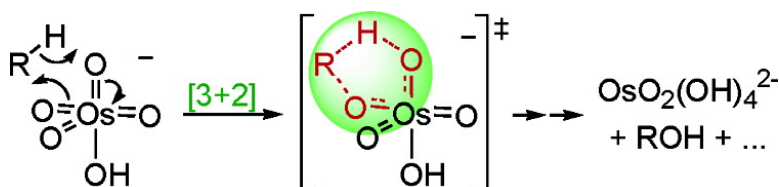


Alkane Oxidation by Osmium Tetroxide

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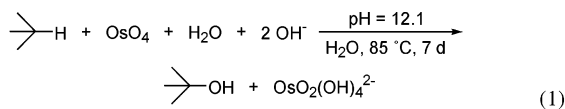
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The selective oxidation of alkanes is of great fundamental and practical importance.¹ Much of the current research in this area utilizes electrophilic late transition metals, such as platinum, and involves initial binding of a C–H bond to the metal center.¹ Alternatively, high oxidation state metal complexes can oxidize alkanes by radical pathways involving hydrogen atom abstraction.² We describe here stoichiometric and catalytic oxidations of alkanes by OsO₄, including primary, secondary, and tertiary C–H bonds. The available evidence suggests a nonradical, nonorganometallic mechanism involving [3+2] addition of a C–H bond to two oxo ligands of OsO₄. This pathway has been previously suggested for RuO₄ oxidations of tertiary and secondary C–H bonds to alcohols and ketones, respectively;³ RuO₄ has not been reported to oxidize primary C–H bonds.

Reaction of an aqueous pH = 12.1 solution of OsO₄ under 10 bar of isobutane (2-methyl-2-propane) at 85 °C for 168 h yields *tert*-butyl alcohol (*t*BuOH) (eq 1).⁴ Reactions were performed in

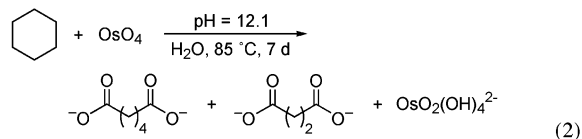


thick-walled glass vessels with a Teflon stopcock and a glass-coated stir bar, or in sealed, medium-walled NMR tubes. The initial reaction pH of 12.1 was set with 300 mM sodium phosphate buffer. Organic products were detected and quantified by ¹H NMR. The osmium product of all of these reactions is the well-known Os^{VI} ion [Os(O)₂(OH)₄]²⁻ (osmate) by comparison of reaction UV–vis spectra to that of an authentic sample. The amount of Os^{VIII} remaining at the end of the reactions was determined by addition of a known quantity of sodium 4-styrenesulfonate. The resulting diol and unreacted alkene were quantitated by ¹H NMR. Replacing the buffer with 64 mM NaOH (pH 12.8) gave the same yields within error. In the absence of organic substrate under these conditions there is <5% decay of OsO₄.⁵

Isobutane oxidations (pH 12.1, 7 d, 85 °C) show 30 ± 3% *t*BuOH formed vs the starting OsO₄ concentration and 30 ± 1% consumption of the initial OsO₄. The yield of *t*BuOH vs the consumed OsO₄ is 97 ± 9%, considering that each OsO₄ acts as a two-electron oxidant (Os^{VIII} → Os^{VI}). No products from the oxidation of primary C–H bonds in isobutane are observed. Oxidation of a methyl C–H bond would give isobutanol (2-methyl-1-propanol), which independent experiments show would be rapidly oxidized to isobutyrate (Me₂CHCO₂⁻) under the reaction conditions. Isobutylene, even in the trace amounts found in some isobutane samples, is rapidly oxidized to acetate under these conditions. Monitoring the reaction in a sealed NMR tube over time shows that ~90% of the *t*BuOH is formed within the first 2 d, after which the reaction slows. The origins of this slowing and of the incomplete conversion of Os^{VIII} are under investigation.

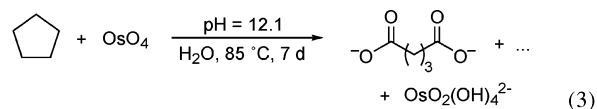
Oxidations of cyclohexane under these reaction conditions (168 h, 85 °C, pH 12.1) gave adipate (4.9 ± 0.2%) and succinate (1.8

± 0.20%) by ¹H NMR (eq 2; amounts vs the starting OsO₄ concentration). Control experiments show that adipate is further



oxidized by OsO₄ under the reaction conditions to give succinate and carbonate (the latter observed by mass spectrometry as CO₂ after acidification). With 54 ± 9% consumption of OsO₄ in this experiment and the stoichiometry requiring 5 and 11 equiv of OsO₄ per mol of adipate and succinate, respectively, the yields based on consumed oxidant are 46 ± 2% for adipate and 37 ± 7% for succinate. Thus the two dicarboxylate products account for 83 ± 7% of the OsO₄ used. The reaction likely proceeds by initial formation of cyclohexanol, which is known to be readily oxidized to adipate by OsO₄ under alkaline conditions.⁶

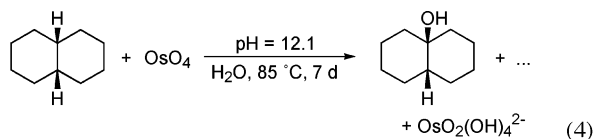
Oxidation of cyclopentane under similar conditions shows only glutarate in ~9% yield based on the stoichiometry and on reacted OsO₄ (eq 3). The low yield is due to the competitive oxidation of glutarate to malonate (⁻O₂CCH₂CO₂⁻), which itself is readily oxidized. The carboxylate oxidations may proceed via low con-



centrations of highly reactive ene-diolate forms. It is surprising that the oxidations of both cyclohexane and cyclopentane only give overoxidation products corresponding to the loss of two carbons. Products corresponding to the loss of only one carbon are not observed, even at short reaction times. Oxidation of hexanoate under similar conditions yields only pentanoate.

OsO₄ in basic solution at 85 °C oxidizes toluene to benzoate in 72 ± 3% yield based on 66 ± 2% consumption of OsO₄ (and 3 Os^{VIII}/PhCO₂⁻). The preference for benzylic oxidation contrasts with the aryl > benzylic selectivity observed for electrophilic late transition metals.^{1a} The oxidation of 2-cyclopropylpropane gives 2-cyclopropyl-2-propanol in low yields (the alcohol product is unstable to the reaction conditions). Ethane and propane both produce acetate in low yields (acetate itself is slowly oxidized). No propionate is formed from propane, although it is stable enough to have been observed. It appears that propane oxidation occurs selectively at the secondary C–H bonds to give acetone, which is rapidly oxidized to acetate (presumably via the enol).

OsO₄ oxidation of *cis*-decalin for 16 h at 85 °C gives *cis*-9-decalinol in low yield by GC/MS (eq 4). Running this oxidation in the presence of *trans*-9-decalinol shows that the *trans* alcohol is not consumed under the reaction conditions, so it would have been observed if it were formed from *cis*-decalin. Hydroxylation of *cis*-



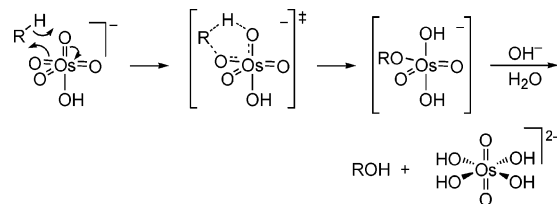
decalin is thus stereoselective, implicating a concerted pathway or rapid trapping of radicals within a solvent cage. *trans*-Decalin is oxidized more slowly than the *cis* isomer, forming unidentified products that do not include *trans*-9-decalinol.

To perform the reaction of alkanes catalytically in OsO_4 , reactions were run in the presence of sodium periodate as a terminal oxidant. Other known oxidants for OsO_4 reactions such as *N*-methylmorpholine *N*-oxide and hydrogen peroxide⁷ are unsuitable because they themselves can be oxidized. Oxidation of excess isobutane by 3.4 mM OsO_4 and 170 mM NaIO_4 for 168 h at 85 °C gave 280% *tert*-butyl alcohol, 140% acetic acid, and 30% isobutyric acid ($\text{Me}_2\text{CHCO}_2\text{H}$). These yields are the mol of product per mol of OsO_4 , not corrected for stoichiometry because of the possible involvement of periodate in the overoxidation steps. The yields suggest that the reactions are mildly catalytic in OsO_4 , ca. 4 turnovers. Similar reactions of cyclohexane give adipic and succinic acids in 22% and 46% molar yields, higher than observed without the periodate but less than 1 turnover. In these reactions the periodate serves as a buffer, $\text{pH} \approx 4.3$. Under these acidic conditions, the *tert*-butyl alcohol is further oxidized to acetic acid, presumably via isobutylene. When higher initial concentrations of OsO_4 are used, less *tert*-butyl alcohol and more acetic acid is observed. The isobutyric acid could result from attack at a primary C–H bond under these conditions.

Preliminary mechanistic data are consistent with a concerted [3+2] pathway for alkane oxidations (Scheme 1), analogous to that proposed for related RuO_4 reactions.^{3,8} Hydroxyl radical is not an intermediate based on the observed selectivities. For instance, aqueous OH^\bullet reacts competitively with the primary and tertiary C–H bonds of isobutane,⁹ but the high-pH OsO_4 reactions have high selectivity for the tertiary position. In addition, OH^\bullet reacts rapidly with *t*-BuOH ($k \geq 5 \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$),¹⁰ while control experiments show *t*-BuOH is stable to OsO_4 at pH 12 and 85 °C for 2 weeks. The stereoselective hydroxylation of *cis*-decalin suggests that free alkyl radicals are not involved. In RuO_4 oxidations, the stereoretentive hydroxylations of *cis*- and *trans*-decalins were taken as evidence for a concerted [3+2] mechanism.³ RuO_4 is reported to react >5 times slower with *trans*-decalin than the *cis* isomer, and other sterically hindered polycyclic tertiary substrates are similarly less reactive.^{3c,11}

The [3+2] mechanism is quite similar to the commonly accepted [3+2] mechanism for olefin dihydroxylation¹² and to the proposed mechanism for H_2 oxidation by OsO_4 in the presence of ligands such as hydroxide.¹³ At $\text{pH} = 12.1$, there are approximately equal concentrations of OsO_4 and $\text{OsO}_4(\text{OH})^-$ present in solution.¹³ The ligation of OsO_4 accelerates its reactions with olefins and H_2 ,^{7b,13} and the same ligand acceleration is observed in the alkane oxidations. No oxidation of isobutane by OsO_4 is observed when the phosphate buffer is adjusted to neutral pH, indicating the need for an OH^- ligand. Preliminary DFT calculations support a ligand-accelerated asynchronous [3+2] pathway and suggest that ligands may also accelerate a hydrogen atom abstraction pathway.¹⁴

Scheme 1. Proposed Concerted [3+2] Mechanism for Alkane Oxidation by $\text{OsO}_4(\text{OH})^-$



In conclusion, OsO_4 oxidizes unactivated alkanes in aqueous base at 85 °C. Isobutane is oxidized to *t*-BuOH, cyclohexane to a mixture of adipate and succinate, toluene to benzoate, and ethane and propane both give low yields of acetate. A couple of turnovers of isobutane oxidation by OsO_4 are observed using NaIO_4 as the terminal oxidant. The reactions are related to the oxidations of saturated hydrocarbons by RuO_4 , but OsO_4 appears to require ligand acceleration, in this case binding of hydroxide. The oxidation of *cis*-decalin gives, in low yield, the corresponding alcohol with retention of configuration. The data are consistent with a concerted [3+2] mechanism, analogous to that proposed for alkane oxidation by RuO_4 , and for alkene and H_2 oxidations by OsO_4 .

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References

- (1) (a) Shilov, A. E.; Shul'pin, G. B. *Activation and Catalytic Reactions of Saturated Hydrocarbons in the Presence of Metal Complexes*; Kluwer: Boston, 2000. (b) *Activation and Functionalization of C–H Bonds*; Goldberg, K. I., Goldman, A. S., Eds.; ACS Symposium Series 885; American Chemical Society: Washington, DC, 2004.
- (2) (a) *Biomimetic Oxidations Catalyzed by Transition Metal Complexes*; Meunier, B., Ed.; Imperial College: London, 2000; (b) Mayer, J. M. *Acc. Chem. Res.* **1998**, *31*, 441–450.
- (3) (a) Spitzer, U. A.; Lee, D. G. *J. Org. Chem.* **1975**, *40*, 2539. (b) Tenaglia, A.; Terranova, E.; Waegell, B. *Tetrahedron Lett.* **1989**, *30*, 5271 and **1992**, *57*, 5523; *J. Chem. Soc., Chem. Commun.* **1990**, 1344. (c) Bakke, J. M.; Frøhaug, A. E. *J. Phys. Org. Chem.* **1996**, *9*, 507.
- (4) General procedure: 34 mM OsO_4 and 10 equiv of substrate (for liquids) in pH 12.1 buffer (300 mM Na_2HPO_4 adjusted to pH 12.1 with 3.0 M NaOH) was freeze–pump–thaw degassed, charged with 1 atm N_2 (or 4–12 atm of a gaseous substrate), sealed, and heated at 85 °C for 168 h.
- (5) Over multiple reactions, corrosion of the Teflon stopcock is observed. Some reactions with phosphate buffer precipitated a small amount of white solid.
- (6) (a) Mehta, S. P. S.; Mehrotra, R. N. *Trans. Met. Chem. (London)* **1991**, *16*, 402. (b) Singh, M. P.; Singh, H. S.; Singh, B. N.; Singh, N.; Kumar, M. *Monatsh. Chem.* **1978**, *109*, 1373.
- (7) (a) Smith, M. B.; March, J. *March's Advanced Organic Chemistry*, 5th ed.; Wiley: New York, 2001; p 1049. (b) Berrisford, D. J.; Bolm, C.; Sharpless, K. B. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1059. (c) Döbler, C.; Mehltretter, G. M.; Sundermeier, U.; Beller, M. *J. Am. Chem. Soc.* **2000**, *122*, 10289.
- (8) The [3+2] mechanism was earlier discussed for Cr^{VI} oxidations: Wiberg, K. B. In *Oxidation in Organic Chemistry Part A*; Wiberg, K. B., Ed.; Academic Press: New York, 1965; pp 69–184.
- (9) Rudakov, E. S.; Volkova, L. K.; Tretyakov, V. P. *React. Kinet. Catal. Lett.* **1981**, *16*, 333.
- (10) Buxton, G.; Greenstock, C. L.; Helman, W. P.; Ross, A. B. *J. Phys. Chem. Ref. Data* **1988**, *17*, 513.
- (11) Bakke, J. M.; Bethell, D. *Acta Chem. Scand.* **1992**, *46*, 644.
- (12) DelMonte, A. J.; Haller, J.; Houk, K. N.; Sharpless, K. B.; Singleton, T. S.; Thomas, A. *J. Am. Chem. Soc.* **1997**, *119*, 9907.
- (13) Dehestani, A.; Lam, W. H.; Davidson, E. R.; Borden, W. T.; Mayer, J. M. *J. Am. Chem. Soc.* **2005**, in press.
- (14) Lam, W.-H.; Davidson, E. R.; Mayer, J. M.; Borden, W. T. Work in progress.

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