Registry No. **3a**, 80958-57-2; **3b**, 83492-42-6; **4a**, 15544-47-5; **4b**, 67508-30-9; **4c**, 69762-22-7; **4d**, 81505-98-8; **4e**, 83492-49-3; **4f**, 83492-50-6; **4g**, 79130-37-3; **4h**, 79130-39-5; **6b**, 80958-64-1; **6c**, 80958-65-2; **6d**, 80958-66-3; **6e**, 80958-67-4; **6f**, 80958-68-5; **6g**, 80958-69-6; **7b**, 84944-16-1; **7c**, 84944-17-2; **7d**, 84944-18-3; **7e**, 84944-19-4; **7f**, 84944-20-7; **7g**, 84959-59-1; **7h**, 84944-21-8; **8**, 84944-22-9; 2′-hydroxy-3,4′-*O*-isopropylidenepyridoxine, 49797-82-2; 1,8-octanedithiol, 1191-62-4.

Supplementary Material Available: Infrared, ultraviolet, and mass spectral data for compounds **6b–g** and **7b–h** (3 pages). Ordering information is given on any current masthead page.

Oxidation of Primary and Secondary Alcohols by the Catalysis of Palladium

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Received August 10, 1982

Saturated and unsaturated secondary alcohols are oxidized to the corresponding ketones in good or excellent yields by using an aryl halide (phenyl bromide or mesityl bromide) as an oxidant and palladium(0) or -(II) as a catalyst (0.6–3 mol % relative to the alcohol) in the presence of a base (NaH or K_2CO_3). The similar oxidation of primary alcohols provides the corresponding aldehydes and/or esters. The aldehyde/ester selectivity is correlated to the steric and electronic features of substrates. The procedure is applied to the oxidation of 1-primary, ω-primary diols to lactones.

The oxidation of alcohols to the corresponding aldehydes and ketones is one of the most fundamental and important processes in organic synthesis. Accordingly, a variety of methods, which show a high chemoselectivity and/or compatibility with other functional groups, have been developed. Many of these necessitate the use of a stoichiometric or excess amount of heavy metals (e.g., Cr, Mn, etc.) or expensive oxidants (e.g., DCC, oxalyl chloride, NCS, etc.). From the economical and environmental points of view, the advantage of the metal-catalyzed oxidation is apparent,[1] and a considerable number of methods have been devised which utilize the catalysis of transition metals (e.g., Ni,[2] Pd,[3] Pt,[4] Ru,[5] etc.). These methods, however, seem to have some drawbacks in manipulation on a laboratory scale, in compatibility with other functionalities, or in their yields or conversions.

Almost at the same time, we[6] and Zask et al.[7] have recognized a novel type of reduction of aromatic halides by alcohols by the catalysis of palladium. In this context, we examined the oxidation of alcohols using aryl halide as an oxidant and palladium as a catalyst and found that a variety of primary and secondary alcohols could be oxidized to the corresponding aldehydes (and/or esters) and ketones, respectively, in good or excellent yields. In this paper, we describe the full scope and some mechanistic aspects of this oxidation reaction.[8]

Results and Discussion

Oxidation of alcohols with aryl halides (1.1–1.2 equiv) was usually carried out in the presence of 0.6–3 mol % of palladium catalyst and a base (1.0–1.1 equiv) in an appropriate anhydrous aprotic solvent under argon at the temperatures ranging from 50 to 120 °C. The reactions were followed mainly by means of VPC. Palladium(II) acetate and tetrakis(triphenylphosphine)palladium(0) are used as catalysts with almost equal efficiency. Triphenylphosphine is an effective cocatalyst, while 1,2-bis(diphenylphosphino)ethane is less effective, with which are suppressed the reaction rates and yields. The optimum amount of cocatalyst ranges from 2 to 4 equiv relative to the catalyst and is variable with the kinds of alcohols, especially in the cases of the unsaturated ones. Use of an excess amount of cocatalyst retards the reaction seriously. As a base, NaH [in tetrahydrofuran (THF) or *N*-methylpyrrolidone (NMP)] or K_2CO_3 [in *N*,*N*-dimethylformamide (DMF) or 1,2-dimethoxyethane (DME)] showed the satisfactory results. Triethylamine or sodium bicarbonate was completely ineffective. As an oxidizing agent, phenyl bromide was mostly employed, and in some special cases *o*-tolyl or mesityl bromide was used. A criterion for the choice of bases, oxidants, and solvents will be discussed elsewhere at the appropriate places.

Oxidation of Secondary Alcohols. The scope of the present procedure is indicated by the results summarized in Table I with 18 representative kinds of secondary alcohols, which might be classified into the saturated (entries 1–11) and unsaturated alcohols (entries 12–26). In most cases examined, the reactions reached 80–100% conversion within periods of 1–8 h, providing the corresponding ketones uniformly in good to excellent yields.

The rate of oxidation largely depends on the bases employed. For example, with triethylamine the oxidation of isoborneol did not proceed to any appreciable extent at 100 °C for 5 h, while with NaH it attained completion

(1) Sheldon, R. A.; Kochi, J. K. "Metal-Catalyzed Oxidations of Organic Compounds", Academic Press, New York, 1981.
(2) (a) Nakagawa, K.; Konaka, R.; Nakata, T. *J. Org. Chem.* **1962**, *27*, 1597. (b) Mitra, M. N.; Elliott, W. H. *Ibid.* **1968**, *33*, 175. (c) *Ibid.* **1968**, *33*, 2814. (d) Doyle, M. P.; Patrie, W. J.; Williams, S. B. *Ibid.* **1979**, *44*, 2955.
(3) (a) Lloyd, W. G. *J. Org. Chem.* **1967**, *32*, 2816. (b) Blackburn, T. F.; Schwartz, J. *J. Chem. Soc., Chem. Commun.* **1977**, 157.
(4) (a) Sneeden, R. P. A.; Turner, R. B. *J. Am. Chem. Soc.* **1955**, *77*, 190. (b) Karrer, P.; Hess, W. *Helv. Chim. Acta* **1957**, *40*, 265. (c) Heyns, K.; Paulsen, H. *Angew. Chem.* **1957**, *69*, 600. (d) Schamma, M.; Rodrignez, H. R. *Tetrahedron* **1968**, *24*, 6583.
(5) (a) Nakata, H. *Tetrahedron* **1963**, *19*, 1959. (b) Capnto, J. A.; Fuchs, R. *Tetrahedron Lett.* **1967**, 4729. (c) Moriarty, R. M.; Gopal, H.; Adams, T. *Ibid.* **1970**, 4003. (d) Rosenthal, A.; Sprinzl, M.; Baker, D. A. *Ibid.* **1970**, 4233. (e) Schroder, M.; Griffith, W. P. *J. Chem. Soc., Chem. Commun.* **1979**, 58. (f) Blum, Y.; Reshef, D.; Shvo, Y. *Tetrahedron Lett.* **1981**, *22*, 1541. (g) Murahashi, S.; Ito, K.; Naota, T.; Maeda, Y. *Ibid.* **1981**, *22*, 5327.
(6) Tamaru, Y.; Yamada, Y.; Yoshida, Z. *Tetrahedron* **1979**, *35*, 329.
(7) Zask, A.; Helquist, P. *J. Org. Chem.* **1978**, *43*, 1619.
(8) (a) Tamaru, Y.; Yamamoto, Y.; Yamada, Y.; Yoshida, Z. *Tetrahedron Lett.* **1979**, 1401. (b) Tamaru, Y.; Inoue, K.; Yamada, Y.; Yoshida, Z. *Ibid.* **1981**, *22*, 1801.

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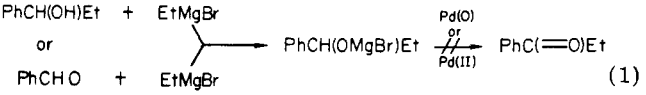
within 1.5 h at 70 °C (entry 8). With K_2CO_3 higher temperatures and prolonged reaction times are generally required for completion of the reaction (entry 9). The oxidation of isoborneol with NaH as a base proceeded about 50 times faster than that with K_2CO_3 as a base (see Experimental Section). Despite its low reactivity, K_2CO_3 is the base of choice for the oxidation of the saturated alcohols, because NaH, in some instances, causes serious depression of yields mainly owing to an aldol condensation of products: 4-methylcyclohexanol (cis/trans mixture) was oxidized to give 4-methylcyclohexanone in 73% yield together with a condensation product, 2-(4-methylcyclohexeny)-4-methylcyclohexanone, in 20% yield (entries 4 and 5).

The efficiency of Grignard reagent as a base was examined in order to explore the one-pot alkylation method of the carbonyl carbon of the aldehyde (umpolung), but unfortunately no oxidation of magnesium alkoxide took place, and the alcohol was recovered (eq 1). The lithium alk-



(1)

oxides, prepared by the reactions of benzaldehyde with *n*-butyl-, *sec*-butyl-, and phenyllithiums, were oxidized sluggishly and provided the ketones in low yields [1 mol % of $Pd(OAc)_2$, 3 mol % of Ph_3P, and 1.1 equiv of PhBr in refluxing DME; *n*-butyl phenyl ketone in 53% yield at 96% conversion (5 h), *sec*-butyl phenyl ketone in 31% yield at 65% conversion (2.5 h), benzophenone in 76% yield at 77% conversion (7 h)].

The oxidation of (3-cyclohexenyl)-*n*-butylmethanol (1) with phenyl bromide–K_2CO_3 in DMF provided the expected ketone only in 24% VPC yield at a 76% conversion (entry 16). The rest of the products consisted of an intractable mixture of phenylated ketones and alcohols.[9] Under similar conditions and with mesityl bromide instead of phenyl bromide, the expected ketone was obtained in 70% yield (entry 15). Interestingly, the combination of phenyl bromide–NaH showed the most satisfactory results, giving the ketone in 81% yield (entry 14). No or only a trace of arylated products was discernible by a VPC analysis of the reaction mixture. For the oxidation of isopulegol (**2**), however, the PhBr–NaH–THF system proved to be completely ineffective, providing a mixture of arylated products as a main portion. No significant improvement was observed by the use of *o*-tolyl bromide–NaH (entry 18). Mesityl bromide was found to be by far the most satisfactory oxidant, and with this was produced pulegone in an almost quantitative yield (entry 17).

The effects of the bases and oxidants on the oxidation/arylation selectivities mentioned above might be rationalized by the following sequential reactions. The intermediate **3**, generated by an oxidative addition of Pd(0) species to aryl bromide (eq 2), reacts either with a hydroxyl

$$Pd^0(Ph_3P)_n + ArBr \xrightarrow{-Ph_3P} \underset{\mathbf{3}}{ArPd(Br)(Ph_3P)_2} \quad (2)$$

$$3 + RR'CHOM \rightarrow \underset{\mathbf{4}}{RR'CHOPd(Ar)(Ph_3P)_2} + MBr \quad (3)$$

$$4 \rightarrow RR'C{=}O + \underset{\mathbf{5}}{HPd(Ar)(Ph_3P)_2} \quad (4)$$

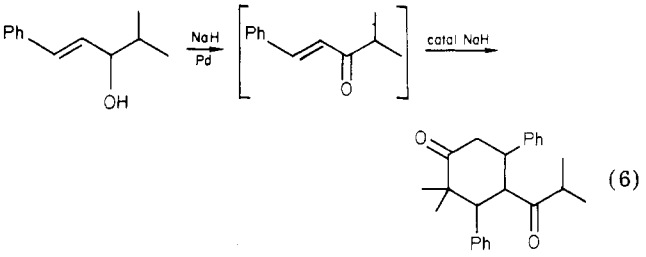
$$5 \xrightarrow{+Ph_3P} Pd^0(Ph_3P)_n + ArH \quad (5)$$

M = H, Li, Na, K, or MgBr

group (or metal alkoxide, eq 3) or olefins to provide alkoxypalladium species (**4**) or β-arylated alkylpalladium species, respectively. The diminished reactivity of magnesium and lithium alkoxides might be attributed to their low ability for the transmetalation with **3** (eq 3, M = Li or Mg). The ineffectiveness of triethylamine or $NaHCO_3$ as a base might be explained in a similar sense. The striking effects exerted by NaH on the oxidation–arylation selectivities (cf. entries 14 and 16) might stem from a kinetic preference of the process of eq 3 (M = Na) over the arylation of olefins. The thus formed alkoxypalladium species **4** might be destined to undergo a β-hydrogen elimination to provide ketone and arylhydridopalladium species (**5**, eq 4).[10-13] In the case of isopulegol (**2**), however, the alkoxypalladium **4** might react in two fashions: the β-hydrogen elimination to give ketone (eq 4) and the arylation of the double bond, which locates at a suitable position for an intramolecular arylation (e.g., entry 18). The result in entry 17 clearly indicates the minimization of this arylation by the use of mesityl bromide.

The amounts of triphenylphosphine were found to be another crucial factor for the successful oxidation of unsaturated secondary alcohols: with 2 equiv (relative to palladium(II) acetate) the oxidation of **2** proceeded smoothly and attained completion within 1 h (entry 17), while with 1 or 4 equiv the oxidation became very sluggish (ca. 10% conversion after 1 h at 50 °C, mesityl bromide–NaH in THF).

On the basis of the results obtained for the alcohols **1** and **2**, the oxidation of other unsaturated secondary alcohols was undertaken mostly by employing mesityl bromide–K_2CO_3 or NaH in the presence of 2 equiv of triphenylphosphine (relative to Pd, entries 12–26). Here again was observed a base-catalyzed dimerization of ketone when NaH was used as a base (eq 6): isopropyl 3,3-di-



(6)

methyl-2,6-diphenyl-4-oxocyclohexyl ketone was isolated as a solid in 80% yield on an oxidation of isopropylstyrylmethanol (entry 23), while the dimerization could be minimized by the use of K_2CO_3 (entry 22).

Among the alcohols examined, cholesterol was exceptionally reluctant, and the reaction ceased essentially at ca. 40% conversion on using phenyl, *p*-methoxyphenyl, *p*-chlorophenyl, or *o*-tolyl bromide (entry 26). Only with

(9) (a) Melpolder, J. B.; Heck, R. F. *J. Org. Chem.* **1976**, *41*, 265. (b) Chalk, A. J.; Magennis, S. A. *Ibid.* **1976**, *41*, 273. (c) Tamaru, Y.; Yamada, Y.; Yoshida, Z. *Ibid.* **1978**, *43*, 3396.

(10) Yoshida, T.; Okano, T.; Otsuka, S. *J. Chem. Soc., Dalton Trans.* **1976**, 993.

(11) The dependence of the present oxidation rates on the counterions (K, Na > Li ≫ Mg) shows an apparent correlation with the bond energies of the H–CRR'OM bonds, which decrease with increasing alkali metal electronegativity (K > Na > Li),[12] and hence another mechanism, pointed out by referee, involving the oxidative addition of **3** to the H–CRR'OM bond[13] also seems probable. Although this and the mechanism shown in eq 4 cannot be discriminated at present, we prefer the latter, only because there are no precedents of the oxidative addition of **3** to the nonallylic C–H bond.

(12) (a) Steigerwald, M. L.; Goddard, W. A., III.; Evans, D. A. *J. Am. Chem. Soc.* **1979**, *101*, 1994. (b) Harada, T.; Oku, A. *Ibid.* **1981**, *103*, 5965 and references cited therein.

(13) Smadja, W.; Czernecki, S.; Ville, G.; Georgoulis, C. *Tetrahedron Lett.* **1981**, *22*, 2479.

Table I. Palladium-Catalyzed Oxidation of Secondary Alcohols[a]

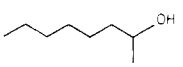
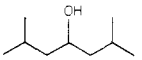
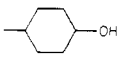
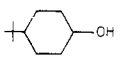
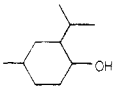
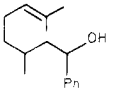
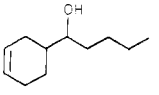
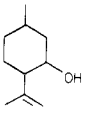
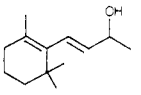
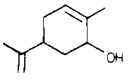
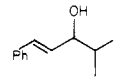
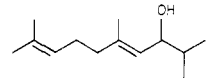
entry	alcohol	catalyst[b] (mol %)	oxid[c]	base	solv[d]	temp, °C	time, h	conv, %	yield,[e] %
1		Tet (1.0)	Ph	K_2CO_3	DMF	110	4.5	84	100
2		Tet (1.0)	Ph	K_2CO_3	DMF	120	6.0	80	92
3		Tet (0.8)	Ph	K_2CO_3	DMF	110	7.5	95	95
4	 I	Tet (1.0)	Ph	K_2CO_3	DMF	110	7.0	86	88
5	I	Pal (0.67), Dip (1.34)	Ph	NaH	DMF	70	3.0	90	73[f]
6		Tet (0.7)	Ph	NaH	THF	50	4.0	95	95
7		Tet (1.0)	Ph	NaH	DMF	50	2.5	95	77
8	 II	Pal (0.67), Tri (1.34)	Ph	NaH	NMP	70	1.5	100	(93)
9	II	Tet (1.3)	Ph	K_2CO_3	NMP	110	3.0	100	(100)
10		Tet (1.3)	Ph	K_2CO_3	NMP	120	8.0	90	(85)
11	$CH_3(CH_2)_5CH(OH)(CH_2)_{10}CO_2H$	Tet (1.3)	Ph	K_2CO_3	DMF	110	8.0	78	78
12	 III	Pal (1.3), Tri (5.2)	Ph	NaH	NMP	70	5.0	95	91
13	III	Pal (1.3), Dip (2.6)	Ph	NaH	NMP	70	5.0	77	73
14	 IV	Pal (3.0), Tri (6.0)	Ph	NaH	THF	50	2.0	97	81
15	IV	Pal (3.0), Tri (6.0)	Mes	K_2CO_3	DMF	100	5.2	85	70
16	IV	Pal (3.0), Tri (6.0)	Ph	K_2CO_3	DMF	90	5.0	76	(24)[g]
17	 V	Pal (3.0), Tri (6.0)	Mes	NaH	THF	50	1.0	99	99
18	V	Pal (3.0), Tri (6.0)	Tol	NaH	THF	50	3.0	92	(37)[g]
19		Pal (3.0), Tri (6.0)	Mes	K_2CO_3	DMF	105	6.0	88	77
20		Pal (3.0), Tri (6.0)	Mes	K_2CO_3	DMF	100	7.5	86	65
21		Pal (3.0), Tri (6.0)	Mes	K_2CO_3	DMF	100	5.5	98	90

Table I (*Continued*)

entry	alcohol	catalyst[b] (mol %)	oxid[c]	base	solv[d]	temp, °C	time, h	conv, %	yield,[e] %
22	 VI	Pal (3.0), Tri (6.0)	Mes	K_2CO_3	DMF	100	2.5	100	66
23	VI	Pal (3.0), Tri (6.0)	Tol	NaH	THF	50	3.5	100	80[h]
24		Pal (3.0), Tri (6.0)	Ph	NaH	THF	50	4.0	93	75
25	cholesterol	Pal (3.0), Tri (6.0)	Mes	K_2CO_3	DMF	120	20	~92	98[i]
26	cholesterol	Pal (3.0), Tri (6.0)	Ph	K_2CO_3	DMF	120	20	~40	

[a] For the details of the procedure, see the Experimental Section. [b] The abbreviations Tet, Pal, Dip, and Tri are meant to refer to tetrakis(triphenylphosphine)palladium, palladium acetate, 1,2-bis(diphenylphosphino)ethane, and triphenylphosphine respectively. [c] Ph, Mes, and Tol are meant to refer to phenyl bromide, mestiyl bromide, and *o*-tolyl bromide, respectively. [d] DMF, NMP, and THF are meant to refer to *N,N*-dimethylformamide, *N*-methylpyrrolidone, and tetrahydrofuran, respectively. [e] The yield is based on the isolated ketone, corrected for the conversion. The value in parentheses is the VPC yield. [f] In addition to 4-methylcyclohexanone (73% yield), 2-(4-methylcyclohexenyl)-4-methylcyclohexanone is isolated in 20% yield. [g] In addition to the expected ketone, many peaks with the longer retention times (due to arylated alcohols and ketones) are observed on VPC. [h] The base-catalyzed dimerization product (isopropyl 3,3-dimethyl-2,6-diphenyl-4-oxocyclohexyl ketone) was obtained as a solid in 80% yield. [i] 4-Cholesten-3-one was isolated as a sole product.

mesityl bromide did the reaction attain completion, though it required an exceptionally prolonged reaction time and an elevated temperature (entry 25). The effect of mesityl bromide in this case might be attributed to the steric acceleration of the β-hydrogen elimination from the alkoxypalladium intermediate **4** (Ar = 2,4,6-trimethylphenyl, eq 4). This explanation seems to be supported by the enhanced reactivity of isoborneol compared with borneol.[14] The oxidation of these alcohols followed well first-order kinetics, and the relative oxidation rate of isoborneol to borneol was found to be as high as 11.4 at 30 °C (see Experimental Section).

Oxidation of Primary Alcohols. The oxidation of primary alcohols was undertaken under conditions similar to those applied to the oxidation of the secondary ones, mostly by employing the phenyl bromide or mesityl bromide/K_2CO_3/DME system. All the alcohols examined were oxidized to the corresponding aldehydes and/or esters in good or excellent yields and with similar ease to the secondary alcohols (eq 7, Table II). Especially rewarding

$$RCH_2OH \rightarrow RCHO \text{ and/or } RCO_2CH_2R \qquad (7)$$

is that the oxidation can accommodate a variety of substituents on the aromatic nuclei, except for a nitro group (entries 1–8, Table II). In the oxidation of *p*-nitrobenzyl alcohol under conditions similar to those of entries 1–8, *p*-nitrobenzaldehyde was obtained in only 45% VPC yield, despite the apparent cleanness of the reaction. The low yield might be attributed partly to a redox reaction between a nitro group and triphenylphosphine.

On examination of Table II there seems to exist the following general correlation between the selectivity (aldehyde vs. ester formation) and steric and electronic features of substrates. (1) The saturated primary alcohols are prone to be oxidized to esters (entries 13–19). (2) By increasing the size of the substituents at the positions β and γ to the hydroxyl group, the population of aldehydes gradually becomes larger and finally reaches a complete reversal of selectivity to provide aldehyde exclusively as observed in the oxidation of 2,3-dimethyl-2-(*p*-chlorophenyl)-1-butanol (entries 20 and 21). (3) The α,β-unsaturated alcohols (allyl alcohols and benzyl alcohols with electron-donating substituents) are oxidized to the corresponding aldehydes selectively (entries 1–5 and 10–12). (4) The benzyl alcohols substituted with the electron-withdrawing groups are oxidized to give a mixture of aldehydes and esters, the latter in an increasing proportion with an increase of the electron-withdrawing ability of substituents (entries 6–8).

The above observations might be rationalized by a mechanism which involves the oxidation of a hemiacetal (**7**).[5g] A mechanism involving the Tischenko-type ester-

$$3 + RCH_2OM \rightarrow \underset{\mathbf{6}}{RCH_2OPd(Ar)(Ph_3P)_2} + MBr \qquad (8)$$

$$6 \rightarrow RCHO + \underset{\mathbf{5}}{HPd(Ar)(Ph_3P)_2} \qquad (9)$$

$$RCH_2OM + RCHO \rightleftarrows \underset{\mathbf{7}}{RCH(OM)OCH_2R} \qquad (10)$$

$$7 + 3 \rightarrow RCH(OPd(Ar)(Ph_3P)_2)OCH_2R + \underset{\mathbf{8}}{MBr} \qquad (11)$$

$$8 \rightarrow RCO_2CH_2R + 5 \qquad (12)$$

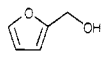
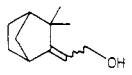
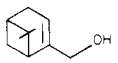
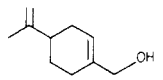
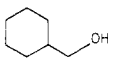
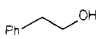
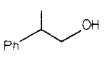
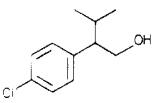
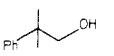
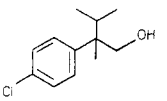
M = H, Na, or K

ification[15] was ruled out by the fact that no *p*-cyanobenzyl *p*-cyanobenzoate was formed from *p*-cyanobenzaldehyde under the oxidation conditions (cf. entry 8). In the equilibrium 10, the primary alcohols with bulky substituents at the β-position to a hydroxyl group might favor the left-hand side due to steric congestion in hemiacetal **7**, and hence the further oxidation to the esters might be suppressed (entries 17–21). In the cases of allyl and benzyl alcohols with electron-donating substituents, the equilibrium 10 might also lie heavily on the left-hand side because of the kinetic stability of the conjugated aldehyde toward a nucleophilic attack of alcohol (or alkoxide). The ester formation for the benzyl alcohols with the electron-withdrawing substituents might be explained by a similar analogy. As can be observed in entries 18 and 20, the

(14) Iwamura, J. *Nippon Kagaku Kaishi* **1977**, 1003.

(15) Ito, I.; Horino, H.; Koshiro, Y.; Yamamoto, A. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 504 and references cited therein.

Table II. Palladium-Catalyzed Oxidation of Primary Alcohols

entry	alcohol[c]	catalyst[a] (mol %)	oxid[a]	base[a]	solv[a]	temp, °C	time, h	conv, %	yield,[b] %	aldehyde/ester product ratio
1	*p*-OCH_3BzylOH	Pal (1.0), Tri (3.0)	Mes	K_2CO_3	DME	85	12	99	(95)	100:0
2	*o*-OHBzylOH	Pal (1.0), Tri (3.0)	Mes	K_2CO_3	DME	85	12	80	(79)	100:0
3	*p*-CH_3BzylOH	Pal (1.0), Tri (3.0)	Mes	K_2CO_3	DME	85	10	100	(96)	100:0
4	*m*-CH_3BzylOH	Pal (1.0), Tri (3.0)	Mes	K_2CO_3	DME	85	12	100	(96)	100:0
5	*o*-CH_3BzylOH	Pal (1.0), Tri (3.0)	Mes	K_2CO_3	DME	85	12	100	(94)	100:0
6	HBzylOH	Pal (1.0), Tri (3.0)	Mes	K_2CO_3	DME	85	12	96	(99)	94:6
7	*p*-ClBzylOH	Pal (1.0), Tri (3.0)	Mes	K_2CO_3	DME	85	10	97	(100)	84:16
8	*p*-CNBzylOH	Pal (1.0), Tri (3.0)	Mes	K_2CO_3	DME	85	12	84	(91)	55:45
9		Pal (1.0), Tri (3.0)	Mes	K_2CO_3	DME	85	12	80	(87)	96:4
10		Tet (0.6)	Ph	NaH	THF	50	3	98	100	100:0
11		Pal (1.6), Tri (3.0)	Ph	NaH	THF	65	1	95	100	100:0
12		Pal (1.0), Tri (3.0)	Mes	K_2CO_3	DME	85	12	96	(92)	100:0
13	*n*-C_8H_{17}OH	Pal (1.0), Tri (3.0)	Ph	K_2CO_3	DME	85	12	84	73	0:100
14		Pal (1.0), Tri (3.0)	Ph	K_2CO_3	DME	85	12	82	81	0:100
15		Pal (1.0), Tri (3.0)	Ph	K_2CO_3	DME	85	12	95	93	0:100
16		Pal (1.0), Tri (3.0)	Ph	K_2CO_3	DME	85	12	95	93	0:100
17	 I	Pal (1.0), Tri (3.0)	Ph	K_2CO_3	DME	85	12	99	89	12:88
18	I	Pal (1.0), Tri (3.0)	Mes	K_2CO_3	DME	85	12	93	85	42:58
19	 II	Pal (1.0), Tri (3.0)	Ph	K_2CO_3	DME	85	10	93	74	13:87
20	II	Pal (1.0), Tri (3.0)	Mes	K_2CO_3	DME	85	10	84	61	80:20
21		Pal (1.0), Tri (3.0)	Ph	K_2CO_3	DME	85	12	87	87	100:0

[a] For the abbreviations, see the footnotes of Table I. [b] The yield is based on isolated product(s), corrected for the recovered alcohol. The value in parentheses is the VPC yield. [c] BzylOH = benzyl alcohol.

increased selectivity of aldehyde formation by the use of mesityl bromide compared with phenyl bromide might be rationalized as a result of the steric acceleration of process 9 and steric deceleration of process 11.

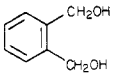
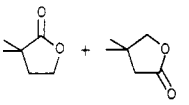
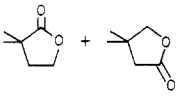
The present procedure was applied to an oxidation of 1-primary, ω-primary diols. Results together with the reaction conditions are summarized in Table III. In every case, the yield of lactone was satisfactory. Despite our expectation of the selective oxidation of the sterically hindered hydroxyl group (vide supra), only moderate chemoselectivities were observed for the oxidation of unsymmetric diols.[16]

Experimental Section

Melting points were determined in capillary tubes with a Büchi apparatus and are not corrected. Unless otherwise indicated, short-path (bulb-to-bulb) distillations were carried out in a Kugelrohr apparatus. Microanalyses were performed by the Microanalysis Center of Kyoto University. Analyses agreed with calculated values within ±0.3% unless otherwise noted. Infrared spectra were measured with a Hitachi Model EPI-G3 grating

(16) Partial support from the Ministry of Education, the Japanese Government (Grants in Aid for Special Project Research No. 56 109 008 and for Scientific Research C No 56 550 588), is gratefully acknowledged.

Table III. Palladium-Catalyzed Oxidative Lactonization of 1-Primary,ω-Primary Diols[a]

entry	1,ω-diol	oxidant[b]	time, h	conv, %	product(s), ratio (yield, %)
1	$HO(CH_2)_4OH$	Ph	12	74.0	 (100)[c]
2		Ph	12	100	 (90.2)[d]
3	$HOCH_2C(CH_3)_2(CH_2)_2OH$	Ph	10	98.7	 70:30 (89.7)[d]
4	$HOCH_2C(CH_3)_2(CH_2)_3OH$	Ph	12	93.7	 62:38 (88.4)[d]
5	$HOCH_2C(CH_3)_2(CH_2)_3OH$	Mes	12	97.4	*e*, 61:39

[a] The usual scale is as follows: diol (2.0 mmol), oxidant (4.2 mmol), $Pd(OAc)_2$ (0.04 mmol), $P(Ph)_3$ (0.12 mmol), K_2CO_3 (4.2 mmol) in 8 mL of 1,2-dimethoxyethane. All the reactions are carried out at 85 °C under argon. [b] Ph and Mes are meant to refer to phenyl bromide and mesityl bromide, respectively. [c] VPC yield, based on conversion. [d] Isolated yield, based on conversion. [e] Same products as entry 4.

spectrophotometer. Proton magnetic resonance (^1H NMR) spectra were determined either at 60 MHz on a JEOL JNM-PMX 60 instrument or at 100 MHz on a Varian HA-100 instrument with tetramethylsilane as an internal standard. Mass spectra were measured either on a Hitachi Model RMU 6C instrument or on a JEOL JMS-OISG-2 instrument (high-resolution mass spectrophotometer).

Solvents and Reagents. Dimethylformamide (DMF), *N*-methylpyrrolidone (NMP), and dimethoxyethane (DME) were dried over CaH_2, and tetrahydrofuran was dried (THF) over sodium/benzophenone. All solvents were distilled and kept under an argon atmosphere. Aryl bromides were dried over CaH_2. Bromomesitylene was prepared according to the literature.[17]

Alcohols. Commercially available alcohols (entries 1–11, 17, 18, 21, 25, and 26 in Table I, entries 1, 3–7, 9–16, and 22 in Table II, and entry 1 in Table III) were used directly without further purification. The other alcohols were prepared according to the standard methods. 1-Phenyl-3,7-dimethyl-6-octen-1-ol (entries 12 and 13, Table I), butyl(3-cyclohexenyl)carbinol (entries 14–16, Table I), 1-phenyl-4-methyl-1-penten-3-ol (entries 22 and 23, Table I), and 2,5,9-trimethyl-4,8-decadien-3-ol (entry 24, Table I) were prepared by the reactions of citronellal with PhMgBr in ether, 3-cyclohexene-1-carboxaldehyde with *n*-BuLi in ether, cinnamaldehyde with *i*-PrMgBr in ether, and citral with *i*-PrMgBr in ether, respectively. 1-(2,6,6-Trimethyl-1-cyclohexenyl)-1-buten-3-ol (entry 19, Table I) and 3,5,5-trimethyl-2-cyclohexen-1-ol (entry 20, Table I) were synthesized by the $LiAlH_4$ reductions of β-ionone and isophorone in ether, respectively. 2-Hydroxybenzyl alcohol (entry 2, Table II) and 4-cyanobenzyl alcohol were prepared by the reduction of the corresponding aldehydes with $LiAlH_4$ in ether and with $NaBH_4$ in ethanol, respectively. 2-(4-Chlorophenyl)-isovaleryl chloride was converted to 2-(4-chlorophenyl)-3-methyl-1-butanol (entry 17, Table II) and 2-(4-chlorophenyl)-2,3-dimethyl-1-butanol (entry 21, Table II) by reduction with $LiAlH_4$ in ether and by (i) $MeOH/Et_3N$, (ii) LDA in THF at −78 °C and then MeI, and (iii) $LiAlH_4$ in ether, respectively. 2,2-Dimethyl-1,4-butanediol (entry 3, Table III), 1,2-bis(hydroxymethyl)benzene (entry 2, Table III), and 2,2-dimethyl-1,5-pentanediol were prepared by the reductions of the corresponding diesters or anhydrides with $LiAlH_4$ in ether.

General Procedure for Oxidation of Alcohols. Into an argon-purged mixture of palladium (0 or II) (0.6–3 mol %), cocatalyst, and base (2.2 mmol) was added a mixture of alcohol (2 mmol) and aryl bromide (2.2–2.4 mmol) in an anhydrous solvent (2 mL) by means of a syringe at an ambient temperature. This slurry mixture was stirred and heated at the temperatures indicated in Tables I–III. The reaction was monitored by VPC. After the reaction was complete or ceased, the mixture was poured into water and extracted twice with ether (20 + 10 mL). The combined ether extracts were washed with saturated NaCl and dried over $MgSO_4$. Evaporation of the solvent and subsequent purification (Kugelrohr distillation, column chromatography on silica gel, or preparative VPC) provided the spectroscopically pure materials in the yields given in Tables I–III. The VPC yields were determined by using biphenyl or diphenylmethane as an internal standard. The spectral and analytical data of the new compounds are as follows.

Phenyl 2,2-dimethyl-5-heptenyl ketone (entries 12, 13, Table I): bp 155 °C (1.5 mmHg); IR (neat film) 1685 (vs), 750 (s), 690 (s) cm^{-1}; NMR δ ($CDCl_3$) 0.97 (3 H, d, J = 6.6 Hz), 1.23–2.56 (5 H, m), 1.62 (3 H, s), 1.69 (3 H, s), 2.74–3.03 (2 H, m), 5.15 (1 H, br t, J = 7.0 Hz), 7.30–8.15 (5 H, m); mass spectrum, m/e (relative intensity) 230 (28.1), 147 (100), 105 (92.6). Anal. Calcd for $C_{16}H_{22}O$: C, 83.43; H, 9.63. Found: C, 83.44; H, 9.65.

Butyl 3-cyclohexenyl ketone (entries 14–16, Table I): bp 160 °C (0.6 mmHg); IR (neat film) 1700 (s), 1650 (m) cm^{-1}; NMR δ (CCl_4) 0.80–2.87 (16 H, m), 5.77 (2 H, br s); mass spectrum, m/e 166 (M^+). Anal. Calcd for $C_{11}H_{18}O$: C, 79.47; H, 10.91. Found: C, 79.57; H, 11.09.

Isopropyl 3,3-dimethyl-2,6-diphenyl-4-oxocyclohexyl ketone (entry 23, Table I): mp 180.5–181.0 °C; IR (KBr) 1780 (s), 1690 (s), 710 (m), 700 (m) cm^{-1}; NMR δ ($CDCl_3$) 0.37 (3 H, d, J = 6.0 Hz), 0.40 (3 H, d, J = 6.0 Hz), 1.03 (3 H, s), 1.37 (3 H, s), 1.93 (1 H, septet, J = 6.0 Hz), 2.60–4.10 (5 H, m), 7.02–7.42 (10 H, m); mass spectrum, m/e 348 (M^+). Anal. Calcd for $C_{24}H_{28}O_2$: C, 82.72; H, 8.10. Found: C, 82.74; H, 8.13.

Isopropyl 2,6-dimethyl-1,5-heptadienyl ketone (entry 24, Table I): bp 190 °C (4 mmHg); IR (neat film) 1680 (s), 1620 (s), 1380 (m) cm^{-1}; NMR δ (CCl_4) 1.07 (6 H, d, J = 7.0 Hz), 1.63 (3 H, s), 1.73 (3 H, s), 2.56 (1 H, septet, J = 7.0 Hz), 5.10 (1 H, br), 6.06 (1 H, br); mass spectrum, m/e 194 (M^+). Anal. Calcd for $C_{13}H_{22}O$: C, 80.35; H, 11.41. Found: C, 80.06; H, 11.66.

4-Chlorobenzyl 4-chlorobenzoate (entry 7, Table II): mp 173–175 °C; IR (KBr) 1715 (vs), 810 (s), 755 (s); NMR δ ($CDCl_3$) 5.30 (2 H, s), 7.33 (4 H, s), 7.23–7.57, 7.83–8.17 (4 H, AA'BB' system); mass spectrum, m/e (relative intensity) 284 (11.5), 282 (66.6), 280 (100), 141 (100), 139 (100) (agreed with the authentic sample, prepared from 4-chlorobenzoyl chloride and 4-chlorobenzyl alcohol).

4-Cyanobenzyl 4-cyanobenzoate (entry 8, Table II): mp 120–121 °C; IR (KBr) 1726 (vs), 1270 (vs), 815 (s), 765 (s) cm^{-1};

(17) "Organic Syntheses"; Wiley, New York, 1943; Collect. Vol. II, p 95.

NMR δ ($CDCl_3$) 5.49 (2 H, s), 7.53–7.95 (6 H, m), 8.07–8.33 (2 H, m); mass spectrum, *m/e* (relative intensity) 263 (19.6), 262 (91.5), 130 (100), 116 (100) (agreed with the authentic sample, prepared from 4-cyanobenzoyl chloride and 4-cyanobenzyl alcohol).

2-Phenylpropyl 2-phenylpropionate (entry 16, Table II): bp 195 °C (0.8 mmHg); IR (neat film) 1730 (vs), 1605 (m), 1165 (s), 695 (s) cm^{-1}; NMR δ (CCl_4) 1.15 (3 H, d, J = 7.2 Hz), 1.42 (3 H, d, J = 7.2 Hz), 2.97 (1 H, q, J = 7.2 Hz), 3.61 (1 H, q, J = 7.2 Hz), 4.00–4.26 (2 H, m), 6.96–7.42 (10 H, br); mass spectrum, *m/e* (relative intensity) 268 (0.4), 119 (100), 118 (100). Anal. Calcd for $C_{18}H_{20}O_2$: C, 80.56; H, 7.51. Found: C, 80.80; H, 7.51.

2-(4-Chlorophenyl)-3-methylbutyraldehyde (entries 17 and 18, Table II): bp 145 °C (5 mmHg); IR (neat film) 2820 (w), 2710 (w), 1725 (vs), 820 (s) cm^{-1}; NMR δ (CCl_4) 0.74 (3 H, d, J = 6.6 Hz), 1.01 (3 H, d, J = 6.5 Hz), 1.91–2.80 (1 H, m), 3.14 (1 H, dd, J = 9.2, 3.0 Hz), 6.97–7.44 (4 H, m), 9.62 (1 H, d, J = 3.0 Hz); mass spectrum, *m/e* (relative intensity) 198 (2.55), 196 (8.57), 169 (24.7), 167 (71.7), 127 (33.8), 125 (100). Anal. Calcd for $C_{11}H_{13}OCl$: C, 67.18; H, 6.66; O, 8.13. Found: C, 67.17; H, 6.80; O, 8.41.

2-(4-Chlorophenyl)-3-methylbutyl 2-(4-chlorophenyl)-3-methylbutyrate (entries 17 and 18, Table II): bp 230 °C (0.2 mmHg); IR (neat film) 1734 (vs), 1495 (s), 820 (s) cm^{-1}; NMR δ (CCl_4) 0.53–1.07 (12 H, m), 1.47–2.77 (3 H, m), 2.91 (1 H, d, J = 10 Hz), 4.28 (2 H, d, J = 6.6 Hz), 6.77–7.33 (8 H, m); mass spectrum, *m/e* (relative intensity) 394 (0.01), 392 (0.02), 351 (0.37), 349 (0.54), 182 (100), 180 (100). Anal. Calcd for $C_{22}H_{26}O_2Cl_2$: C, 67.18; H, 6.66; Cl, 18.11. Found: C, 66.96; H, 6.61; Cl, 18.03.

2-Methyl-2-phenylpropionaldehyde (entries 19 and 20, Table II): bp 150 °C (10 mmHg); IR (neat film) 2820 (w), 2720 (w), 1725 (vs), 700 (s) cm^{-1}; NMR δ (CCl_4) 1.40 (6 H, s), 7.23 (5 H, br s), 9.41 (1 H, s); mass spectrum, *m/e* (relative intensity) 148 (0.99), 121 (23.4), 119 (100), 91 (45.7). Anal. Calcd for $C_{10}H_{12}O$: C, 81.04; H, 8.16. Found: C, 81.11; H, 8.37.

2-Methyl-2-phenylpropyl 2-methyl-2-phenylpropionate (entries 19 and 20, Table II): bp 190 °C (0.3 mmHg); IR (neat film) 1728 (vs), 1150 (s), 695 (ms) cm^{-1}; NMR δ (CCl_4) 1.20 (6 H, s), 1.46 (6 H, s), 4.06 (2 H, s), 7.20 (10 H, s); mass spectrum, *m/e* (relative intensity) 296 (3.6), 132 (33.1), 119 (100). Anal. Calcd for $C_{20}H_{24}O_2$: C, 81.04; H, 8.16. Found: C, 81.06; H, 8.34.

2-(4-Chlorophenyl)-2,3-dimethylbutyraldehyde (entry 21, Table II): bp 140 °C (0.3 mmHg); IR (neat film) 2800 (w), 2700 (w), 1725 (vs), 820 (m) cm^{-1}; NMR δ (CCl_4) 0.67 (3 H, d, J = 7.0 Hz), 0.92 (3 H, d, J = 6.8 Hz), 1.34 (3 H, s), 2.50 (1 H, septet, J = 7.0 Hz), 7.27 (4 H, br s), 9.45 (1 H, s); mass spectrum, *m/e* (relative intensity) 212 (1.2), 210 (4.0), 183 (47.2), 181 (100), 127 (43.7), 125 (98.5). Anal. Calcd for $C_{12}H_{15}OCl$: C, 68.41; H, 7.18; O, 7.59. Found: C, 68.71; H, 7.15; O, 7.29.

Competition Reactions. Borneol (3.0 mmol), isoborneol (3.0 mmol), bromobenzene (6.6 mmol), β-methylnaphthalene (1.5 mmol, an internal standard), NaH (7 mmol), $Pd(Ph_3P)_4$ (0.06 mmol), and DMF (5 mL) were charged in an argon purged flask at 0 °C. After subsidence of the foaming, the flask was immersed in a temperature-controlled bath. Aliquots (1–2 μL) were sampled at appropriate intervals and subjected directly to VPC analysis. The amounts of decrease of alcohols and increase of ketones showed a good balance. The reaction obeyed good first-order kinetics up to more than 90% reaction of isoborneol. The relative rates of oxidation of isoborneol to borneol were calculated by the least-squares method to be 11.2 (30 °C), 10.6 (40 °C), and 10.0 (50 °C). The competition reaction using K_2CO_3 as a base was carried out similarly. The relative oxidation rate of isoborneol to borneol was 2.2 at 110 °C.

Registry No. Phenyl bromide, 108-86-1; mesityl bromide, 576-83-0; *o*-tolyl bromide, 95-46-5; tetrakis(triphenylphosphine)palladium, 14221-01-3; palladium acetate, 3375-31-3; 1,2-bis(diphenylphosphino)ethane, 1663-45-2; triphenylphosphine, 603-35-0; 2-octanol, 123-96-6; 2,6-dimethyl-4-heptanol, 108-82-7; α-methylbenzenemethanol, 98-85-1; 4-methylcyclohexanol, 589-91-3; 4-(1,1-dimethylethyl)cyclohexanol, 98-52-2; 4-methyl-2-(1-methylethyl)cyclohexanol, 1490-07-9; isoborneol, 10334-13-1; borneol, 464-43-7; 12-hydroxyoctadecanoic acid, 106-14-9; 1-phenyl-3,7-dimethyl-6-octen-1-ol, 72237-37-7; butyl(3-cyclohexenyl)carbinol, 78932-49-7; isopulegol, 89-79-2; (*E*)-1-(2,6,6-trimethyl-1-cyclohexenyl)-1-buten-3-ol, 472-80-0; 3,5,5-trimethyl-2-cyclohexen-1-ol, 470-99-5; 2-methyl-5-(1-methylethenyl)-2-cyclohexen-1-ol, 99-48-9; 1-phenyl-4-methyl-1-penten-3-ol, 17137-22-3; 2,5,9-trimethyl-4,8-decadien-3-ol, 78932-50-0; cholesterol, 57-88-5; 4-methoxybenzyl alcohol, 105-13-5; 2-hydroxybenzyl alcohol, 90-01-7; 4-methylbenzyl alcohol, 589-18-4; 3-methylbenzyl alcohol, 587-03-1; 2-methylbenzyl alcohol, 89-95-2; benzyl alcohol, 100-51-6; 4-chlorobenzyl alcohol, 873-76-7; 4-cyanobenzyl alcohol, 874-89-5; 2-furanmethanol, 98-00-0; 2-(3,3-dimethylbicyclo[2.2.1]hept-2-ylidene)ethanol, 2226-05-3; 6,6-dimethylbicyclo[3.1.1]hept-2-ene-2-methanol, 515-00-4; 4-(1-methylethenyl)-1-cyclohexene-1-methanol, 536-59-4; 1-octanol, 111-87-5; cyclohexanemethanol, 100-49-2; benzeneethanol, 60-12-8; β-methylbenzeneethanol, 1123-85-9; 2-(4-chlorophenyl)-3-methyl-1-butanol, 65079-44-9; β,β-dimethylbenzeneethanol, 2173-69-5; 2-(4-chlorophenyl)-2,3-dimethyl-1-butanol, 84877-65-6; 2-octanone, 111-13-7; 2,6-dimethyl-4-heptanone, 108-83-8; 1-phenylethanone, 98-86-2; 4-methylcyclohexanone, 589-92-4; 2-(4-methylcyclohexenyl)-4-methylcyclohexanone, 13705-82-3; 4-(1,1-dimethylethyl)cyclohexanone, 98-53-3; 4-methyl-2-(1-methylethyl)cyclohexanone, 1654-31-5; (*R*)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-one, 464-49-3; 12-oxooctadecanoic acid, 925-44-0; phenyl 2,6-dimethyl-5-heptenyl ketone, 72237-38-8; butyl 3-cyclohexenyl ketone, 70242-56-7; isopulegone, 29606-79-9; 2-methyl-5-(1-methylethenyl)-2-cyclohexen-1-one, 99-49-0; 4-methyl-1-phenyl-1-penten-3-one, 3160-32-5; isopropyl 3,3-dimethyl-2,6-diphenyl-4-oxocyclohexyl ketone, 78932-53-3; isopropyl 2,6-dimethyl-1,5-heptadienyl ketone, 78932-52-2; 4-cholesten-3-one, 601-57-0; 4-methoxybenzaldehyde, 123-11-5; 4-methylbenzaldehyde, 104-87-0; 3-methylbenzaldehyde, 620-23-5; 2-methylbenzaldehyde, 529-20-4; benzaldehyde, 100-52-7; 4-chlorobenzaldehyde, 104-88-1; phenylmethyl benzoate, 120-51-4; 4-chlorobenzyl 4-chlorobenzoate, 19048-85-2; 4-cyanobenzyl 4-cyanobenzoate, 84877-66-7; 2-furancarboxaldehyde, 98-01-1; 2-furanylmethyl 2-furancarboxylate, 615-11-2; (3,3-dimethylbicyclo[2.2.1]hept-2-ylidene)acetaldehyde, 2226-09-7; 6,6-dimethylbicyclo[3.1.1]hept-2-ene-2-carboxaldehyde, 564-94-3; 4-(1-methylethenyl)-1-cyclohexene-1-carboxaldehyde, 2111-75-3; octyl octanoate, 2306-88-9; cyclohexylmethyl cyclohexanecarboxylate, 2611-02-1; 2-phenylethyl benzeneacetate, 102-20-5; 2-phenylpropyl 2-phenylpropionate, 66255-91-2; 2-(4-chlorophenyl)-3-methylbutyl 2-(4-chlorophenyl)-3-methylbutyrate, 84877-67-8; 2-(4-chlorophenyl)-3-methylbutyraldehyde, 74408-48-3; 2-methyl-2-phenylpropionaldehyde, 3805-10-5; 2-methyl-2-phenylpropyl 2-methyl-2-phenylpropionate, 84877-68-9; 2-(4-chlorophenyl)-2,3-dimethylbutyraldehyde, 84895-11-4; 1,4-butanediol, 110-63-4; 1,2-bis(hydroxymethyl)benzene, 612-14-6; 2,2-dimethyl-1,4-butanediol, 32812-23-0; 2,2-dimethyl-1,5-pentanediol, 3121-82-2; tetrahydro-3,3-dimethyl-2*H*-pyran-2-one, 4830-05-1; dihydro-2(3*H*)-furanone, 96-48-0; 1(3*H*)-isobenzofuranone, 87-41-2; dihydro-3,3-dimethyl-2(3*H*)-furanone, 3709-08-8; dihydro-4,4-dimethyl-2(3*H*)-furanone, 13861-97-7; tetrahydro-5,5-dimethyl-2*H*-pyran-2-one, 1679-55-6; citronellal, 106-23-0; 3-cyclohexene-1-carboxaldehyde, 100-50-5; citral, 5392-40-5; isopropyl bromide, 75-26-3; β-ionone, 79-77-6; isophorone, 78-59-1; 2-hydroxybenzaldehyde, 90-02-8; 4-cyanobenzaldehyde, 105-07-7; 2-(4-chlorophenyl)isovaleryl chloride, 51631-50-6; cinnamaldehyde, 104-55-2; *p*-nitrobenzyl alcohol, 619-73-8; *p*-nitrobenzaldehyde, 555-16-8.