ORGANIC SYNTHESIS AND INDUSTRIAL ORGANIC CHEMISTRY

Oxidation of *p*-Cresol with Ozone in Acetic Anhydride

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Abstract—Preparation of aromatic alcohols and aldehydes by oxidation of *p*-cresol with ozone in acetic anhydride in the presence of sulfuric acid, manganese acetate, and potassium bromide was studied. The optimal oxidation conditions were determined.

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p-Cresol (*p*-Cr) oxidation products, *p*-hydroxybenzyl alcohol (*p*-HBA) and *p*-hydroxybenzaldehyde (*p*-HBAd), are used in production of synthetic drugs and products of fine organic synthesis [1]. These products are prepared by oxidation of *p*-cresol with sodium dichromate or chromic anhydride in concentrated sulfuric acid [2]. The disadvantages of this procedure are formation of large amounts of difficult to utilize toxic waste and relatively low selectivity. To overcome these disadvantages, environmentally clean oxidizing agent, ozone, can be used.

Ozone is used to oxidize methylbenzenes in acetic acid to the corresponding benzenecarboxylic acids [3]. The possible intermediates, aromatic alcohols and aldehydes, are readily oxidized under these conditions and cannot be isolated.

To decelerate the oxidation at the step of formation of p-HBA and p-HBAd and to develop a low-waste technology of their production, we studied the reaction of p-Cr with ozone in acetic anhydride in the presence of a strong mineral acid. Under these conditions, acetic anhydride is a strong acylating agent and reacts with the intermediate reaction products to form the acetate and acylal derivatives which are more resistant to oxidation [4].

It is known [5] that *p*-Cr readily reacts with ozone in the liquid phase with opening of the aromatic ring to form peroxides ($k = 2 \times 10^3 \text{ 1 mol}^{-1} \text{ s}^{-1}$, CCl₄, 293 K). In acetic acid, one *p*-Cr molecule is consumed per three ozone molecules, which suggests that this process occurs in two steps by Scheme 1 [6].

In the first step, ozone attacks the O–H bond to form the phenoxy radical. Then hydroxy radical is added to phenoxy radical with opening of the aromatic ring. The product reacts with two ozone molecules to form the aliphatic peroxide. To stabilize the aromatic ring of *p*-cresol, its OH group was acylated. Weighed portions of *p*-Cr and acetic anhydride were loaded in a flask. A mixture of acetic anhydride and phosphoric acid taken in a 10 : 1 weight ratio was added in small portions at 5°C. The reaction mixture was poured into water after 20 min. The oil was separated, washed with a 5% solution of sodium hydroxide and water, and distilled in a vacuum. The yield of *p*-cresyl acetate (*p*-CrA) was 80%.

An ozone–air mixture with an ozone concentration of 4×10^{-4} M was bubbled through a *p*-CrA solution in acetic anhydride. The kinetic experiments showed that the reactivity of *p*-CrA with respect to ozone substantially decreases: the rate constant of this reaction at 20°C is $k = 1.3 \text{ l mol}^{-1} \text{ s}^{-1}$. This fact and the stoichiometric coefficient of ozone in this reaction (one ozone molecule per substrate molecule) confirm the change in the oxidation mechanism. In this case, in accordance with the classical concept on ozonolysis of





Fig. 1. Kinetic curves of (1) *p*-CrA consumption and accumulation of (2) peroxides, (3) *p*-ABA, and (4) *p*-ABDA in oxidation of *p*-CrA with an ozone–air mixture in acetic anhydride at 5°C. $[p\text{-Cr}]_0 = 0.4$, $[\text{H}_2\text{SO}_4]_0 = 1.2$, $[\text{O}_3]_0 = 4 \times 10^{-4}$ M; $v_{\text{air}} = 8.3 \times 10^{-3}$ 1 s⁻¹. (c) Concentration and (τ) time; the same for Fig. 2.



Fig. 2. Rate and selectivity of *p*-CrA oxidation with an ozone–air mixture in acetic anhydride at 5°C in the presence of (1, 2) H₂SO₄ and (1', 2') H₃PO₄. [p-Cr]₀ = 0.4, $[acid]_0 = 1.2$, $[O_3]_0 = 4 \times 10^{-4}$ M; $v_{air} = 8.3 \times 10^{-3}$ l s⁻¹. (1, 1') Consumption of *p*-CrA and (2, 2') total accumulation of *p*-ABA and *p*-ABDA.

alkylbenzenes [6], ozone attacks the aromatic ring to form peroxide monomers by Scheme 2:



Under these conditions, virtually no aromatic alcohol and aldehyde are formed. In the presence of acylation catalyst (mineral acid such as sulfuric and phosphoric acid) in the reaction mixture, *p*-HBA and *p*-HBAd do not decompose and are converted into *p*-acetoxybenzyl acetate (*p*-ABA) and *p*-acetoxybenzylidene diacetate (*p*-ABDA) having lower reactivity with respect to ozone. However, under these conditions the total yield of the aromatic products is still as low as 10% (Fig. 1). It should be noted that the selectivity of the oxidation of the methyl group is independent of the type of the mineral acid but the reaction is accelerated in going from phosphoric to sulfuric acid (Fig. 2).

The selectivity of oxidation of the side chain increases in the presence of an oxidation catalyst, variable-valence metal salt [3]. We studied the oxidation of *p*-CrA catalyzed by manganese(II) acetate (Table 1). This reaction is fast and yields mainly *p*-ABA. The oxidation is complete in 1 h at the manganese(II) acetate concentration of 0.18 M and temperature of 5°C. The selectivity of oxidation of the methyl group is 77%; the yield of *p*-ABA and *p*-ABDA is 56 and 21%, respectively (Table 1).

After the oxidation completion, the reaction mixture was diluted with a fivefold volume of water and then was extracted with ether. The organic layer was distilled under atmospheric pressure to remove the ether and then in a vacuum (10 mm Hg) to remove the unchanged *p*-CrA. Th residue was refluxed in 5% NaOH. The resulting *p*-HBA was extracted with ether; the yield based on reacted *p*-CrA was 51%.

The methyl group is selectively oxidized in two steps with ozone in the presence of manganese(II) acetate. Under these conditions, ozone reacts mainly with Mn^{2+} {reaction (1), $k_1 = 4.7 \times 10^3$ [7]; $k_{\text{AcOC}_6\text{H}_4\text{CH}_3\text{-}p+\text{O}_3} = 1.3 \text{ 1 mol}^{-1} \text{ s}^{-1}$, our data} to form reactive Mn^{3+} species which rapidly and selectively oxidize the methyl group of *p*-CrA [reaction (2)]:

$$Mn^{2+} + O_3 + H^+ \rightarrow Mn^{3+} + HO^{\bullet} + O_2,$$
 (1)

$$AcOC_6H_4CH_3 p + Mn^{3+} \rightarrow AcOC_6H_4CH_2 p + Mn^{2+} + H^+.$$
(2)

For reaction (1) to occur, ozone should be continuously fed into the system. When the ozone supply is stopped, the process is decelerated up to its complete cessation. This fact additionally confirms formation of reactive catalytic species by reaction (1). Since the concentration of molecular oxygen under the experimental conditions is higher by one and half orders of magnitude than that of ozone, the benzyl radical formed by reaction (2) reacts mainly with molecular oxygen by reaction (3) to form the peroxy radical which is converted into *p*-ABA by reactions (4)–(6):

$$AcOC_6H_4CH_2^{\bullet}-p + O_2 \longrightarrow AcOC_6H_4CH_2O_2^{\bullet}-p$$
, (3)

$$\operatorname{AcOC}_{6}\operatorname{H}_{4}\operatorname{CH}_{2}\operatorname{O}_{2}^{\bullet}p + \operatorname{O}_{3} \longrightarrow \operatorname{AcOC}_{6}\operatorname{H}_{4}\operatorname{CH}_{2}\operatorname{O}^{\bullet}-p + 2\operatorname{O}_{2},$$
(4)

$$AcOC_6H_4CH_2O^{-}p + Mn^{2+} \rightarrow AcOC_6H_4CH_2O^{-}p + Mn^{3+},$$
(5)

$$AcOC_6H_4CH_2O^--p + Ac_2O + H^+ \rightarrow AcOC_6H_4CH_2OAc-p$$

$$+$$
 AcOH. (6)

Introduction of potassium bromide in the system increases the conversion and selectivity of catalytic oxidation of the methyl group of *p*-CrA to 84%. The major reaction product is *p*-ABDA. Its yield reaches 67% (Table 2).

After the reaction completion, the reaction mixture was poured into a glass beaker filled by two thirds with finely divided ice and then was diluted to 100 ml with cold water. The mixture was vigorously stirred until the oil solidified. The solid product was filtered off, washed with cold water, and dried. Concentrated HCl (20 ml), water (20 ml) and alcohol (4 ml) were added to crude *p*-ABDA. The mixture was refluxed with stirring for 1 h. The reaction mixture was cooled, and *p*-HBAd precipitate was filtered off. The yield based on *p*-CrA was 62%.

Potassium bromide reacts with manganese(II) acetate catalyst to form $Mn^{2+}Br^{\bullet}$ which is more reactive than Mn^{3+} :

$$Mn^{2+} + Br^{-} \rightleftharpoons Mn^{2+}Br^{-},$$
 (7)

$$Mn^{2+}Br^{-} + O_3 \rightarrow Mn^{2+}Br^{\bullet} + HO^{\bullet} + O_2.$$
 (8)

 $Mn^{2+}Br^{\cdot}$ oxidizes the methyl group of *p*-ABA by the following scheme:

$$AcOC_{6}H_{4}CH_{2}OAc-p + Mn^{2+}Br^{-} \rightarrow AcOC_{6}H_{4}C^{\bullet}HOAc-p$$
$$+ Mn^{2+} + Br^{-} + H^{+}, \qquad (9)$$

$$AcOC_6H_4C^{\bullet}HOAc_{-p} + O_2 \rightarrow AcOC_6H_4C(OO^{\bullet})HOAc_{-p},$$
(10)

$$AcOC_{6}H_{4}C(OO^{\bullet})HOAc-p + O_{3} \rightarrow AcOC_{6}H_{4}C(O^{\bullet})HOAc-p + 2O_{2}, \qquad (11)$$

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Table 1. Yield of the products of oxidation of the methyl group in *p*-CrA at 5°C and various concentration of
$$Mn(OAc)_2$$
. $[p-Cr]_0 = 0.4$, $[H_2SO_4]_0 = 1.2$, $[O_3]_0 = 4 \times 10^{-4}$ M; $\tau = 1$ h

[Mn(OAc) ₂] ₀ , M	Yield, %	
	p-ABA	p-ABDA
$\begin{array}{c} 0.05 \\ 0.10 \\ 0.14 \\ 0.18 \\ 0.20 \end{array}$	30.1 42.4 51.3 56.1 54.2	8.7 12.5 17.2 21.3 20.1

Table 2. Yield of the oxidation products of the methyl group in *p*-CrA at 5°C and various KBr concentrations. $[p\text{-Cr}]_0 = 0.4$, $[\text{Mn}(\text{OAc})_2]_0 = 0.18$, $[\text{H}_2\text{SO}_4]_0 = 1.2$, $[\text{O}_3]_0 = 4 \times 10^{-4}$ M; $\tau = 50$ min

[KBr] ₀ , M	Yield, %	
	<i>p</i> -ABA	<i>p</i> -ABDA
0.02	40.2	39.8
0.06	24.2	51.9
0.08	19.3	60.3
0.10	17.2	67.1
0.12	17.1	66.3

$$AcOC_{6}H_{4}C(O^{\bullet})HOAc-p + Mn^{2+}Br^{-}$$

$$\rightarrow AcOC_{6}H_{4}C(O^{-})HOAc-p + Mn^{2+}Br^{\bullet}, \qquad (12)$$

$$AcOC_{6}H_{4}C(O^{-})HOAc-p + Ac_{2}O + H^{+}$$

$$\rightarrow AcOC_{6}H_{4}CH(OAc)_{2}-p + AcOH. \qquad (13)$$

The increase in the oxidative conversion of *p*-CrA in the presence of potassium bromide is due to accumulation of reactive complex $Mn^{2+}Br^{\bullet}$ in the system. Oxidation of *p*-ABA in the presence of this complex is faster than that in the presence of Mn^{3+} [9].

EXPERIMENTAL

Analytically pure grade acetic anhydride and manganese(II) acetate were used as received. Crystalline p-Cr was recrystallized repeatedly from water.

The experiments were performed in a glass column with a porous partition. Acetic anhydride (10 ml), p-Cr (0.4 M), appropriate mineral acid (1.2 M), and a weighed portion of the catalyst were placed in the

column. The column was thermostated and an ozone– air mixture (ozone concentration 4×10^{-4} M) was passed through at a flow rate of 30 l h⁻¹ under the steady operation conditions of the ozonizer. The ozone concentration in the gas phase was determined spectrophotometrically by the absorption in the range 254–290 nm.

The oxidation products were identified and their concentration in the solution was determined by gas–liquid chromatography on an LKhM-80 chromatograph with a flame ionization detector using a 2 m×4 mm column packed with Chromaton N-AW. The stationary phase was SE-30 in the 5% amount of the support weight. The analysis was performed under the following conditions: vaporizer temperature 250°C; thermostat temperature 180°C; flow rate of the carrier gas (nitrogen) 1.8, hydrogen 1.8, and air 18 1 h⁻¹. *p*-Nitrochlorobenzene was used as the internal reference.

CONCLUSION

p-Cresol was oxidized with ozone in acetic anhydride in the presence of mineral acid, manganese(II) acetate, and potassium bromide as catalysts. In the presence of manganese(II) acetate, the reaction can be stopped at the step of formation of p-hydroxybenzyl alcohol in the form of the corresponding diacetate (yield 56%). Introduction of potassium bromide into the catalytic system allows preparation of p-hydroxy-benzaldehyde in the form of triacetate in a 67% yield.

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