Pergamon

Tetrahedron Letters 39 (1998) 2261–2264

TETRAHEDRON
LETTERS

Catalytic Oxidation of Para-Substituted Phenols with Nitrogen Dioxide and Oxygen.

Joseph J. Bozell* and John O. Hoberg

National Renewable Energy Laboratory, 1617 Cole Boulevard, Golden, CO 80401

Donald R. Dimmel

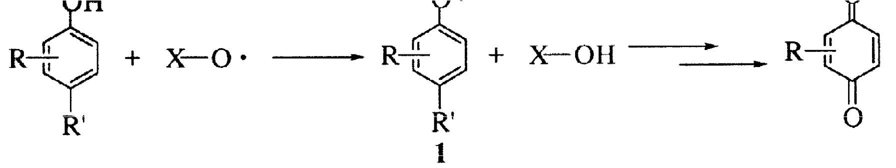
Institute of Paper Science and Technology, 500 10th Avenue N. W., Atlanta GA 31520

Received 24 November 1997; revised 21 January 1998; accepted 22 January 1998

ABSTRACT: A series of para-substituted phenols was oxidized to the corresponding benzoquinones in moderate to high yield with catalytic amounts of NO_2 under O_2 in MeOH. Little or no oxidation is observed under argon. Substrates of lower reactivity gave quinones when treated with stoichiometric amounts of NO_2 in CCl_4, but nitration of the aromatic ring became a significant side product. © 1998 Elsevier Science Ltd. All rights reserved.

Many methods are known for the oxidation of phenols to benzoquinones if the phenol does not possess a substituent para to the hydroxyl group. However, selective oxidations of para-substituted phenols are unusual.[1] We have investigated the oxidation of para-substituted phenols as a model for conversion of lignin to novel products and recently reported a method for their conversion to benzoquinones using O_2 and Co-Schiff base catalysts.[2] Lignin, a renewable biopolymer, will become an important raw material for the production of chemicals if methodology can be developed to convert it cleanly and selectively into single compounds in high yield.[3] The unifying structural feature of lignin is a network of para-substituted oxygenated phenolic rings.[4] These rings could be useful chemical precursors if selectively released from the polymer.

The oxidation of para-substituted phenols with Co-Schiff base complexes and O_2 depends on the formation of phenoxy radical **1** by an intermediate Co-superoxo complex (equation 1, X=(salen)CoO).



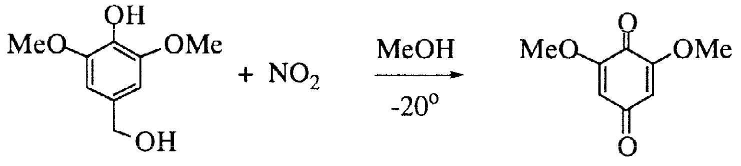
[1]

Because of the tendency of Co(salen)/O_2 complexes to undergo deactivation during oxidation,[5] we are investigating other species that contain an oxygen centered free radical as a structural feature, and recently reported that stoichiometric NO_2 could be used for this conversion.[6] We now report preliminary results showing that *catalytic* NO_2 in the presence of O_2 can be used to convert para-substituted phenols to benzoquinones.

In initial experiments, alcohol **2** was treated with a stoichiometric amount of $NaNO_2$ and 100 μL of concentrated HNO_3 or HCl (a convenient source of NO_2) in MeOH under argon at -20°C. Quinone **3** was

0040-4039/98/$19.00 © 1998 Elsevier Science Ltd. All rights reserved.
PII: S0040-4039(98)00242-1

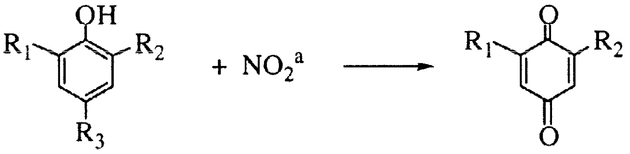
isolated in low yield (equation 2).



2 **3** [2]

However, introduction of 1 atmosphere of O_2 to this reaction has a dramatic effect, allowing isolation of **3** in much higher yields (80-90%). In addition, we find that in the presence of O_2, only catalytic amounts of $NaNO_2$ were required to produce 80-90% yields of **3**. With $NaNO_2$ levels as low as 5%, compound **3** is formed in yields of 70-75%. A summary of results is found in Table 1.[7]

Table 1 - Oxidation of Para-Substituted Phenolics with NO_2 and O_2



R_1	R_2	R_3	conditions	% yield
OMe	OMe	CH_2OH	20% $NaNO_2$, -20°C, MeOH	88
OMe	OMe	CH_2OH	5% $NaNO_2$, -20°C, MeOH	72
OMe	OMe	$CH(CH_3)OH$	20% $NaNO_2$,-20°C, MeOH	56
OMe	OMe	CHO	20% $NaNO_2$, 0°C, MeOH	50
OMe	OMe	Me	20% $NaNO_2$, -10°C, MeOH	12
t-Bu	t-Bu	CH_2OH	20% $NaNO_2$, -20°C, MeOH	0^b
t-Bu	t-Bu	CH_2OH	1 eq $NaNO_2$, rt, CCl_4	37^c
Me	Me	CH_2OH	1 eq $NaNO_2$, rt, CCl_4	9^d
Me	Me	OH	20% $NaNO_2$, -10°C, MeOH	100
t-Bu	t-Bu	OMe	20% $NaNO_2$, -10°C, MeOH	99

[a] NO_2 generated by the reaction of $NaNO_2$ with 100 µL of concentrated HNO_3 or HCl. [b] The corresponding methyl benzyl ether was isolated in 81% yield. [c] 4-Nitro-2,6-di-t-butylphenol was isolated in 31% yield. [d] 4-Nitro-2,6-dimethylphenol was isolated in 17% yield.

For most reactions, lower temperatures are more effective because of the increased concentration of volatile NO_2 in solution. MeOH is the optimal solvent for most reactions. Solvents such as MeCN, CH_2Cl_2, ethylene dichloride, i-PrOH, and EtOAc resulted in the formation of significant amounts of side products, predominantly oxidation of the benzylic alcohols to the corresponding benzaldehyde or nitration of the aromatic ring. For example, treatment of **2** with $NaNO_2$ in MeCN gave a 63% yield of the corresponding aldehyde. Substrates with strongly electron donating substituents exhibit a greater ability to form quinone. However, substrates unreactive toward quinone formation under catalytic conditions (e.g., R_1, R_2 = t-Bu, R_3 = CH_2OH) can be converted to quinone in the presence of stoichiometric amounts of $NaNO_2$ in CCl_4 solvent. Hydroquinones and hydroquinone monoalkyl ethers can be converted to the corresponding benzoquinones in high yield.[8] The results with the benzyl alcohols are particularly interesting since Coombes has reported that similar phenols undergo reaction with NO_2 under inert atmosphere to give the corresponding aldehyde and aromatic ring nitration; no quinone is observed.[9] The addition of oxygen in our system is apparently diverting the normal aromatic nitration pathway. Overall, these results indicate that para-substituents similar to those found in lignin undergo cleavage, a necessary step for the removal of the phenolic units present in lignin.

The mechanism of NO_2 promoted oxidation is complex due to the number of different oxides of nitrogen that can be formed under these conditions.[10] However, Kochi has shown that NO_2 oxidation of hydroquinone dialkyl ethers to quinones occurs via a radical cation that results from the reaction of the substrate with the NO_2 disproportionation product $NO^+NO_3^-$.[11] Substrates used in our study are assumed to undergo conversion to radical cation **4** upon reaction with NO^+. Formation of the quinone occurs via reaction of **4** with nitrate anion (Figure 1). This sequence forms HONO which is converted back to NO_2 via N_2O_3 formation and subsequent O_2 oxidation of N_2O_3 to N_2O_4, continuing the catalytic cycle.

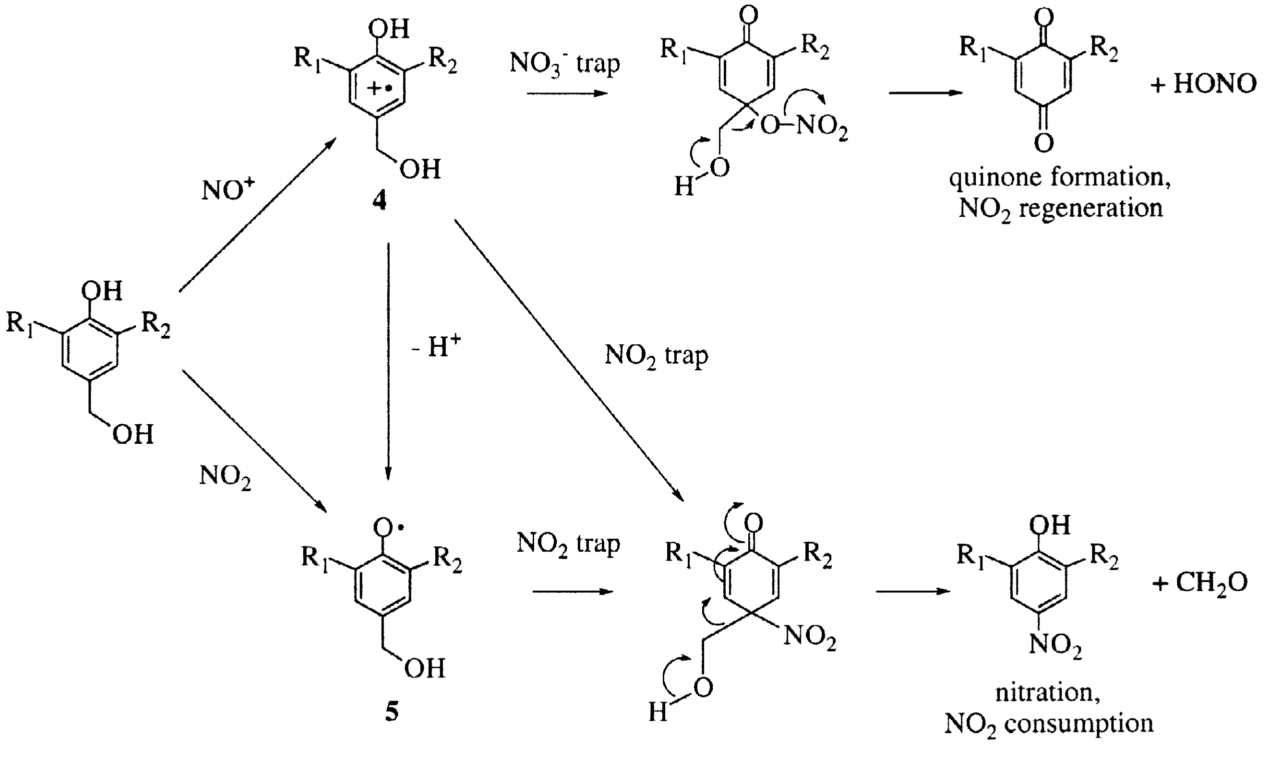


Figure 1 - Possible Mechanism for the Conversion to Benzoquinones

Nitrogen dioxide is also a useful aromatic nitration reagent.[12] We observe ring nitration as a side product in low yield in several of the reactions shown in Table 1. Ring nitration can proceed from radical cation **4** in a process that leads to the nitration products and consumption of NO_2.[11] Interestingly, we observe an increase in the relative amount of ring nitration when a stoichiometric quantity of $NaNO_2$ is used in nonpolar CCl_4 as a solvent. In contrast, Kochi reported an increase in ring nitration when hydroquinone dialkyl ethers were treated with stoichiometric NO_2 in polar solvents. We suggest that ring nitration of these phenols in nonpolar media may be occurring via phenoxy radical **5**, formed upon abstraction of the phenolic hydrogen atom by NO_2. Subsequent reaction of **5** with NO_2 would lead to the observed nitration products. This mechanistic path is similar to that described for the reaction of phenols with Co-Schiff base complexes and O_2.[13] Direct reaction of the starting phenol with NO_2 might occur under these conditions because the formation of ionic $NO^+NO_3^-$ would be expected to be poor in nonpolar media. In this case, nitration could be occurring via direct reaction of **4** with NO_2[11] or through **5** formed by loss of H^+ from **4** and trapping of **5** by NO_2.

These results suggest that NO_2 may be a suitable agent for the selective conversion of lignin into useful chemicals. We are currently investigating methods to extend the generality of this reaction to other phenolic substrates.[14]

References

1. (a) Patai, S.; Rapoport, Z., eds., The Chemistry of the Quinonoid Compounds; Wiley: New York, 1988; Volume 2, parts 1-2; (b) Saa, J. M.; Morey, J.; Rubido, C. *J. Org Chem.* **1986**, *51*, 4471.
2. Bozell, J. J.; Hames, B. R.; Dimmel, D. R. *J. Org. Chem.* **1995**, *60*, 2398.
3. Bozell, J. J.; Hoberg, J. O.; Claffey, D.; Hames, B. R.; Dimmel, D. R. in Green Chemistry: Frontiers in Benign Chemical Synthesis and Processing; Anastas, P. T.; Williamson, T., eds. Oxford University Press, in press.
4. Fengel, D.; Wegener, G.; Wood: Chemistry, Ultrastructure and Reactions; Walter DeGruyter: New York, 1984.
5. Busch, D. H. in Oxygen Complexes and Oxygen Activation by Transition Metals; Martell, A. E.; Sawyer, D. T. eds., Plenum,: New York, 1988; p. 61.
6. Dimmel, D. R.; Karim, M. R.; Savidakis, M. C.; Bozell, J. J. *J. Wood Chem. Tech.* **1996**, *16*, 169.
7. Typical experimental conditions: The substrate and $NaNO_2$ are mixed in the reaction solvent, placed under an oxygen atmosphere, and cooled to the reaction temperature. The solution is treated with 100 µL of either concentrated HNO_3 or HCl and stirred until no starting material is observed by thin layer chromatography (1-24 h). The quinone is isolated either by solvent removal and column chromatography of the residue on silica gel or by simple filtration.
8. Kochi has reported the oxidation of hydroquinone monoalkyl ethers to quinones with stoichiometric NO_2: Rathore, R.; Bosch, E.; Kochi, J. K. *J. Chem. Soc. Perkin Trans. 2* **1994**, 1157.
9. Coombes, R. G.; Hadjigeorgiou, P.; Jensen, D. G. J.; Morris D. L. In Nitration: Recent Laboratory and Industrial Developments; Albright, L. F.; Carr, R. V. C.; Schmitt, R. J., eds., ACS Symposium Series 623, American Chemical Society; Chapter 3 (1996).
10. Bosch, E.; Rathore, R.; Kochi, J. K. *J. Org. Chem.*, **1994** *59*, 2529.
11. Rathore, R.; Bosch, E.; Kochi, J. K. *Tetrahedron*, **1994** *50*, 6727.
12. (a) Pervez, H.; Onyiriuka, S. O.; Rees, L.; Rooney, J. R.; Suckling, C. J. *Tetrahedron*, **1988** *44*, 4555; (b) Bosch, E.; Kochi, J. K. *J. Org. Chem.*, **1994** *59*, 3314; (c) Ohi, H; McDonough, T. J. *Mokuzai Gakkaishi*, **1992** *38*, 570; (d) Hartshorn, M. P.; Robinson, W. T.; Sutton, K. H.; Vaughan, J. *Aust. J. Chem.*, **1985** *38*, 161.
13. Nishinaga, A.; Tomita, H.; Nishizawa, K.; Matsuura, T.; Ooi, S.; Hirotsu, K. *J. Chem. Soc. Dalton Trans.*, **1981** 1504.

14. This work was funded by the U. S. Department of Energy, Office of Industrial Technologies.