Aerobic Oxidation

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Selective Aerobic Oxidation of Benzylic Alcohols Catalyzed by Carbon-Based Catalysts: A Nonmetallic Oxidation System**

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Selective oxidation is of great importance in organic synthesis,[1] and green, efficient, selective oxidation techniques are highly sought after in the chemical industry.[2] In particular, selective oxidation of alcohols is a fundamental transformation in the synthesis of fine chemicals.[3] Recently, aerobic oxidation processes have received increasing attention, as oxygen or air are used as the terminal oxidant to replace the stoichiometric metal oxides such as chromates and manganese oxides. The use of oxygen has great benefits from both economic and green chemistry viewpoints, because oxygen is relatively cheap and produces water as the only by-product. Accordingly, varied heterogeneous and homogenous catalysts derived from precious metals have been developed for this purpose, for example, Pt, Ru, Pd, Au, and Ag.[4] However, because of their rarity and high price, precious metals are impractical for industrial use. Despite this, few efforts have been made to seek out nonprecious metal catalysts. One example is the 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO)/Br_2/$NaNO_2$ aerobic oxidation system reported by Liu et al.,[5] in which TEMPO was used as a homogeneous catalyst, and the in situ generated NO played a crucial role in the activation of O_2. Our interests are in the exploration of the potential of carbon-based materials to be applied as metal-free catalysts for selective aerobic oxidation of alcohols. Several studies of carbon catalyst materials have already revealed the ability to replace metal-based catalysts in several important transformations, such as the Friedel–Crafts reaction[6] and the oxidative dehydrogenation of aromatic hydrocarbons[7] and alkanes.[8] Interestingly, carbon catalysts with an ordered nanoshell structure or doped with heteroatoms have been reported to possess surprisingly high oxygen reduction reaction (ORR) activities.[9] However, to date there is no report on the selective aerobic oxidation of alcohols using the same catalyst. Herein, we present a novel protocol: nitric acid assisted carbon-catalyzed oxidation System (NACOS), by which benzyl alcohol and its substituted derivatives can be smoothly oxidized by oxygen under mild reaction conditions, affording high conversions and good selectivities into the corresponding aldehydes.

The nanoshell carbon (NSC) used in this investigation was prepared by pyrolization of a blend of phenol resin and iron phthalocyanine, similar to methods reported by Ozaki et al.,[10] and subsequent acid washes using concentrated HCl. The iron metal on the carbon surface can be thoroughly removed by acid washes,[10] and the metal-free surface was characterized by energy dispersive X-ray spectroscopy (EDS) (Figure 1 a) and X-ray photoelectron spectroscopy (XPS; Table 4). The specific surface area of NSC was 330 $m^2 g^{-1}$, determined by N_2 adsorption. Initial experiments with benzyl alcohol showed that the NSC alone could not activate oxygen and no alcohol conversion was observed. It was postulated that the catalyst might take effect in the presence of an additive, so several acid and base additives were tested. Among all the tested additives, concentrated nitric acid

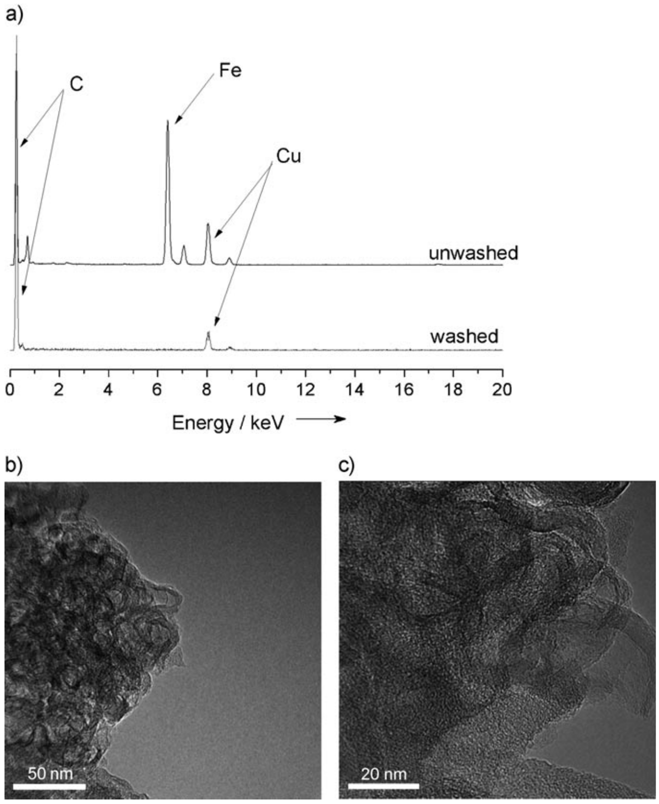

Figure 1. a) Comparison of EDS spectra between acid washed and unwashed nanoshell carbon. The Cu characteristic emission results from the sample holder grid, not from the carbon catalysts. b) and c) TEM images of NSC.

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proved to be the most effective. Subsequent studies suggest that HNO_3 plays a critical role in the activation of O_2.

With concentrated nitric acid as an additive, the NSC was initially investigated for the oxidation of benzyl alcohol at 90 °C, with O_2 (1 atm) as the oxidant and 1,4-dioxane as the solvent. The reaction proceeded smoothly under these conditions, with a conversion of 96 %. Notably, the selectivity for aldehyde formation was 92 %, with benzoic acid being the main by-product (Table 1, entry 1). From the viewpoint of green chemistry,[11] it is desirable to avoid the use of organic solvents, therefore the oxidation of benzyl alcohol was evaluated under solvent-free conditions. For a shorter reaction time (6 h), medium conversion was observed (65 %) and the selectivity remained high (82 %) (Table 1, entry 2). For a longer reaction time (10 h), a good conversion was obtained (97 %), however the selectivity for aldehyde dropped below 40 % (Table 1, entry 3), with benzoic acid being the major product.

Table 1: Aerobic oxidation of benzyl alcohol to benzaldehyde with carbon-based catalysts.

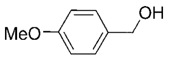
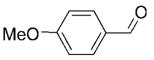
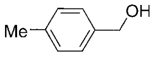
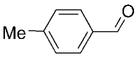
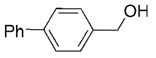
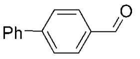
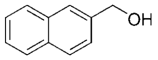
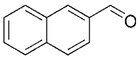
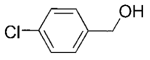
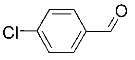
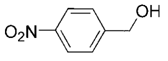
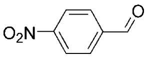
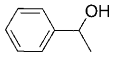
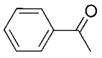
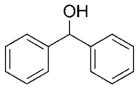
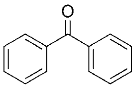
Entry	Catalyst	Solvent	*t* [h]	Conv. [%][b]	Sel. [%][b,f]
1	NSC	1,4-dioxane	5	96	92
2[c]	NSC	–	6	65	82
3[d]	NSC	–	10	97	38
4	–	1,4-dioxane	5	<3	98
5[e]	–	1,4-dioxane	5	3	96
6	AC	1,4-dioxane	5	88	70
7	wAC	1,4-dioxane	5	90	68
8	XC72	1,4-dioxane	5	91	58
9	VGCF	1,4-dioxane	5	3	99

[a] General conditions: catalyst (10 mg), alcohol (0.5 mmol), 1,4-dioxane (2 mL), 67%HNO_3 (1 mmol), 90 °C. [b] Determined by gas chromatography mass spectrometry methods with an internal standard (naphthalene). [c] Alcohol (20 mmol), 67%HNO_3 (2 mmol), solvent free. [d] Alcohol (20 mmol), 40%HNO_3 (4 mmol), solvent free. [e] $NaNO_2$ (0.1 mmol) added. [f] Benzoic acid was the main by-product.

Following the success of benzyl alcohol oxidation, we applied NACOS to a series of benzylic alcohols having substitutions ranging from electron-donating groups to electron-withdrawing groups (Table 2). For all these derivatives, good conversions and selectivities could be easily obtained. Generally, the substrates with electron-donating groups showed higher activity. For example, 4-methoxylbenzyl alcohol and 4-phenylbenzyl alcohol had conversions of around 95 % at 90 °C after three and two hours respectively (Table 2, entries 1 and 3). In contrast, 4-nitrobenzyl alcohol resulted in conversion of less than 60 % after a five hour reaction at 90 °C. However, excellent results could be achieved simply by raising the temperature to 100 °C (Table 2, entry 6). Secondary benzylic alcohols were also tested, giving good yields as expected (Table 2, entries 7 and 8).

To study the mechanism of NACOS, first efforts focused on elucidating the role of the additive. Nitric acid is one of the most commonly produced compounds in the chemical industry and has been studied intensively as an oxidizing agent for alcohol oxidation. These reactions were carried out either with concentrated acid (sulphuric acid or nitric acid) as the reaction media[12a,b] or with $NaNO_2$ as the catalyst.[12c] Therefore it could be postulated that nitric acid ultimately serves as the oxidant in NACOS. However in the absence of NSC, it was shown that nitric acid alone was not active and was unable to catalyze the transformation (Table 1, entry 4). With the addition of 10 mol % $NaNO_2$ (relative to HNO_3), still no improved conversion was obtained (Table 1, entry 5), which indicates clearly a different mechanism with the $NaNO_2$ catalyzed system.[12c] To demonstrate that O_2 rather than HNO_3, is the ultimate oxidant, we tracked the HNO_3 remaining after the reaction. As shown in Table 3, nitric acid was almost all recovered after the reaction in which the ratio of substrate to acid was 1:2 (Table 3, entry 1). Even when the substrate and acid ratio was 10:1, over 90 % of the acid was recovered (Table 3, entry 3). These results clearly indicate that HNO_3 does not serve as the ultimate oxidant, but O_2 does. To additionally clarify the role of HNO_3, a well-designed reaction conducted under a N_2 atmosphere (closed system) provided some interesting results (Table 3, entry 2). In the absence of oxygen, around 90 % of the HNO_3 was consumed, suggesting that in the presence of the catalyst, HNO_3 itself is

Table 2: Oxidation of varied primary and secondary benzylic alcohols.

Entry[a]	Substrate	Product	*t* [h]	Conv. [%][b]	Sel. [%][b]
1			3	97	84
2			4	92	83
3			2	94	98
4			5	95	82
5[c]			4	92[d]	78
6[c]			5	98[e]	99
7			5	90	98
8			4	98	100

[a] General conditions: substrate (0.5 mmol), NSC (10 mg), 1,4-dioxane (2 mL), 67 % HNO_3 (1 mmol), 90 °C. [b] Conversion and selectivity were determined by gas chromatography mass spectrometry methods using an internal standard (naphthalene). [c] Substrate was 1 mmol and temperature was 100 °C. [d] Under general conditions, conversion and selectivity were 76 % and 91 %, respectively. [e] Under general conditions, conversion and selectivity were 58 % and 100 % respectively.

Table 3: Comparison of recoveries of HNO_3 in benzyl alcohol oxidations conducted under oxygen and nitrogen atmosphere.

Entry	alcohol:HNO_3[a]	Atmosphere	HNO_3 Recovery [%]	Conv. [%]	Sel. [%]
1	1:2	O_2	96	96	92
2	1:2	N_2	13	95	42
3	10:1	O_2	90	81	51

able to oxidize alcohol, and serves as a stoichiometric oxidant under these conditions. Moreover, brown gas was observed above the mixture during the reaction, indicating the formation and accumulation of NO_2. As the reaction proceeded, the brown color faded gradually, probably as a result of the reaction between NO_2 and benzaldehyde, which produces benzoic acid as by-product. This reaction explains the poor selectivity (42 %).

Since the activation of HNO_3 does not involve O_2, NO_2 should also be generated in the presence of O_2. However, brown gas was not observed under O_2 bubbling. So NO_2 did not accumulate in the gas phase, but quickly reacted. Considering the high recovery of HNO_3, NO_2 must largely react with O_2 towards the regeneration of HNO_3. Thus under an O_2 atmosphere, there is a HNO_3 consumption/regeneration cycle in which HNO_3 plays a role as primary oxidant for alcohol oxidation, and O_2 acts as secondary oxidant for HNO_3 recovery. Therefore, HNO_3 serves as a catalytic mediator, and to the best of our knowledge, this is the first example of the utilization of an in situ HNO_3 recycling system in organic synthesis.

Alcohol conversion was not observed when the HNO_3 additive was replaced by HBr or $NaNO_3$, all other reaction parameters remaining the same. This result shows that the hydrogen cation and the nitrate ion alone cannot catalyze the reaction. Furthermore, reactions carried out for five hours in a 1,4-dioxane/water (1:1 to 1:4) mixed solvent showed a significant drop in conversion with increasing water content (Figure 2). Recall that HNO_3 has a large dissociation constant, as the ratio of water increases in the solvent, H^+ and NO_3^- ions become more abundant. Thus we suggest that the H^+ and NO_3^- ions have no catalytic activity and only the pseudo-acidic form of HNO_3 is active for this type of reaction.

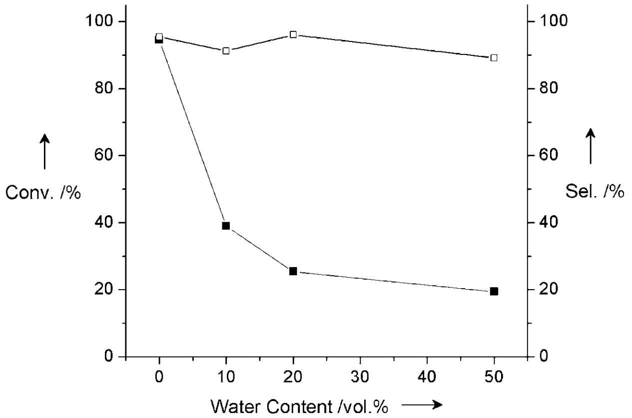


Figure 2. Comparison of benzyl alcohol oxidations conducted with 1,4-dioxane/water mixture at various ratios. Solid squares: conversion, open squares: selectivity to aldehyde. Reaction conditions: 1,4-dioxane/water mixture (2 mL), benzyl alcohol (0.5 mmol), NSC (10 mg), 67% HNO_3 (1 mmol), 90 °C, atmospheric pressure, 5 h.

In contrast, nitric acid has been widely employed in the surface modification of carbon materials.[13] And recent studies have revealed the surface carbonyl groups as the active sites for the oxidative dehydrogenation of aromatic hydrocarbons[7] and alkanes.[8] Therefore it is likely that the NSC surface is oxidized by HNO_3 under our reaction conditions and the surface oxygen-containing group plays an important role in this type of reaction. To examine this assumption, the used catalyst (uNSC) was collected after the reaction and analyzed by XPS (Table 4). The surface oxygen content was shown to be increased from 6% to 9.5%. However, IR spectrum of uNSC does not show a significant increase at 1730 cm^{-1} (Figure 3 b), which is associated with the C=O stretching in lactones and carboxylic anhydrides.[13b] In contrast, oNSC, prepared by treating NSC with 5 M HNO_3 solution under refluxing for five hours, shows a very strong peak at 1750 cm^{-1}. Therefore, the increased surface oxygen detected by XPS is probably a result of a sum of a small degree of surface oxidation and increased physical adsorption of oxygen containing species. To evaluate the effect of surface oxidation, three parallel reactions were conducted simultaneously under the same conditions with NSC, uNSC, and oNSC respectively, using a multireactor. However, the conversions were at the same level after one hour of reaction, indicating same catalytic performances of three catalysts. So increased surface oxidation does not lead to higher reaction rate.

Table 4: [a] The reported ratio is a molar ratio.Table 4
XPS results of nanoshell carbon (NSC) and nanoshell carbon collected after reaction (uNSC).

Sample	C [%]	N [%]	O [%]	Fe [%]
NSC	93	0.7	6.0	n.d.
uNSC	89	0.9	9.5	n.d.

n.d. = not determined.

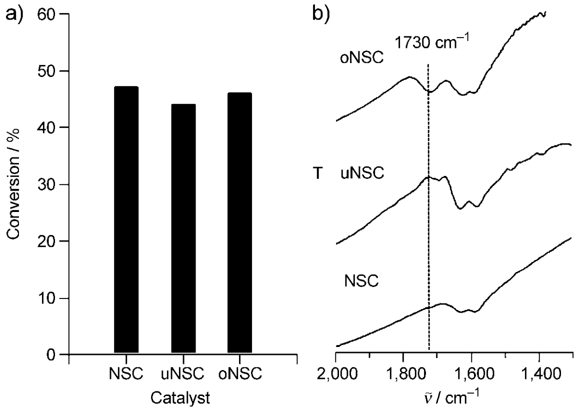
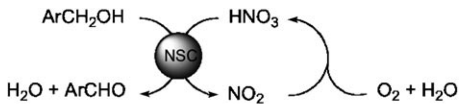


Figure 3. a) Comparison of benzyl alcohol oxidations using NSC, uNSC, and oNSC under the identical reaction conditions: 1,4-dioxane (2 mL), benzyl alcohol (0.5 mmol), catalyst (10 mg), HNO_3 (1 mmol), 90 °C, 1 hour. b) IR spectra of NSC, uNSC, and oNSC.

On the basis the evidence presented herein, we propose an overall mechanism for NACOS (Scheme 1). HNO_3 is firstly adsorbed onto the NSC surface and activated. The activation process probably starts from the weakening of the N–O single bond of HNO_3. Upon heating, a nearby alcohol molecule is attacked by the activated HNO_3 to yield the



Scheme 1. Overall mechanism of NACOS.

aldehyde product accompanied with the rupture of N−O bond of HNO_3 and the release of NO_2. Then NO_2 reacts with surrounding O_2 and water to regenerate HNO_3. Therefore considering the whole catalytic cycle, the net effect is that the alcohol is oxidized by O_2.

As shown in entries 6–9 in Table 1, several other candidates for the oxidation of benzyl alcohol were tested, including activated carbon (AC), carbon black (XC72), and carbon nanofiber (VGCF). AC and XC72 showed good conversions of around 90 % after five hours, but the selectivity was worse than that with NSC. Since the NSC used in our study was washed by concentrated HCl, we treated AC with the same acid-washing process to see whether it has any effect on the selectivity. As shown in entry 7 of Table 1, it seems to not help in the improvement of the selectivity. The high conversions of AC and XC72 hint at the generality of this mechanism, and the broad applicability of this method. In contrast, VGCF had a much lower conversion of 3 %. The low catalytic activity of VGCF is probably because of the low surface area ($13\,m^2\,g^{-1}$) compared to AC and XC72 (1100 and $250\,m^2\,g^{-1}$, respectively). In the case of NSC, the good conversion can be explained by the high surface area ($330\,m^2\,g^{-1}$), however the reason for the excellent oxidation selectivity may require an additional mechanism. It has been reported that the carbonization of polymeric materials in the presence of iron can result in the formation of hollow shell-like crystalline carbon structures, leading to an improvement in oxygen reduction activity.[10] Such crystalline structures were also observed in this work in transmission electron microscope (TEM) images (Figure 1 b,c). The Raman spectra obtained for these four carbon structures provides additional support (Figure 4). As expected, AC and XC72 show very broad bands at $1600\,cm^{-1}$ (G band), whereas VGCF gives a very sharp peak and a shift from $1600\,cm^{-1}$ to $1580\,cm^{-1}$, due to the formation of organized structure similar to the multi-walled carbon nanotube. The spectrum for NSC has a sharper peak and a slight shift from $1600\,cm^{-1}$ to $1590\,cm^{-1}$ compared with AC and XC72, which has been reported to be signs of the formation of ordered carbon structures.[10] These findings indicate that NSC not only possesses large surface area ($330\,m^2\,g^{-1}$) but also has a degree of crystallinity. Because the active sites of the NSC are likely to be on the carbon atoms along exposed zigzag edges of graphitic layers,[14] the crystalline feature of NSC may be partially responsible for the improved selectivity compared with AC and XC72, which are both amorphous carbon structures with a low degree of crystallinity.

This study revealed the feasibility of replacing costly precious metals in selective aerobic oxidation with cheap and abundant carbon materials. An efficient nitric acid assisted carbon-catalyzed oxidation system (NACOS) was established. The activation and recovery mechanism of HNO_3 was elucidated. This newly discovered method of O_2 activation may have more potential applications in line with the notion of green chemistry. NACOS works at mild temperatures and at atmospheric pressure, using low cost and environmentally benign reactants, offering great ease of operation and high potential for scalability. These factors make NACOS an extremely attractive process for industrial application.

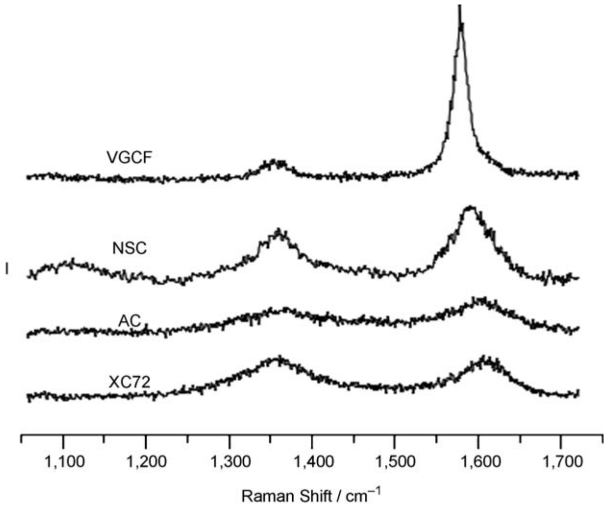


Figure 4. X-ray photoelectron spectra of the different carbon surfaces. The peaks represent ordered carbon structures.

Additional work is now in progress to study the detailed reaction mechanism and to expand the scope of this process.

Experimental Section

Energy dispersive X-ray spectroscopy (EDS) and transmission electron spectroscopy (TEM) was performed using a JEOL JEM-2010F transmission electron microscope (accelerating voltage 200 kV). X-ray photoelectron spectroscopy (XPS) analysis was performed with a PHI Quantum 2000 spectrometer. IR measurements were conducted with JEOL JIR-SPX200 spectrometer. RAMAN spectra were recorded with JASCO NRS-2100 spectrometer. The samples were analyzed with a SHIMAZDU GCMS-QP2010 Plus, using a Restek Rxi-1 ms column. An internal standard method (naphthalene) was used for quantitative analysis.

Preparation of nanoshell carbon (NSC): 1.00 g of iron phthalocyanine was blended with 3.725 g of phenol resin in 300 mL of acetone in a glass flask. The materials were well dispersed by sonication and then acetone was removed by evaporation. After drying the residue under reduced pressure, the blend was heated at 800 °C under N_2 flow for 1 h. The obtained material was pulverized by ball milling to obtain small particles. The pulverized black powder was washed in concentrated hydrochloric acid (37 %) for 12 h. The washed NSC was filtered and thoroughly washed by deionized water, then dried in a vacuum oven for 24 h at 80 °C.

Determination of HNO_3 recovery: The resultant mixture was collected by filtration using a 45 μm syringe filter. In a beaker, 1 mL of the filtrate was diluted to 40 mL with deionized water. The solution was stirred for several minutes and then filtrated to remove insoluble substances. A pH meter was used to determine the pH value of the solution. Based on the pH value, the recovery of HNO_3 after the reaction was calculated.

General oxidation method: The oxidation reactions were conducted in a 25 mL three-necked flask. The flask was charged with benzyl alcohol (54.1 mg, 0.5 mmol), NSC (10 mg), naphthalene (12.8 mg, 0.1 mmol) as an internal standard, and 1,4-dioxane (2 mL). After the mixture was sonicated for 20 s, 67.6 μL (1 mmol) of 67 % nitric acid was added dropwise into the reaction mixture. Oxygen gas was bubbled through a glass capillary. The reaction mixture was heated to 90 °C for 5 h. Samples were taken at appropriate intervals through a silicon septum using a hypodermic needle.

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