Electrophilic Catalysis in Iodosylbenzene Oxidation of Aromatic Derivatives**

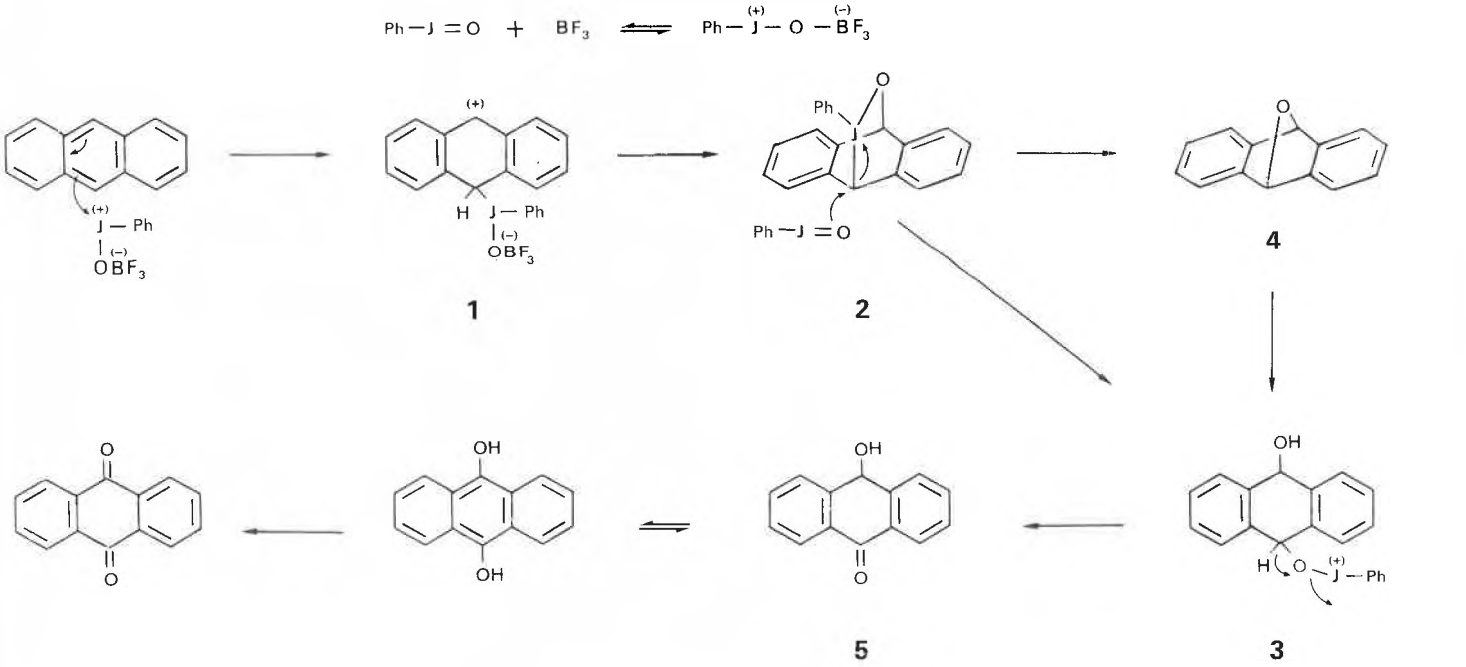
Paul Müller* and David Manuel Gilabert

Abstract: The oxidation of activated aromatic compounds (phenols and hydroquinones) is catalyzed by BF_3 or $RuCl_2(PPh_3)_3$. The catalytic effect of the ruthenium is ascribed to electrophilic catalysis, due to complexation between iodosylbenzene and the Ru species, in analogy to the effect of BF_3.

The Fe-porphyrin catalyzed oxygen transfer from iodosylbenzene (PhIO) to organic substrates serves as model for cytochrome P450-mediated oxygenases[1]. These reactions are of interest for the understanding of the mechanism of action of other metalloenzymes[2] and for the development of catalytic methods for preparative oxidation[3]. Several such systems have been described over the recent years, based on Fe-phthalocyanines[4a], Fe-tetraphenylporphyrin[4b], or on PhIO in conjunction with BF_3[4c,d]. The mechanism of catalysis is not the same for all systems. Fe-porphyrin catalyzed reactions proceed via an Fe^V=O intermediate[1]; however, in other cases involving metal ions, electrophilic catalysis[5] analogous to that with BF_3 appears to be involved. *Barton* et al.[6] were first to recognize the significance of electrophilic catalysis in the related oxidations with iodylbenzene ($PhIO_2$).

We have recently reported preparative applications of Ru-catalyzed PhIO oxidations with alcohols, aldehydes, alkynes, and sulfides[7]. Subsequently, model studies, using anthracene as substrate, were carried out in order to extend the applicability of the catalytic system. However, anthracene reacts only sluggishly with PhIO/Ru and yields of anthraquinone are poor. The situation improves significantly if the reactions are carried out in presence of BF_3–OEt_2. Indeed, we find that for anthracene oxidation catalysis by BF_3 is superior to Ru catalysis. The quinone is produced in ca. 65% yield (3 equivalents of PhIO, 1 equivalent of BF_3–OEt_2, 2 h, 25 °C, in CH_2Cl_2) together with some 9,10-dichloroanthracene, which must originate from decomposition of the solvent. In presence of $AlCl_3$ 9,10-dichloroanthracene is the main reaction product (79% yield).

A tentative mechanism for the reaction of BF_3-activated iodosylbenzene is shown in the Scheme. We propose electrophilic attack of BF_3-coordinated PhIO[5] on anthracene in the key step. Cyclization of the zwitterion **1** affords a bicyclic intermediate **2** which suffers nucleophilic attack by PhIO. Alternatively, intermediate **3** is obtained via 9,10-oxaanthracene. The subsequent steps involve β-elimination of **3** to the hydroxyketone **5**, which is further oxidized via the tautomeric hydroquinone by an analogous sequence.



$PhIO/BF_3$ can be applied towards oxidation of substituted phenols (Table 1) giving yields of quinones in the range of 60–70%. In some cases PhIO in acetic acid affords higher yields, but the presence of Ru salts leads mainly to decomposition products, except when *m*-PhIO(COOH)/Ru is used. This latter result could however be ascribed to acid catalysis due to the presence of the carboxyl group in the iodosylbenzene, in analogy to the effect of PhIO/AcOH.

While PhIO alone is inefficient for oxidation of phenols, the 1,2- and 1,4-hydroquinones are readily converted to quinones (Table 2)[8], and the presence of a Ru catalyst is only of minor importance. Similarly,

* *Correspondence:* Prof. Dr. P. Müller
Département de Chimie Organique
Université de Genève
30, quai Ernest Ansermet, CH-1211 Genève 4

** *Acknowledgement:* This work was supported by the Schweizerischer Nationalfonds zur Förderung der wissenschaftlichen Forschung (grant No. 2.034-0.83).

Ru-catalyzed hydroquinone oxidations proceed with comparable yields with *N*-methyl-*N*-morpholin oxide (MMNO)[9] and *tert*-butylhydroperoxide[10]. The sterically hindered 3-methyl-6-*tert*-butyl-1,2-hydroquinone leads to product mixtures with all the systems tried. For this compound PhIO without catalyst is the least unsatisfactory oxidant.

The oxidation of phenols and hydroquinones should proceed by an analogous scheme as that of anthracene as far as BF_3 catalysis is concerned. For the Ru-catalyzed reactions the situation is more complex. It is believed that in oxidations with MMNO[9], *t*-BuOOH[10], H_2O_2[11], and O_2[12] the role of the oxidant consists in regenerating the active Ru species after the oxidation step. This should however not apply to PhIO, because the reactivity of the latter depends upon the electron-donating ability of the substituent in the phenyl ring. Accordingly, the PhIO and Ru should be associated in the oxidation step. Therefore the catalytic effect of Ru should be similar to that of BF_3, i.e. to enhance the electrophilic nature of the iodine by complexation at the oxygen atom. Evidence for electrophilic activation of PhIO with Fe^{III}, Fe^{III}-bleomycin, and Zn^{II}-bleomycin has recently been reported by *Moriarty* et al.[5].

Received: March 25, 1986 [FC 56]

Table 1. Oxidation of phenols with iodosylbenzene (PhIO), isolated yield of *p*-quinone [%].

Phenol	$PhIO/BF_3(OEt_2)$[c]	$PhIO/CH_3COOH$[a]	*m*-PhIO(COOH)/Ru[b]
2,3,6-Trimethylphenol	70[d]	75	74 [1] 21 [0]
2,3,5-Trimethylphenol	42[d]	73	
2,3,5,6-Tetramethylphenol	58	80	43 [1]
2-Methylnaphthol	61	50	≈ 30 [1] 18 [1][e]

[a] 2 eq. of PhIO, 2–5 min/R.T. [b] In CH_2Cl_2, mol% of $[RuCl_2(PPh_3)_3]$ in brackets. [c] 1 eq. of $BF_3(OEt_2)$. [d] 20 min/R.T. [e] 2 eq. of PhIO in CH_2Cl_2, 2 min/R.T.

Table 2. Ru-catalyzed and uncatalyzed oxidation of hydroquinones, isolated yield of quinone [%].

Hydroquinone	PhIO[a] uncatalyzed	PhIO/Ru[c]	MMNO/Ru[g]	*t*-BuOOH/Ru
1,4-Dihydroxybenzene	70[b]	93 [0.2][b]	43 [1][b]	
1,4-Dihydroxynaphthalene	92[c] (86)[d]	85 [1.7][c]		
3-Methyl-5-*tert*-butyl-1,2-hydroquinone	70	98 [0.3]	95 [0.2]	56
3-Methyl-6-*tert*-butyl-1,2-hydroquinone	48	42 [0.2]	mixture	mixture
3,5-Di-*tert*-butyl-1,2-hydroquinone	98	86 [0.5] 100 [0.5][f]	95 [2]	92 (100)[f]

[a] In CH_2Cl_2, room temperature (R.T.), 1.1–2-fold excess of PhIO, ca. 1.5 h. [b] In Et_2O. [c] In acetone. [d] Ref. [16]. [e] Conditions as in[a]; mol% of $[RuCl_2(PPh_3)_3]$ in brackets. [f] With *m*-PhIO(COOH). [g] Conditions as in[a], reaction time 1.5–6 h; MMNO = *N*-methyl-*N*-morpholine oxide. [h] 3 eq. of *t*-BuOOH in CH_2Cl_2, 1 mol% of $[RuCl_2(PPh_3)_3]$. [i] Ref. [10].

[1] a) J.T. Groves, T.E. Nemo, R.S. Myers, *J. Am. Chem. Soc. 101* (1979) 1032; J.T. Groves, T.E. Nemo, *ibid. 105* (1983) 5786, 6243; b) J.R. Lindsay Smith, D.N. Mortimer, *J. Chem. Soc. Chem. Commun.* (1985) 64, 410; J.R. Smith, P.R. Sleath, *J. Chem. Soc. Perkin Trans. II* (1982) 1009; c) J.P. Collman, T. Kodadek, S.A. Raybuck, J.I. Brauman, L.M. Papazian, *J. Am. Chem. Soc. 107* (1985) 4343; W.A. Lee, T.C. Bruice, *ibid. 107* (1985) 513.

[2] a) C.C. Franklin, R.B. Van Atta, A.F. Tai, J.S. Valentine, *J. Am Chem. Soc. 106* (1984) 814; b) N. Murugesan, S.M. Hecht, *ibid. 107* (1985) 493.

[3] a) J.A. Smegal, C.L. Hill, *J. Am. Chem. Soc. 105* (1983) 3515; J.A. Smegal, B.C. Schardt, C.L. Hill, *ibid. 105* (1983) 3510; b) J.T. Groves, R.S. Myers, *ibid. 105* (1983) 5791.

[4] a) R. Rohde, G. Neef, G. Sauer, R. Wiechert, *Tetrahedron Lett. 26* (1985) 2069; b) W. Ando, R. Tajima, T. Takata, *ibid. 23* (1982) 1685; c) R.M. Moriarty, S.C. Gupta, H. Hu, D.R. Berenschot, K.B. White, *J. Am. Chem. Soc. 103* (1981) 686; R.M. Moriarty, H. Hu, S.C. Gupta, *Tetrahedron Lett. 22* (1981) 1283; R.M. Moriarty, O. Prakash, M.P. Duncan, *Synthesis* (1985) 943; d) M. Ochiai, E. Fujita, M. Arimoto, H. Yamaguchi, *J. Chem. Soc. Chem. Commun.* (1982) 1108; M. Ochiai, K. Sumi, Y. Nagao, E. Fujita, M. Arimoto, H. Yamaguchi, *ibid.* (1985) 697; M. Ochiai, T. Ukita, Y. Nagao, E. Fujita, *ibid.* (1985) 637.

[5] R.M. Moriarty, R. Penmasta, I. Prakash, *Tetrahedron Lett. 26* (1985) 4699.

[6] a) D.H.R. Barton, J.W. Morzycki, W.B. Motherwell, *J. Chem. Soc. Chem. Commun.* (1981) 1044; D.H.R. Barton, C.R.A. Godfrey, J.W. Morzycki, W.B. Motherwell, A. Stobie, *Tetrahedron Lett. 23* (1982) 957; b) R. Barrel, F. Pautet, M. Daudon, H. Fillion, *Bull. Soc. Chim. Belg. 94* (1985) 157.

[7] P. Müller, J. Godoy, *Tetrahedron Lett. 22* (1981) 2361; *23* (1982) 3661; *Helv. Chim. Acta 64* (1981) 2531; *66* (1983) 1790.

[8] T. Takata, R. Tajima, W. Ando, *J. Org. Chem. 48* (1983) 4764.

[9] K.B. Sharpless, K. Akashi, K. Oshima, *Tetrahedron Lett. 17* (1976) 2503.

[10] Y. Tsuji, T. Ohta, T. Ido, H. Minbu, Y. Watanabe, *J. Organomet. Chem. 270* (1984) 333.

[11] S. Ito, K. Aihara, M. Matsumoto, *Tetrahedron Lett. 24* (1983) 5249.

[12] M. Matsumoto, K. Kuroda, *J. Am. Chem. Soc. 104* (1982) 1433.