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RUTHENIUM-CATALYZED OXIDATION OF PHENOLS WITH HYDROGEN PEROXIDE

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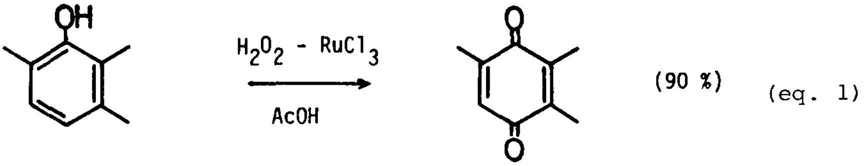
Summary: $RuCl_3$ catalyzed the oxidation of trimethylphenol with 30% H_2O_2 in acidic medium to give the corresponding *p*-benzoquinone in high yield.

Selective oxidation of phenols with hydrogen peroxide is one of attractive problems from a synthetic point of view as well as in biological oxygenation.

Transition metals, such as Fe, Cu, and Mo, are well known to catalyze oxidation of phenols with hydrogen peroxide.[1] However, these systems gave in most cases complex results so that they could hardly be applicable to organic synthesis.

One of important phenolic oxidations to be developed is the conversion of 2,3,6-trimethylphenol to the corresponding *p*-benzoquinone, which is a key intermediate in the synthesis of tocophelol (Vitamin E).[2] We now wish to report here that this problem can easily be solved by the use of catalysis of ruthenium, especially $RuCl_3$, in the oxidation of the phenol with hydrogen peroxide (equation 1).



(eq. 1)

1 2

When a solution of 2,3,6-trimethylphenol (1) (0.37 M) and a catalytic amount of $RuCl_3.3H_2O$ (1 mol%) was treated with 2 eq. of 30% H_2O_2 at ambient temperature, the oxidation occurred smoothly to afford trimethyl-*p*-benzoquinone (2) (within 5 h) in a 90% yield together with a slight amount of dimeric phenol (< 10%).

Following table showed the results of H_2O_2-oxidation of the phenol 1 in the presence of various metal salts;

Table I. Transition Metal-Catalyzed Oxidation of 1 by 30% H_2O_2 to 2*

Catalysts	cat ratio (mol%)	conv(%)	yield(%)
H_2SO_4	4 drops	50	73
$FeCl_2.4H_2O$	2	98	56
$FeCl_3$	2	98	73
$[Fe_3O(OAc)_6py_3]^+$	0.5	26	29
$RuCl_3.3H_2O$	1	99	90
$[Ru_3O(OAc)_6aq_3]^+$	0.4	99	61
$RuCl_2(PPh_3)_3$	0.6	59	56
$RuH(PPh_3)_3OAc$	0.7	60	61
CuCl	3	99	37
$CuCl_2$	2	99	32
$ZnCl_2$	2	32	29
$CoCl_2$	2	36	40
$NiCl_2$	2	27	37
$RhCl_3.3H_2O$	1	39	50
$PdCl_2$	2	23	29
$SnCl_4$	1	52	40
$AlCl_3$	1	28	66
$CeCl_3.7H_2O$	2	13	63
$BF_3(OEt)_2$		80	64
$VO(acac)_2$	1	59	51
$Na_2MoO_4.2H_2O$	1	58	13
$MoO_2(acac)_2$	1	42	53
$La(OAc)_3.2H_2O$	0.8	23	59
$P_2O_5.24WO_3.nH_2O$	0.1	42	53

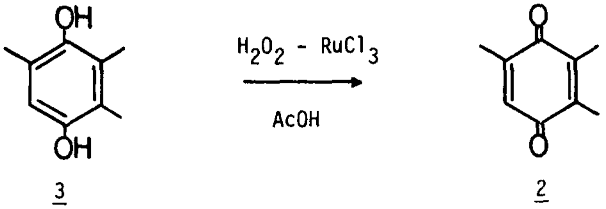
* Carried out in acetic acid at ambient temperature.

** Isolation yield by column chromatography (SiO_2; eluted with CH_2Cl_2)

i) This oxidation prefered the redox type catalysts (Fe^{2+}, Cu^+, etc.) more than the peroxy type catalysts (Mo, V, etc.) and ruthenium, especially $RuCl_3$, showed remarkable catalytic activity.[3,4] Strong Lewis acid BF_3, a typical catalyst for H_2O_2-oxidation, could not overcome $RuCl_3$ in the catalytic activity.

As a solvent, acetic acid could be replaced by the other carboxylic acid, such as formic acid or acidic (HCl) methanol, though methanol solvent was of no use.[5,6]

The oxidation of eq. 1 required two equivalents of H_2O_2. Thus, this oxidation seemed to proceed through the hydroxylation at *p*-position of the phenol 1, followed by the oxidative dehydrogenation to yield benzoquinone 2 as shown in the equation 2. In fact, trimethyl-*p*-hydroquinone (3) was smoothly converted to 2 by an equimolar amount of H_2O_2 under the same conditions.

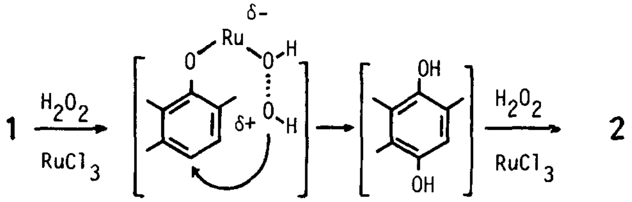


(eq. 2)

However, we could not detect 3 in the reaction mixture of 1 and H_2O_2. These facts suggested that the oxidation of 3 to 2 is far more rapid than the process of 1 to 3.

A plausible mechanism is depicted in Scheme 1. Phenoxide type of coordination of 1 to the Ru metal seems to be essential because methyl ether of 1 could hardly be converted to 2. Possibility of peracetic acid as an active oxidant species was excluded by the result using H_2SO_4 catalyst in the Table I and by the result in acidic methanol mentioned above. $RuCl_3$ probably acts as a Lewis acid to activate H_2O_2 rather than a one-electron oxidant. It is known that one-electron oxidation of propenylsesamol, a certain substituted phenol, by moleuclar oxygen in the presence of ruthenium catalyst leads to the formation of carpanone.[7] While the oxidation of propenylsesamol by $RuCl_3$-H_2O_2 system could produce no carpanone.

Scheme 1

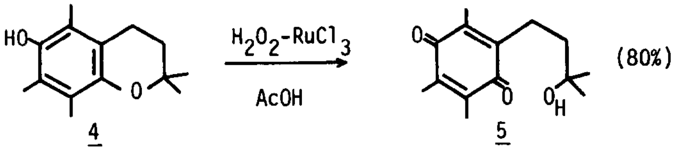


Oxidation of the other substituted phenols was attempted by the present system ($RuCl_3$-H_2O_2-AcOH). As shown in Table II, one of important characteristics of this oxidation system was the preference of *p*- oxygenation of phenols, though the efficiency was very sensitive to the substituents.[8]

Table II. Substituent Effect on the Oxidation of Phenols with $RuCl_3$-H_2O_2

Phenols	Quinones(%)	Phenols	Quinones(%)
o-cresol	trace	3,5-di-*t*-butylphenol	0
o-*t*-butylphenol	trace	2,3,5-trimethylphenol	41
o-phenylphenol	20	2,3,6-trimethylphenol	90
2,3-dimethylphenol	10	2,3,5,6-tetramethylphenol	55

At the end, we show effective conversion of monomethyl ether of *p*-hydroquinones to *p*-quinones. 4-Methoxy-2,3,6-trimethylphenol was oxidized into 2 in a 77% yield. Similarly, a model compound 4 of vitamin E was easily converted to the corresponding quinone 5 in an 80% yield.



References and Notes

1. For examples, see: a) M. L. Mihailovic, Z. Cekovic, "The Chemistry of Hydroxy Group," Ed., S. Patai, Chapter 10, Interscience, 1971. b) G. Sosnovsky, "Organic Peroxides," Ed., D. Swern, Vol. II, p. 269, 1971.
2. P. Schudel, H. Mayer, O.Isler, "The Vitamines," Ed., W. H. Sebrell, Jr., and R. S. Harris, 2nd. Ed., Vol. V, p. 165, Academic Press, 1972.
3. The reaction proceeded without catalyst, though the efficiency was less than the $RuCl_3$-system (conv. 23%, yield 46%).
4. 5% Ru on Carbon (heterogeneous system) showed the catalytic activity as follows: cat ratio-conv(%)-yield(%) = 0.4 - 99 - 79.
5. Oxidation potential is known to relate to the pH of the reaction medium.[6]
6. G. E. Peneth, J. Appl. Chem., 7, 512 (1957).
7. M. Matsumoto, K. Kuroda, Tetrahedron Lett., 22, 4437 (1981) and unpublished results.
8. *o*-*t*-Butylphenol derivatives did not produce the corresponding quinone derivatives but yielded dimeric coupling products.

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