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FURTHER STUDIES ON THE UTILITY OF SODIUM HYPOCHLORITE IN ORGANIC SYNTHESIS. SELECTIVE OXIDATION OF DIOLS AND DIRECT CONVERSION OF ALDEHYDES TO ESTERS

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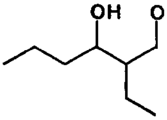
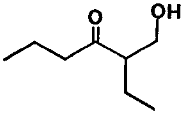
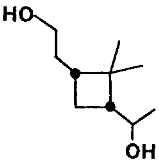
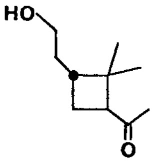
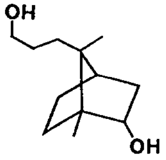
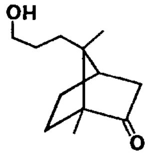
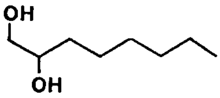
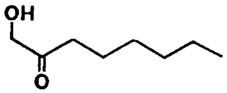
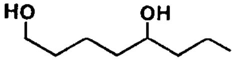
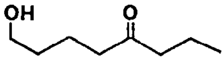
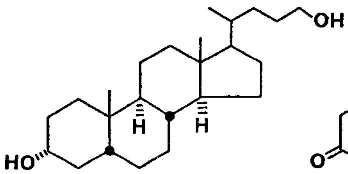
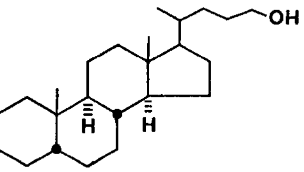
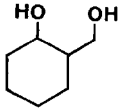
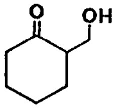
Summary: Sodium hypochlorite in acetic acid solution selectively oxidizes secondary alcohols to ketones in the presence of primary alcohols and converts aldehydes to methyl esters in the added presence of methanol.

Recently, we reported a convenient and inexpensive procedure for the oxidation of secondary alcohols to ketones using NaOCl in acetic acid.[1] During the course of that study we also observed that this procedure oxidized primary alcohols to the corresponding dimeric ester (e.g., 1-decanol to decyl decanoate) but that these oxidations occurred much more slowly than those involving secondary alcohols. These qualitative observations suggested that this procedure might be useful for the selective oxidation of secondary alcohols to ketones in the presence of primary alcohols and that a slight variation of the procedure may allow conversion of aldehydes to esters in a single operation. We now wish to report the realization of these hypotheses. As in our previous study we employed concentrated aqueous solutions of NaOCl which are available as "Swimming Pool Chlorine."[2]

In the first study a variety of diols were oxidized by the reagent with the results shown in Table I. Good yields of the corresponding hydroxy-ketones were obtained, usually without further purification. Dimeric esters contaminated the product when more than one equivalent of oxidant was employed with the exception of entry 5. The best yield obtained in this case was with 1.84 equivalents of oxidant. Use of only 1.05 equivalents gave only a 31% yield of the hydroxy-ketone. Presumably the hemiacetal form of the product competes with the starting material for oxidant. A typical procedure is provided for entry 2: the diol (0.637 g, 3.71 mmol) was dissolved in 3 mL of glacial acetic acid and stirred magnetically. Aqueous 1.86 M NaOCl (2.1 mL, 1.05 equiv) added dropwise at room temperature over 15 minutes initiated a rapid exothermic reaction. Stirring was continued for one hour at room temperature, after which 2 mL of isopropanol was added to quench any remaining oxidant followed by 50 mL of water. The solution was extracted 3 times with CH_2Cl_2, washed with aqueous $NaHCO_3$ and dried over $MgSO_4$. Removal of the solvent left 0.61 g (97%) of crude material which was judged to be 95% pure by gas chromatography. Further purification could be achieved by column chromatography on florisil with 35% ethyl acetate in hexane as the eluant to give 0.523 g (83%) of hydroxy-ketone as a colorless oil of >99% purity as determined by vpc. Upon standing for 24 hr at room temperature 10-15% epimerization was observed. It is noteworthy that epimerization was not observed in the oxidation itself.

TABLE I

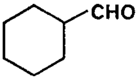
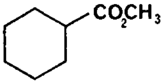
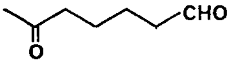
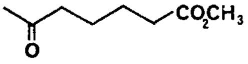
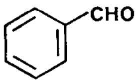
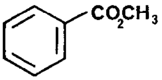
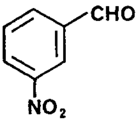
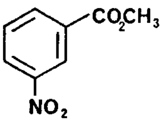
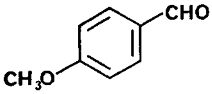
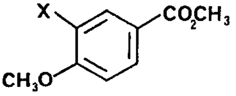
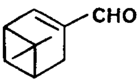
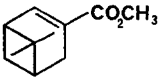
ENTRY	DIOL	PRODUCT	% YIELD[a]
1			85
2			83
3			91
4			73[b]
5			70
6			75
7			90

[a] All yields represent isolated pure products

[b] Isolated as the benzoate ester

Our assumption that dimeric ester formation in the primary alcohol oxidation studies proceeds via hemiacetal intermediates led to a second study. In this investigation an aldehyde was dissolved in methanol and 1-2 equivalents of acetic acid, presumably resulting in equilibrium concentrations of the methyl hemiacetal. The addition of 1-2 equivalents of the aqueous $NaOCl$ solution usually resulted in the rapid conversion of the aldehyde to the corresponding methyl ester in good yield. Our results are shown in Table II. Although the yields are generally good, a few limitations of the method should be mentioned. Activated aromatic aldehydes (entry 6) give low yields due to competing ring chlorination reactions. Certain olefins are also susceptible to electrophilic attack by the reagent (entry 7 and citral, which both gave a multitude of chlorine containing by-products). However, competitive ketone α-chlorination did not lead to reduced yields in the case of entry 3. In some cases (entry 4 and other aldehydes not shown) the only

TABLE II

ENTRY	ALDEHYDE	PRODUCT	% YIELD[a]
1			89
2			58
3			90
4			60
5			73
6			X = H 35[b] X = Cl 35
7			22[b]

[a] All yields represent isolated pure products

[b] Isolated by medium-pressure liquid chromatography

other compound observed was the starting aldehyde which was separable by medium-pressure liquid chromatography or extraction with aqueous sodium bisulfite. A typical procedure is given for entry 1: heptaldehyde (1.70 g, 14.9 mmol) was dissolved in acetic acid (1.8 g, 29 mmol) and 10 mL of CH_3OH. The reaction mixture was cooled to 0-5 °C and stirred while the NaOCl solution (22.5 mmol) was added dropwise over 20 minutes. The cooling bath was removed and the mixture was allowed to come to room temperature. After 1 hr the excess oxidant was quenched by the addition of 2-3 mL of aqueous $NaHSO_3$ solution. The resulting mixture was extracted 3 times with ether and washed successively with aqueous saturated $NaHCO_3$ and brine. The ether was dried over Na_2SO_4 and removed *in vacuo* to leave 1.87 g of colorless methyl heptanoate, shown to be the sole product by 60 MHz NMR.

Although other procedures exist for both selective alcohol oxidation[3] and aldehyde to ester conversion,[4] the simplicity and low cost of our procedures designates them as practical alternatives.

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References and Notes

1. Stevens, R.V.; Chapman, K.T.; Weller, H.N. *J. Org. Chem.* **1980**, *45*, 2030.
2. We employed "Sani-Clor Pool Sanitizer" which is sold as a 12.5% by weight solution. As obtained, these solutions were found to be 1.8 - 2.2 molar. On standing at room temperature in their original containers, these solutions decreased in concentration by about 20% per month. However, refrigerated solutions retain their original strength for months. Alternatively, concentrated solutions may be prepared from Cl_2 and NaOH as described by Boido, V.; Edwards, O.E. *Can. J. Chem.* **1971**, *49*, 2664. For precise work, samples may be titrated according to the procedure of Kolthoff, I.M.; Belcher, R. *Volumetric Analysis*; Interscience: New York, 1957; p 262.
3. (a) Veno, Y.; Okawara, M. *Tetrahedron Lett.* **1976**, 4597. (b) Wicha, J.; Zarecki, A. *ibid.* **1974**, 3059. (c) Posner, G.H.; Perfetti, R.B.; Runquist, A.W. *ibid.* **1976**, 3499. (d) Jung, M.E.; Speltz, L.M. *J. Amer. Chem. Soc.* **1976**, *98*, 7882. (e) Johnson, W.S.; *et al. ibid.* **1963**, *85*, 1409. (f) Jones, R.E.; Kocher, F.W. *ibid.* **1954**, *76*, 3682. (g) Kritchevsky, T.H.; *et al. ibid.* **1952**, *74*, 483.
4. (a) Castells, J.; Pujol, F.; Llitjós, H.; Moreno-Mañas, M. *Tetrahedron*, **1982**, *38*, 337. (b) Keehn, P.; Nwaukwa, S.O. *Tetrahedron Lett.* **1982**, 35. (c) Sundararaman, P.; Walker, E.C.; Djerassi, C. *ibid.* **1978**, 1627. (d) Nishihara, A.; Kubota, I. *J. Org. Chem.* **1968**, *33*, 2525. (e) Pinnick, H.W.; Lajis, N.H. *ibid.* **1978**, *43*, 371. (f) Ogawa, T.; Matsui, M. *J. Amer. Chem. Soc.* **1976**, *98*, 1629.

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