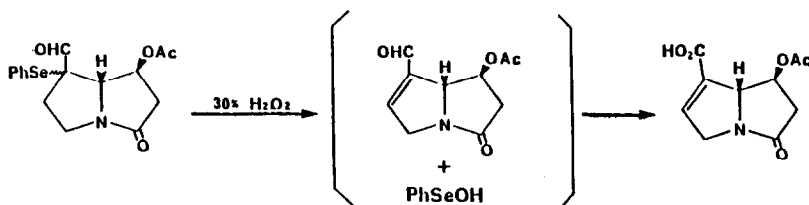


CATALYTIC OXIDATION OF ALDEHYDES TO CARBOXYLIC ACIDS
WITH HYDROGEN PEROXIDE AS OXIDANT[#]

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Summary: Alkyl and aryl aldehydes were catalytically oxidized to carboxylic acids in high yields with hydrogen peroxide as oxidant using benzeneselenenic acid as catalyst.

On the basis of recent report about obtaining an unsaturated carboxylic acid from an α -phenylselenoaldehyde with excess hydrogen peroxide by Choi and Hart,¹ we decided to look at the possible catalytic function of benzeneselenenic acid in the oxidation of aldehydes to carboxylic acids. It could be viewed that the compound was first converted to enal and benzeneselenenic acid by hydrogen peroxide, then the enal was further oxidized to unsaturated carboxylic acid by the action of benzeneselenenic acid and hydrogen peroxide.



Many ways of oxidizing aldehydes to carboxylic acids have been developed.² Among many oxidants used, acidic permanganates and chromates are most widely used. Other examples are aqueous potassium permanganate, fuming nitric acid, aqueous sodium hydroxide - silver oxide, Jones' reagent, and cyanide - silver oxide. In one instance, hydrogen peroxide - acetic acid was used to oxidize an aldehyde to carboxylic acid, *i. e.* 2-(4-isobutylphenyl)propionaldehyde to ibuprofen, an antiinflammatory agent.³

Recently, organoselenium reagents have attracted much attention among synthetic organic chemists.⁴ Benzeneselenenic acids have been used with hydrogen peroxide in epoxidation⁵ and glycol formation⁶ of alkenes, in Baeyer - Villiger type reaction of cyclic ketones,⁷ and in oxidation of sulfides.⁸ In most of these cases, benzeneselenenic acid was used as reagents except in sulfide oxidations.

Couple of enals, cinnamaldehyde and crotonaldehyde, were subjected to the reaction condition, a tetrahydrofuran solution of the aldehyde with 1.6 equi-

TABLE. CATALYTIC OXIDATION OF ALDEHYDES WITH HYDROGEN PEROXIDE*

Entry	Aldehydes	Hydrogen Peroxide		Time(h)	Yields(%)
		Concn.(%)	Equivalents		
1	<u>p</u> -chlorobenzaldehyde	30	1.6	12	1.1 ^{a,b}
2	"	30	1.6	5	94 ^b
3	"	30	1.6	5	20 ^{b,c}
4	"	30	1.6	5	50 ^{b,d}
5	<u>p</u> -bromobenzaldehyde	30	1.6	7	97 ^b
6	<u>p</u> -tolualdehyde	30	1.6	20	90 ^b
7	<u>m</u> -fluorobenzaldehyde	30	1.6	8	94 ^b
8	<u>m</u> -tolualdehyde	30	1.6	20	90 ^b
9	<u>m</u> -anisaldehyde	30	1.6	20	96 ^b
10	3,4-dichlorobenzaldehyde	30	1.6	8	98 ^b
11	<u>m</u> -nitrobenzaldehyde	30	1.6	4	97 ^b
12	<u>o</u> -fluorobenzaldehyde	30	1.6	20	91 ^b
13	<u>o</u> -chlorobenzaldehyde	30	1.6	21	53 ^b
14	"	45	1.6	21	55 ^b
15	"	45	4.0	21	75 ^b
16	"	45	10	21	75 ^b
17	"	45	4.5	21	74 ^{b,e}
18	<u>o</u> -tolualdehyde	30	1.6	20	57 ^b
19	"	45	1.6	20	61 ^b
20	"	45	4.0	20	88 ^b
21	2,6-dichlorobenzaldehyde	30	1.6	20	4.4 ^b
22	2-chloro-6-fluorobenzaldehyde	30	1.6	45	39 ^b
23	"	45	4.0	45	41 ^b
24	3-pyridinecarboxaldehyde	30	1.6	3	50 ^{b,f}
25	propionaldehyde	30	1.6	2.5	82 ^g
26	butyraldehyde	30	1.6	2.5	90 ^g
27	isobutyraldehyde	30	1.6	2	91 ^g
28	decanal	30	1.6	2	88 ^b
29	pivalaldehyde	30	1.6	2	82 ^g
30	2-ethylbutyraldehyde	30	1.6	2	84 ^g
31	3,3-dimethylbutyraldehyde	30	1.6	2	76 ^g

* All the reactions were carried out with 1.00 g of aldehyde and 5 mole % of benzeneseleninic acid in 10 mL of tetrahydrofuran under reflux.

a: No catalyst was added.

b: The products were identified by m. p. and NMR, and reactions were followed by TLC. The yields were for isolated products.

c: Chloroform was used as the solvent.

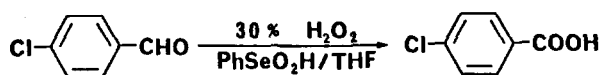
d: Acetone was used as the solvent.

e: Each equivalent of hydrogen peroxide was added every five hours.

f: N-Oxidation was accompanied with the intended reaction.

g: G. C. was used for identification of the products and determination of the yields.

valents of 30 % hydrogen peroxide and 5 mole % of benzeneseleninic acid under reflux. Not only oxidation to carboxylic acid, epoxidation of the double bond was also accompanied. Then we turned to *p*-chlorobenzaldehyde. *p*-Chlorobenzoic acid was obtained in 94 % yield after five hours' reflux (Entry 2). Only 1.1 % of the acid was obtained without the catalytic amount of benzeneseleninic acid (Entry 1). Thus the oxidizing power of hydrogen peroxide itself is negligible for conversion of aldehyde to carboxylic acid, and catalytic amount of benzeneseleninic acid played a major role in this reaction. The effect of different solvents was also studied. In chloroform and acetone, the yields were lowered to 20 % and 50 %, respectively, under the same conditions (Entries 3 and 4).



To see the electronic effects, *p*-bromobenzaldehyde and *p*-tolualdehyde were subjected to the reaction condition. *p*-Bromobenzoic acid was obtained in 97 % yield after 7 hours' reflux, but *p*-tolualdehyde required 20 hours' reflux to give 90 % yield (Entries 5 and 6). Thus electron-withdrawing groups may enhance the rate, while electron-donating groups lower the rate. For *meta*-substituted benzaldehydes, similar effects were also observed. Whereas *m*-fluorobenzaldehyde showed 94 % yield after 8 hours, it took 20 hours for *m*-tolualdehyde to show 90 % yield (Entries 7 and 8). *m*-Anisaldehyde, 3,4-dichlorobenzaldehyde, and *m*-nitrobenzaldehyde showed similar trends (Entries 9, 10 and 11).

While electronic effect of the ring substituents did not affect the yields significantly, steric effects were significant. *o*-Chlorobenzaldehyde and *o*-tolualdehyde showed low yields of 53 % and 57 %, respectively (Entries 13 and 18), while *o*-fluorobenzaldehyde gave 91 % of corresponding acid (Entry 12). Moreover, 2,6-disubstituted compounds with higher steric hindrance, for example, 2-chloro-6-fluorobenzaldehyde and 2,6-dichlorobenzaldehyde showed 39 % and 4.4 %, respectively (Entries 21 and 22).

To see the effect of other factors of the reaction, several series of the experiments were also performed. First, the concentration of the hydrogen peroxide was raised to 45 % from 30 %, and showed little effect on the yields. The yields were raised slightly from 53 % to 55 % for *o*-chlorobenzaldehyde (Entries 13 and 14), and from 57 % to 61 % for *o*-tolualdehyde (Entries 18 and 19). When the amount of hydrogen peroxide was increased from 1.6 equivalents to 4.0 equivalents, the yield was substantially increased to 75 % from 55 % in case of *o*-chlorobenzaldehyde. But further increase to 10 equivalents did not improve the yield significantly (Entries 14, 15 and 16). Also incremental addition of hydrogen peroxide, *i. e.* one equivalent of hydrogen peroxide at every five-hour, did not increase the yield appreciably (Entry 17). Although same trend was observed for *o*-tolualdehyde (Entries 19 and 20), it was not evident for 2-chloro-6-fluorobenzaldehyde (Entries 22 and 23).

Aliphatic aldehydes were also easily oxidized by the system in excellent yields. Steric effect does not seem to play any significant role for the reaction (Entries 25 to 31).

Although the reaction mechanism is not clear at this point, the reaction seems to proceed through tetrahedral intermediate considering the observed steric effect. The reaction was largely affected by the size of o-substituents, possibly at the stage of addition of benzeneseleninic acid to the carbonyl group for benzaldehydes. Another point which should be made is the reaction did not proceed in the presence of sodium bicarbonate or excess triethylamine, *i. e.* under weakly basic conditions.

Since it is well known that many derivatives of phenyl selenides give benzeneseleninic acids under various conditions,⁹ other selenium derivatives were also tried as catalysts. Benzeneselenenyl chloride and diphenyldiselenide also gave satisfactory results.

As a conclusion, benzeneseleninic acid, PhSeO_2H and aqueous hydrogen peroxide was shown to be an efficient and mild reagent for the conversion of both aromatic and aliphatic aldehydes into the corresponding carboxylic acids. The oxidation of aromatic aldehydes usually took longer than aliphatic ones. Both steric hindrance and concentration of hydrogen peroxide seemed to affect the reaction. The bulkier groups at ortho position reduced the yields whereas higher concentration of hydrogen peroxide enhanced the yields for benzaldehydes. But such effect was not evident for aliphatic aldehydes.

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References and Notes

- # Part of this work was applied for Korean Patent (1987) and also presented at the 61st Meeting of the Korean Chemical Society.
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