

# SYNTHESIS OF 1,4-BENZOQUINONE: “IN” AND “ON WATER”

Dr Niharika Verma

Associate Professor

Shri JNPG College, Lucknow

**Key words:** “on water”, co-solvent, benzoquinone, hydroquinone

## ABSTRACT

The objective of this study is to evaluate the impact of “*on water*” reaction conditions on the oxidation of organic compounds under the atmosphere of molecular oxygen. Experiments highlighted herein utilize water as the sole reaction solvent or as a major co-solvent. The study describes standardization of the method for the oxidation of phenolic compounds utilizing “*on water*” reaction concepts using molecular oxygen.

## INTRODUCTION

Quinones are a large class of organic compounds having rich and fascinating chemistry<sup>1</sup>. 1,4-Benzoquinone or p-benzoquinone (**1**) is the basic structure of quinonoid compounds. They are abundantly distributed in the natural world<sup>2</sup>, play major role in the biological functions including oxidative phosphorylation and electron transfer<sup>3</sup>. A large number of chemical derivatives having 1,4-benzoquinone as the basic moiety shows prominent pharmacological applications as antibiotic<sup>4</sup>, antitumor<sup>5</sup>, antimalarial<sup>6</sup> and herbicidal activity<sup>7</sup>. Quinones also have wide applications in the field of synthetic organic chemistry<sup>8</sup>. In coordination chemistry quinones are used for designing magnetic materials<sup>9</sup>.

The keen interest on quinone chemistry has been observed from the middle of 19<sup>th</sup> century<sup>10</sup>. **1** was the first synthesized quinone in late 1830 from the oxidation of quinic acid with manganese dioxide and sulfuric acid<sup>11</sup> (Scheme 1). The commonly used oxidizing agents applied for quinone synthesis are silver oxide<sup>12</sup>, manganese oxide<sup>13</sup>, nitric acid<sup>14</sup>, salcomine/O<sub>2</sub><sup>15</sup>, chromium oxidants<sup>16</sup>, benzene selenic anhydride<sup>17</sup>, ceric ammonium nitrate(CAN)<sup>18</sup> and DDQ<sup>19</sup>. The

combination of solvent and oxidizing agents, such as ferric chloride in DMF<sup>20</sup>, ceric ammonium nitrate in acetonitrile-water<sup>21</sup>, silver oxide in benzene<sup>22</sup>, and sodium hypochlorite<sup>23</sup>, and nitric acid-impregnated manganese dioxide in methylene chloride<sup>24</sup> have been utilized for the oxidation of hydroquinones to 1,4-benzoquinones. Among polymers, polyaniline is known to have various oxidation states, which permits the reversible redox cycle for the catalytic reactions<sup>25</sup>.

Various techniques have been reported for the oxidation of phenol to benzoquinones. The Teuber reaction<sup>26</sup> (Scheme 2), which uses Fremy's salt,  $(\text{KSO}_3)_2\text{NO}$  as oxidizing agent has been the earliest reported and widely used method. The nitric acid oxidation of phenols into the corresponding quinones is very well known<sup>27</sup>. The electrosynthesis of benzoquinone is achieved by the anodic oxidation of phenol in acetonitrile-water mixtures using  $\text{PbO}_2$  electrodes (Scheme 3)<sup>28</sup>. The recent advancement in the quinone synthesis from phenol is following the green chemistry route. The solar chemical synthesis of quinones by the photo-oxygenation of phenols was carried out by Oelgemollar and co-workers<sup>29</sup>. One of the earliest synthetic route of 1,4-benzoquinones from hydroquinone was revealed by Vliet<sup>30</sup> around 70 years back, using Cr (VI) salt for the oxidation. Bernini et al<sup>31</sup> disclosed the first catalytic methodology to obtain p-benzoquinone by oxidation of catechin and epicatechin derivatives with the hydrogen peroxide/methyltrioxo rhenium catalytic system (Scheme 4). "Telescoped process", discovered by Bjorsvik and colleges<sup>32</sup>, constitutes a green and environment friendly synthesis of 1,4-Benzoquinone in the following three steps: i) oxidation using hydrogen peroxide in the presence of a Bronsted acid, nitric acid as a catalyst; ii) elimination of excess oxidant using sodium metasulfite; iii) oxidation using concentrated nitric acid (Scheme 5).

### **Synthesis of 1, 4-Benzoquinone from unique precursors**

Several reports are mentioned in the literature about the synthesis of quinones from organic moieties other than commonly applied phenols.

1. Coombes and Moody<sup>33</sup> synthesized the product from brown algae *Perithalia capillaries* (Scheme 6).

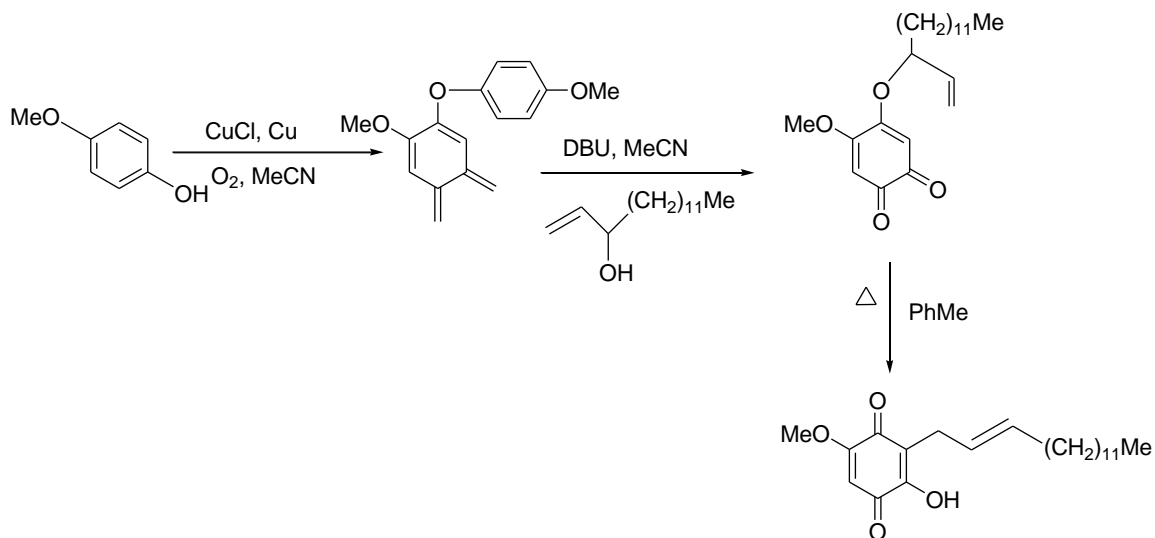
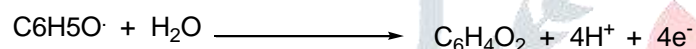
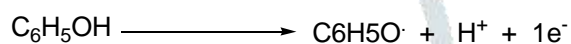
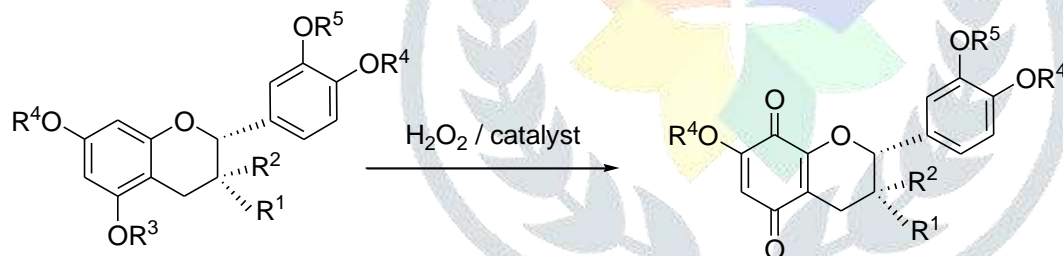
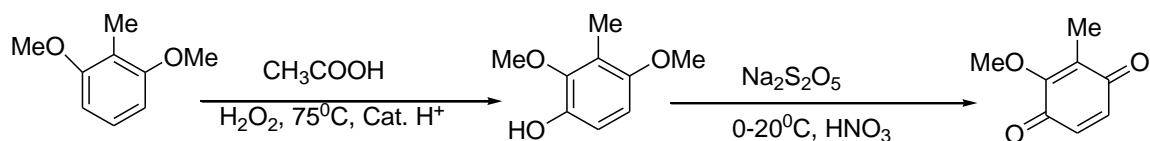
2. N-Arylsulphonamides gave p-benzoquinone on oxidation with ceric ammonium nitrate (Scheme 7)<sup>34</sup>.
3. Synthesis of annelated quinones was reported by Moore and co-workers<sup>35</sup> (Scheme 8). The reaction proceeds via thermal rearrangement.
4. Mathur et al<sup>36</sup> reported a photochemically promoted one-step synthesis of 1,4-benzoquinones (Scheme 9).
5. Moody and co-workers<sup>37</sup> reported microwave-mediated Claisen rearrangement followed by phenol oxidation to give the desired product. Wide range of 1,4-benzoquinone were designed by Pardasani and co-workers following this method<sup>34</sup> (Scheme 10).

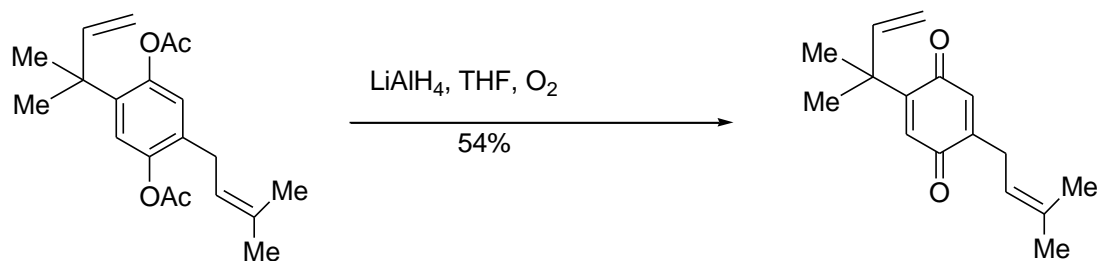
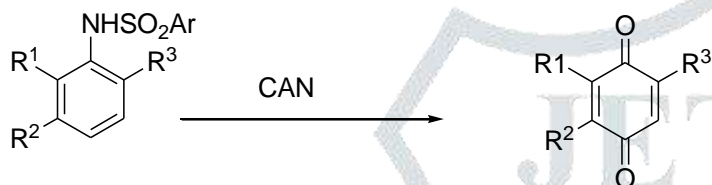
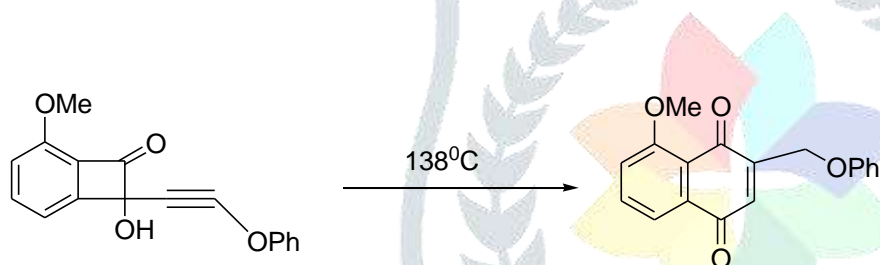
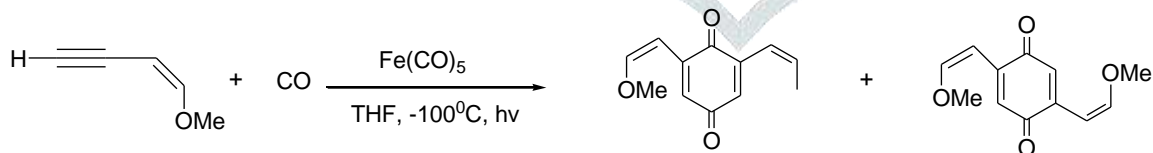
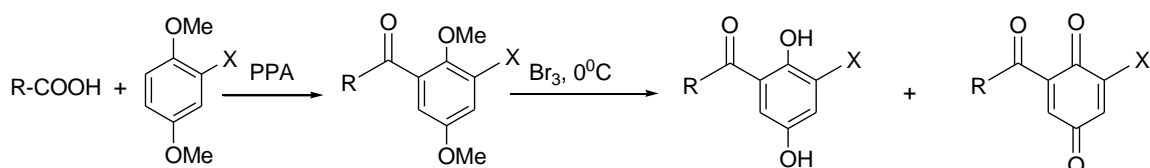
The oxidation of hydroquinone to benzoquinone is marked as an important physiological reaction, which is most efficiently catalyzed by copper metal<sup>38, 39</sup>. This particular reaction prompts me to use the copper salt as a catalyst in my experiment.

### Oxidation of hydroquinone to 1,4- benzoquinone using various oxidising agents



**Scheme 1. First synthesis of benzoquinone.**

**Scheme2. Mechanism of Teuber reaction****Scheme3 . Electrosynthesis of benzoquinone.****Scheme 4 . Synthesis of benzoquinone by Bernini et al.****Scheme 5 . A green telescoped process for the synthesis of quinones**

**Miscellaneous synthesis of 1,4-benzoquinones from unique precursors****Scheme 6 . Synthesis of benzoquinone by Coombes and Moody****Scheme 7 . Conversion of N-arylsulphonamides to benzoquinone****Scheme 8 . Synthesis of benzoquinone by Moore and co-worker****Scheme 9 . Synthesis of benzoquinone by Mathur et al.**

**Scheme 10. Synthesis of benzoquinone by Pardasani and coworkers.****EXPERIMENTAL SECTION****Materials**

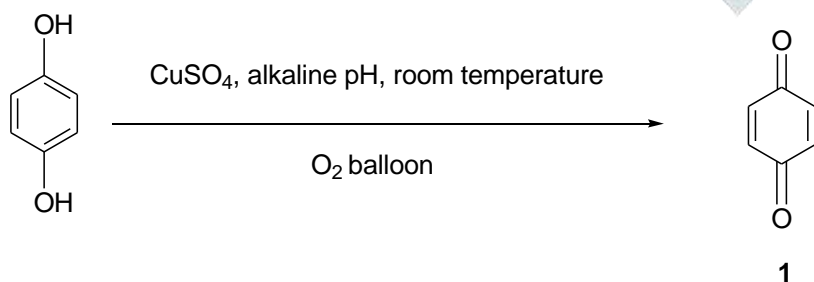
Hydroquinone was purchased from Loba Chemie Pvt. Ltd., India. Copper sulphate was supplied by Fisher Scientific Qualigens, India.

**i) “In water” catalytic oxidation of hydroquinone to 1**

In a 25 ml round-bottomed flask, hydroquinone (2 mmol) and water (6 ml) were added and the reaction mixture was stirred at room temperature for one and a half hour under the atmosphere of molecular oxygen (oxygen balloon) in presence of alkaline medium and catalytic amount of copper sulphate (20 mole%) (Scheme 11).

**ii) “On water” catalytic oxidation of hydroquinone to 1**

Slurry of 5 mmol of hydroquinone was made in hexane, and then it was quenched with minimum amount of water to achieve a heterogeneous mixture. “On Water” catalytic oxidation of this heterogeneous mixture was proceeded in the similar manner as mentioned above. The oxidative conversion of hydroquinone to **1** (obs. m.p 114-116<sup>0</sup>C; reported m.p 115<sup>0</sup>C) was achieved within 45 min. The conversion rate was up to 80-90%, which is higher in comparison to the “in water” oxidation (70-80%).

**Scheme 11. Catalytic oxidation of hydroquinone to 1**



## RESULT AND DISCUSSION

The optimization of the process obviously depends on ascertaining the role of pH, catalyst and molecular oxygen in the reaction.

### pH selection

The oxidation of hydroquinone with molecular oxygen is very sensitive to the pH. Experiments were also performed at neutral and acidic pH under the similar conditions but no oxidation was observed.

### Role of the catalyst

From the optimization study on the reaction conditions, I found that when hydroquinone was stirred at room temperature under atmospheric oxygen at alkaline pH, without the addition of catalyst a small amount (<1%) of **1** was formed. On addition of catalytic amount (20 mole %) of copper sulphate at neutral pH the conversion of hydroquinone to **1** was about 5%. By making the reaction mixture alkaline the oxidative conversion exceeds up to 40-50%.

### Role of molecular oxygen

Similar experimental conditions (pH, amount of catalyst) were used to compare the oxidation of hydroquinone under atmospheric oxygen and molecular oxygen. Maximum oxidative conversion (80-90%) was obtained when the oxidation was proceeded under the atmosphere of molecular oxygen (oxygen balloon). For these reasons, the use of molecular oxygen seems to be very promising, as the oxidizing agent.

Hence, this screening process reveals that here, the catalyst, pH and molecular oxygen are all equally essential for facilitating the oxidation of hydroquinone to 1,4- benzoquinone. The conclusion drawn from the above experiment was that hydroquinone was partially oxidized to benzoquinone even on addition of catalyst to the reaction mixture at alkaline pH under

atmospheric oxygen. But the rate of oxidation was very high when the reaction was proceeded under similar conditions in the presence of molecular oxygen.

## CONCLUSION

In conclusion, a new protocol has been developed for the oxidation of hydroquinone to benzoquinone. This process is rapid and easy to perform at room temperature. The methodology developed here is environmentally benign, as it uses molecular oxygen as an oxidant and found to be highly efficient for the oxidation of hydroquinone to **1** with the efficacy of 80-90%.

## REFERENCES

1. Patai, S.; Rappaport, Z.; The Chemistry of Quinonoid Compounds, *Wiley publications* New York 1988.
2. Thomson, R.H.; Naturally Occuring Quinones IV. Recent Advances, *Blackie* London 1997.
3. Morton, R.A.; Biochemistry of Quinones, *Academic Press* New York 1965.
4. Hartley, J.A.; Reszka, K.; Lown, J.W.; Photosensitization by antitumor agents, *Photochem. Photobiol.* **48** (1988) 19.
5. Gupta, S.P.; Quantative structure-activity relationship studies on anticancer agents, *Chem. Rev.* **94** (1994) 1507.
6. Anthony, R.A.; Grey, G.O.; Udo, B.; Peter, S.; Larry, W.R.; Metabolic activation of PCBs to quinones: Reactivity towards nitrogen and sulfur nucleophiles and influence of superoxide dismutase, *Chem. Res. Toxicol.* **9** (1996) 623.
7. Gonzalez, I.; Farfan, M.; Trejo, N.; Uribe, C.; Lotina, S.; Henssen, B.; Selective herbicide activity of 2,5-di(benzylamine)-p-benzoquinone against the monocot weed, *J. Agric. Food Chem.* **53** (2005) 3415.
8. George, J.H.; Baldwin, J.E.; Adlington, R.M; Enantiospecific biosynthetically inspired formal total synthesis of (+)- Liphagal *Org. Lett.* **12**(2010) 2394.



9. Hasegawa, T.; Mochida, T.; Kondo, R.; Kagoshima, K.; Iwasa, Y.; Akutagawa, T.; Mixed stack organic charge-transfer complexes with intercolumnar networks, *Phys. Rev. B*: **62** (2000) 10059.
10. Abraham, I.; Joshi, R.; Pardasani, P.; Pardasani, R.T.; Recent advances in 1,4-benzoquinone chemistry, *J. Braz. Chem. Soc.* **22** (2011) 385.
11. Fieser, L.F.; Fieser, M.; Organic Chemistry, 3<sup>rd</sup> ed. *Health and Comp*, Boston, 1956.
12. Koning, C.B.; Giles, R.G.F.; Knight, L.S.; Niven, M.L.; Yorke, C.S.; Asymmetrische synthese, *J. Chem. Soc.* **1** (1988) 2477.
13. Mackenzie, A.R.; Moody, J.C.; Rees, C.W.; Synthesis of the bacterial coenzyme methoxatin, *Tetrahedron* **42** (1986) 3259.
14. Tashiro, M.; Koya, K.; Yamato, T.; Metacyclophanes and related compounds. 7. Preparation and reduction of [2,2] metacyclophanequinone, *J. Am. Chem. Soc.* **104** (1982) 104, 3707.
15. Dockal, E.R.; Cass, Q.B.; Brocksom, T.J.; Brocksom, U.; Correa, A.G.; Solid state oxidation of phenols to quinones, *Synth Commun.* **15** (1985) 1033.
16. Trost, B.M.; Pearson, W.H.; A synthesis of naphthalene core of streptovaricin D via synthon of NH<sub>2</sub><sup>+</sup>, *Tetrahedron Lett.* **24** (1983) 269.
17. Preston, P.N.; Will, S.G.; Winwick, T.; Morley, J.O.; Preparation of 3,4-dihydroanthracene-1(2H)-ones, *J. Chem. Soc.* **1** (1983) 1001.
18. Wulff, W.D.; McCallum, J.S.; Kunng, F.A.; Two regiocomplementary approaches to angular furanocoumarins with chromium carbene complexes, *J. Am. Chem. Soc.* **110** (1988) 7419.
19. Sato, M.; Katsumata, N.; Ebine, S.; A convenient synthesis of benzocyclobutene-4, 5-dione, *Synthesis* **8** (1984) 685.
20. Scheib, S.; Cava, M.P.; Baldwin, J.W.; Metzger, R.M.; In search of molecular rectifiers. The donor-s-acceptor system derived from triptycenequinone, *J. Org. Chem.* **63** (1998) 1198.
21. Valderrama, J.A.; Gonzalez, M.F.; Studies on quinones: synthesis and cyclisation of substituted 2-acetylamino 1,4-benzoquinones, *Heterocycles* **45** (1997) 1703.

22. Taing, M.; Moore, H.W.; Synthesis and cyclization of substituted 2-acetylamino-1,4 benzoquinones, *J. Org. Chem.* **61** (1996) 329.
23. Lockshin, M.P.; Filosa, M.P.; Zuraw, M.J.; Carlier, P.R.; Formation of a novel sulfonated enedione, *J. Org. Chem.* **61** (1996) 2556.
24. Cassis, R.; Valderrama, J.A.; Synthesis of quinones from hydroquinones by using manganese dioxide and acid impregnated manganese di-oxide, *Synth. Commun.* **13** (1983) 347.
25. Cao, Y.; Heeger, A.J.; Magnetic susceptibility of polyaniline in solution in non-polar organic solvents, *J. Synth. Met.* **52** (1992) 193.
26. Teuber, H.J.; Glosaer, O.; Reaktionen mit nitrosodisulfonal, *Chem. Ber.* **98** (1965) 2643.
27. Nakao, H.; Arakawa, M.; Antileukemic agents: Some 2,5-disubstituted p-benzoquinones, *Chem. Pharm. Bull.* **20** (1972) 1962.
28. Tamer, S. Abaci, S. U.; Pekmez, K.; Yildiz, A.; Electrosynthesis of benzoquinone from phenol on surface of PbO<sub>2</sub>, *Electrochim. Acta* **50** (2005) 53655.
29. Haggiage, E.; Coyle, E.E.; Joyce, K.; Oelgemoller, M.; Green photochemistry: solar chemical synthesis of 5-amido-1,4-naphthoquinones, *Green Chem.* **11** (2009) 318.
30. Vliet, E.B.; Organic syntheses *Wiley and sons*, New York (1932).
31. Bernini, R.; Mincione, E.; Provenzano, G.; Fabrizi, G.; Catalytic oxidation of catechins to p-benzoquinones with hydrogen peroxide, *Tetrahedron Lett.* **46** (2005) 2993.
32. Gonzalez, R.R.; Gambarotti, C.; Liguori, L.; Bjorsvik, H.R.; Efficient and green telescoped process to 2-methoxy-3-methyl-[1,4] benzoquinone, *J. Org. Chem.* **71** (2006) 1703.
33. Coombes, C.L.; Moody, C.J.; First synthesis of novel prenylated quinone derivatives from the New Zealand brown alga *Perithalia capillaris* *J. Org. Chem.* **73** (2008) 6758.
34. Hewson, T.; Sharpe, D.A.; Wadsworth, A.H.; Synthesis of p-benzoquinones by oxidation of N-Arylsulphonamides *Synth. Commun.* **19** (1989) 2095.
35. Perri, S.T.; Foland, L.D.; Decker, O.H.; Moore, H.W.; Rearrangement of cyclobutenones to annulated hydroquinones and quinones, *J. Org. Chem.* **51** (1986) 3067.

36. Mathur, P.; Avasare, V.D.; Mobin, S.M.; Iron pentacarbonyl assisted photochemical route to 2,5 and 2,6-divinyl substituted 1,4-benzoquinones from 1-ene-3-yne, *Tetrahedron* **64** (2008) 8943.
37. Davis, C.J.; Hurst, T.E.; Jacob, A.M.; Moody, C.J.; Microwave mediated Claisen rearrangement followed by phenol oxidation, *J. Org. Chem.* **70** (2005) 4414.
38. Saladino, R.; Neri, V.; Minicone, E.; Filipone, P.; Selective oxidation of phenol and anisole derivatives to quinone with hydrogen peroxide and polymer supported methylrhenium trioxide, *Tetrahedron* **58** (2002) 8493.
39. Jakubiak, A.; Owsik, A.; Kolarz, B.; The oxidation of hydroquinone catalyzed by Cu (II) ions immobilized on acrylic resins, *React. Funct. Polym.* **65** (2005) 161.

