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Mechanism of the oxidation of *para*-substituted 1-phenylethanols with sodium hypochlorite in acetic acid

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Abstract

The ρ-value of −1.8 for the oxidation of *para*-substituted 1-phenylethanols by sodium hypochlorite in acetic acid suggests that ketone is formed directly from alcohol by loss of a hydride. The kinetic isotope effect is 3.0. When the disappearance of oxidant is followed by iodometric titration, 5-nonanol is oxidized about 20 times faster than 1-butylpentyl hypochlorite decomposes. However, when NaCl is added to the alkyl hypochlorite, the reaction rates are about the same. © 2000 Elsevier Science Ltd. All rights reserved.

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Sodium hypochlorite (bleach) in acetic acid provides an inexpensive and relatively non-toxic method for alcohol oxidation.[1] The previously suggested mechanism proposed the rapid formation of an alkyl hypochlorite intermediate, which is converted to ketone in an E2 type reaction.[1] Our study of substituent effects on this reaction indicates that an alternative mechanism may be occurring.

A series of *para*-substituted 1-phenylethanols was treated with a limiting amount of bleach in acetic acid.[2] Since 1-phenylethanol and 1-(4-methylphenyl)ethanol gave 6 and 20% yields of ring chlorinated products, respectively, 5-nonanol was used as the reference alcohol, and the relative reactivities were adjusted to account for ring chlorination.[3] The data is given in Table 1. A Hammett plot gives a ρ-value of -1.80 ± 0.06 (r=0.9878).

Alcohols also have been oxidized with bleach in a two-phase system using a phase transfer catalyst (PTC).[4] For comparison to oxidation in acetic acid, we measured substituent effects for bleach oxidations in ethyl acetate. Since ring chlorination was not a problem in the two-phase reaction, 1-phenylethanol was used as the reference.[5] The results, shown in Table 1, give a ρ-value of $+0.98\pm0.02$ (r=0.9943). This agrees very well with the ρ-value of +1.03 reported by Bradley for the oxidation of benzyl alcohols.[6] We have also measured kinetic isotope effects for these reactions with 1-phenylethanol-d_1 using 5-nonanol as the reference. The k.i.e. values are 3.0 in acetic acid and 3.6 in ethyl acetate. Therefore, in either

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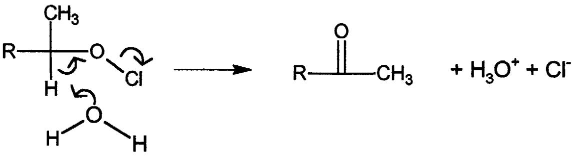
Table 1
Oxidation of *para*-substituted 1-phenylethanol by bleach in acetic acid and ethyl acetate

Compound	k_{rel} acetic acid[a]	k x$10^3$$s^{-1}$ ethyl acetate[b]	k x$10^3$$s^{-1}$ ethyl acetate[c]	k_{rel} ethyl acetate
NO_2-PhCHOHCH$_3$	0.024	11.2	1.61	6.96
CF_3-PhCHOHCH$_3$	0.048	5.22	1.18	4.42
Cl-PhCHOHCH$_3$	0.17	2.86	1.40	2.04
F-PhCHOHCH$_3$	0.31			
CH_3-PhCHOHCH$_3$	1.5[d]	1.64	1.91	0.863
CH_3O-PhCHOHCH$_3$		1.29[e]	1.82	0.708
H-PhCHOHCH$_3$	0.42[d]			3.9[f]
H-PhCDOHCH$_3$	0.14			1.1[f]

[a] Average of two experiments; details in ref. 2.
[b] Rate constants for substituted 1-phenylethanols; details in ref 5.
[c] Rate constants for 1-phenylethanol.
[d] Corrected for formation of ring chlorinated product.[3]
[e] Based on rate of formation of ketone.
[f] Relative to 5-nonanol, average of two experiments.

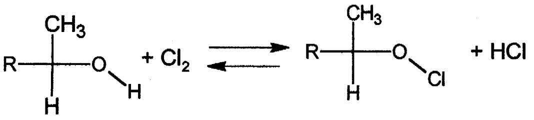
solvent, the carbon–hydrogen bond is being broken in the transition state of the rate determining step but the electronic effects of substituents are opposite.

It is apparent that these two reactions have different mechanisms. Although it has not been established, the likely mechanism for the two-phase system is an E2 elimination of an intermediate alkyl hypochlorite. We have shown by ^{1}H NMR that 1-methyl-1-phenylethyl hypochlorite is rapidly formed in the dichloromethane–bleach–PTC reaction of 2-phenyl-2-propanol.[7] An E2 type reaction should be accelerated by electron withdrawing groups. Positive ρ-values have been reported for the formation of benzaldehyde in the reaction of benzyl nitrate with ethoxide ($\rho=+3.40$)[8] and for eliminations of a number of 2-substituted-1-phenylethanes.[9] If the rate determining step in the bleach/acetic acid system was elimination of HCl from an alkyl hypochlorite, as shown in Eq. (1), the ρ-value for the reaction should be positive.

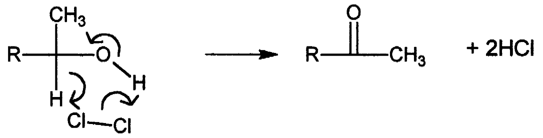


(1)

An alternate mechanism for the bleach/acetic acid oxidation consistent with the observed substituent effects is shown in Eqs. (2) and (3). An alkyl hypochlorite intermediate is rapidly formed, but the reaction is reversible (Eq. (2)). Chloride ions react with alkyl hypochlorites in acidic solution to give chlorine.[10] While elimination of HCl from the alkyl hypochlorite is possible (Eq. (1)), we believe it is a relatively slow reaction, and the oxidation is the result of a fast concerted reaction of alcohol with chlorine (Eq. (3)). Although hypochlorous acid as well as chlorine could be the oxidant, earlier work by Kudesia and Mukherjee indicates chlorine.[11]



(2)



(3)

Negative ρ-values have been reported for the oxidations of benzyl alcohol with quinolinium dichromate ($\rho=-1.67$)[12] and for oxidations of substituted ethanols with pyridinium chlorochromate ($\rho^*=-1.75$).[13] The proposed mechanism for these reactions is an intramolecular loss of hydride from a chromate ester.[12,14] Cyclic mechanisms as in Eq. (3) also have been suggested for the oxidations of benzyl alcohol with benzyltrimethylammonium tribromide ($\rho_I=-1.07$, $\rho_R=-1.36$)[15] and for the reaction of 1-phenylethanol with *t*-butyl hypochlorite ($\rho=-0.66$).[16] A ρ-value of -1.66 was reported for the oxidation of benzyl alcohol with chloramine T, which forms chlorine in situ.[17]

For our mechanism to be correct, alkyl hypochlorite must be formed reversibly and must react relatively slowly with water. We have followed the disappearance of oxidant by iodometric titration for bleach reactions and for reactions of 1-butylpentyl hypochlorite (**1**) in the absence of bleach.[18] Our results are given in Table 2. Graphs of ln [oxidant] versus time were linear for all reactions except for the slower reactions of **1** without added NaCl (6–8). For these slower reactions, the rate increased after an induction period of at least 35 min;[19] the reported rate constants are for the initial slow reactions.

Table 2

Rate constants for reactions of 5-nonanol and **1**[a]

Number	$[ROH]_0$	$[Bleach]_0$	$[\mathbf{1}]_0$[b]	Added Salt	$k \times 10^3\ s^{-1}$
1	0.530[c]	0.072	--	--	9.9
2	0.308[c]	0.072	--	--	4.1
3	0.146[c]	0.072	--	--	2.4
4	0.175[d]	0.072	--	--	2.4
5	0.088[d]	0.072	--	--	1.2, 1.0
6	0.008	--	0.072	--	0.052
	0.005	--	0.076	--	0.056
7	0.008	--	0.074	0.064 M NaOAc	0.078
	0.006	--	0.068	0.091 M NaOAc	0.065
8	0.007	--	0.068	0.09 M KF	0.051
	0.005	--	0.076	0.10 M KF	0.042
9	0.007	--	0.068	0.10 M NaCl	1.3, 1.2
10	0.006	--	0.068	0.252 M NaCl	1.3

[a] 0.20 mL aliquots titrated with 0.010 M $Na_2S_2O_3$.

[b] 1.25 mL of approximately 0.3 M **1** in CH_2Cl_2 diluted to 5 mL with acetic acid and 0.70 mL water or 0.70 mL water containing added salt.

[c] Alcohol diluted to 5.0 mL with acetic acid and 0.70 mL bleach added.

[d] Alcohol and 1.25 mL CH_2Cl_2 diluted to 5.0 mL with acetic acid and 0.70 mL bleach added.

The first five entries in Table 2 show the effect of changing alcohol concentration. When alcohol is in excess, the reaction rate is approximately first order in alcohol. For an E2 reaction of a rapidly formed alkyl hypochlorite, the reaction rate should be independent of alcohol concentration when alcohol is in excess. Furthermore, if Eq. (1) were the rate determining step, the decomposition of **1** in aqueous acetic acid (**6**) should have the same rate constant as alcohol oxidation (**5**). Bleach oxidation, however, is 20 times faster than the disappearance of oxidant in the reaction of **1**. The addition of sodium acetate (**7**), which would be formed in the reaction of sodium hypochlorite with acetic acid, has little effect on the rate constant for reaction of **1**.

Bleach contains NaCl,[20] and when NaCl is added to **1** (9,10), the rate constant is essentially the same as that of alcohol in bleach. We believe that the added chloride ions rapidly react with **1** to give alcohol and chlorine. When fluoride, which does not react with alkyl hypochlorites,[10a] is added to **1** (8), the rate is not increased. Furthermore, the decomposition of **1** in acetic acid without added chloride would be expected to exhibit autocatalytic behavior; the initial reaction is slow until chloride is formed and then the reaction accelerates.

In summary, the rate acceleration by chloride supports the reversibility of Eq. (2). The initial stability of **1** in the absence of chloride shows that reaction of **1** with water is slower than the reaction of 5-nonanol with bleach. The ρ-value of −1.8 is consistent with the reaction of chlorine or hypochlorous acid with alcohol being the rate determining step. The mechanism also explains the necessity of a chlorocarbon solvent in the preparation of alkyl hypochlorites from secondary alcohols.[10b,c] Extraction of the alkyl hypochlorite, as it is formed, into the organic layer isolates it from the chloride ions in bleach and prevents the reverse reaction.

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2. A 10 mL acetic acid solution containing 0.10 M 5-nonanol, 0.10 M substituted 1-phenylethanol and 0.10 M chlorobenzene was divided into two 5.0 mL aliquots. One aliquot was stirred with 0.70 mL bleach at 21°C for 30 min. Both aliquots were worked up by adding 10 mL of water and 10 mL of CH_2Cl_2. The CH_2Cl_2 layer was separated and washed with 10% aqueous sodium carbonate. Relative areas were measured by GC and relative reactivities were calculated by k_{rel}=log (rel. area A_t/rel. area A_0)/log (rel. area B_t/rel. area B_0) where A is substituted 1-phenylethanol and B is 5-nonanol.
3. The relative reactivity was corrected by k_{corr}=k_{rel}/[1+(rel. area of ring chlorinated compounds)/(rel. area of ketone)].
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5. A 20 mL solution of bleach buffered with 0.2 M sodium carbonate at pH 9 with 0.075 mmol tetra-*n*-butylammonium hydrogen sulfate was added to 15 mL ethyl acetate containing 0.05 M 1-phenyl-1-ethanol, 0.05 M chlorobenzene internal standard and 0.05 M substituted 1-phenylethanol at 21°C. Rate constants are the slope of a graph of $\ln[\text{alcohol}]_t$ versus time.
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18. In a typical preparation of **1**, 0.581 g (4.03 mmol) of 5-nonanol and 0.234 g (2.08 mmol) chlorobenzene were dissolved in 10 mL of CH_2Cl_2 and cooled in an ice bath. Then 20 mL of bleach at pH 7.5 cooled in an ice bath was added dropwise. The solution was stirred in the ice bath for 30 min. After washing two times with 10% aqueous sodium carbonate and drying over

sodium sulfate, the organic layer was diluted to 10 mL with CH_2Cl_2. This stock solution of **1**, analyzed by GC and iodometric titration, was 0.35 M **1** and 0.023 M 5-nonanol. The solution was stable for several days at −78°C, but decomposed within a few hours at room temperature. For the reactions in Table 2, 1.25 mL of the stock solution of **1** was diluted to 5.0 mL with acetic acid and 0.70 mL water with or without added salts was added.

19. All of the faster reactions in Table 2 were at least 93% complete within 35 min.
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