A New OsO_4-Mediated Carbon–Carbon Bond Cleavage Reaction Leading to the Formation of Anthraquinone

Shouhai Gao, Wei Wang, and Binghe Wang*
Department of Chemistry, North Carolina State University, Raleigh, NC 27695-8204, U.S.A.

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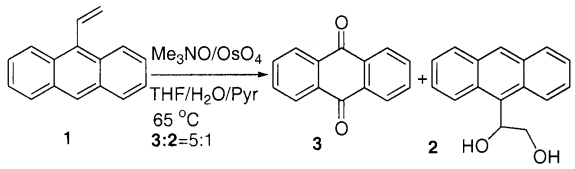
A new OsO_4-mediated carbon–carbon bond cleavage reaction leading to the formation of anthraquinone was observed. The reaction goes through the dihydroxylated intermediate and is aided by the presence of pyridine.

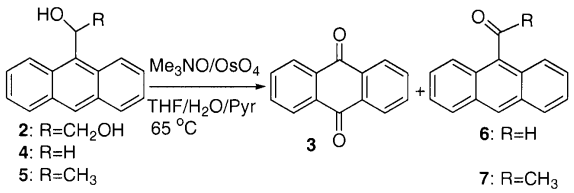
Osmium tetroxide (OsO_4) is widely used for the *cis*-dihydroxylation of alkenes.[1,2] Herein, we report an unusual carbon–carbon bond cleavage reaction mediated by OsO_4 resulting in the formation of anthraquinone.

When 9-vinylanthracene (**1**) was treated with 3 equivalents of trimethylamine *N*-oxide (TMO) in the presence of catalytic amount of OsO_4 (5%) at 65 °C, anthraquinone (**3**) was obtained in 39% yield together with the expected diol (**2**) in a 5:1 ratio (Scheme 1). Apparently, the reaction leading to the formation of anthraquinone involves a carbon–carbon bond cleavage. Such a carbon–carbon bond cleavage reaction is unusual. Aimed at achieving a better understanding of the reaction pathway, we also subjected the diol (**2**) to the same reaction conditions and found that the diol (**2**) was converted to anthraquinone completely indicating that the diol (**2**) was probably the intermediate for the formation of anthraquinone.



Scheme 1.

Because hydroxy groups are known to be able to coordinate to osmium,[3,4] it was thought that the hydroxy group probably plays a critical role in this reaction leading to the carbon–carbon bond cleavage. This was confirmed with the experiment using anthracene and 9-methylanthracene, which lack the hydroxy group and were not affected when subjected to the same reaction conditions. In contrast, 9-(hydroxymethyl)anthracene (**4**, Scheme 2) was converted to anthraquinone under the same conditions in over 30% yield with the formation of 9-anthraldehyde (**6**) (10%) (Entry 2, Table 1). Therefore, the oxidation of **4** could take on two different pathways, one involving carbon–carbon bond cleavage and the other one involving the simple oxidation of the alcohol to give the aldehyde. It needs to be noted that with 3 equivalents of TMO, the reaction did not proceed to completion



Scheme 2.

Table 1. OsO_4-mediated oxidation of 9-(1-hydroxyalkyl)-anthracene[a]

Entry	Substrate	Yield of **3** / %[b]	Conversion / %[c]	Product (ratio)[d]
1	**2**	71	86	**3**
2	**4**	33	57	**3, 6** (2.1:1)
3[e]	**4**	14	64	**3, 6** (1:2.7)
4	**5**	48	55	**3**
5[e]	**5**	11	70	**3, 7** (1:4.7)
6[f]	**4**	33	45	**3, 6** (3.0:1)

[a]THF/H_2O/Pyridine (5:1:0.1, v/v) was used as the solvent. [b]The yield was calculated based on the total amount of starting material. [c]The conversion was calculated based on the recovered starting material. [d]The ratio was estimated based on ^1H-NMR. [e]Using OsO_4 (1.0 equiv) as the only oxidant. [f]The reaction was conducted in the dark.

and about 43% of the starting material was recovered (Table 1), which was the reason for the somewhat low yield of anthraquinone. Similar results were observed with the oxidation of 9-(1-hydroxyethyl)anthracene (**5**, Scheme 2) under the same conditions (Entry 4, Table 1).

To further examine the role of the hydroxy group in this oxidation reaction, 9-anthraldehyde (**6**), 9-(methoxymethyl)-anthracene, and 9-acetylanthracene, which all lack the hydroxy group at the benzylic position, were subjected to the same reaction conditions and it was found that none of them was converted to anthraquinone. Such results further indicate that a hydroxy group was essential for this type of cleavage reaction. It is interesting to note that there are literature reports that anthracene and its certain derivatives can be transformed into anthraquinone via a photochemical process in the presence of OsO_4.[5] However, such photochemical reactions could not cleave carbon–carbon bonds.[5] This is in direct contrast to the reactions under study, which involves a carbon–carbon bond cleavage leading to the formation of anthraquinone. Aimed at examining the effect of light on the reactions under study, we conducted the OsO_4-mediated oxidation of **4** in the dark and found that the same results were obtained as compared to the reactions without shielding the reaction flask away from normal daylight (Entry 6, Table 1). Furthermore, anthracene itself was not converted to anthraquinone under our experimental conditions. Therefore, we conclude that the reactions under study are not a light driven process and the reaction mechanism is also different from that reported in a photochemical process.

To understand the role of TMO in this reaction, we also studied the reaction without added TMO using stoichiometric amount of OsO_4. Similar to the reaction in the presence of TMO, **4** underwent both the carbon–carbon bond cleavage reaction and simple oxidation, leading to the formation of **3** and **6**, respectively. However, the ratio between **3** and **6** was much lower (1:2.7) than that of the reaction in the presence of 3.0 equivalents of TMO (2.1:1) (Entries 2 and 3, Table 1). This indicates that the presence of TMO does play a role, which is more than to regenerate OsO_4. The situation with the oxidation of **5** is similar (Entries 4 and 5, Table 1).

Table 2. The influence of reaction conditions on the product distribution in the oxidation of 9-(hydroxymethyl)anthracene (**4**) at 65 °C

Entry	Oxidant (eq.) TMO	Oxidant (eq.) OsO_4	Solvent[a]	Yield of **3** / %[b]	Conversion / %[c]	Product (ratio)[d]
1	3.0	0.05	5:1:0.1	33	57	**3,6** (2.1:1)
2	3.0	0.05	5:1:0	15	60	**3,6** (1:2.5)
3	3.0	0.05	5:1:1	27	33	**3,6** (>10:1)
4	10.0	0.05	5:1:0.1	65	100	**3,6** (3.4:1)
5	10.0	0.05	5:1:0	41	100	**3,6** (1:1)
6	10.0	0.05	5:1:1	33	45	**3,6** (4.9:1)
7	20.0	0.05	5:1:1	31	45	**3,6** (4.1:1)
8	0	1.0	5:1:0.1	14	64	**3,6** (1:2.7)
9	0	1.0	5:1:0.2 (THF/H_2O/TEA)	4	57	**3,6** (1:10.7)
10	3.0	0.05	5:1:1 (THF/H_2O/TEA)	3	48	**3,6** (1:12.3)

[a]THF/H_2O/Pyr was used as the solvent, unless specified otherwise. [b]The yield was calculated based on the total amount of starting material. [c]The conversion was calculated based on recovered starting material. [d]The ratio was calculated based on ^{1}H-NMR.

Ligand coordination to OsO_4 is known to affect its reactivity.[6–8] We suspect that the coordination of TMO or its reduced form, trimethylamine, to OsO_4 might be the reason for the different outcome of the reactions with and without added TMO. Therefore, we were interested in studying the effect of added amines on the product distribution in the oxidation of **4** (Table 2). We chose to study the effect of pyridine and triethylamine (TEA) as model amines. In one set of studies, we changed the amount of pyridine added to the reaction mixture. In the absence of pyridine (Entry 2, Table 2), catalytic amount of OsO_4 in the presence of 3.0 equivalents of TMO was able to give both **3** and **6** in a ratio of 1:2.5. This ratio was much lower than that (2.1:1) of the reaction when pyridine was added to the reaction mixture in a ratio of 5:1:0.1 for THF, water, and pyridine (Entry 1, Table 2). When a higher concentration of pyridine was used (Entry 3, Table 2), the product ratio between **3** and **6** was over 10:1. These results clearly indicate that pyridine plays an important role in determining the product distribution. The higher the pyridine concentration, the higher ratio of anthraquinone over aldehyde was observed. However, the addition of TEA to the reaction mixture resulted in a higher ratio of anthraldehyde in the product distribution (Entries 8 and 9, 3 and 10, Table 2), which indicates that the effect of TEA is opposite to that of pyridine in such reactions.

As described earlier, the reaction was not 100% complete when 3 equivalents of TMO was used in the presence of catalytic amount of OsO_4. On the other hand, a large excess of TMO could drive the reaction to completion when a lower ratio of pyridine was used (Entries 4 and 5, Table 2). However, it is interesting that in the presence of a higher concentration of pyridine, the reaction did not proceed to the completion even with 20 equivalents of TMO (Entries 6 and 7, Table 2). We suspect that the different effects observed with pyridine and TEA were most likely due to their coordination to osmium, which modified the reactivity of OsO_4. Similar effects are certainly well documented in the literature.[6–8] However, proving such a mechanism is beyond the scope of this study.

To examine whether the same type of reactions occurs with other vinyl aromatic compounds, we also examined the oxidation of styrene using TMO in the presence of OsO_4 in a mixture of THF–H_2O–pyridine (5:1:0.1). Complete disappearance of the starting material was observed at the end of the reaction. However, no benzoquinone was observed, which is understandable. If quinone is formed upon the oxidation of styrene following the same pathway as the oxidation of vinylanthracene, the double bonds of the quinone product are not expected to be stable and can undergo further oxidation mediated by OsO_4 to give other degradation products. The fact that the starting material disappeared implies that the oxidation reaction indeed occurred with styrene.

In a typical experiment, to a suspension of **4** (164 mg, 0.787 mmol) and TMO (262 mg, 2.36 mmol, 3.0 equiv) in THF (5 mL) and pyridine (0.1 mL) was added the solution of OsO_4 (10 mg, 0.039 mmol, 5% equiv) in water (1 mL). The reaction mixture was stirred at 65 °C under nitrogen for 24 h. After cooled to room temperature, a 10% aqueous solution of sodium hydrosulfite (10 mL) was added and the mixture was stirred for 10 min. After extraction with EtOAc (3 × 50 mL), the combined organic layers was dried over anhydrous $MgSO_4$. The final product was obtained from silica gel column chromatography using a mixture of ethyl acetate and hexanes.

In conclusion, 9-(1-hydroxyalkyl)anthracene can be converted to anthraquinone using TMO as the oxidant in the presence of catalytic amount of OsO_4 with the best yield in the range of 60–70%. The hydroxy group is essential for this reaction. The presence of pyridine favors the formation of the anthraquinone product, while the presence of TEA favors the simple oxidation of the starting alcohols to the corresponding aldehydes. Such reactions can be used for the preparation of biologically important anthraquinone compounds[9] and will also be very useful in analyzing functional group compatibilities in designing reactions involving OsO_4.

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