OXIDATIVE CLEAVAGE OF α -DIOLS, α -DIONES, α -HYDROXY-KETONES AND α -HYDROXY- AND α -KETO ACIDS WITH CALCIUM HYPOCHLORITE [Ca(OC1)₂].

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Summary: α -Diols, α -diones, α -hydroxy ketones, and α -hydroxy- and α -keto acids are easily cleaved oxidatively with calcium hypochlorite. The reaction is carried out at ambient temperature in aqueous acetonitrile/acetic acid solution. The yields are good to excellent and the products, depending on the starting material, are aldehydes, ketones or acids.

The oxidative cleavage of α -diols and related compounds can be carried out with a number of reagents. These include sodium bismuthate^{2,3} which is effective in water, aqueous dioxane or acetic acid,⁴ iodo triacetate⁵ and aryl iodoso acetates,^{4,6,7} whose mode of action is similar to, but slower than lead tetraacetate, and manganic pyrophosphate,^{8,9} which is stable only in acid solutions. Other oxidants which have been found useful are xenic acid,¹⁰ mchloroperbenzoic acid,¹¹ silver salts,¹² ceric salts^{9,13} and a variety of other oxidants coupled with periodate.⁹

The most classical and versitile reagents however are periodic $\operatorname{acid}^{14,15}$ and lead tetraacetate. ^{14,16} Between these two reagents most carbon-carbon bond fissions of α -diols, α -diones, α -keto and hydroxy acids and α -hydroxy ketones can be carried out selectively and in good yield. However, large scale oxidations using these reagents are expensive and lead tetraacetate is difficult to store and handle. Our recent work on the use of Ca^(OCL)₂ in alcohol, ether¹⁷ and aldehyde oxidation¹⁸ lead us to consider the utility of this reagent in oxidative cleavage reactions. We herein report our results on the use of this versitile, inexpensive and easily stored oxidant for the above oxidative cleavage reactions.

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With $Ca(OCl)_2$, 1,2-diols are oxidatively cleaved to aldehydes while α -hydroxy ketones and acids are converted to aldehydes and carboxylic acids. α -Diketones and α -keto acids are cleaved to acids. The reactions are carried out using at least a molar equivalent of oxidant per bond to be cleaved. Aqueous acetonitrile (with acetic acid added for solution purposes) is used as the solvent and the reactions are done at ambient temperature. Reaction times are frequently less than four hours and yields average better than 75%. Our results are summarized in Table I.

Some important points are worth mentioning with respect to these oxidations. For reactions where the products are aldehydes, one molar equivalent of calcium hypochlorite per mole of substrate is employed. If poor yields are obtained, more oxidant should be used. However, excess reagent should be avoided since further oxidation of the resultant aldehydes will take place.¹⁸ For cases where ketones are the expected products, two molar equivalents of the oxidant are employed.

With benzoin, (entry 8), a solubility problem arose which led to the use of a mixture of CH_2Cl_2 , CH_3CN and water in a 1:5:5 ratio. With this mixture of solvents, the desired acid and aldehyde products were obtained in a good yield. However, when a mixture of benzene and water (1:1) was used as solvent (two phase system), the only isolated product was benzil (95% yield).

A representative experimental procedure is herein described for the oxidative cleavage of benzil to benzoic acid. (Oxidative cleavage of the other functionalities are carried out in the same manner.) Thus, benzil (2.289 g, 10.9 mmole) was dissolved in methylene chloride (10 ml) and acetonitrile (20 ml) in a round bottomed flask and the resultant solution stirred at room temperature. Calcium hypochlorite¹⁹ (4.80 g, 21.8 mmole) was added to water (50 ml) and swirled in an Erlenmeyer flask until the resultant solution was cloudy. Glacial acetic acid (5 ml) was then added dropwise until a clear yellow solution was obtained. This oxidizing solution was added dropwise, with stirring, to the solution of benzil over a period of 15 minutes. The reaction was slightly exothermic. The yellow colour that resulted after the addition. disappeared after 20 minutes. The solution was then stirred for another one and a half hours after which 10% Na₂SO₃ (20 ml) was added and the resultant solution extracted with CH_2Cl_2 (3 x 40 ml). The CH_2Cl_2 portions were combined, washed with saturated sodium bicarbonate (3 x 40 ml) and dried with anhydrous MgSO4. Solvent removal by evaporation left no residue, indicating the complete oxidation of benzil. All the NaHCO3 portions were

Table I

The Oxidation of α -Diols, α -Hydroxy Ketones, α -Diones, α -Hydroxy Acids and α -Keto Acids Using Ca(OCl)₂.

Run	Substrate	Product	Molar Equiv	$\frac{\texttt{Time}}{(\texttt{hr})}$	$\frac{\texttt{Yield}^{\texttt{a}}}{(\%)}$
1	Benzopinacol	Benzophenone	2	2	92
2	Pinacol	Acetone	2	1	80
3	Cyclohexanone- pinacol	Cyclohexanone	2	1	82
4	1,2-Diphenylethylene Glycol	Benzaldehyde	1	1	92
5	2,3-Dihydroxybutane	Acetaldehyde	1	1	b
6	l-Phenylethylene Glycol	Benzoic Acid	2 ^{c,d}	3.5	86
7	Propylene Glycol	Acetic Acid	1	4	e
8	Benzoin	Benzaldehyde; Benzoic Acid	2 ^f	17	90 _a
9	α-Hydroxyaceto- phenone	Benzoic Acid	2	17	93
10	α-Hydroxycyclohexan- one	Adipic Acid	2	2	55
11	Benzil	Benzoic Acid	2 ^f	2	79
12	Biacetyl	Acetic Acid	1	1	e
13	α-Hydroxyphenylace- tic Acid	Benzaldehyde	1	1	84
14	α-Hydroxyisoc a proic Acid	Isovaleric Acid	2	1	70
15	Sodium α-Ketoiso- caproate	Isovaleric Acid	2	2	92
16	Sodium α -Ketovaler- ate	Butyric Acid	2	3	96

a. Isolated. b. GC analyzed. Acetaldehyde was the only product. c. Using 1 molar equivalent, 55% yield of α -hydroxyacetophenone was isolated. d. Using 4 molar equivalents, 85% yield of p-chlorobenzoic acid was isolated. See ref. 18. e. GC analyzed. Acetic acid was the only product. f. CH₂Cl₂ added for solubility purposes. g. Total yield. Ratio of aldehyde:acid = 1:1.

combined and acidified using concentrated hydrochloric acid. Benzoic acid (2.0823 g, 79%) precipitated and was filtrated, washed with water and dried in an oven. The melting point (121.5-123°C), and infrared and NMR spectra were identical with authentic material. It should be noted that in this

procedure CH_2Cl_2 is necessary as a co-solvent only for compounds which are not soluble in acetonitrile. In addition, when the substrate is water soluble (cases 5,6,7,10,12,13,14,15) acetonitrile is unnecessary.

Further studies in the use of $Ca(OCL)_2$ as an oxidant are underway.

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