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ORGANIC SYNTHESIS AND INDUSTRIAL ORGANIC CHEMISTRY

Oxidation of 4-Aminotoluene by Ozone–Air Mixture in the Presence of a Stop-Reagent

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Abstract—A study of the liquid-phase oxidation of 4-aminotoluene by ozone to 4-amino benzaldehyde in the presence of a manganese/bromide catalyst demonstrated that introduction of potassium bromide into the oxidizing system makes it possible to obtain 4-aminobenzaldehyde in the form of 4-(acetylamino)benzylidene diacetate (84.5%) as the main product. A reaction scheme accounting for the results obtained was suggested.

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4-Aminobenzaldehyde (4-AB) is widely used in manufacture of pharmaceutical preparations and organic dyes [1–4]. It is for the most part industrially produced by reduction of 4-nitrotoluene with sulfides in an alkaline medium [5]. Among disadvantages of this method are the low yield of the product and formation of large amounts of a toxic wastewater.

This study is devoted to analysis of the oxidation process of 4-aminotoluene (4-AT) by an air–ozone mixture in order to develop a low-waste method for production of 4-AB in high yield.

It has been shown previously [6] that AT-4 reacts with ozone as 4-acetylaminotoluene (4-AAT) in a solution of acetic anhydride in the presence of sulfuric acid. This fact is accounted for by the high rate of acylation by acetic anhydride, which ends under the experimental conditions while a mixture for ozonation is prepared. Ozone attacks 4-AAT predominantly at the aromatic ring [reaction (2)], and the selectivity of oxidation at the methyl group [reaction (1)] does not exceed 26%:

$$\mathrm{AcNHArCH_3 + O_3 \rightarrow AcNHArC^{\cdot}H_2 + OH^{\cdot} + O_2}, \qquad (1)$$

$$\mathrm{AcNHArCH_3 + O_3 \rightarrow Ozonolysis\ products}. \qquad (2)$$

It was shown in [7] that the selectivity of oxidation at the ethyl group increases to 84.5% in the presence of a catalyst, manganese(II) acetate. The main oxidation products are 4-(acetylamino)benzyl acetate (4-AABA, 65%) and 4-(acetylamino)benzylidene diacetate (4-AABDA, 19.5%). It is impossible to oxidize 4-AT to predominantly obtain 4-AB (in the acylated form) under these conditions.

Proceeding with these studies, we examined the possibility of making deeper the oxidation of 4-AAT by its ozonation in the presence of a mixed manganese/bromide catalyst, because it is known [8, 9] that the catalytic activity of variable-valence metal ions grows in a mixture with alkali metal bromides.

Our study demonstrated (Table 1) that addition of potassium bromide to the oxidizing system at 30°C does improve the selectivity and depth of oxidation at the methyl group of 4-AAT with predominant formation of 4-AABDA. The content of 4-AABDA in the reaction products increases with the potassium bromide concentration and reaches the maximum value at [KBr] = 0.08 M (Table 1). At a $[\mathrm{ArCH_3}] : [\mathrm{Mn(OAc)_2}] : [\mathrm{KBr}]$ ratio of 5 : 1 : 1, the reaction yields, at an overall selectivity in the system of 94.8%, 84.5% 4-AABDA, 10.3% 4-AABA, and trace amounts of 4-(acetylamino)benzyl bromide (4-AABB).

Based on our experimental results and published data

Table 1. Effect of the reagent concentrations on the composition of the products formed in oxidation of 4-acetylaminotoluene with ozone in acetic anhydride at 30°C

Run no.	Concentration of reagents, M				Concentration of reaction products, M (%)		Overall selectivity of oxidation at the methyl group, %
	ozone	4-AAT	$Mn(Oac)_2$	KBr	4-AABA	4-AABDA	
1	0.50×10^{-4}	0.40	0.080	0.08	Trace amounts	0.106 (27.0)	27.0
2	1.00×10^{-4}	0.40	0.080	0.08	0.020 (5.5)	0.216 (54.0)	59.5
3	2.00×10^{-4}	0.40	0.080	0.08	0.025 (6.4)	0.292 (73.5)	79.9
4	4.00×10^{-4}	0.40	0.080	0.08	0.040 (10.3)	0.338 (84.5)	94.8
5	4.00×10^{-4}	0.40	0.040	0.08	0.024 (6.1)	0.305 (76.5)	82.6
6	4.00×10^{-4}	0.40	0.020	0.08	0.024 (6.1)	0.239 (59.0)	65.1
7	4.00×10^{-4}	0.40	0.005	0.08	0.017 (4.5)	0.179 (44.3)	48.8
8	4.00×10^{-4}	0.40	0.080	0.10	0.039 (10.0)	0.338 (84.5)	94.5
9	4.00×10^{-4}	0.40	0.080	0.04	0.073 (18.2)	0.280 (70.0)	88.2
10	4.00×10^{-4}	0.40	0.080	0.01	0.106 (26.1)	0.203 (52.5)	78.6
11	4.00×10^{-4}	0.40	0.080	–	0.224 (56.0)	0.075 (18.7)	74.7

[9–13], we suggested the following scheme of catalytic oxidation of 4-AAT:

$$Mn^{2+} + Br^- \rightarrow Mn^{2+}Br^-, \quad (3)$$

$$Mn^{2+}Br^- + O_3 + H^+ \rightarrow Mn^{2+}Br^{\cdot} + HO^{\cdot} + O_2, \quad (4)$$

$$AcNHArCH_3 + Mn^{3+} \rightarrow AcNHArCH_2^{\cdot} + Mn^{2+} + H^+, \quad (5)$$

$$AcNHArCH_2OAc + Mn^{3+} \rightarrow AcNHArCH^{\cdot}OAc + Mn^{2+} + H^+, \quad (6)$$

$$AcNHArCH_3 + Mn^{2+}Br^{\cdot} \rightarrow AcNHArCH_2^{\cdot} + Mn^{2+}Br^- + H^+, \quad (7)$$

$$AcNHArCH_2OAc + Mn^{2+}Br \rightarrow AcNHArCHOAc + Mn^{2+}Br^- + H^+, \quad (8)$$

$$AcNHArCH_2^{\cdot} + O_2 \rightarrow AcNHArCH_2O_2^{\cdot}, \quad (9)$$

$$2AcNHArCH_2O_2^{\cdot} \rightarrow \text{Reaction products.} \quad (10)$$

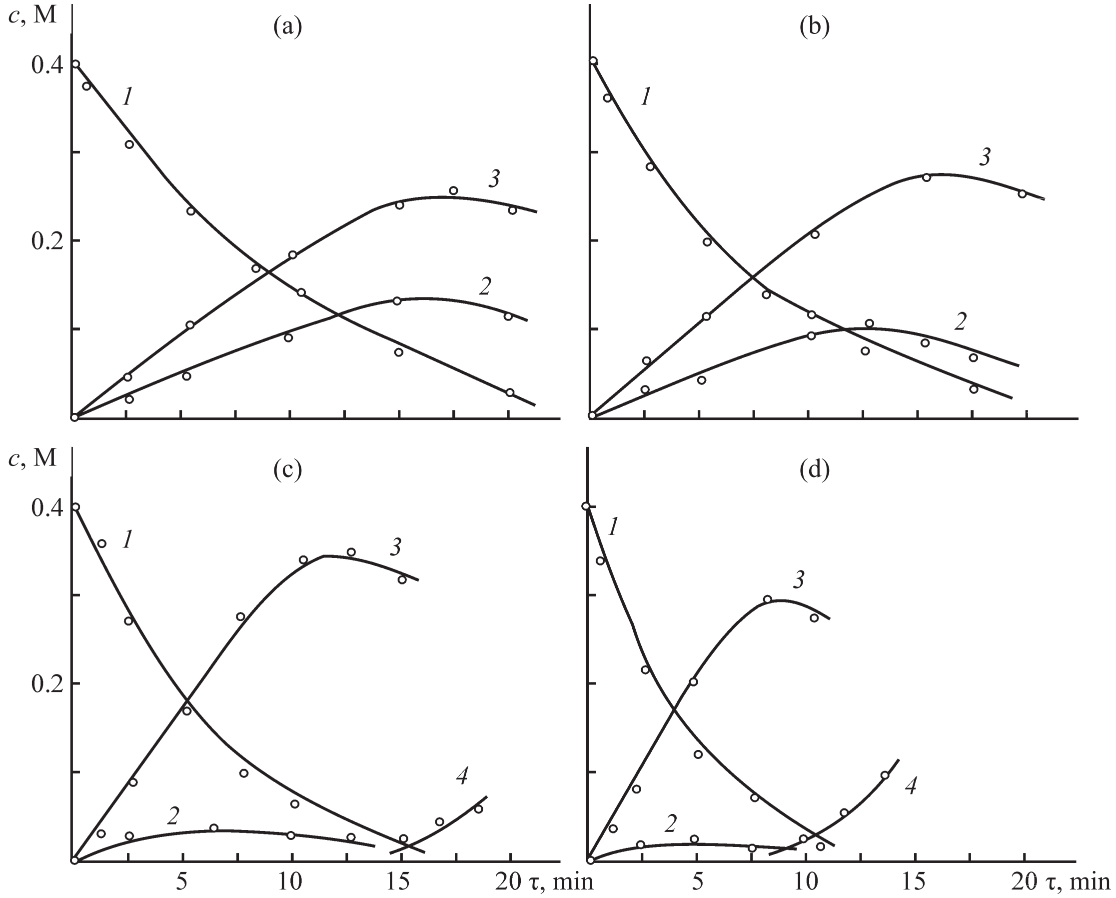
The catalytic activity of manganese(II) acetate increases in the presence of potassium bromide due to the formation of a highly active manganese bromide complex $Mn^{2+}Br^{\cdot}$ [reactions (3) and (4) [8, 9], which can oxidize the 4-AAT and 4-AABA molecules faster than Mn^{3+} does (Table 2). At the initial instant of time, when hardly any oxidation products are present in the system, active species are formed by reactions (5) and (7). The continuous delivery of ozone into the system makes it possible to maintain a sufficiently high concentration of the active form of the catalyst, $Mn^{2+}Br^{\cdot}$, and, consequently, also a high formation rate of benzyl radicals.

At $[O_2]_0 >> [O_3]_0$, the benzyl radical being formed are converted to peroxide radicals [reaction (9)] whose further transformation occurs due to their recombination by reaction (10) to give oxidation products.

Without ozone, 4-AAT is slowly oxidized by molecular oxygen in the presence of the manganese bromide catalyst. Only 10% of the substrate is consumed in 11 h of the reaction. Trace amounts of 4-AABA and 5% 4-AABDA (relative to the consumed 4-AAT) were

Table 2. Rate constants of the elementary stages of the catalytic cycle at 20°C

Reaction	k, M^{-1} s^{-1}
4-AAT + O_3 (1)	0.850
4-AAT + Mn^{3+} (2)	0.200
4-AAT + $Mn^{2+}Br^{\cdot}$ (3)	0.270
4-AABA + Mn^{3+} (4)	0.060
4-AABA + $Mn^{2+}Br^{\cdot}$ (5)	0.090
4-AABDA + Mn^{3+} (6)	0.010
4-AABDA + $Mn^{2+}Br^{\cdot}$ (7)	0.016



Effect of temperature on the kinetics of 4-AAT oxidation in acetic anhydride. $[ArCH_3]_0 = 0.4$, $[O_3]_0 = 4 \times 10^{-4}$, $[Mn(OAc)_2]_0 = 0.08$, $[KBr]_0 = 0.08$, $[H_2SO_4]_0 = 0.8$ M; gas flow rate 8.3×10^{-3} L s^{-1}. (c) Concentration of 4-AAT and its conversion products and (τ) process duration. T (°C): (a) 10, (b) 20, (c) 30, (d) 40. (*1*) 4-AAT, (*2*) 4-AABA, (*3*) 4-AABDA, and (*4*) 4-AABA.

found among the reaction products. Introduction of ozone into the system leads to a substantial increase in the oxidation rate of the methyl group, with predominant formation of 4-AABDA (Table 1). As indicated by the experimental data (Table 1), the oxidation selectivity depends on the ozone concentration in the ozone–air mixture: a decrease in this concentration from 4.0×10^{-4} to 0.5×10^{-4} M results in that the overall selectivity falls by nearly 68%.

An analysis of the data obtained demonstrated that this dependence, only observed in the presence of sulfuric acid, is due to the change in the reaction rate ratio $r_2 : r_4 : r_7$. If ozonation is performed without sulfuric acid, varying the ozone concentration within the range under study hardly affects the oxidation selectivity. The reason is that r4 always exceeds r_7 ($r_4 : r_7 = 21$–66) and manganese acetate is present in solution in the oxidized form, which promotes ozonation of 4-AAT at the methyl group (at $[O_3] = 4.0 \times 10^{-4}$, [4-AAT] = 0.4, $[Mn(OAc)_2] = 0.08$, [KBr] = 0.08 M; $k_4 = 2.0 \times 10^3$, $k_7 = 27 \times 10^{-2}$ M^{-1} s^{-1}, where k is the reaction rate constant; $r_4 = 4.8 \times 10^{-2}$, $r_7 = 6.1 \times 10^{-3}$ M s^{-1}, i.e., $r_4 : r_7 = 23$). At $[O_3]_0 = 1.25$ M, $r_4 : r_7 = 7$ (r is the reaction rate).

In the presence of sulfuric acid, k_4 decreases to 12.1 M^{-1} s^{-1} ($T = 30$°C), which leads to a strong deceleration of reaction (4). Under these conditions, $r_4 : r_7 = 0.46$, i.e., the rate of manganese reduction by reaction (7) substantially exceeds the rate of its oxidation by reaction (4). It is known that, in a system simultaneously containing oxidized and reduced forms of manganese, binuclear complexes with a strongly lowered redox potential and lower catalytic activity than that of Mn^{3+} are formed [14]. Thus, as the ozone concentration in the ozone–air mixture decreases, reaction (7) becomes slower and the $r_2 : r_7$ ratio increases (in the presence of sulfuric acid, k_2 remains nearly unchanged and equal to 2.68 M^{-1} s^{-1}, and just this circumstance leads to a decrease in the oxidation selectivity for the methyl group).

The rate and selectivity of 4-AAT oxidation to

4-AABDA depend on the reaction temperature. The optimal temperature is 30°C. At lower temperatures, the overall selectivity remains nearly unchanged, but the fraction of the acylated alcohol grows. Raising the temperature leads to an increase in the rate and depth of oxidation: 4-AABDA becomes an intermediate product further converted to 4-(acetylamino)benzoic acid (4-AABA) (see figure).

Thus, it was found that, with the reaction of ozone with 4–AAT catalyzed by a mixture of manganese(II) acetate and potassium bromide in acetic anhydride in the presence of sulfuric acid at a temperature of 30°C, it is possible to preclude ozonolysis of the aromatic ring and direct the process to oxidation of the methyl group to give predominantly 4-AABDA (84.5%).

EXPERIMENTAL

We used acetic anhydride of analytically pure grade. Crystalline 4-AT was purified by multiple recrystallization from ethanol. Manganese(II) acetate of analytically pure grade and potassium bromide of pharmacopoeia grade were used without preliminary purification.

The reactor having the form of a glass column equipped with a porous partition for dispersion of the ozone–air mixture was charged with 5 mL of acetic anhydride, 0.4 M of 4-AT, and calculated amounts of the catalyst and sulfuric acid. After that the device was thermostated and an ozone–air mixture (4.8×10^{-4} M of ozone) was passed in the steady-state operation mode of the ozonizer at a rate of 30 L h^{-1}. The content of ozone in the gas phase was determined by spectrophotometry from the absorption at 254–290 nm. The oxidation products were identified and quantitatively determined in solution by GLC on a chromatograph with a flame-ionization detector on a 3 m × 4 mm column packed with Inerton AW-DMCS support treated with a 10% alkali solution, coated with Apiezon-L fixed phase deposited in an amount of 10% relative to the support mass, under the following conditions: temperature (°C); evaporator 250 and thermostat 100–240; flow rate (L h^{-1}): carrier gas (nitrogen) 1.8, hydrogen 1.8, and air 18. Nitrobenzene served as the internal standard. The effective rate constants were spectrophotometrically determined for the reaction of ozone with $Mn^{2+}Br^{\cdot}$ and 4-AAT by the procedure described in [15] and were calculated for the reaction of 4-AAt with Mn^{3+} and $Mn^{2+}Br^{\cdot}$ in terms of the irreversible second-order reaction model.

CONCLUSIONS

(1) It was shown that 4-aminotoluene can be oxidized to the corresponding 4-(acetylamino)benzylidene acetate with ozone in acetic anhydride in the presence of a mixed manganese/bromide catalyst. The yield of the acylated aldehyde is 84.5%.

(2) A reaction scheme accounting for experimental data was considered.

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