

Selective Nitrous Oxide Oxidation for C-H Oxidation and Aromatization of 9,10-Dihydroanthracene Derivatives

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During the nitrous oxide oxidation of 9,10-dihydroanthracene derivatives catalyzed by the ruthenium-porphyrin complexes, anthraquinones were selectively afforded by the C-H oxidation of the benzylic carbon under the appropriate reaction conditions, whereas anthracenes as a result of oxidative aromatization were selectively obtained in the presence of sulfuric acid.

Oxidative aromatization is one of the important chemical reactions; e.g., P-450 aromatase produces estrogens in the human metabolism.¹ While very few artificial systems that mimic these enzymes can be found,² many chemical methods for aromatization are usually carried out as a dehydrogenative process, such as the dehydrogenation by platinum and palladium metals, or DDQ aromatization.³ Owing to their vigorous reaction conditions or large amount of waste, development of a catalytic system for oxidative aromatization is still desired. When 9,10-dihydroanthracene was subjected to some oxidative systems, it was reported that a mixture of anthraquinone and anthracene was produced with no chemo-selectivity.⁴ There are few effective methods to control the ratio of this mixture; limited examples of oxidative⁵ or hydrogen abstraction⁶ catalysts are known to give either anthraquinone or anthracene, respectively. Recently, a stoichiometric procedure was proposed for the effective aromatization of highly alkyl-substituted substrates.⁷ In this paper, we describe that during the nitrous oxide (N₂O)⁸ oxidation^{9,10} catalyzed by a ruthenium-porphyrin complex, quinones were selectively afforded as a result of the oxidation of the benzylic carbon under the appropriate reaction conditions, whereas the aromatized product was selectively obtained in the presence of sulfuric acid.

Various reaction conditions and solvents were initially examined for the N₂O oxidation of 9,10-dihydroanthracene (**1**) (Table 1). When the reaction was performed in benzene at 120 °C, the oxidized product resulted in a mixture of anthraquinone (**2**) and anthracene (**3**) with moderate conversion (Entry 1). In the presence of 10 mol% of the ruthenium catalyst at 200 °C, it was found that **2** was selectively produced in 90% yield as a result of the oxidation of the benzylic carbon (Entry 2: Conditions A). An examination of various reaction solvents revealed that the ratio of these products **2** and **3** varied in each solvent; e.g., in 1,2-dichloroethane the product ratio of **2** to **3** was 34% vs. 57% yields (Entry 3) and in cyclohexane 47% vs. 53% yields (Entry 4). Various additives were then used in the oxidation reaction in order to improve the selectivity towards the aromatized product **3**. As the intermediate for the aromatized product **3** is assumed to be a benzylalcoholic derivative, some dehydration reagents should enhance the aromatization reaction. Neither bases nor molecular sieves worked at all, whereas several strong acids, for example, hydrochloric acid (Entry 5) or trifluoroacetic acid (Entry 6) was

Table 1. N₂O Oxidation of 9,10-Dihydroanthracene

Entry ^b	Solvent	Additive	Temp. / °C	Time / h	Yield / % ^c	
					2	3
1	benzene	—	120	4	17	56
2 ^d		—	200	20	90	9
3	Cl—CH ₂ —CH ₂ —Cl	—	160	4	34	57
4	cyclohexane	—	160	4	47 ^e	53 ^e
5	benzene	HCl ^f	120	4	—	24 (26) ^g
6		CF ₃ CO ₂ H	120	4	—	16 (17) ^g
7		H ₂ SO ₄	120	4	—	99
8 ^h		H ₂ SO ₄	120	4	—	9
9 ⁱ		H ₂ SO ₄	120	4	—	5

^atmp: 5,10,15,20-tetramesitylporphyrin. ^bReaction conditions: 0.15 mmol of 9,10-dihydroanthracene and 5.0 mol% of Ru(tmp)(O)₂ in solvent (14.0 ml) under 10 atm of N₂O. ^cIsolated yield. ^d10 mol% of catalyst. ^eGC yield. ^f1.0 M ether solution. ^gConversion / % in parenthesis. ^hUnder 10 atm of argon. ⁱWith no catalyst.

revealed to improve the selectivity toward aromatization but resulting in low conversions. Finally it was found that sulfuric acid was an efficient additive to selectively afford the aromatized product, anthracene, in quantitative yield (Entry 7: Conditions B). The combined use of an oxo-metal catalyst with sulfuric acid should be a novel and effective system for N₂O oxidation catalyzed by the ruthenium porphyrin complex, though several additives, such as *N*-methylimidazole,¹¹ HCl/HBr,¹² or a carboxylic acid,¹³ were reported to regulate and/or enhance the oxidation processes. It was confirmed that under an argon atmosphere the oxidized product was yielded in the yield corresponded to the amount of the dioxoruthenium complex catalyst (Entry 8) and that the reaction scarcely proceeded without catalyst (Entry 9).

The present selective transformation for the benzylic oxidation and aromatization were successfully applied to several bisbenzylic compounds to afford the corresponding benzylic ketones and 9,10-dihydroanthracene derivatives to afford the corresponding aromatized product, respectively (Table 2). When fluorene (Entry 1) and xanthene (Entry 2) were subjected to reaction conditions A, benzylic methylenes were smoothly oxidized to afford the corresponding ketones in good-to-high yields. The reaction procedure was applied to alkyl substituted 9,10-dihydroanthracenes, such as 2-methyl-(Entry 3), 2-ethyl-(Entry 5), and 2,3-dimethyl-(Entry 7) derivatives, to afford the corresponding anthraquinones in high yields under reaction conditions A. In the presence of sulfuric acid (reaction conditions B), the corresponding aromatized products, the anthracene derivatives, were selectively obtained from each 9,10-dihydroan-

Table 2. N₂O Oxidation of Various Substrates

Entry	Substrate	Conditions ^{a, b}	Product	Yield /% ^c
1		A		85
2		A		92
3		A		88
4		B		98
5		A		98
6		B		99
7		A		86
8		B		96
9		A		47 ^d
10		B		95 ^e

^aConditions A: 0.05 mmol of substrates and 10.0 mol% of Ru(tmp)(O)₂ in 14 ml benzene at 200 °C under 10 atm N₂O. ^bConditions B: 0.15 mmol of substrates and 5.0 mol% of Ru(tmp)(O)₂ in 14 ml benzene with 1 eq. of H₂SO₄ at 120 °C under 10 atm N₂O. ^cIsolated yield. ^d42% of anthraquinone was obtained. ^e10 mol% of catalyst.

thracene in high yields (Entries 4, 6, and 8). Although the reaction rate of the nitrous oxide oxidation of 9-ethyl-9,10-dihydroanthracene under reaction conditions A and B decreased, 10 mol% of the ruthenium catalyst was loaded to complete the reaction (Entries 9 and 10). Under conditions A, the corresponding ketone was obtained in 47% yield along with 42% yield of anthraquinone, while 9-ethylanthracene was selectively obtained under reaction conditions B.

The reaction pathways to produce both the aromatized product and the benzylic oxidation product were explained as follows (Figure 1). In the first step, 9,10-dihydroanthracene (I) should be oxidized into 9-hydroxy-9,10-dihydroanthracene (II)¹⁴ as the common intermediate both for anthracene (III) and anthraquinone (IV). Under reaction conditions A, further oxidation catalyzed by the oxo-ruthenium complex would then proceed to similarly afford the corresponding ketone on another benzylic carbon, and anthraquinone (IV) was finally obtained in high selectivity. On the other hand, in the presence of a strong acid (the conditions B) protonation to II followed by dehydration could proceed to selectively afford the aromatized product, anthracene (III). It should be mentioned that the oxidation of the resulting anthracene (III) was inhibited under conditions B. Anthracene (III) was oxidized to anthraquinone (IV) in 53% yield under vigorous conditions, e.g., at 160 °C with a 5 mol% ruthenium-complex catalyst. However, in the presence of sulfuric

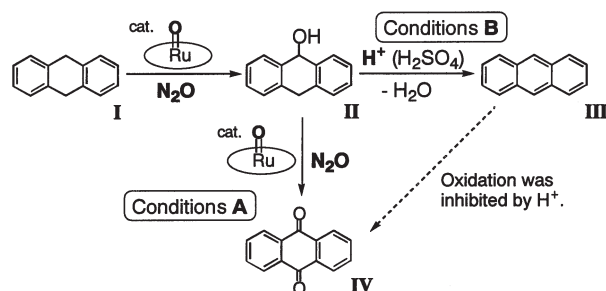


Figure 1. Proposed mechanism for selective oxidation of 9,10-dihydroanthracene.

acid, anthracene (III) was recovered in 94% yield even after exposure to the vigorous conditions of 200 °C for 20 h. Although the remarkable effect of sulfuric acid as the appropriate additive for the oxidative aromatization could not be clearly explained yet, similar effects by several metal sulfates were observed in the N₂O oxidation catalyzed by the oxo-ruthenium complex. The total yield of the benzylic oxidation and aromatization of 9,10-dihydroanthracene was remarkably improved in the presence of the several metal sulfates: 97% yield with CuSO₄ and 93% yield with FeSO₄ vs. 74% yield without any additive. The results that copper chloride or acetate is not effective on the total yield¹⁵ suggested that sulfate anions should work to enhance the oxidation reaction. Further investigations of this phenomenon and the details of the reaction mechanism are currently under way.

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