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Metal Dependence in Gif-type Reactions. The Cu(II)-catalyzed Olefination of Saturated Hydrocarbons by tert-Butyl Hydroperoxide.

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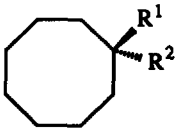
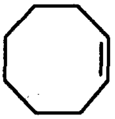
Abstract: Cycloalkanes are transformed into the corresponding cycloalkenes by treatment with *tert*-butyl hydroperoxide (TBHP) in pyridine/acetic acid solution in the presence of $Cu(OAc)_2.H_2O$. When iron salts are used instead of copper salts, the major reaction product is the corresponding ketone. Differences between the iron-catalyzed and the copper-catalyzed reactions support a metal-dependent reaction pathway.

Early studies on the mechanistic pathway and the chemical characteristics of the Fe(III)-catalyzed TBHP-based ketonization of saturated hydrocarbons in pyridine/acetic acid solution (GoAgg^{IV} system) showed many similarities between this process and the one based on H_2O_2 as the oxidant.[1,2] For the two reactions there is a single major linear pathway *alkane* → *alkyl hydroperoxide* → *ketone* or *alcohol*, and dioxygen (O_2) is the precursor of the oxygen atoms in the alkyl hydroperoxide, the alcohol, and the ketone. Thus, cyclooctane (**1**, 50.0 mmol) in pyridine (30 mL) and acetic acid (3 mL) was oxidized by TBHP (5.0 mmol, 90% + 5% H_2O + 5% *tert*-BuOH) in the presence of $Fe(OAc)_3$ (0.2 mmol) at 60°C under air (closed system), affording cyclooctanone (**2**, 4.12 mmol), and cyclooctanol (**3**, 0.73 mmol). The reaction efficiency[3] (based on TBHP, the limiting reagent) was nearly quantitative (97%).



1: R^1=R^2=H
2: R^1; R^2=O
3: R^1=OH; R^2=H



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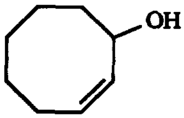

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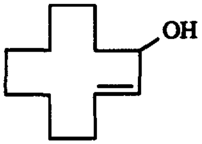
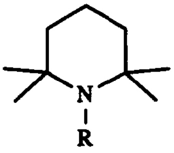


6 *(cis + trans)*



7: R=O•
8: R=OMe

What happens when a Cu(II)-catalyst is used instead of an Fe(III)-catalyst? Remarkably, the olefin is the major reaction product instead of the ketone usually formed under iron catalysis. Thus, when cyclooctane (1, 50 mmol) in pyridine (30.0 mL) and acetic acid (3.0 mL) was oxidized by TBHP (5.0 mmol) in the presence of $Cu(OAc)_2.H_2O$ (5.0 mmol) at 60°C in a closed system for 24 h (all the TBHP was consumed), cyclooctene (4, 3.47 mmol), cyclooctanone (2, 0,23 mmol), and cyclooctanol (3, 0.02 mmol) were obtained.[4] The ratio olefin/ketone was ca. 15. The total reaction efficiency was high (74.4% based on TBHP). In the corresponding blank experiment in the absence of Cu(II)-catalyst no oxidation of cyclooctane 1 was observed.

We have previously shown that the formation of ketones under Gif-type conditions requires stoichiometric amounts of dioxygen (O_2). When the Cu(II)-catalyzed oxidation of cyclooctane was performed under an atmosphere of Ar instead of air, the reaction proceeded in high yield, affording the olefin in a higher ratio olefin/ketone (>33).[5] When the Cu(II)-catalyzed reaction was carried out in the presence of the radical trap Tempo (7), normal olefination was observed.[6] No cyclooctyl-Tempo adduct was detected (GC-MS analysis). Under these experimental conditions carbon radicals *do react* with Tempo. Even a small fraction of methyl radicals, generated from

TBHP through a minor homolytic pathway,[7] could be trapped *in situ* as the adduct **8**. The excess Tempo remains stable throughout the reaction.[6]

The selectivity of the copper-catalyzed oxidation was studied by allowing pairs of hydrocarbons to compete with each other. The order of reactivity found (normalized by the number of C-H bonds) was: cyclooctane (2.38) > cycloheptane (1.75) > cyclododecane (1.36) > cyclohexane (1.00, by definition).

Allylic C-H bonds are also reactive under these reaction conditions. When cyclooctene **4** was the reaction substrate the allylic alcohol (**5**, 1.44 mmol) was the major reaction product. The reaction efficiency was 28.8%. The competition between non-activated C-H bonds and allylic C-H bonds was also examined. Cyclododecene (25 mmol, 1:1 mixture of *cis* and *trans* isomers) and cyclooctane (25 mmol) were competed affording the allylic alcohol **6** (1.53 mmol), cyclooctene (1.75 mmol), and cyclooctanone (0.11 mmol). The normalized reactivity ratio cyclooctane/cyclododecene was 0.30. In the reciprocal experiment, cyclooctene and cyclododecane were competed, affording cyclododecene (1.73 mmol), cyclododecanone (0.12 mmol), and the allylic alcohol **5** (0.54 mmol). In this case, the normalized reactivity ratio was 0.57. Thus, the reactivity of allylic C-H bonds seems to be of the same order of magnitude as for non-activated C-H bonds, a well known characteristic of Gif chemistry.[1a] No epoxide was detected in any of these experiments.

In Cu^{II} based reactions, an intermediate **A** is formed and postulated to contain a Cu^{IV}-carbon (or possibly Cu^{III}-carbon) bond. Insertion of oxygen into this bond, or a reduced form of it, affords intermediate **B** which is again the hydroperoxide.[8] The breakage of the Cu-carbon bond of Cu-A, concerted with loss of a proton, would afford the olefin and Cu^{II} (or Cu^{I}).

Acknowledgments. We are indebted to the National Science Foundation, British Petroleum of America, and Quest International for financial support of this work.

References

(1) For some examples of hydrocarbon oxidation systems based on O_2 or H_2O_2, see: *a.* Barton, D. H. R.; Bévière, S. D.; Chavasiri, W.; Csuhai, E.; Doller, D.; Liu, W.-G. *J. Am. Chem. Soc.* **1992**, *114*, 2147-2156 and references therein cited. *b.* Tung, H.-C.; Kang, C.; Sawyer, D. T. *J. Am. Chem. Soc.* **1992**, *114*, 3445-3455. *c.* Oxygen Chemistry. Sawyer, D. T.; Oxford University Press: New York, 1991, Chapter 4, pp 82-119. *d.* Leising, R. A.; Brennan, B. A.; Que, Jr, L.; Fox, B. G.; Münck, E. *J. Am. Chem. Soc.* **1991**, *113*, 3988-3990. *e.* Fish, R. H.; Konings, M. S.; Oberhausen, K. J.; Fong, R. H.; Yu, W. M.; Vincent, J. B.; Coggin, D. K.; Buchanan, R. M. *Inorg. Chem.* **1991**, *30*, 3002-3006. *f.* Geletii, Yu. V.; Lavrushko, V. ; Lubimova, G. V. *J. Chem. Soc., Chem. Commun.* **1988**, 936-937. For other oxidation systems based on TBHP, see: Faraj, M; Hill, C. L. *J. Chem. Soc., Chem. Commun.* **1987**, 1487-1489. Fish, R. H.; Fong, R. H.; Vincent, J. B.; Christou, G. *J. Chem. Soc., Chem. Commun.* **1988**, 1504-1506. Leising, R. A.; Norman, R. E.; Que, Jr, L. *Inorg. Chem.* **1990**, *29*, 2555-2557. Sarneski, J. E.; Michos, D.; Thorp, H. ; Didiuk, M.; Poon, T.; Blewitt, J.; Brudvig, G. W.; Crabtree, R. *Tetrahedron Lett.* **1991**, *32*, 1153-1156.

(2) Barton, D. H. R.; Bévière, S. D.; Chavasiri, W.; Doller, D.; Hu, B. *Tetrahedron Lett.* **1992**, *33*, 5473-5476.

(3) The reaction efficiency is calculated considering that one equivalent of TBHP is required for the formation of the alkyl hydroperoxide, and thus ketone and alcohol. Two oxygen atoms from dioxygen are introduced during hydroperoxide formation but are not included in the calculation.

(4) 5.0 mmol of Cu(II)-catalyst was used to increase the reaction rate, which is very slow when ca. 0.2 mmol of $Cu(OAc)_2.H_2O$ is used.

(5) Reaction conditions: $Cu(OAc)_2.H_2O$ (5.0 mmol), TBHP (5.0 mmol), pyridine (30.0 mL), acetic acid (3.0 mL), hydrocarbon (50 mmol), 60°C, 24 h in a closed system under Ar atmosphere. Under these experimental conditions the reaction products distribution was: cyclooctene (4 , 3.64 mmol), cyclooctanone (2 , 0.11 mmol), cyclooctanol (3 , traces); reaction efficiency=75.0%.

(6) Experimental conditions: as in reference 5 plus Tempo (3.0 mmol). The product distribution was: cyclooctene (3.30 mmol), Methyl-Tempo adduct (0.11 mmol), Tempo (recovered, 2.85 mmol); reaction efficiency=66.0%.

(7) Sheldon, R. A.; Kochi, J. K. Metal-Catalyzed Oxidations of Organic Compounds. Academic Press: New York; 1981; Chapter 3, pp 33-70.

(8) Barton, D. H. R.; Bévière, S. D.; Chavasiri, W.; Csuhai, E. and Doller, D. *Tetrahedron* **1992**, *48*, 2895-2910.

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