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LITHIUM HYPOCHLORITE-CLOROX AS A NOVEL OXIDATIVE MIXTURE FOR METHYL KETONES AND METHYL CARBINOLS

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New, mild methods were needed to oxidize methyl ketones and related systems regioselectively. The conversion of methyl ketones into carboxylic acids with one less carbon has been historically accomplished with hypohalites in alkaline media;¹⁻⁴ sodium hypochlorite and hypobromite are the most common reagents utilized. Although sodium hypoiodite has been used for many years in the iodoform test,¹ it has not been employed frequently for synthetic purposes. Interestingly, sodium hypochlorite was recently shown to oxidize cyclic ketones to dicarboxylic acids under phase-transfer catalysis.⁴

In contrast, the use of lithium hypochlorite has not been well explored. It was thought that lithium hypochlorite might prove a more effective reagent in this type of oxidation because lithium might coordinate better with the oxygen atom of the carbonyl group. Thus, enhancement of the electron-deficit on the carbon atom would increase the acidity of the α -hydrogens. We have discovered that common pool-spa oxidants,⁵ labelled 'Bioguard Burnout 35' or just 'Bioguard', in combination with 'Clorox' bleach, readily cleaves methyl ketones, secondary methyl carbinols, and even one "non-acetyl" alkyl aryl ketone under mild conditions (77°) in short reaction times and with an easy workup. Consistently high yields of the corresponding, highly pure carboxylic acids were obtained (see Table) with little or no purification required in most instances. 'Bioguard Burnout 35' contains 29.5% LiOCl and 70.5% inert ingredients while 'Bioguard' has 29% LiOCl and 71% inert ingredients. An alternate agent, Bioguard Burnout-Ca(OCl)₂ containing 65% Ca(OCl)₂, effected the conversion, albeit in lower yields. All oxidants were purchased locally,⁵ as was the 'Clorox', which contains 5.25% NaOCl and 94.5% inert ingredients.

In a typical experiment, acetophenone (1) was treated for 2 h with LiOCl/Clorox solution in 95% EtOH to yield benzoic acid (95%); without the Clorox or with only a one-hour reaction time, the yield was only 69%. The mp. of the unrecrystallized benzoic acid, as well as those of other solid acids

**Table.** Oxidation of Ketones and Alcohols to Carboxylic Acids with LiOCl/Clorox

Ketone	Yield ^a (%)	mp. ^b (°C)	lit. mp. ^c (°C)	n _D	lit. n _D
C ₆ H ₅ COCH ₃ (1)	95 ^d	122.5-123.5	122.4 ⁶		
4-(Me) ₃ CC ₆ H ₄ COCH ₃ (2)	94	163-165	164 ⁷		
2,4-(Me) ₂ C ₆ H ₃ COCH ₃ (3)	92	125-127	127 ⁸		
3-HOC ₆ H ₄ COCH ₃ (4)	83 ^e	201-202	200 ⁹		
2-MeOC ₆ H ₄ COCH ₃ (5)	93 ^f	101-102	101.5 ¹⁰		
4-MeOC ₆ H ₄ COCH ₃ (6)	92	181-181.5	185 ¹¹		
2-MeC ₆ H ₄ COCH ₃ (7)	89 ^g	104-105	107-108 ¹²		
2-O ₂ NC ₆ H ₄ COCH ₃ (8)	71	146-147	146 ¹³		
1-Acetyladamantane (9)	58	173-174	181 ¹⁴		
CH ₃ (CH ₂) ₈ COCH ₃ (10)	94 ^h		28.5	(1.4455 ²⁹) ⁱ	(1.4319 ⁴⁰) ^{i,15}
(CH ₃) ₃ CCOCH ₃ (11)	80 ^j		33-35	(1.4100 ²⁸) ⁱ	(1.4030 ²⁵) ^{i,16}
(C ₆ H ₅) ₂ CHCOCH ₃ (12)	95	145-147	147-149 ¹⁷		
(CH ₃) ₂ C=CHCOCH ₃ (13)	56 ^k	67-69.5	66-67.5 ¹⁸		
CH ₃ (CH ₂) ₅ CH(OH)CH ₃ (14)	65 ^l		-8.9 to -8.7	(1.4209 ²⁸) ⁱ	(1.4236 ¹⁴) ^{i,19}
C ₆ H ₅ CH(OH)CH ₃ (15)	73 ^m	120-121	121-122 ²⁰		
C ₆ H ₅ COCH ₂ CH ₃ (16)	48	119-120	121-122 ²⁰		

a) The yields are the average of two separate experiments (2-h at reflux unless otherwise specified) and are based upon the weight of isolated acid *without* recrystallization. b) The mp. of the *unrecrystallized* acids. c) Literature mps. d) The reaction was performed under argon. e) With Bioguard Burnout-Ca(OCl)₂; yield of acid was 73%. f) With Bioguard Burnout-Ca(OCl)₂; yield of acid-76%. g) With Bioguard Burnout-Ca(OCl)₂; yield of acid-76%. h) The reaction time was 4 h, and the extraction method was required. i) Refractive index of the oil at the temperature specified in the superscript. With decanoic acid obtained from **10**, HCCl₃ was used as the extractant. The acid obtained was pure by comparison with spectral data from the known compound. In the case of pivalic acid obtained from **11**, an ether extract proved useful to remove pure acid as an oil whose spectral data were identical to that of the pure compound. With heptanoic acid obtained from **14**, hexane was the extractant and gave the acid in pure form as evidenced by spectral analysis. j) Reaction time: 4 h; reaction time: 8 h (84% yield of acid) k) Reaction time-8 h; acid had to be extracted (HCCl₃, 4 x 20 mL) for the maximum yield. The isolation of the acid required basification of a HCCl₃ solution, and the aqueous layer was separated and reacidified to obtain pure acid. Distilled mesityl oxide gave highly pure acid. l) Methanol as the solvent gave a similar yield (64%) of acid. Extraction of the aqueous layer with hexane was required to achieve the yields with either ethanol or methanol. m) Extraction of the aqueous layer with H₂CCl₂ and the use of methanol as solvent were required to achieve the yield shown. With ethanol as solvent, the yield of benzoic acid was ~25-50% less than that obtained using methanol.

studied, was essentially the same as the literature value. The use of Bioguard-Ca(OCl)₂ for LiOCl-Clorox for the oxidation of acetophenone resulted in decreased yields (76%) after 2 hours. Alkyl methyl ketones (9-13,16) and the secondary methyl carbinols 14 and 15 behaved similarly with LiOCl/Clorox as illustrated in the Table. It is clear that neither electron-donating groups (2-7) nor electron-withdrawing groups (8) appreciably affect the reaction. Moreover, steric hindrance by a group *ortho* or adjacent to the acetyl group (as in 3, 5, 7, 8, 9, 11, 12), also appears to have relatively little influence on the cleavage. The conjugated double bond in 13 is not detrimental although the yield of the corresponding acid is moderate because high solubility in the aqueous medium made extraction difficult. Secondary alcohols 14 and 15 were easily converted to the respective acids in a smooth manner. The cleavage of ketone 16 to benzoic acid was especially interesting since it is *not* a methyl ketone. The mild reaction conditions which generate benzoic acid in moderate yield has potential significance in such oxidations of alkyl aryl ketones.

It is known that isomeric methylacetophenones with NaOCl are converted to the corresponding phthalic acids,²¹ but, under our conditions, 2-methylacetophenone was oxidized to *o*-toluic acid without any phthalic acid being formed. The usual conditions were initially employed to cleave *m*-hydroxyacetophenone (4) but resulted in a mixture even when the reaction was performed under nitrogen. However, when the procedure was performed under argon, a good yield (83%) of the corresponding acid was achieved.²² This contrasts with the report that *o*-hydroxyacetophenone, as well as 8, was unaffected by NaOCl.²³ Compounds 4 and 8 were smoothly oxidized under our conditions. Thus, the method described may be applicable to systems with aryl rings bearing groups which are susceptible to overoxidation by other oxidants.

EXPERIMENTAL SECTION

All mps. of the acids were determined on a Thomas-Hoover melting point apparatus and were uncorrected. The identity of the products was verified by comparison of IR (Perkin-Elmer 2000 FT-IR) and ¹H NMR spectra (Varian Omega 300 MHz) with those of authentic samples. Purity was checked by TLC. All substrates used in this study were purchased from Aldrich Chemical Company and were used as received.

General Procedure for the Preparation of Oxidizing Mixtures. LiOCl/Clorox solutions.- A mixture of either Bioguard Burnout 35 or Bioguard (50 g) and Clorox (200 mL) was stirred at RT for 1 h. Solid, inert materials were filtered in initial experiments, but it was later found that such filtration was not necessary since the yields of acids were unaffected.

Ca(OCl)₂/Clorox solutions.- A mixture of Bioguard Burnout-Ca(OCl)₂ (50 g) and Clorox (200 mL) was stirred at RT for 1 h and the solid inert ingredients were filtered off.

These solutions may be stored for at least one week (cool/dark) without a diminution in yields of the acids. The concentration of the oxidizing solution used was 1.24 M in LiOCl, and the ratio of this agent to the ketone was approximately 4:1. The concentration of LiOCl in solution was

determined from the specified concentration of LiOCl in the sample used and included consideration of the dilution effect with Clorox.

General Procedure For Oxidations.- The following procedure is typical. In a round-bottomed flask were placed acetophenone (0.500 g, 4.2 mmol) and 95% EtOH (10 mL). The LiOCl/Clorox solution (15 mL) was then added dropwise (CAUTION: exothermic), and the resulting mixture was heated (77°) at reflux for 2 h. The reaction mixture was allowed to cool to RT (~1 h), and then an aqueous solution (25%) of Na₂S₂O₅ was added (~2 mL). The residual insoluble, inert ingredients were filtered off, and then water (~10 mL) was added to the filtrate which was then acidified with conc HCl (pH ~ 1) and then stirred for 1 h. The flask was cooled (10°) overnight, and the resulting precipitated benzoic acid was collected, washed with cold H₂O (~4 mL), and air dried.

The acids could be obtained more rapidly, albeit in lower (10%) yields, by extraction of the acidic solution with CH₂Cl₂ (4 x 20 mL). The organic solution were washed with cold H₂O (~ 5 mL), and then NaOH (10%, 20 mL) was added. Two layers formed immediately and were separated. The aqueous layer was chilled (ice bath) and then acidified (conc HCl) until the acid precipitated. The mixture was allowed to stand (0.5 h) in the cold, and the solid acid was collected and washed quickly (ice-cold water; ~5 mL).

In the experimental procedure leading to 3-hydroxybenzoic acid, starting ketone **4** was dissolved in ethanol at 0° under argon. When the oxidation was completed, the mixture was allowed to cool to room temperature (1 h) and then was cooled to 0°. In the workup and after acidification (conc HCl, pH ~1), the new solution was treated with a saturated aqueous solution of NaCl (~25 mL), and the resulting mixture was allowed to stand overnight (10°). The remainder of the procedure was identical to that above. Specific workups for liquid acids are given in the Table.

The yields and mps. of the solid acids are provided in the Table along with literature mps. and refractive indices for the liquid acids.

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