A Selective and Efficient Method for Alcohol Oxidations Mediated by *N*-Oxoammonium Salts in Combination with Sodium Bromite

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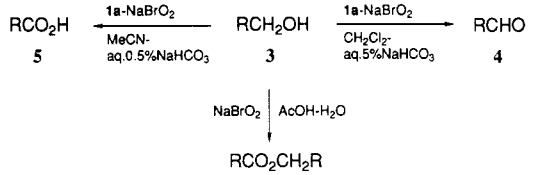
The oxidation of primary and secondary alcohols leading to aldehydes, carboxylic acids, and ketones has been carried out in a *N*-oxoammonium salts–$NaBrO_2$ system. Sodium bromite as a stoichiometric oxidizing reagent activates *N*-oxyl compounds (recycling catalysts) to their *N*-oxoammonium salts in a weakly basic medium, which oxidize primary hydroxyl groups preferentially rather than secondary ones to the corresponding aldehydes. Calcium hypochlorite is used as an alternative terminal oxidant in the same media. The procedure, applicable to the selective formation of γ- and δ-lactones, β-hydroxy aldehydes, and 2-acetoxy ketones, is advantageous in terms of reagent cost, safety, and ease of operation.

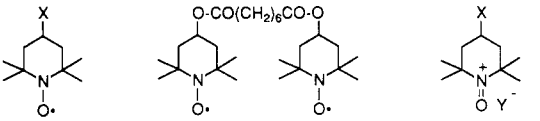
Oxidation of alcohols using metallic or nonmetallic catalysts with stoichiometric amounts of cooxidants is currently a practical operation.[1] However, use of even a catalytic amount of hazardous metallic reagents is a matter of economic and environmental concern.[2] *N*-Oxoammonium salts[3] as nonmetallic oxidizing reagents are available easily from the corresponding *N*-oxyl radicals by treating with following reagents and methods: (a) positive halogen sources,[4] (b) *m*-chloroperbenzoic acid,[5] (c) high-valency metal salts,[6] and (d) electrooxidation.[7] In particular, the search for a recycling system with *N*-oxoammonium salts has led to the development of efficient procedures by use of NaOCl–KBr[8] and $CuCl_2$–O_2[9] as a cooxidant. However, problems associated with these methods are, sooner or later, loss of the oxidizing power of the *N*-oxoammonium salts due to concurrently generated hydrogen peroxide[4c] and molecular chlorine. We describe here a versatile procedure for the oxidation of alcohols with *N*-oxyl compounds (catalysts)–sodium bromite ($NaBrO_2$, cooxidant)[10] (Scheme I).

Two-phase or mixed solvent systems were chosen for the following reasons: (a) different solubilities of organic and inorganic reagents, (b) easy operation and workup, and (c) instability of *N*-oxoammonium salts in aqueous media.[11]

Scheme I



After a survey on solvent effects, methylene chloride was found to be the best choice for the oxidation of primary alcohols to the corresponding aldehydes. The pH of the aqueous phase was maintained slightly basic with buffer solutions. Thus, the reaction of undecanol (**3a**) with a catalytic amount of 4-(benzoyloxy)-2,2,6,6-tetramethylpiperidine-1-oxyl (**1a**, 1 mol %) and 3 equiv of sodium



1a, X = OCOPh
1b, X = CN
1c, X = OMe

1d

2, Y = Br, Cl

bromite in a CH_2Cl_2–H_2O (buffered at pH 8.6 with $NaHCO_3$, 1:2 v/v) system afforded undecanal (**4a**) in 93% yield (Table I, entry 1). The oxidation of **3a** to the corresponding carboxylic acid **5a** was performed in 92% yield with the two-reagents combination in a homogeneous MeCN–H_2O (1:1 v/v) system (entry 2). The conversion of the reagent **1a** to *N*-oxoammonium salt **2a** is probably enhanced in the homogeneous medium so that further oxidation of the aldehyde **4a** to the carboxylic acid **5a** proceeds smoothly. On the other hand, the reaction of **3a** with sodium bromite in an AcOH–H_2O (1:5 v/v) system produced only the dimeric ester **6a** in 92% yield (entry 3) in accordance with the results reported by Kageyama et al.[12] The ester **6a** was partially formed when the oxidation of **3a** was carried out in a **1a**–$NaBrO_2$ system under neutral to weakly acidic conditions (entries 4 and 5).

The time-dependence curves of the conversion yields of **4a** from **3a** under various added amounts of the oxidant **1a** are plotted in Figure 1. The oxidation of **3a** to **4a** is

(1) (a) Zhang, N.; Mann, C. M.; Shapley, P. A. *J. Am. Chem. Soc.* **1988**, *110*, 6591. (b) Giddings, S.; Millis, A. *J. Org. Chem.* **1988**, *53*, 1103. (c) Ishii, Y.; Yamawaki, K.; Ura, T.; Yamada, H.; Yoshida, T.; Ogawa, M. *J. Org. Chem.* **1988**, *53*, 3587. (d) Morris, P. E.; Kiely, D. E. *J. Org. Chem.* **1987**, *52*, 1149. (e) Dess, D. B.; Martin, J. C. *J. Org. Chem.* **1983**, *48*, 4155, and references therein.

(2) Kauffman, J. M.; Mckee, J. R. *J. Chem. Educ.* **1982**, *59*, 862.

(3) Rozantsen, E. G.; Sholle, V. D. *Synthesis* **1971**, 401.

(4) Cl_2 or Br_2: (a) Miyazawa, T.; Endo, T.; Shiihashi, S.; Okawara, M. *J. Org. Chem.* **1985**, *50*, 1332. (b) Miyazawa, T.; Endo, T. *J. Org. Chem.* **1985**, *50*, 3930. (c) Endo, T.; Miyazawa, T.; Shiihashi, S.; Okawara, M. *J. Am. Chem. Soc.* **1984**, *106*, 3877. XeF_2: (d) Golubev, V. A.; Salmina, N. N.; Korsunskii, B. L.; Aleinikov, N. N. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1978**, 778; *Chem. Abstr.* **1978**, *89*, 42006z. HOCl: (e) Petrov, A. N.; Kozlov, Yu. N.; Purmal, A. P.; Uskov, A. M. *Zh. Fiz. Khim.* **1984**, *58*, 2109; *Chem. Abstr.* **1984**, *101*, 210302e. $FClO_3$: (f) Vigalok, A. A.; Lukashina, S. G.; Petrova, G. G.; Vigalok, I. V.; Levin, Ya. A. *Zh. Org. Khim.* **1987**, *23*, 489; *Chem. Abstr.* **1987**, *107*, 235828t.

(5) Cella, J. A.; Kelley, J. A.; Kenehan, E. F. *J. Org. Chem.* **1975**, *40*, 1860.

(6) $K_3[Fe(CN)_6]$: (a) Miyazawa, T.; Endo, T. *J. Mol. Catal.* **1985**, *31*, 217. CuX_2 (X = Cl, Br, OAc, etc.): (b) Miyazawa, T.; Endo, T. *J. Mol. Catal.* **1985**, *32*, 357.

(7) Semmelhack, M. F.; Chou, C. S.; Cortes, D. A. *J. Am. Chem. Soc.* **1983**, *105*, 4492.

(8) Anelli, P. L.; Biffi, C.; Montanari, F.; Quici, S. *J. Org. Chem.* **1987**, *52*, 2559.

(9) Semmelhack, M. F.; Schmid, C. R.; Cortes, D. A.; Chou, C. S. *J. Am. Chem. Soc.* **1984**, *106*, 3374.

(10) Review on $NaBrO_2$ as an oxidant: Okawara, M. *J. Synth. Org. Chem. Jpn.* **1984**, *42*, 751.

(11) Dagonneau, M.; Kagan, E. S.; Mikhailov, V. I.; Rozantsev, E. G.; Sholle, V. D. *Synthesis* **1984**, 895. Our attempts to isolate the oxoammonium salt **2a** (Y = Br) from **1a** by the oxidation with $NaBrO_2$ (3 equiv) in a CH_2Cl_2–aqueous 5% $NaHCO_3$ (1:1 v/v) were unsuccessful, but the starting **1a** was recovered quantitatively presumably because of rapid reduction of the formed oxoammonium salt **2a** with water.

(12) Kageyama, T.; Kawahara, S.; Kitamura, K.; Ueno, Y.; Okawara, M. *Chem. Lett.* **1983**, 1097.

0022-3263/90/1955-0462$02.50/0

Table I. Oxidation of Undecanol (3a) by *N*-Oxyl (1a)–$NaBrO_2$ and/or $Ca(OCl)_2$ Cooxidants[a]

entry	solvent (pH, v/v)	oxidizing reagent	product yield, % 4a	5a	6a
1	CH_2Cl_2–H_2O (pH 8.6, 1:2)	**1a** (1 mol %)–$NaBrO_2$ (3 equiv)	93		
2	MeCN–H_2O (pH 8.6, 1:1)	**1a** (1 mol %)–$NaBrO_2$ (3 equiv)		92	
3	AcOH–H_2O (pH 2.2, 1:5)	$NaBrO_2$ (3 equiv)[b]			92
4	CH_2Cl_2–H_2O (pH 7, 1:2)	**1a** (1 mol %)–$NaBrO_2$ (3 equiv)	80		5
5	CH_2Cl_2–H_2O (pH 4, 1:2)	**1a** (1 mol %)–$NaBrO_2$ (3 equiv)	45		34
6	CH_2Cl_2–H_2O (pH 8.6, 1:2)	**1a** (1 mol %)–$Ca(OCl)_2$ (2.2 equiv)	90[c]		

[a] Unless otherwise noted, reactions were carried out by using **3a** (1.0 mmol) in organic solvent (5 mL) and aqueous solution (5–10 mL) at room temperature for 15–180 min. [b] *N*-Oxyl **1a** was not present. [c] 50 mmol of **3a** was used; see Experimental Section.

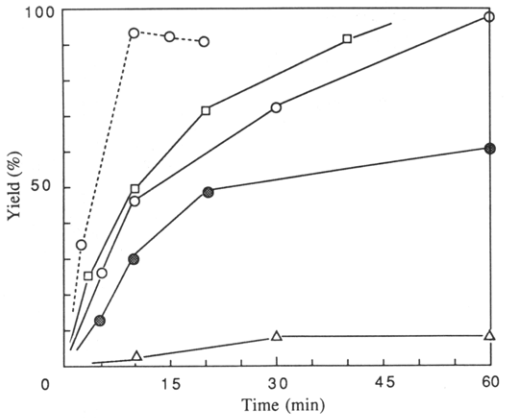


Figure 1. Time-dependence curves for oxidation of undecanol (**3a**) with *N*-oxyl (**1a**)–$NaBrO_2$ (—) or **1a**–$Ca(OCl)_2$ (- - -) system. Symbols are as follows: 5 mol % of **1a** (□); 1 mol % of **1a** (○); 0.2 mol % of **1a** (●); in the absence of **1a** (△). Data points were obtained by GC analyses based on an internal standard (bromononane).

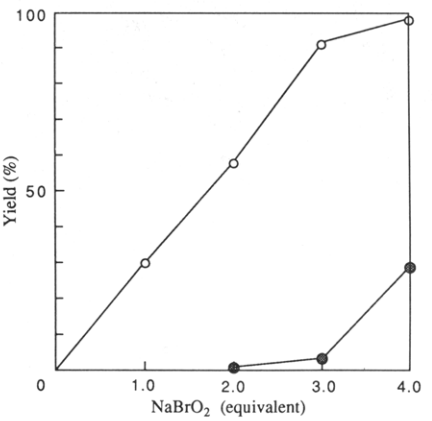


Figure 2. Competitive oxidation of undecanol (**3a**) and 2-undecanol. Symbols are as follows: undecanal (○), 2-undecanone (●). Data points were based on isolated products.

accelerated by increasing the catalyst amount and reasonable rates were obtained in the range 1–5 mol % of **1a**. Routinely, we used 1 mol % of **1a** (based on the substrate) for the oxidation, which facilitated the separation of products from the catalyst **1a** by distillation or chromatography.[13]

Subsequently, the oxidation of **3a** to **4a** was attempted using the tetramethylpiperidine-1-oxyl derivatives **1b**, **1c**, and **1d**, affording **4a** in 98% (with **1b**), 85% (with **1c**), and 97% yields (with **1d**). In contrast, di-*tert*-butylnitroxyl was not useful as a recycling catalyst.

Competitive oxidation of 1-undecanol (**3a**) and 2-undecanol (**7a**) under the conditions of entry 1 (Table I) was examined at 0 °C, and the yields of undecanal (**4a**) and 2-undecanone (**8a**) are plotted in Figure 2 as a function of the amount of sodium bromite. Aldehyde **4a** was exclusively formed when less than 3 equiv of sodium bromite was used. Similarly, treatment of a 1:1 mixture of 1-dodecanol (**3b**) and 4-dodecanol (**7b**) with **1a** (1 mol %)–$NaBrO_2$ (4 equiv) at 0 °C afforded dodecanal (**4b**) and 4-dodecanone (**8b**) in 92% and 2% yields, respectively. In the latter case, the relative oxidation rates for **4b** and **8b** can be estimated to be in a ratio of 46:1. This value compares well with that obtained by the oxidation with ruthenium dichloride tris(triphenylphosphine) complex, ($RuCl_2(PPh_3)_3$), as a stoichiometric oxidant in benzene.[14]

As an alternative oxygenated halogen oxidant, calcium hypochlorite ($Ca(OCl)_2$) could be used for the present purpose.[15] As shown in entry 6 (Table I), the oxidation of **3a** in a CH_2Cl_2–H_2O (buffered at pH 8.6, 1:2 v/v)–**1a** (1 mol %)–$Ca(OCl)_2$ (2.2 equiv) system at 0–5 °C gave aldehyde **4a** in 90% yield. The oxidation of **3a** with a **1a**–$Ca(OCl)_2$ system proceeded more rapidly than that with a **1a**–$NaBrO_2$ system.[16] On the other hand, the use of sodium chlorite ($NaClO_2$) and sodium periodide ($NaIO_4$) as a stoichiometric oxidizing reagent was unsuccessful.

In contrast to our present method, the recently developed 4-methoxy-2,2,6,6-tetramethylpiperidine-1-oxyl (**1d**, catalytic)–KBr (catalytic)–NaOCl (stoichiometric) system[8] needs ultrarapid agitation to complete the reaction quickly. Furthermore, the **1a**–$NaBrO_2$ system can be operated easily in a large-scale preparation.[17]

The results from oxidation of a variety of primary and secondary alcohols are listed in Table II. The oxidation of terminal 1,4- and 1,5-diols can lead to γ- and δ-lactones (entries 16–19), while terminal 1,3-diols are converted to β-hydroxy aldehydes (aldols) due to mild reaction conditions (entries 13–15). For the oxidation of secondary alcohols in 1,3-diol derivatives, the sodium hypochlorite–acetic acid system, a typically economical method, has been recognized as a particularly useful one.[18] The present

(13) After completion of the reaction, excess oxidants can be removed by adding ethanol in the aldehyde synthesis or aqueous 5% sodium hydrogen sulfite in the ketone synthesis.

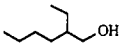
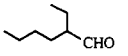
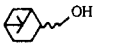
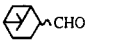
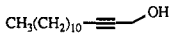
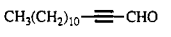
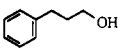
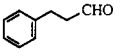
(14) Tomioka, H.; Takai, K.; Oshima, K.; Nozaki, H. *Tetrahedron Lett.* **1981**, *22*, 1605.

(15) Oxidation with $Ca(OCl)_2$ in acetic acid: Nwauka, S. D.; Keehn, P. M. *Tetrahedron Lett.* **1982**, *23*, 3131.

(16) The oxidation with **1a**–$Ca(OCl)_2$ was carried out with a 0.2 M solution of substrate in CH_2Cl_2, and $Ca(OCl)_2$ was added portionwise to the reaction mixture. At about 1 M concentration loss of *N*-oxyl compounds occurred prior to the end point.

(17) The oxidation of **3a** (10 mmol) with a combination of **1a** (0.1 mmol) and KBr (1 mmol)–NaOCl (30 mmol) in a CH_2Cl_2 (50 mL)–aqueous 5% $NaHCO_3$ (45 mL) at 0–5 °C for 3 h resulted in the formation of **4a** (35%) and recovery of the starting **3a** (64%).

Table II. Oxidation of Primary and Secondary Alcohols by *N*-Oxyl (1a)–$NaBrO_2$ or 1a–$Ca(OCl)_2$[a]

entry	substrate	oxidant[b] (equiv/time)	product	yield,[c] %
1	octanol	A (2.5/3 h)	octanal	80
2	dodecanol	A (2.5/3 h)	dodecanal	98
3	octadecanol	A (6/6 h)	octadecanal	96
4		A (4.5/4 h)		57
5		A (7/3 h)		90
6		A (3/3 h)		95
6′		B (3/5 min)		96
7		A (3/5 h)		96
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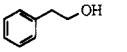
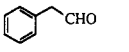
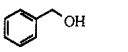
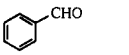
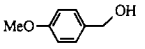
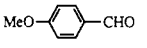
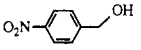
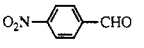
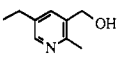
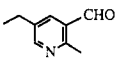
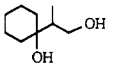
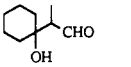
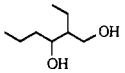
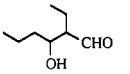
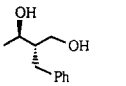
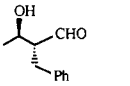
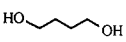
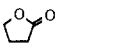
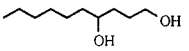
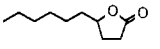
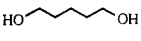
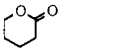
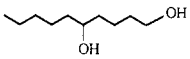
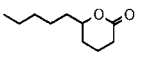
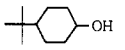
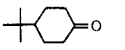
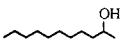
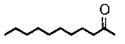
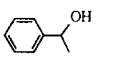
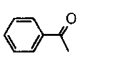
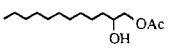
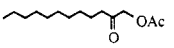
8		A (3/4 h)		68
9		A (2.5/4 h)		76
10		A (4/72 h)		53
11		A (2/1 h)		69
12		A (3/0.5 h)		77
13		A (2/3 h)		86
14		A (3/3 h)		96
15		A (3/3 h)		94
16		A (5/3 h)		95
17		A (4/3 h)		99
18		A (5/3 h)		94
19		A (5/3 h)		86
20		A (4/3 h)		97
20′		B (3/15 min)		89
21		A (6/2 h)		99
21′		B (3/1 h)		76
22		A (6/4 h)		92
22′		B (4/3 h)		81
23		A (6/4 h)		95
24		A (4/3 h)		87

[a] Substrate (1 mmol) was reacted with **1a** (0.01 mmol) in CH_2Cl_2 (5 mL)–aqueous 5% $NaHCO_3$ (10 mL). [b] Oxidant A, $NaBrO_2$; oxidant B, $Ca(OCl)_2$. [c] Yields based on isolated products.

procedure provides a complement to the above method for the selective oxidation of 1,3-diols in the reverse manner without noticeable isomerization (entries 14 and 15).[19]

1,2-Diol monoacetates yielded the corresponding 2-acetoxy ketones without cleaving the carbon–carbon bond (entries

(18) Stevens, R. V.; Chapman, K. T.; Weller, H. N. *J. Org. Chem.* **1980**, *45*, 2030.

(19) Optically active 2-benzyl-3-hydroxybutanal was unstable to chromatography on SiO_2 or Florisil column and isomerized on standing at room temperature for few hours. Optical purity and the elemental analysis of this compound were not determined.

23 and 24).

Sodium bromite ($NaBrO_2$)[20] is intermediate in oxidation state between sodium hypobromite (NaOBr) and sodium bromate ($NaBrO_3$), the latter of which is not useful for the present purpose as a cooxidant. An aqueous solution of $NaBrO_2$ at pH 6–8 is proposed to be trimeric, and due to self-decomposition property at this pH region, the reactivity as an oxidant is mild, in contrast to that under acidic conditions.[21,22] Such a characteristic nature of sodium bromite, being specifically effective as an oxidant for the conversion of *N*-oxyl **1** to *N*-oxoammonium salts **2**, is adequate for a selective oxidation of alcohols under mild conditions without loss of the catalyst activity. Furthermore, as far as $NaBrO_2$ is employed as a cooxidant, the operation described here is quite safe since the reaction proceeds at a moderate rate (Figure 1), and $NaBrO_2$ in basic media liberates no molecular bromine.[21]

Experimental Section

General Procedures.[23] Sodium bromite ($NaBrO_2 \cdot 3H_2O$, 65% pure as $NaBrO_2$, Kanto Kagaku, Japan) and calcium hypochlorite (60% pure, Santoku Chemical, Japan) were used as received. 2,2,6,6-Tetramethylpiperidine-1-oxyls (**1a–d**) were prepared from the corresponding 2,2,6,6-tetramethylpiperidine according to the method reported[24] and purified by recrystallizations or column chromatography. Starting alcohols were purified by distillation or column chromatography (SiO_2) prior to use.

Oxidation of Primary Alcohols to Aldehydes. Typical Procedure. Undecanol (**3a**, 1.72 g, 10 mmol) and 4-(benzoyloxy)-2,2,6,6-tetramethylpiperidine-1-oxyl (**1a**, 28 mg, 0.1 mmol) were dissolved in CH_2Cl_2 (50 mL) and combined with aqueous 5% $NaHCO_3$ (100 mL). On cooling to 0–5 °C, $NaBrO_2 \cdot 3H_2O$ (6.2 g, 30 mmol) was added to the above mixture with moderate stirring. Stirring was continued for an additional 3 h at room temperature, and ethanol (5 drops) was added. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2. Combined extracts were washed with brine, dried (Na_2SO_4), and concentrated. Flash chromatography of the residue on silica gel (hexane–AcOEt 10:1) gave 1.58 g (93%) of undecanal (**4a**) as an oil: bp 113 °C (9 mmHg); IR (neat) 2716, 1729 (C=O), 1466 cm^{-1}; ^1H NMR (500 MHz) δ 0.88 (t, J = 7.0 Hz, 3, CH_3), 1.26 (br s, 14, CH_2), 1.62 (m, 2, CH_2), 2.41 (dt, J = 7.3, 2.0 Hz, 2, CH_2CO), 9.76 (t, J = 2.0 Hz, 1, CHO); ^{13}C NMR (126 MHz) δ 14.1, 22.1, 22.7, 19.2, 29.29, 29.34, 29.4, 29.5, 31.9, 43.9, 203.0.

Oxidation of Primary Alcohol to the Carboxylic Acid. The alcohol **3a** (1.72 g, 10 mmol) and **1a** (28 mg, 0.1 mmol) were dissolved in MeCN (100 mL) and mixed with aqueous 5% $NaHCO_3$ (100 mL). To this homogeneous solution was added portionwise $NaBrO_2 \cdot 3H_2O$ (8.30 g, 40 mmol) at 0–5 °C, and the mixture was stirred vigorously for an additional 3 h at room temperature. The mixture was acidified with 10% tartaric acid and taken up in AcOEt (50 mL × 3). Extracts were washed with brine, dried (Na_2SO_4), and concentrated under vacuum. Chromatographic purification (hexane–AcOEt 1:1) of the crude products gave 1.71 g (92%) of undecanoic acid (**5a**): mp 28 °C; IR (KBr) 3500–2500 (COOH), 1698 (C=O), 1468, 1435, 1412, 1290, 932 cm^{-1}; ^1H NMR (60 MHz) δ 0.87 (t, 3, CH_3), 1.25 (br s, 16, CH_2), 2.31 (t, J = 6.7 Hz, 2, CH_2CO), 11.37 (br s, 1, COOH).

Oxidation of Primary Alcohol to the Dimeric Ester. To a solution of **3a** (172 mg, 1 mmol) in AcOH (0.2 mL) was added aqueous $NaBrO_2 \cdot 3H_2O$ (622 mg, 3 mmol) in H_2O (1 mL) at room temperature over 30 min. After stirring for 12 h, the mixture was neutralized with aqueous $NaHCO_3$ and extracted with CH_2Cl_2. Extracts were washed with brine, dried (Na_2SO_4), and concentrated. Chromatographic purification (hexane–AcOEt 15:1) of the crude products gave 158 mg (92%) of undecanyl undecanoate (**6a**) as an oil: IR (neat) 1742 (COO), 1466, 1379, 1241, 1170, 1114 cm^{-1}; ^1H NMR (500 MHz) δ 0.88 (t, J = 7.5 Hz, 6, CH_3), 1.26 (br s, 30, CH_2), 1.61 (m, 4, CH_2), 2.28 (t, J = 7.5 Hz, 2, CH_2), 4.05 (t, J = 6.5 Hz, 2, CH_2O).

Oxidation of Secondary Alcohols to the Ketones. Typical Procedure. A solution of 4-*tert*-butylcyclohexanol (7.81 g, 50 mmol) and 4-(benzoyloxy)-2,2,6,6-tetramethylpiperidine-1-oxyl (**1a**, 138 mg, 0.5 mmol) in CH_2Cl_2 (100 mL) was combined with aqueous 5% $NaHCO_3$ (100 mL). To this biphase mixture was added portionwise $NaBrO_2 \cdot 3H_2O$ (31.2 g, 150 mmol) with vigorous stirring and cooling in an ice bath. Stirring was continued for an additional 3 h at room temperature, and the reaction was quenched with aqueous 5% sodium bisulfate (3 mL). The mixture was worked up in the usual manner, and the crude products were distilled to give 6.86 g (89%) of 4-*tert*-butylcyclohexanone: mp 48–49 °C (from hexane).

Oxidation of 1,4-Dihydroxyl Compounds to the γ-Lactones. Typical Procedure. 1,4-Decanediol (174 mg, 1.0 mmol) and **1a** (2.8 mg, 0.01 mmol) were dissolved in CH_2Cl_2 (5 mL) and combined with aqueous 5% $NaHCO_3$ (10 mL). To this two-phase solution was added $NaBrO_2 \cdot 3H_2O$ (832 mg, 4 mmol) with vigorous stirring and cooling with an ice bath. Stirring was continued for an additional 3 h at room temperature. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2. Combined extracts were washed with 5% sodium bisulfate, dried (Na_2SO_4), and concentrated. Chromatographic purification of the crude products gave 168 mg (99%) of decan-4-olide: bp 136–138 °C (9 mmHg) (lit.[25] bp 84 °C (0.2 mmHg)); IR (neat) 1770 (C=O), 1465, 1170, 900 cm^{-1}; ^1H NMR (200 MHz) δ 0.88 (t, J = 6.6 Hz, 3, CH_3), 1.29 (m, 6, CH_2), 1.4–1.80 (m, 4, CH_2), 1.80–1.98 (m, 2, CH_2), 2.32–2.68 (m, 2, CH_2CO), 4.20–4.35 (m, 1, CHO); ^{13}C NMR (50 MHz) δ 14.6, 19.1, 23.1, 25.2, 28.4, 30.1, 32.2, 36.4, 81.2, 172.6.

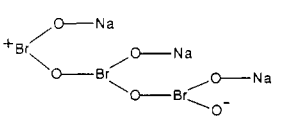
Oxidation of 1,3-Diols to the Corresponding Aldols. A solution of 2-ethyl-1,3-hexanediol (4.39 g, 30 mmol; 1.3–1.4:1 stereoisomers on ^{13}C NMR) in CH_2Cl_2 (50 mL) was combined with aqueous 5% $NaHCO_3$ (100 mL) and cooled to 0–5 °C. To this two-layer solution was added **1a** (83 mg, 0.3 mmol) and then $NaBrO_2 \cdot 3H_2O$ (18.7 g, 90 mmol) with moderate stirring. After this stirred for an additional 3 h at room temperature, ethanol (5 drops) was added. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2. Combined extracts were washed with brine, dried (Na_2SO_4), and concentrated to give 4.14 g (96%) of 2-ethyl-3-hydroxyhexanal (1.3–1.4:1 stereoisomers on ^{13}C NMR): bp 101 °C (9 mmHg) (lit.[26] bp 107–110 °C (16 mmHg)); IR (neat) 3330 (OH), 2734, 1721 (C=O), 1464, 1381, 1149, 1125, 977 cm^{-1}; ^1H NMR (500 MHz) δ 0.94, 0.95, 0.99 (t, J = 8 Hz, 6, CH_3), 1.30–1.58 (m, 4, CH_2), 1.62–1.84 (m, 4, CH_2), 1.94, 2.13 (br, 1, OH), 2.26, 2.31 (m, 1, CHCO), 3.88, 3.98 (m, 1, CHO), 9.75, 9.77 (d, J = 3, 2 Hz, 1, CHO); ^{13}C NMR (126 MHz) δ 11.5, 12.2, 13.83, 13.85, 17.5, 18.7, 19.1, 19.4, 36.5, 37.1, 58.61, 58.70, 70.5, 70.8, 205.6, 205.9.

(2*R*,3*R*)-2-Benzyl-3-hydroxybutanal (93:7 stereoisomers on ^{13}C NMR) was obtained in 94% yield by the similar oxidation of (2*S*,3*R*)-2-benzyl-1,3-butanediol (95:5 stereoisomers on ^{13}C NMR) as above at 0 °C. The starting diol was prepared by reduction of ethyl (2*R*,3*R*)-2-benzyl-3-hydroxybutanoate with $LiAlH_4$.[27] Spectral data of the crude aldol:[19] IR (neat) 3332 (OH), 2735,

(20) Crystalline $NaBrO_2$ is stable in the dark and undergoes disproportionation on heating.[21] Aqueous $NaBrO_2$ solution is shown to be trimeric at pH 6–8.[22]

$$3NaBrO_2 \rightarrow 2NaBrO_3 + NaBr \quad (\text{at } 109\ ^\circ C)$$

$$2NaBrO_3 \rightarrow 2NaBr + 3O_2 \quad (\text{at } 359\ ^\circ C)$$



(21) Kageyama, T. *J. Chem. Soc. Jpn.* **1972**, 1064.

(22) Techinical Bulletin on sodium bromite from Nippon Silica Industrial Co., 1984.

(23) All reactions were carried out under an argon atmosphere. Melting points and boiling points indicated by an air-bath temperature are uncorrected. GC analyses were carried out on a Yanagimoto Model G6800 with a Quadrex bond-fused silica capillary column (methylsilicone: 0.25-μm film thickness, 25 m × 0.25-m i.d.). ^1H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$.

(24) Rozantsev, E. G.; Neiman, M. B. *Tetrahedron* **1964**, *20*, 131.

(25) Kharasch, M. S.; Skell, P. S.; Fisher, P. *J. Am. Chem. Soc.* **1948**, *70*, 1055.

(26) Blanc, P. Y.; Perret, A.; Teppa. F. *Helv. Chim. Acta* **1964**, *47*, 567.

(27) Frater, G. *Helv. Chim. Acta* **1979**, *62*, 2825.

1717, 1605, 1497, 1456, 1379, 1267, 1118, 917, 739, 702 cm^{-1}; ^1H NMR (200 MHz) δ 1.25 (d, J = 6.4 Hz, 3, CH_3), 2.60 (m, 1, CHCO), 2.82–3.01 (m, 2, CH_2), 3.95 (m, 1, CHO), 7.11–7.28 (m, 5, PhH), 9.73 (d, J = 2 Hz, 1, CHO); ^{13}C NMR (50 MHz) δ 21.5, 32.3, 51.9, 67.0, 126.4, 128.7, 128.8, 138.1, 205.0.

Oxidation of a Mixture of Primary and Secondary Alcohols, a Competition Reaction. A mixture of **3a** (172 mg, 1.0 mmol), 2-undecanol (**7a**, 172 mg, 1.0 mmol), and **1a** (5.6 mg, 0.02 mmol) was dissolved in CH_2Cl_2 (10 mL) and combined with aqueous 5% $NaHCO_3$ (20 mL). To this mixture was added $NaBrO_2 \cdot 3H_2O$ (624 mg, 3 mmol) with vigorous stirring under cooling on an ice bath. The mixture was stirred for an additional 1 h at 0 °C and worked up in the usual manner. Purification of the crude oils by column chromatography (hexane–AcOEt 10:1) gave 157 mg (91%) of **4a**, 14 mg (8%) of **3a**, and 163 mg (95%) of 2-undecanol (**7a**).

Similarly, a mixture of 1-dodecanol (**3b**, 186 mg, 1.0 mmol) and 4-dodecanol (**7b**, 186 mg, 1.0 mmol) in CH_2Cl_2 (10 mL) was oxidized with **1a** (2.8 mg, 0.01 mmol) and $NaBrO_2 \cdot 3H_2O$ (832 mg, 4.0 mmol) at 0 °C for 2 h. Usual workup followed by purification on SiO_2 (hexane–AcOEt 15:1) gave dodecanal (**4b**, 170 mg, 92%) and 4-dodecanone (**8b**, 4 mg, 2%). 4-Dodecanone (**4a**):[14] IR (neat) 1717 (C=O) cm^{-1}; ^1H NMR (500 MHz) δ 0.86 (t, J = 7.1 Hz, 3, CH_3), 0.90 (t, J = 7.4 Hz, 3, CH_3), 1.26 (br, 8, CH_2), 1.54 (m, 2, CH_2), 1.58 (m, 2, CH_2), 2.36, 2.37 (q, J = 7.4 Hz, 4, CH_2).

Oxidation of Primary Alcohols to Aldehydes by a 1a–$Ca(OCl)_2$ System. Typical Procedure. Undecanol (**3a**, 8.62 g, 50 mmol) and **1a** (138 mg, 0.5 mmol) was placed in a biphase solution of CH_2Cl_2 (250 mL)–aqueous 5% $NaHCO_3$ (500 mL). On cooling to 0–5 °C, $Ca(OCl)_2$ (13.1 g, 55 mmol) was added portionwise to this mixture with a vigorous stirring. Stirring was continued for an additional 10 min at 10–15 °C. Precipitates were filtered, and the combined filtrates and washings were washed with 5% sodium bisulfate, dried (Na_2SO_4), and concentrated. Purification of the crude products by distillation gave 7.66 g (90%) of undecanal (**4a**): bp 113 °C (9 mmHg).

Spectral data of some selected products listed in Table I are as follows.

2-Tetradecynal: bp 98–100 °C (0.2 mmHg) (lit.[28] bp 94–98 °C (0.3 mmHg)); IR (neat) 2740, 2282, 2204, 1673 (C=O), 1466, 1139; ^1H NMR (200 MHz) δ 0.88 (t, J = 6.5 Hz, 3, CH_3), 1.25 (br s, 16, CH_2), 1.52–1.63 (m, 2, CH_2), 2.40 (t, J = 7 Hz, 2, CH_2), 9.17 (t, J = 1 Hz, 1, CHO); ^{13}C NMR (50 MHz) δ 14.1, 19.1, 22.7, 27.5, 28.8, 29.0, 29.3, 29.4, 29.6 (2C), 31.9, 81.7, 99.4, 177.3.

5-Ethyl-3-formyl-2-methylpyridine: bp 115–117 °C (15 mmHg); IR (neat) 2740, 1692 (C=O), 1603, 1557, 1466, 1288, 1151, 1009, 729 cm^{-1}; ^1H NMR (500 MHz) δ 1.25 (t, J = 7.5 Hz, 3, CH_3), 2.68 (q, J = 7.5 Hz, 2, CH_2), 2.82 (s, 3, CH_3), 7.90 (s, 1, CH=C), 8.50 (s, 1, CH=C), 10.30 (s, 1, CHO); ^{13}C NMR (126 MHz) δ 15.28, 21.95, 25.66, 129.27, 137.29, 137.70, 153.31, 157.83, 191.83. Anal. Calcd for $C_9H_{11}NO$: C, 72.46; H, 7.43; N, 9.39. Found: C, 72.08; H, 7.21; N, 9.38.

2-(1-Hydroxycyclohexyl)propanal: IR (neat) 3426 (OH), 2738, 1719 (C=O) cm^{-1}; ^1H NMR (500 MHz) δ 1.13 (d, J = 7.0 Hz, 3, CH_3), 1.24 (m, 1, CH_2), 1.42 (m, 1, CH_2), 1.50–1.66 (m, 8, CH_2), 2.04 (s, 1, OH), 2.43 (m, 1, CHCO), 9.83 (d, J = 2 Hz, 1, CHO); ^{13}C NMR (126 MHz) δ 8.6, 21.4, 21.5, 25.5, 34.4, 36.2, 55.1, 72.8, 206.2. Anal. Calcd for $C_9H_{16}O_2$: C, 69.19; H, 10.32. Found: C, 68.81; H, 10.51.

(28) Wailes, P. C. *Aust. J. Chem.* **1959**, *12*, 173.

1-Acetoxy-2-dodecanone: mp 64–65 °C (from hexane); IR (KBr) 1754 (COO), 1725 (C=O), 1462, 1410, 1379, 1234, 1085, 1052, 1036 cm^{-1}; ^1H NMR (500 MHz) δ 0.87 (t, J = 7 Hz, 3, CH_3), 1.25, 1.27 (br, 14, CH_2), 1.57–1.64 (m, 2, CH_2), 2.16 (s, 3, OAc), 2.40 (t, J = 7.5 Hz, 2, CH_2CO), 4.64 (s, 2, CH_2O); ^{13}C NMR (126 MHz) δ 14.1, 20.5, 22.6, 23.3, 29.1, 29.26, 29.30, 29.40, 29.51, 31.9, 38.8, 67.9, 170.2, 204.0. Anal. Calcd for $C_{14}H_{26}O_3$: C, 69.38; H, 10.81. Found: C, 69.14; H, 11.22.

2-Acetoxycyclohexanone: bp 114–116 °C (9 mmHg) (lit.[29] bp 120–123 °C (12 mmHg)); IR (neat) 1748 (COO), 1727 (C=O), 1454, 1435, 1379, 1241, 1085, 1071 cm^{-1}; ^1H NMR (500 MHz) δ 1.56–1.65 (m, 1, CH_2), 1.66–1.80 (m, 2, CH_2), 1.96 (m, 1, CH_2), 2.05–2.11 (m, 1, CH_2), 2.15 (s, 3, OAc), 2.28 (m, 1, CH_2), 2.35–2.42 (m, 1, CH_2CO), 2.48–2.53 (m, 1, CH_2CO), 5.16 (m, 1, CHOAc); ^{13}C NMR (126 MHz) δ 20.7, 23.7, 27.1, 33.0, 40.7, 76.5, 170.0, 204.5.

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Registry No. **1a**, 3225-26-1; **3a**, 112-42-5; **3b**, 112-53-8; **4a**, 112-44-7; **4b**, 112-54-9; **5a**, 112-37-8; **6a**, 42231-61-8; **7a**, 1120-06-5; **7b**, 10203-32-4; **8a**, 112-12-9; **8b**, 6137-26-4; $NaBrO_2$, 7486-26-2; $Ca(OCl)_2$, 7778-54-3; $HgC(CH_2)_7OH$, 111-87-5; $H_3C(CH_2)_6CHO$, 124-13-0; $H_3C(CH_2)_{17}OH$, 112-92-5; $H_3C(CH_2)_{16}CHO$, 638-66-4; $H_3C(CH_2)_3CH(CH_2OH)CH_2CH_3$, 104-76-7; $H_3C(CH_2)_3CH(CHO)CH_2CH_3$, 123-05-7; $H_3C(CH_2)_{10}C{\equiv}CCH_2OH$, 51309-22-9; $H_3C(CH_2)_{10}C{\equiv}CCHO$, 101098-99-1; $C_6H_5(CH_2)_3OH$, 122-97-4; $C_6H_5(CH_2)_2CHO$, 104-53-0; $C_6H_5(CH_2)_2OH$, 60-12-8; $C_6H_5CH_2CHO$, 122-78-1; $C_6H_5CH_2OH$, 100-51-6; C_6H_5CHO, 100-52-7; 4-$MeOC_6H_4CH_2OH$, 105-13-5; 4-$MeOC_6H_4CHO$, 123-11-5; 4-$O_2NC_6H_4CH_2OH$, 619-73-8; 4-$O_2NC_6H_4CHO$, 555-16-8; $H_3C(CH_2)_2CH(OH)CH(CH_2OH)CH_2CH_3$, 94-96-2; $H_3C(CH_2)_2CH(OH)CH(CHO)CH_2CH_3$, 496-03-7; (2*R*,3*S*)-$H_3CCH(OH)CH(CH_2Ph)CH_2OH$, 124018-63-9; (2*R*,3*R*)-$H_3CCH(OH)CH(CH_2Ph)CHO$, 123903-26-4; $HO(CH_2)_4OH$, 110-63-4; $HO(CH_2)_3CH(OH)(CH_2)_5CH_3$, 37810-94-9; $HO(CH_2)_5OH$, 111-29-5; $HO(CH_2)_4CH(OH)(CH_2)_4CH_3$, 4203-48-9; $C_6H_5CH(OH)CH_3$, 98-85-1; $AcOCH_2CH(OH)(CH_2)_9CH_3$, 78209-66-2; $C_6H_5COCH_3$, 98-86-2; $AcOCH_2CO(CH_2)_9CH_3$, 123903-27-5; 7,7-dimethyl-2-(hydroxymethyl)bicyclo[3.1.1]heptane, 514-99-8; 7,7-dimethylbicyclo[3.1.1]heptan-2-al, 4764-14-1; 5-ethyl-3-(hydroxymethyl)-2-methylpyridine, 123903-23-1; 5-ethyl-3-formyl-2-methylpyridine, 123903-24-2; 2-(1-hydroxycyclohexan-1-yl)propanol, 90676-81-6; 2-(1-hydroxycyclohexan-1-yl)propanal, 123903-25-3; tetrahydrofuran-2-one, 96-48-0; 5-hexyltetrahydrofuran-2-one, 706-14-9; tetrahydropyran-2-one, 542-28-9; 6-pentyltetrahydropyran-2-one, 705-86-2; 4-*tert*-butylcyclohexanol, 98-52-2; 4-*tert*-butylcyclohexanone, 98-53-3; 2-acetoxycyclohexanol, 22241-34-5; 2-acetoxycyclohexanone, 17472-04-7.

Supplementary Material Available: Spectral data for 2-ethyl-3-hydroxyhexanal and (2*R*,3*R*)-3-benzyl-3-hydroxybutanal (5 pages). Ordering information is given on any current masthead page.

(29) Williamson, K. L.; Keller, R. T.; Fonken, G. S.; Szmuszkovicz, J.; Johnson, W. S. *J. Org. Chem.* **1962**, *27*, 1612.