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# Osmium Tetroxide-Promoted Catalytic Oxidative Cleavage of Olefins: An Organometallic Ozonolysis

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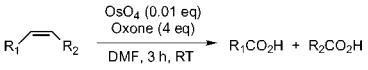
Oxidative cleavage of olefins is one of the paramount reactions developed in organic chemistry. Many oxidative pathways discussed in the literature can be summarized into two main methodologies: (i) Transformation of olefins into 1,2-diols followed by cleavage with $NaIO_4$ or other oxidants[1] or (ii) ozonolysis, in which the olefin is directly cleaved into a variety of functionalized products depending on the workup conditions.[2]

The standard method for the direct oxidative cleavage of olefins is ozonolysis. This reaction has been well-developed and yields aldehydes or carboxylic acids upon reductive or oxidative workup, respectively. As important as ozonolysis has proved to be in synthetic chemistry, there are relatively few alternate reactions that duplicate the same transformation, that is, the direct cleavage of olefins without the intermediacy of 1,2-diols.[3] Also, a notable issue with ozonolysis is the major concern for safety; serious accidents due to explosions have been reported.[4] Alternatively, the Lemieux−Johnson reaction and its variants are widely used for the oxidative cleavage of 1,2-diols and can be coupled to the dihydroxylation of olefins with Os, Mn, Ru, and W oxides.[5] Direct oxidation of olefins with $OsO_4$, without the intermediacy of 1,2-diols, has been suggested by using either hydrogen peroxide or *tert*-butyl hydrogen peroxide as co-oxidants, albeit in low yields.[6] Herein, we report initial observations on a mild, organometallic alternative to ozonolysis using Oxone as the co-oxidant for oxidative cleavage of olefins with $OsO_4$ proceeding without the intermediacy of 1,2-diols.

Our interest in this area stemmed from previous work in the oxidative cyclization of 1,4-dienes, in which $OsO_4$ and various co-oxidants were used to promote the cyclization pathway.[7] Low yields of cyclized products were attributed to a substantial amount of over-oxidized products resulting from an oxidative cleavage of the olefin functionality. Further investigation into the nature of the over-oxidized products and optimization of the reaction has led to a selective oxidative cleavage of olefins to yield carboxylic acids using catalytic $OsO_4$ and Oxone in DMF (Scheme 1).

***Scheme 1***




Initially, we investigated the oxidative cleavage of olefins in simple alkyl and aromatic compounds (Table 1). Both *cis*- and *trans*-stilbene (**1** and **2**) cleanly provided 2 equiv of benzoic acid (**1a**) in 95% yield. *trans*-Cinnamic acid (**3**), styrene (**4**), and methyl cinnamate (**5**) were also easily converted to **1a** in 97, 94, and 96% yields, respectively. Cyclohexene (**6**) and cyclooctene (**7**) provided the corresponding adipic acid (**6a**) and suberic acid (**7a**) in good yields. Additionally, simple alkyl olefins such as 1-decene (**8**), 1-nonene (**9**), and *trans*-2-nonene (**10**), all provided the appropriate alkyl carboxylic acids in 93, 90, and 93%, respectively. Similarly, methyl oleate (**11**) provided a clean conversion to nonanoic acid (**8a**) and nonanedioic acid monomethyl ester (**11a**).

***Table 1.*** Oxidative Cleavage of Simple Olefins[a]

| entry | substrate | product | yield[b] (%) |
|---|---|---|---|
| 1 | *cis*-stilbene, **1** | benzoic acid, **1a** | 95 |
| 2 | *trans*-stilbene, **2** | **1a** | 95 |
| 3 | *trans*-cinnamic acid, **3** | **1a** | 97 |
| 4 | styrene, **4** | **1a** | 94 |
| 5 | methyl cinnamate, **5** | **1a** | 96 |
| 6 | cyclohexene, **6** | adipic acid, **6a** | 50 (94)[c] |
| 7 | cyclooctene, **7** | suberic acid, **7a** | 82 (92)[c] |
| 8 | 1-decene, **8** | nonanoic acid, **8a** | 93 |
| 9 | 1-nonene, **9** | octanoic acid, **9a** | 90 |
| 10 | 2-*trans*-nonene, **10** | heptanoic acid, **10a** | 93 |
| 11 | methyl oleate, **11** | **8a** + **11a** | 80 (93)[c] |

[a] All reactions were performed with olefin (1 equiv), Oxone (4 equiv), and $OsO_4$ (0.01 equiv) in DMF for 3 h at rt. [b] Isolated yields. [c] GC yield.

A number of monosubstituted, 1,1-disubstituted, 1,2-disubstituted, trisubstituted, and tetra-substituted olefins containing a variety of functional groups were also subjected to the oxidative cleavage (Table 2). In most cases a yield of 80% or greater of the desired ketone or carboxylic acid was obtained.

Hydroxyalkene **12** reacted smoothly to provide the carboxylic acid **12a** in 85% yield. Similarly, the corresponding acetate **13** was also cleanly oxidized in high yields. (−)-Isopulegol (**14**) was oxidized to furnish the desired ketoalcohol **14a** and formate **14b** in 78% total yield. The same reaction was performed in $d_7$-DMF but resulted in no incorporation of labeled formate. This suggests that the nearby terminal olefinic carbon that was oxidized during the cleavage was transferred intramolecularly, resulting in the observed formyl group. The formate could be easily hydrolyzed with base; therefore, it is clear that the alcohol functionality is immune to oxidation. The benzyl-protected isopulegol **15** provided 80% of the desired ketone **15a**. Substituted stilbenes, **16** and **17**, were also cleanly converted into the corresponding acid products, **16a** and **17a**, without difficulty in 91 and 95% yield, respectively.

Interestingly, α-methyl cinammic acid (**19**) and 1-methyl cyclohexene (**20**) (examples of trisubstituted olefins) did not deliver the desired product in high yields under standard conditions. Seemingly, the hydrolysis of the osmate intermediate leads to the formation of the observed diol side product, presumably as a result of the acidity of Oxone. However, addition of solid $NaHCO_3$ to the reaction substantially improved the cleavage of **19** and **20**, leading to high yields of the oxidatively cleaved products. Cleavage of the tetrasubstituted olefin **21** in the presence of $NaHCO_3$ was also successful in yielding acetophenone (**21a**).

α,β-Unsaturated systems pose an interesting case since their cleavage would yield an α-dicarbonyl functionality. Oxidation of 2-cyclohexenone (Table 2, entry 6) provided pentanedioic acid, most probably via the α-dicarbonyl intermediate which decarboxylates under the oxidative conditions. Baeyer−Villiger-like oxidative cleavage of α-dicarbonyls has been reported previously with peroxy

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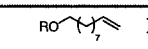
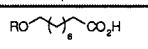
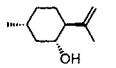
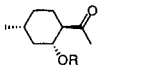
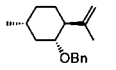
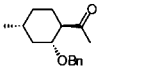
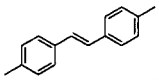
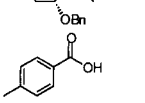
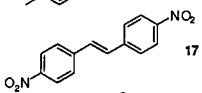
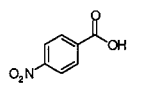
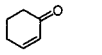
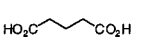
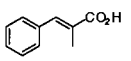
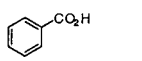
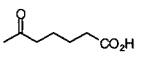
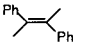
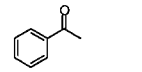
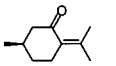
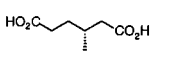
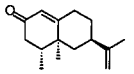
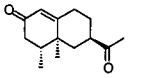
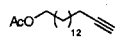
***Table 2.*** $OsO_4$/Oxone Promoted Oxidative Cleavage[a]

| entry | substrate | | product | yield (%) |
|---|---|---|---|---|
| 1 |  | **12** R=H<br>**13** R=Ac |  | **12a**, (R=H) 85<br>**13a**, (R=Ac) 93 |
| 2 |  | **14** |  | **14a**, (R=H) 44<br>**14b**, (R=CHO) 34 |
| 3 |  | **15** |  | **15a**, 80 |
| 4 |  | **16** |  | **16a**, 91 |
| 5 |  | **17** |  | **17a**, 95 |
| 6 |  | **18** |  | **18a**, 92[b] |
| 7 |  | **19** |  | **1a**, 82 (90)[b,c] |
| 8 |  | **20** |  | **20a**, 80 (85)[b,c] |
| 9 |  | **21** |  | **21a**, 85[c] |
| 10 |  | **22** |  | **22a**, 67[c] |
| 11 |  | **23** |  | **23a**, 60[d] |
| 12 |  | **24** | recovered **24** (96%) | — |

[a] All reactions were performed with olefin (1 equiv), Oxone (4 equiv), and $OsO_4$ (0.01 equiv) in DMF (0.2 M) for 3 h at rt. [b] GC yield. [c] 4 equiv $NaHCO_3$. [d] Only 2 equiv of Oxone was used.

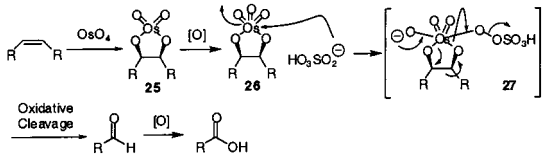
compounds and is likely the operative route in the latter oxidation.[8] 1,2-Cyclohexanedione, subjected to the same reaction conditions (without $OsO_4$) was also oxidized to adipic acid (see Supporting Information), thus demonstrating the lability of the α-dicarbonyl functionality. In a similar fashion, (+)-pulegone (**22**) yielded the dicarboxylic acid **22a** via the intermediacy of an α-diketone.

Treatment of nootkatone (**23**) containing dissimilar olefins under standard conditions furnished ketone **23a** showing that selectivity in oxidation is also obtainable. Last, alkyne **24** was subjected to the cleavage conditions; however, it proved immune to oxidation, and the starting material was recovered, thus indicating selectivity for alkenes versus alkynes.

Oxone, a monopotassium peroxysulfate salt, is known to be an effective oxidant for numerous transformations. For instance, Oxone is well-known in the preparation of sulfones or sulfoxides from sulfides,[9] oxides of both phosphorus[10] and nitrogen,[11] and several reports have shown that Oxone can also be used to oxidize aldehydes to carboxylic acids.[12] We believe that in this system Oxone functions in three distinct oxidizing roles: (1) oxidizes the initially formed osmate back to Os(VIII), (2) promotes the oxidative cleavage to an intermediate aldehyde, and (3) independently oxidizes the aldehyde to the carboxylic acid.

We are not certain as to the mechanism of the oxidative cleavage; however, we do propose the intermediacy of an osmate ester which undergoes the cleavage. We do not believe that 1,2-diols are intermediates in this reaction for the following two reasons: (i) The oxidation of olefins with the $OsO_4$/Oxone system proceeds just as well under anhydrous conditions, that is there is no hydrolysis of the osmate ester. (ii) Submission of 1,2-diols such as styrene glycol to this reaction does not yield products, and in fact starting diol is recovered quantitatively.[13] Scheme 2 depicts our proposed mechanism, in which osmate **25** is oxidized by Oxone to furnish

***Scheme 2***




**26**, which is subsequently attacked by the same to yield intermediate **27**. Fragmentation of **27** regenerates $OsO_4$ and produces two aldehydes, which can undergo further oxidation to yield carboxylic acids (Scheme 2). We believe that the nucleophilicity of Oxone, and the fact that it contains an excellent leaving group (i.e., bisulfate) drives the reaction forward. On the other hand, as compared to other routinely used co-oxidants such as $NaIO_4$ and Cr oxides, Oxone does not oxidize alcohols or diols independently.[13]

To highlight the utility of this reaction, the oxidative cleavage of **2** was successfully scaled to 50 mmol (9 g), and the amount of $OsO_4$ required was greatly reduced from 1 to 0.02 mol % (5000 turnovers). The isolated yield of this reaction remains high at 95% (88% after crystallization from chloroform).

During the course of our investigation we have been able to show that a simple, mild, and efficient oxidative cleavage of olefins takes place with $OsO_4$ and Oxone in DMF, to provide ketones or carboxylic acids. Modification of the reaction to deliver aldehydes exclusively is in progress. This reaction can be considered as an alternate to ozonolysis.

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**Supporting Information Available:** Experimental procedures and spectral data for compounds **12a**−**23a** (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(13) See Supporting Information for details.

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