[d]
		12	**5**, 1%	8	20min	72%[d] (72%)
		13	none	6	50min	6%[d]
		14	**1**, 2%	3	2h	0%[d,e]

[a] 50 μL of substrates were used. [b] Yield obtained by NMR with 1,3,5-trimethoxybenzene as the internal standard unless stated otherwise. The yield is based on total starting material, yield based on converted starting material in parentheses. [c] Estimated from GC-MS. [d] D_2O as solvent, yield obtained by NMR with L-leucine as the internal standard. [e] 82% unreacted starting material recovered. [f] 3:1 AcOMe/H_2O as solvent. [g] Reactions were run at room temperature (21 °C) under nitrogen or argon in 1:1 *t*BuOH/H_2O solvent unless stated otherwise.

THF was converted to lactone (entries 10−12). No product was seen in pyrrolidine oxidation (entry 14). No other products were detected in >1% for *cis*-decalin, >3% for cyclooctene and ethylbenzene, and >8% for thf.

Alternative terminal oxidants, including pyridine *N*-oxides, iodosobenzene, iodosobenzene diacetate, oxone, and mCPBA, were far less efficient for catalytic epoxidation and C−H oxidation (see Supporting Information (SI)). Various other solvents, mostly miscible with water, proved less satisfactory (see SI).

This work shows that Cp*Ir complexes can catalyze both alkane C−H oxidation and alkene epoxidation with a simple 1e primary oxidant, Ce(IV). Moreover, the C−H hydroxylation of alkanes proceeds with a remarkably high degree of retention of stereochemistry, contrary to the usual expectation from radical H atom abstraction. The mechanism can only be speculative until computational work[15] is completed, but an oxene-like insertion into the C−H bond is possible. Since the source of the O incorporated is water, this reaction may also be useful for isotope incorporation into organic molecules.

General Procedure for C−H Oxidation. In 4 mL of degassed 1:1 *t*BuOH/H_2O, 1 g of CAN, 50 μL of *cis*-decalin, and 7.5 mg of **3** were added sequentially. The reaction was stirred under nitrogen for 12 h. Additional DCM and water were then added, and the organic layer was collected. The aqueous layer was extracted with DCM (2×). The combined organic solution was washed twice with water and once with brine and then dried over sodium sulfate. The product was isolated by column chromatography with 15% AcOEt in hexane. The eluent was monitored by GC-MS. The products were identified by comparing the GC-MS with that of the authentic samples.[14]

Acknowledgment. This material is based upon work supported as part of the Center for Catalytic Hydrocarbon Functionalization, an Energy Frontier Research Center funded by the U.S. Department of Energy, Office of Science, Office of Basic Energy Sciences under Award Number DE-SC-0001298 (R.H.C. and M.Z.) and the DOE catalysis program DE-FG02-84ER13297 (N.D.S.).

Supporting Information Available: Synthetic details for the complexes and screening of different solvents and primary oxidants. This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) Conley, B.; Tenn, W.; Young, K.; Ganesh, S.; Meier, S.; Ziatdinov, V.; Mironov, O.; Oxgaard, J.; Gonzales, J.; Goddard, W.; Periana, R. *J. Mol. Catal. A: Chem.* **2006**, *220*, 7.
(2) Bergman, R. *Nature* **2007**, *446*, 391.
(3) Fraunhoffer, K.; Bachovchin, D.; White, M. *Org. Lett.* **2005**, *7*, 223.
(4) Gunay, A.; Theopold, K. *Chem. Rev.* **2010**, *110*, 1060.
(5) Hull, J.; Balcells, D.; Sauer, E.; Raynaud, C.; Brudvig, G.; Crabtree, R.; Eisenstein, O. *J. Am. Chem. Soc.* **2010**, *132*, 7605.
(6) Cady, C.; Crabtree, R.; Brudvig, G. *Coord. Chem. Rev.* **2008**, *252*, 444.
(7) Hay-Motherwell, R.; Wilkinson, G.; Hussain-Bates, B.; Hursthouse, M. *Polyhedron* **1993**, *12*, 2009.
(8) Jacobi, B.; Laitar, D.; Pu, L.; Wargocki, M.; DiPasquale, A.; Fortner, K.; Schuck, S.; Brown, S. *Inorg. Chem.* **2002**, *41*, 4815.
(9) Janowicz, A.; Bergman, R. *J. Am. Chem. Soc.* **1982**, *104*, 352.
(10) Sau, Y.; Yi, X.; Chan, K.; Lai, C.; Williams, I.; Leung, W. *J. Organomet. Chem.* **2010**, *695*, 1399.
(11) Hirai, Y.; Kojima, T.; Mizutani, Y.; Shiota, Y.; Yoshizawa, K.; Fukuzumi, S. *Angew. Chem., Int. Ed.* **2008**, *47*, 5772.
(12) Hull, J.; Balcells, D.; Blakemore, J.; Incarvito, C.; Eisenstein, O.; Brudvig, G.; Crabtree, R. *J. Am. Chem. Soc.* **2009**, *131*, 8730.
(13) Hara, M.; Waraksa, C.; Lean, J. T.; Lewis, B.; Mallouk, T. *J. Phys. Chem. A* **2000**, *104*, 5275.
(14) Prepared by the literature procedure:Lee, S.; Fuchs, P. *J. Am. Chem. Soc.* **2002**, *124*, 13978.
(15) Balcells, D.; Eisenstein, O. Personal communication, 2010.

JA1058247