

THE OXIDATION OF ALDEHYDES TO ACIDS WITH CALCIUM HYPOCHLORITE [Ca(OCl)₂]

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Summary: Calcium hypochlorite is an efficient reagent for the oxidation of aldehydes to the corresponding acids. Reactions are carried out at ambient temperature in aqueous acetonitrile-acetic acid solution. Aliphatic aldehydes and aromatic aldehydes with electron withdrawing groups afford good to excellent yields. Nuclear chlorination is the preferred reaction in aromatic aldehydes with electron donating groups.

We have recently reported on the use of calcium hypochlorite as a reagent for the oxidation of alcohols and ethers.² We now wish to report on the further use of this reagent in the smooth and facile oxidation of certain aldehydes to carboxylic acids. In an accompanying communication we will also report on the use of this reagent for the oxidative cleavage of α -diols, α -diones, α -hydroxy ketones, and α -hydroxy- and keto- acids.³

Several conventional reagents are generally used for CHO \rightarrow COOH transformation⁴ chief among which are the dichromate and permanganate ions.⁵ These reagents are normally employed in strongly acidic or basic media, however, and enolizable aldehydes generally suffer from carbon-carbon bond cleavage giving reduced yields of the desired acid.^{6,7} Substantial improvements in the yields have been realized recently with the use of chromium (V and VI)^{8,9} and permanganate ion¹⁰ in non-aqueous media. The use of MnO₂ for aldehyde oxidation has been reported but the reaction is usually carried out at elevated temperatures.¹¹ Other methods of aldehyde oxidation have recently appeared involving the use of 2-hydroperoxyhexafluoro-2-propanol¹² and O₃.¹³ Though the yields are good, basic conditions and non-ambient temperatures are employed in both cases. Silver salts are perhaps the most widely used aldehyde oxidants because of the mild conditions employed and specificity, but these reagents are prohibitively expensive on a preparative scale.¹⁴⁻¹⁷

In contrast to the above, calcium hypochlorite, an inexpensive reagent,

can be used to oxidize most aldehydes to their corresponding acids at ambient temperature, in good yield and without attendant side reactions. Though the reaction is carried out in the presence of acetic acid, this does not seem to constitute a problem even for those aldehydes which are enolizable.

A general procedure is described for the oxidation of m-nitrobenzaldehyde. To a solution of calcium hypochlorite¹⁸ (7.0 g, 33 mmol) in water (100 ml), was added, in a dropwise manner, glacial acetic acid (10 ml) until all the reagent dissolved. A clear yellow solution was obtained which was then added dropwise (15 min), at ambient temperature, to a stirred solution of m-nitrobenzaldehyde (5 g, 33 mmol) in acetonitrile (40 ml). The mixture became cloudy while the yellow color of the oxidant slowly disappeared. Stirring was continued for 16 hrs with the precipitation of a flocculent white precipitate. The solution was then diluted with water (50 ml) and extracted with ether. The ether extract was washed with sodium bicarbonate (2 x 50 ml) and the combined bicarbonate washings acidified with concentrated hydrochloric acid. The m-nitrobenzoic acid (4.62 g, 84%) precipitated from the acidified solution and was filtered, washed and dried in a vacuum oven. The m.p. (140-142° lit. 140-142°),¹⁹ infrared and NMR spectra were identical with those of authentic material. (In cases where the products were liquid, the acidified bicarbonate extracts were reextracted with ether. The acid was obtained by evaporating the ether.) The ether extracts, after aqueous washing and drying afforded no unreacted starting material.

Table 1 summarizes the results of aldehyde-acid oxidation using $\text{Ca}(\text{OCl})_2$. Usually, one molar equivalent of $\text{Ca}(\text{OCl})_2$ was employed per mole of aldehyde. Unreacted starting material was recovered in all cases where the yield of the acid fell below 80%. All reactions were carried out at ambient temperature though addition of the oxidant to the aldehyde almost always resulted in an exothermic reaction. In general the reaction mixture was stirred overnight, though the disappearance of the yellow color of the oxidant (which usually occurred within 4 hrs) roughly indicated the completion of the oxidation.

A number of other points are also noteworthy. All aliphatic aldehydes are easily converted to the corresponding acids despite the potential for enolization. In these cases (entries 8-10) no attempts were made to optimize yields and 10-25% of the starting aldehyde was recovered after the oxidation. The yields are thus potentially higher. Aromatic aldehydes with electron withdrawing groups afford excellent yields of the corresponding benzoic acids. In the case of o-chlorobenzaldehyde (entry 3) the usual one molar equivalent

Table 1. The Oxidation of Aldehydes to Acids by $\text{Ca}(\text{OCl})_2$.

Run	Substrate	Product	Isolated Yield (%)	Reference
1	Benzaldehyde	Benzoic Acid	86	19a,b
2	m-Nitrobenzaldehyde	m-Nitrobenzoic Acid	84	19a,b
3	o-Chlorobenzaldehyde	o-Chlorobenzoic Acid	81 ^a	19a,b
4	p-Chlorobenzaldehyde	p-Chlorobenzoic Acid	92	19a,b
5	α -Chlorocinnamaldehyde	α -Chlorocinnamic Acid	60	20
6	4-Methylbenzaldehyde	3-Chloro-4-methylbenzoic Acid	76	20
7	2-Methoxybenzaldehyde	5-Chloro-2-methoxybenz- aldehyde	93 ^b	21
8	Cyclohexanecarboxaldehyde	Cyclohexanecarboxylic Acid	77	19a,b
9	2-Ethylbutanal	2-Ethylbutanoic Acid	75	20
10	Heptanal	Heptanoic Acid	70	19a,b

a. Two molar equivalents of oxidant was used.

b. Nuclear chlorination took place instead of aldehyde oxidation.

of oxidant afforded only 36% yield of the acid (perhaps due to the proximity of the chlorine atom to the center being oxidized). Two molar equivalents of $\text{Ca}(\text{OCl})_2$ however, gave an excellent yield.

Aromatic aldehydes containing electron donating groups undergo a competing reaction. Thus, preferential nuclear chlorination occurs with strongly donating groups (entry 7) while both chlorination and aldehyde oxidation take place in the presence of weakly donating groups²² (entry 6). A similar reaction also seems to take place with α,β -unsaturated aldehydes where preferential α -chlorination occurs.^{23,24} Once deactivated however these systems undergo normal $\text{CHO} \rightarrow \text{COOH}$ oxidation (entry 5).

Despite the above limitations with electron rich aromatic aldehydes and the limitation of carrying out the oxidation in the presence of other reactive groups (-OH, -OR, active alkenes) the $\text{Ca}(\text{OCl})_2$ method for aldehyde \rightarrow acid conversion is competitive with existing methods. The reactions can be carried out at ambient temperature, on a large scale and with an inexpensive reagent. Further studies on the mechanism of these reactions and on the use of this oxidant for aromatic chlorination is under way.

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22. Nuclear chlorination occurs first. After deactivation of the ring the aldehyde group is oxidized. This has been demonstrated by (a) the isolation of 3-chloro-4-methylbenzaldehyde (50%) in the early stages of $\text{Ca}(\text{OCl})_2$ oxidation of 4-methylbenzaldehyde and (b) the subsequent aldehyde oxidation of this chlorinated compound with $\text{Ca}(\text{OCl})_2$ to the acid (62%). It should also be noted that reaction of $\text{Ca}(\text{OCl})_2$ with toluene under the same conditions affords p-chloro-toluene (50%).
23. Cinnamaldehyde affords α -chloro cinnamaldehyde in 68% yield under the reaction conditions given.
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