New Strategies in Carbonylation Chemistry: The Synthesis of δ-Lactones from Saturated Alcohols and CO

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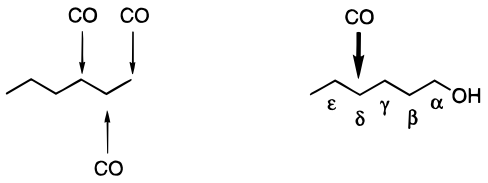
Abstract: This paper describes the δ-carbonylation of saturated alcohols which uses a 1,5-hydrogen-transfer reaction of alkoxyl radicals and subsequent carbonylation at the δ-carbon atoms as the key. The carbonylation reactions of five classes of saturated alcohols, namely, primary alcohols having primary δ-carbons, primary alcohols having secondary δ-carbons, primary alcohols having tertiary δ-carbons, secondary alcohols having primary δ-carbons, secondary alcohols having secondary δ-carbons, were carried out, in which lead tetraacetate (LTA) was used as a one-electron oxidant to generate the alkoxyl radicals. Carbonylation of these saturated alcohols, except for primary alcohols having tertiary δ-carbons, took place to afford δ-lactones in moderate to good yields. The mechanism of the remote carbonylation likely involves (1) alkoxyl radical generation via LTA oxidation of a saturated alcohol, (2) conversion of this alkoxyl radical to a δ-hydroxyalkyl radical by a 1,5-hydrogen-transfer reaction, (3) CO trapping of the δ-hydroxyalkyl radical yielding an acyl radical, and (4) oxidation and cyclization of the acyl radical to give a δ-lactone. A metal salt-free system was also tested for a substrate derived from a tertiary alcohol having a secondary δ-carbon; the photolysis of an alkyl 4-nitrobenzenesulfenate under CO pressures gave a δ-lactone in moderate yield.

Introduction

Despite the efforts of many research groups, the selective and efficient introduction of carbon monoxide into unactivated hydrocarbons has remained elusive.[1] Current methods, irrespective of whether they employ transition metals or free radicals, for the carbonylations of alkanes are generally not selective for different types of C−H bonds (left-hand side of Scheme 1). Only reactions of symmetrical alkanes, such as methane and ethane, and cyclic alkanes are certain to give uniform products. A notable exception reported by Tanaka and co-workers is the photochemical conversion of alkanes into aldehydes catalyzed by $[RhCl(CO)(PMe_3)_2]$,[1a,c,o] which prefers methyl groups to methylene groups. Our approach relies upon well-precedented radical methodology for the activation and functionalization of a particular C−H bond. By employing a 1,5-hydrogen-transfer reaction, it is possible to prepare δ-hydroxyalkyl radicals selectively from the corresponding carbinols (remote functionalization).[2] Treatment of the resulting radicals with CO would result in the δ-selective carbonylation of saturated alcohols (right-hand side of Scheme 1). Alkoxyl radical generation/1,5-H shift sequences have been used extensively in C-heteroatom bond-forming reactions, such as the Barton reaction.[2−10] However, as for the related C−C bond-forming reactions, examples are generally restricted to intramolecular cases.[11,12]

Scheme 1. Possible Reaction Sites for Carbonylation of Alkane and Alcohol



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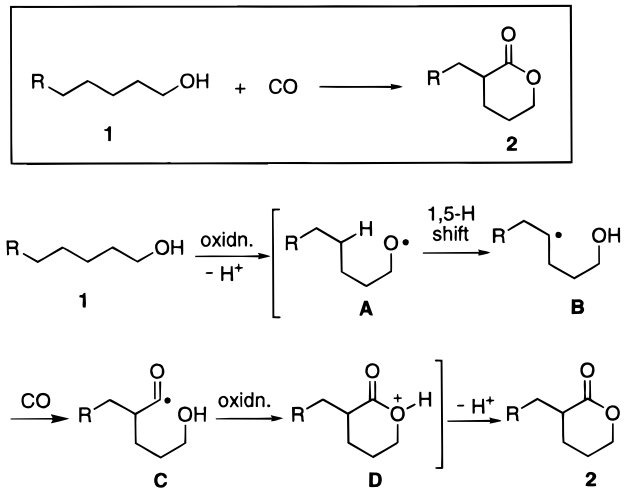
We became interested in the early work in this area which described the preparation of substituted tetrahydrofurans (THFs) from saturated alcohols by lead tetraacetate (LTA) induced oxidative cyclization[13] in refluxing benzene, since Alper and one of us previously observed that one-electron metal oxidation systems are compatible with radical carbonylation systems.[14] This THF synthesis, originally discovered in the late 1950s and mainly pursued by Mihailović and co-workers,[13] is thought to involve a 1,5-hydrogen transfer from the δ-carbon to an alkoxyl radical **A**, which is formed by the one-electron oxidation of saturated alcohol, and the subsequent oxidative cyclization. We envisioned that the putative intermediate **B** would undergo carbonylation with CO to give an acyl radical **C**[15] and that the subsequent oxidation of **C** leading to an acyloxonium ion **D** would be followed by facile deprotonation, providing a carbonylative route to δ-lactones from saturated alcohols (Scheme 2). This has proven to be the case.[16]

Scheme 2



In this paper, we provide the scope and limitations of this unique LTA-induced δ-carbonylation, which achieved the C-carbonylation of saturated alcohols for the first time, as well as a proposed mechanism for this oxidative carbonylation, and the potential for related δ-carbonylations using metal free systems.

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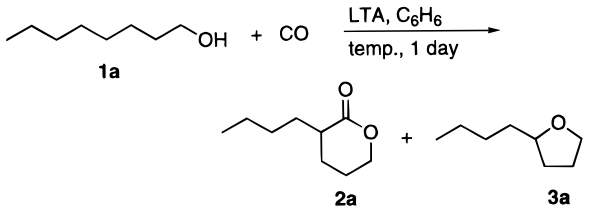
Table 1. Control Experiments for Carbonylation of 1-Octanol



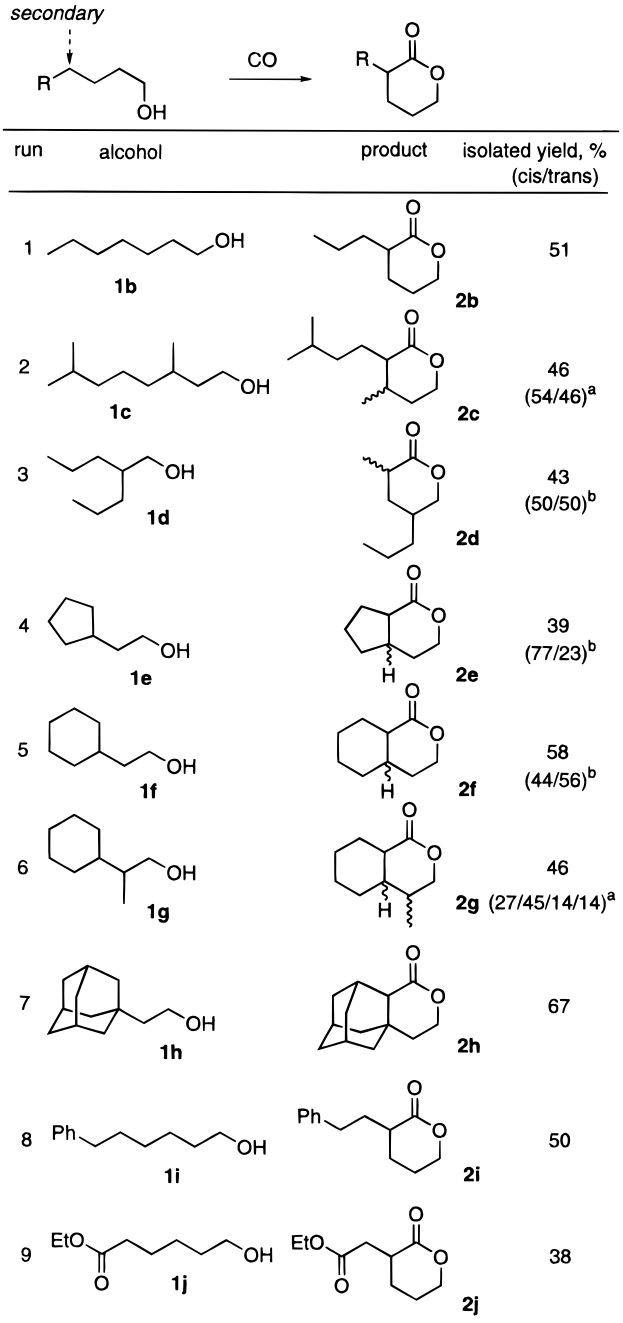
run[a]	[**1a**] M	LTA equiv	CO atm	temp °C	**2a**[b]	**3a**[b]	**2a**/**3a**
1	0.5	1.5	80	80	21	42	0.5
2	0.02	1.5	105	40	63	9	7.0
3	0.02	1.5	80	40	53	15	3.5
4	0.04	1.5	80	40	46	22	2.1
5	0.02	1.1	80	40	39	8	4.9
6	0.02	2	80	40	47	23	2.0
7	0.02	1.5	20	40	31	27	1.1
8	0.02	1.5	50	40	44	19	2.3
9	0.02	1.5	80	80	36	26	1.4
10[c]	0.02	1.5	80	40	7	<1	>7.0
11[c,d]	0.02	1.1	80	80	23	15	1.5

[a] Recovery of **1a**: run 5, 29%; run 10, 85%; run 11, 10%. [b] GC yield (%). [c] Reaction was conducted in CH_2Cl_2. [d] Octyl acetate was formed in 10%.

Results and Discussion

Carbonylation of Primary Alcohols at the Secondary *δ*-Carbons. Detailed control experiments were carried out for the conversion of 1-octanol (**1a**) to a *δ*-lactone **2a** (Table 1). In the LTA/CO system, the major competing reaction is direct oxidation of the *δ*-hydroxyalkyl radical to give a THF derivative **3a**.[13] Thus, some parameters, such as concentration, amount of LTA, CO pressure, and temperature, were varied as deemed appropriate in order to suppress the undesirable direct oxidation. Higher concentrations of **1a** caused an increase in the amount of uncarbonylated product **3a** (run 4). However, at concentrations less than 0.02 M, the reaction slowed considerably. With equimolar amounts of LTA, the ratio of carbonylated/uncarbonylated product (**2a**/**3a**) was improved, but larger amounts of the starting alcohol remained unreacted (run 5), whereas with 2 mol equiv of LTA, the formation of **3a** became largely competitive (run 6). Consequently, 1.5 mol equiv of LTA was chosen. High CO pressures are desirable for this reaction (run 2). Indeed, when CO pressure was reduced to 20 atm (run 7), the ratio of **2a**/**3a** decreased to 1.1. Interestingly, lower reaction temperatures gave better **2a**/**3a** ratios (runs 3 vs 9), but at temperatures below 30 °C, the reaction became very sluggish. Besides benzene, CH_2Cl_2 was also tested as a solvent; however, the reaction was sluggish at 40 °C, and 85% of the starting alcohol was recovered (run 10). Even at 80 °C, the reaction was not complete, and octyl acetate was detected as a principal byproduct in this case (run 11). It is known that 1,5-H shifts compete with 1,6-H shifts to some extent.[4f,g,13c] In these experiments a byproduct containing CO, 2-propyl-6-hexanolide (**4a**), which is formed via 1,6-hydrogen transfer[17] followed by carbonylation, was detected in <1/10 ratio relative to **2a**, but as will be referred to later, the formation of this byproduct depends on the structure of the starting alcohols.[18] Under optimal conditions (run 2, 0.02 M, 105 atm, 40 °C), alcohol **1a** is carbonylated to give *δ*-lactone **2a** in 63% yield, with a 7/1 ratio of **2a**/**3a**. In conclusion, as can be seen in Table 1, lower concentrations of 1-octanol, smaller amounts of LTA, higher pressures of CO, and lower reaction temperatures all favored the carbonylation of the *δ*-hydroxyalkyl radical over the undesirable direct oxidation.

Table 2. Carbonylation of Primary Alcohols at the Secondary *δ*-Carbons[c]



[a] Determined by GC. [b] Determined by ^1H NMR. [c] Conditions: ROH (0.4-0.8 mmol), LTA (1.5−2.0 equiv), C_6H_6 (20−40 mL), CO (80 atm), 40 °C, 3 days (except for run 1: 1 day, runs 6 and 8: 5 days).

Table 2 summarizes the carbonylations of substrates containing secondary *δ*-carbon atoms, under the now standard conditions ([ROH] = 0.02 M, 1.5−2.0 equiv of LTA, 40 °C, 80 atm

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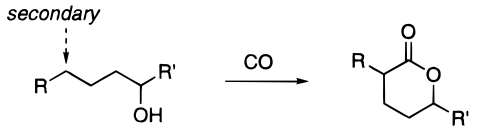
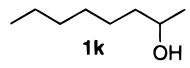
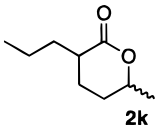
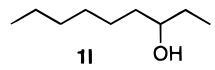
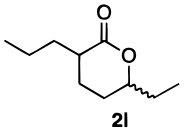
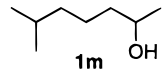
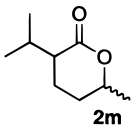
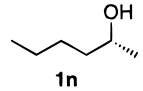
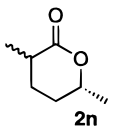
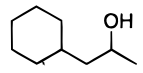
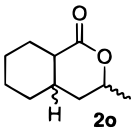
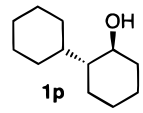
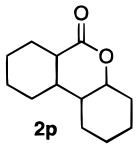
Table 3. Carbonylation of Secondary Alcohols at the Secondary δ-Carbon[e]



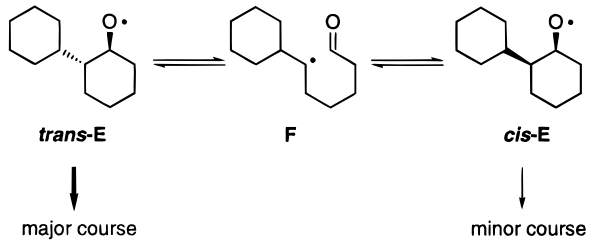
run	alcohol	product	isolated yield, % (cis/trans)
1			57 (55/45)[a]
2			57 (55/45)[a]
3			58 (52/48)[a]
4			53 (55/45)[a]
5			75 (22/26/24/28)[b]
6[d]			50[c]

[a] Determined by GC. [b] Determined by ^{1}H NMR (600 MHz). [c] Mixture of eight diastereomers. [d] ROH (1 mmol) and C_6H_6 (5 mL) were used. [e] Conditions: ROH (0.4−0.8 mmol), LTA (1.5−2.0 equiv), C_6H_6 (20−40 mL), CO (80 atm), 40 °C, 3−7 days.

of CO). Both α,β- and α,γ-disubstituted δ-lactones were obtained in reasonable yields from the corresponding branched primary alcohols (runs 2 and 3). Carbonylation of 2-cycloalkylethanols also took place to give bicyclic δ-lactones (runs 4−7). δ-Lactones having phenyl and ethoxycarbonyl groups on the α-side chains were obtained from alcohols **1i** and **1j**, respectively (runs 8 and 9). In all cases, the major competing reaction is oxidation to give THF derivatives. Small quantities of ϵ-lactones (via 1,6-H shifts) were observed in runs 1 (4%), 2 (5%), and 8 (4%) and could be eliminated by careful flash chromatography on silica gel to afford pure δ-lactones (ϵ-lactones come out faster). In the other cases examined, competitive 1,6-hydrogen-transfer reactions were negligible.

Carbonylation of Secondary Alcohols at the Secondary δ-Carbons. The δ-carbonylations of secondary alcohols at the secondary δ-carbons were examined. As expected, all of secondary alcohols listed in Table 3 underwent carbonylation to give α,δ-disubstituted δ-lactones. In general, the yields of δ-lactones are higher than those from primary alcohols. This may be due to a decrease in the rate of the reaction leading to THF derivatives from these secondary alcohols (vide infra).

Scheme 3



Secondary alcohols **1k** and **1l** also produced ϵ-lactones via a 1,6-hydrogen-transfer reaction, but the amounts were very small (<3%, runs 1 and 2). For the other cases examined, the formation of ϵ-lactones was negligible.[19] Bicyclic δ-lactone **2o** was obtained from **1o** in good yield (run 5).

This δ-carbonylation was successfully applied to a concise synthesis of carpenter bee pheromone[20] from optically pure (*R*)-(−)-2-hexanol (**1n**), a commercially available alcohol. Thus, treatment of **1n** with CO in the presence of LTA yielded a cis and trans mixture of 2-methyl-5-hexanolide (**2n**) (Table 3, run 4). Preparative HPLC separation of the mixture afforded pure *cis*-(*2S,5R*)-2-methyl-5-hexanolide (ee ≈ 100%),[21] a sex pheromone of the carpenter bee *Xylocopa hirutissima*. The observed quantitative optical yield confirmed that the absolute configuration of the hydroxyl-bearing carbon was completely retained.

Although the reaction of *trans*-2-cyclohexyl-1-cyclohexanol (**1p**) under standard conditions (0.02 M) was sluggish, the reaction at a higher concentration (0.2 M) yielded tricyclic δ-lactone **2p** in moderate yield (Table 3, run 6). To our surprise, analysis of the NMR spectra (600 MHz) indicated that tricyclic δ-lactone **2p** was a mixture of eight diastereomers even though only four diastereomers were possible from **1p**. The mixture was composed of four major diastereomers assigned as trans isomers with retention of the original stereochemistry, in the ratio of 55/15/12/6, and four minor diastereomers assigned as cis isomers with inversion of original stereochemistry, in the ratio of 4/3/3/2. A possible rationale for this observation is detailed in Scheme 3. The initially generated alkoxyl radical *trans*-**E** may undergo β scission[22] to give a fragment radical **F**. The cyclization of radical **F** back onto the internal aldehyde would afford an isomerized radical *cis*-**E** or the original radical *trans*-**E**.[23] The isomerized radical *cis*-**E** would undergo 1,5-hydrogen transfer, CO trapping, and oxidation to give the four minor products, while radical *trans*-**E** would afford the four

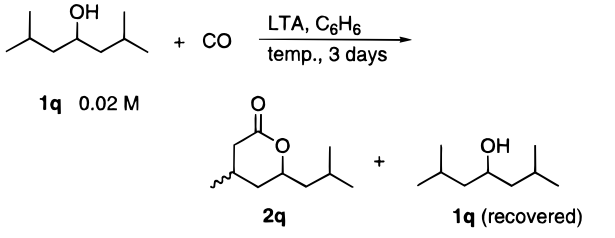
(19) For example, with **1m**, ϵ-lactone was not detected. We speculate that, in this case, 1,6-H transfer yields a tertiary radical, which would easily undergo the subsequent oxidation to give the carbocation rather than CO trapping (Table 3, run 3).

(20) Wheeler, J. W.; Evans, S. L.; Blum, M. S.; Velthius, H. H. V.; de Camargo, J. M. F. *Tetrahedron Lett.* **1976**, 4029.

(21) (a) Pirkle, W. H.; Adams, P. E. *J. Org. Chem.* **1978**, *43*, 378. (b) Bacardit, R.; Moreno-Mañas, M. *J. Chem. Ecol.* **1983**, *9*, 703. (c) Mori, K.; Senda, S. *Tetrahedron* **1985**, *41*, 541. (d) Bäckvall, J.-E.; Byström, S. E.; Nyström, J. E. *Tetrahedron* **1985**, *41*, 5761. (e) Narasaka, K.; Ukaji, Y. *Chem. Lett.* **1986**, 81. (f) Gerth, D. B.; Giese, B. *J. Org. Chem.* **1986**, *51*, 3726. (g) White, J. D.; Somers, T. C.; Reddy, G. N. *J. Am. Chem. Soc.* **1986**, *108*, 5352. (h) Ikuba, T.; Nakao, T.; Nishii, S.; Yamamoto, Y. *J. Am. Chem. Soc.* **1986**, *108*, 7420. (i) Katsuki, T.; Yamaguchi, M. *Tetrahedron Lett.* **1987**, *28*, 651. (j) Bernardi, R.; Ghiringhelli, D. *Synthesis* **1989**, 938. (k) Harada, T.; Matsuda, Y.; Imanaka, S.; Oku, A. *J. Chem. Soc., Chem. Commun.* **1990**, 1641. (l) Schink, H. E.; Bäckvall, J.-E. *J. Org. Chem.* **1992**, *57*, 1588. (m) White, J. D.; Somers, T. C.; Reddy, G. N. *J. Org. Chem.* **1992**, *57*, 4991. (n) Jacobs, H. K.; Mueller, B. H.; Gopalan, A. S. *Tetrahedron* **1992**, *48*, 8891.

(22) For LTA-induced carbonylation via β scission of cyclic alkoxyl radicals, see: Tsunoi, S.; Ryu, I.; Tamura, Y.; Yamasaki, S.; Sonoda, N. *Synlett* **1994**, 1009.

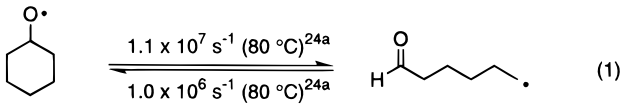
Table 4. Control Experiments for Carbonylation of 2,6-Dimethyl-4-heptanol



run	LTA equiv	CO atm	temp °C	**2q** %[a]	**1q** (recovered) %[a]
1	1.5	80	40	81 (71) (cis/trans = 59/41)[c]	7
2	1.5	20	40	62	12
3	1.5	5	40	13	71
4[b]	2.0	80	80	61	6

[a] GC yield (isolated yield). THF derivatives are always produced in trace amount (<2%). [b] Reaction was run for 1 day. [c] Determined by ^{1}H NMR.

major products. This result is supported by kinetic data reported by Beckwith and Hay which show that the cyclization/fragmentation process is in equilibrium (eq 1).[24a] On the other

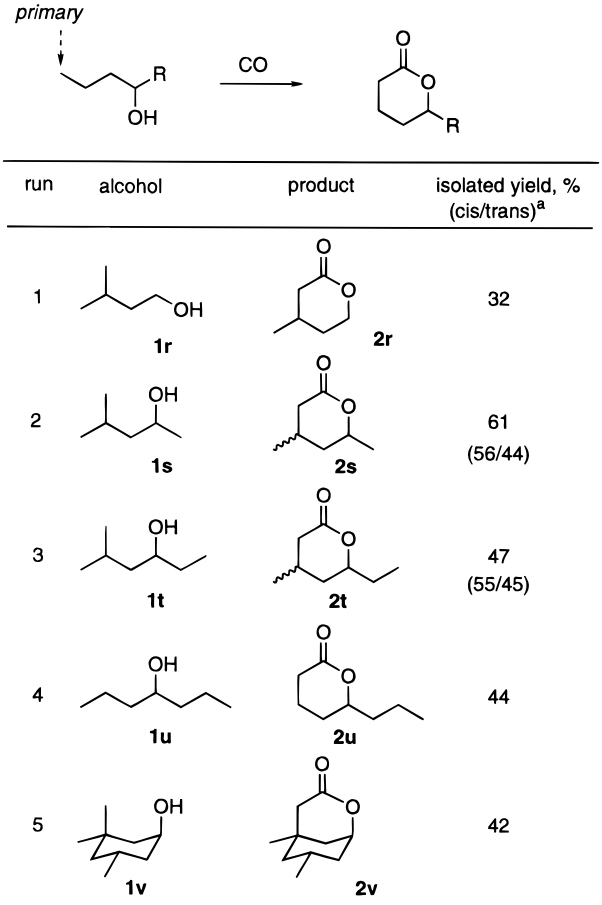


hand, complete retention of stereochemistry in the case of **1n** can be easily understood since in this case β scission yields two fragments, whose recombination is entropically unlikely.

Carbonylation of Primary and Secondary Alcohols at the Primary δ-Carbons. All of the examples shown above involve alcohols having secondary δ-carbons. The carbonylation of alcohols having primary δ-carbons was also examined. A symmetrical secondary alcohol, 2,6-dimethyl-4-heptanol (**1q**), which contains four methyl groups on both side chains, was chosen to conduct control experiments (Table 4). Treatment of **1q** with 1.5 equiv of LTA at 80 atm of CO gave δ-lactone **2q** in good yield (run 1). The remarkable efficiency of the carbonylation of **1q** in comparison with that of 1-octanol (Table 1) indicates that primary alkyl radicals prefer to react with CO rather than to be oxidized with Pb(III or IV). In fact, very little competitive oxidation of **1q** leading to the THF derivative was observed. This is ascribed to the slower oxidation of primary radicals compared to that of secondary radicals. The slow side reaction may enable us to carbonylate alcohols, which have primary δ-carbons, at relatively low CO pressures and at high temperatures (80 °C) (runs 2 and 4). On the other hand, when we carried out the same reaction at 5 atm of CO, the yield of the δ-lactone was dramatically reduced, and the starting alcohol was largely recovered (run 3).[25]

Table 5 lists the results of carbonylations of primary and secondary alcohols possessing primary δ-carbons. Since the carbonylation of alcohols having primary δ-carbons is essentially

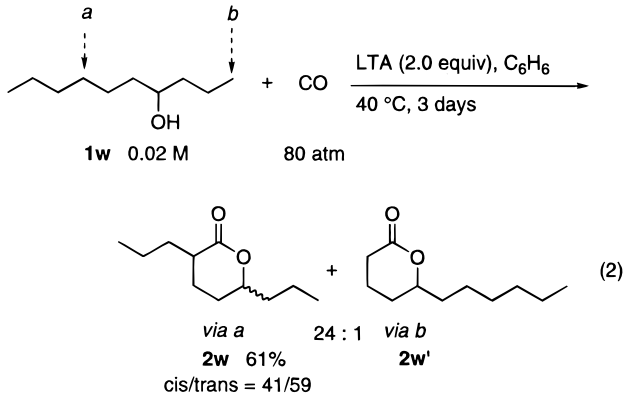
Table 5. Carbonylation of Secondary Alcohols at the Primary δ-Carbons[b]



[a] Determined by ^{1}H NMR. [b] Conditions: ROH (0.4−0.8 mmol), LTA (1.5−2 equiv), C_6H_6 (20 mL), CO (80 atm), 60 °C, 2−5 days.

free of contamination by THF derivatives, the carbonylation can be conducted at a somewhat higher temperature (60 °C).

This low reactivity of the primary carbon permits the selective carbonylation of alcohol **1w** which has both secondary and primary δ-carbons, *a* and *b*. In this case, carbon monoxide could be incorporated at the secondary δ-carbon *a*, with high regiochemical selectivity (eq 2). Thus, 2-propyl-5-octanolide (**2w**)

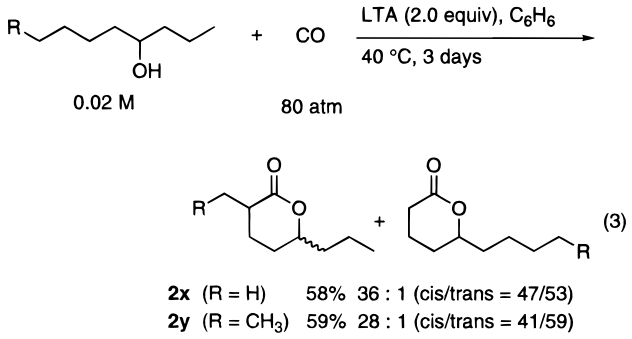


was formed predominantly over 5-undecanolide (**2w′**) in a 24/1 ratio. Purification of **2w** to eliminate the minor product **2w′** was easily accomplished by flash chromatography on silica gel. The preferential formation of **2w** is reasonable in light of the weaker C−H bond strength of methylene relative to that of

(23) Heusler, K.; Kalvoda, J.; Anner, G.; Wettstein, A. *Helv. Chim. Acta* **1963**, *46*, 352.

(24) (a) Beckwith, A. L. J.: Hay, B. P. *J. Am. Chem. Soc.* **1989**, *111*, 2674. The rate constant for 1,5-H shift from C to O• has been estimated to be $>10^8$ s^{-1} (for *n*-hexyloxy radical), see: (b) Gilbert, B. C.; Holmes, R. G. G.; Laue, H. A. H.; Norman, R. O. C. *J. Chem. Soc., Perkin Trans. 2* **1976**, 1047.

(25) The reason for the observed low conversion under low CO pressure conditions remains uncertain.

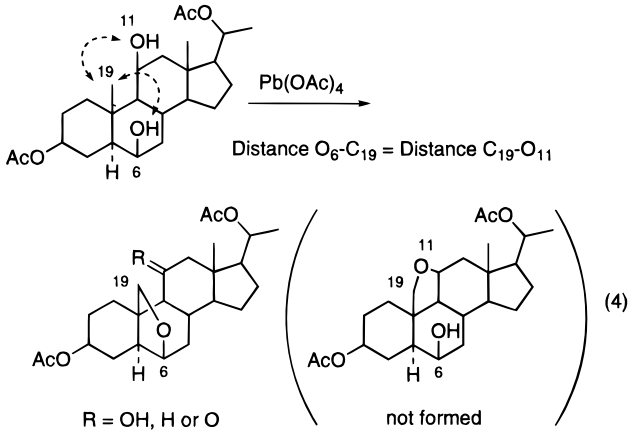


methyl (ΔE = ca. 3 kcal/mol).[26] Similar results were obtained in the case of 4-octanol and 4-nonanol (eq 3).

Mechanistic Insights

It is notable that unlike primary alcohols, secondary alcohols having secondary δ-carbons produced only a small amount of THF byproducts. For example, 2-octanol (**1k**) gave δ-lactone **2k** in 57% yield along with less than 5% yield of 2-methyl-5-propyltetrahydrofuran.[27] Table 6 summarizes the ratio of δ-lactone/THF for primary alcohol **1b** and secondary alcohols **1k** and **1l**, which have δ-methylene carbons. The relatively low δ-lactone/THF ratio in primary alcohols compared to that in secondary alcohols may be a reflection of the relative ease of THF formation for a primary alcohol. As outlined in Scheme 4, the reactivity difference for the direct oxidation of δ-radicals may be explained by assuming that the hydroxyl group coordinates to the Pb(III or IV) center, making the second oxidation easier. In cyclic intermediate **H**, a substituent at the hydroxyl-bearing carbon as found in secondary alcohols would cause steric congestion.

It was previously observed by Heusler and Kalvoda that 6β,11β-dihydroxysteroid,[13d] in which the C-19 methyl group is equidistant from 6β- and 11β-oxygen atoms (eq 4), undergoes



selective oxidative cyclization. This may lend support to the intermediacy of Pb-coordinated species. The reaction afforded only the 6β,19-ether resulting from the attack on the 6β-oxygen which is less crowded compared with the 11β-oxygen. If we hypothesize a free cation at C-19, there is no reason for the cation to choose 6-OH to 11-OH. This, along with the result shown in Table 6, probably suggests that coordination of the hydroxyl group to Pb(III or IV) center (in **G**) or the intervention of cyclic intermediate **H**[28,29] is essential for the second oxidation and cyclization step. More work is needed to clarify the precise mechanism with respect to the intermediacy of **H**.

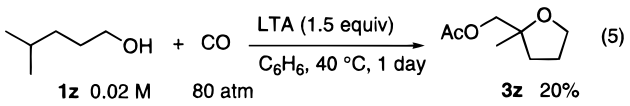
Table 6. Comparison of the Ratio of δ-Lactone/THF[b]

	ROH	δ-lactone/THF[a]
primary alcohol	**1b**	4
secondary alcohol	**1k**	10
	1l	12

[a] Determined by GC. [b] Conditions: [ROH] = 0.02 M (in C_6H_6), LTA (1.5−2.0 equiv), CO (80 atm), 40 °C, 1−3 days.

Limitations and Prospects for the LTA-Free System

In contrast to the successful carbonylation of alcohols having secondary and primary δ-carbons, alcohols having a tertiary δ-carbon, such as **1z**, did not undergo δ-carbonylation. Acetoxytetrahydrofuran **3z** was isolated as the major product (20%), and the starting alcohol was detected (33%) (eq 5). Both



rapid oxidation of the generated tertiary radical to lead to an olefin[30] and rapid decarbonylation of the tertiary acyl radical[31] conspire to prevent carbonylation of this substrate. Further oxidation of the resultant alkenyl alcohol consumed LTA to give the THF derivative **3z** and the recovered **1z** (Scheme 5).[32,33]

In contrast to primary and secondary alcohols, tertiary alcohol **5a** was virtually inert under the reaction conditions employed (97% recovery of **5a** after 3 days) (eq 6). This is presumably because of the difficulty of the formation of the lead alkoxide species at the initial step under the standard conditions.[13c]

(26) Wayner, D. D. M.; Griller, D. In *Advances Free Radical Chemistry*; Tanner, D. D., Ed.; JAI Press: Greenwich, 1990; Vol. 1, p 159. The preference of methylene over methyl in the competitive 1,5-H abstraction of alkoxyl radical has been documented. See refs 4e−g.

(27) The material balance is fairly poor (70−80%), which may be attributed in part to the formation of fragmentation products.

(28) Rubottom and co-workers proposed the formation of $RCOCH_2CH_2$-$Pb(OAc)_3$ in the ring opening of bicyclic siloxycyclopropanes with LTA, see: Rubottom, R. G.; Beedle, E. C.; Kim, C.-W.; Mott, R. C. *J. Am. Chem. Soc*. **1985**, *107*, 4230.

(29) Čeković and co-workers proposed that in the case of the LTA-oxidation system, the δ-hydroxyalkyl radical is in a tight radical pair with Pb(III) since the major product from 8-nonen-1-ol was the THF derivative formed via oxidative cyclization rather than the cyclopentane derivative formed via 5-*exo* cyclization. See ref 11l. Also see: Mihailović, M. L.; Konstantinović, S.; Vukićević, R. *J. Serb. Chem. Soc.* **1987**, *52*, 175.

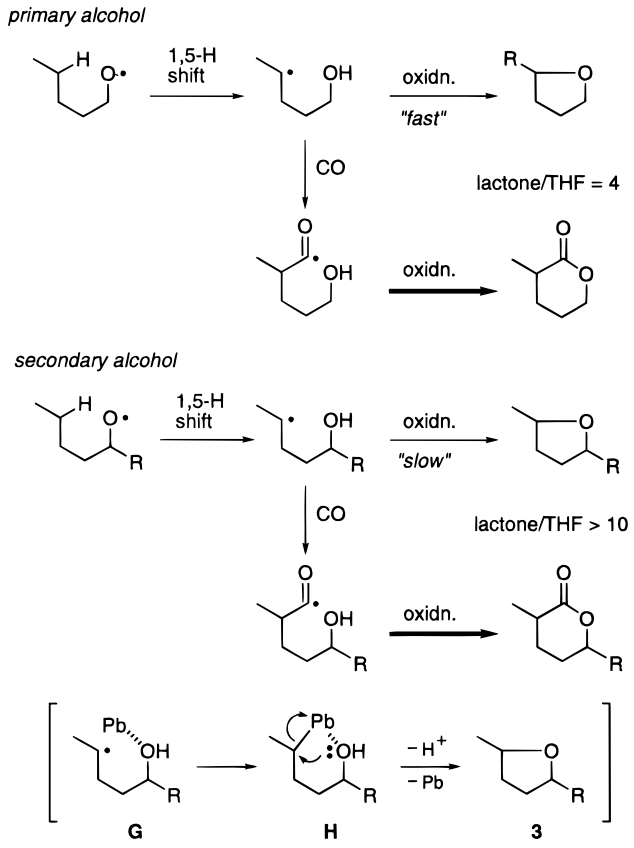
(30) Hauser, D.; Schaffner, K.; Jeger, O. *Helv. Chim. Acta* **1964**, *47*, 1883.

(31) For the decarbonylation order of the acyl radical being tertiary > secondary > primary acyl radical, see: (a) Chatgilialoglu, C.; Lucarini, M. *Tetrahedron Lett.* **1995**, *36*, 1299. (b) Chatgilialoglu, C.; Ferreri, C.; Lucarini, M.; Pedrielli, P.; Pedulli, G. F. *Organometallics* **1995**, *14*, 2672.

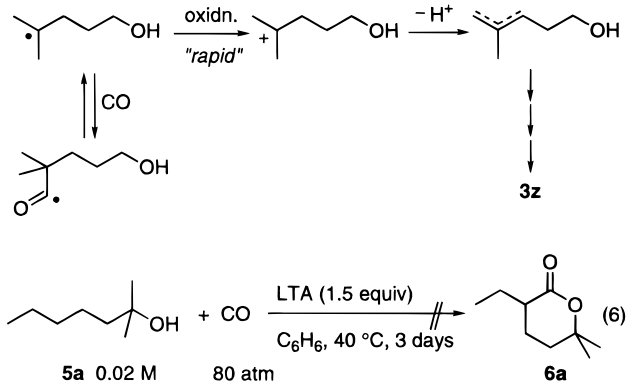
(32) (a) Mihailović, M. L.; Čeković, Ž.; Stanković, J.; Pavlović, N.; Konstantinović, S.; Dokić-Mazinjanin, S. *Helv. Chim. Acta* **1973**, *56*, 3056. (b) Bortrand, M. P.; Surzur, J. M.; Boyer, M.; Mihailović, M. L. *Tetrahedron* **1979**, *35*, 1365.

(33) The formation of **3z** may be accounted for by the cyclization of the alkoxyl radical onto internal C=C and the subsequent oxidation of the cyclized primary radical. The carbonylation of the primary radical does not appear to compete well with the oxidation to yield the acetoxylated product. It seems probable that stabilization of the three-membered oxonium cation contributes to this facile oxidation of the primary radical β to oxygen. For an alternative pathway involving coordination of C=C to Pb, see: (a) Moriarty, R. M.; Kapadia, K. *Tetrahedron Lett.* **1964**, 1165. (b) Moon, S.; Lodge, J. M. *J. Org. Chem.* **1964**, *29*, 3453.

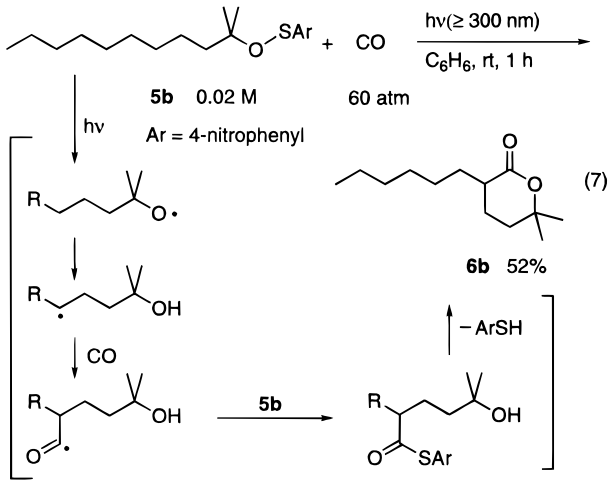
Scheme 4



Scheme 5



To demonstrate the generality of our new δ-carbonylation protocol and to circumvent the limitations, we considered generating the alkoxyl radical without LTA.[2,11,34,35] It is already known that O−S bonds undergo homolytic cleavage to give alkoxyl radicals, as does O−O homolysis. It has been reported that photolytic cleavage of the O−S bond in alkyl 4-nitrobenzenesulfenates,[36] which are readily prepared by the reaction of the alcohols with 4-nitrobenzenesulfenyl chloride, provides a convenient method for the generation of alkoxyl radicals. Thus, the reaction of an alkyl 4-nitrobenzenesulfenate **5b** derived from a tertiary alcohol with CO was conducted under xenon lamp irradiation in the hope of effecting δ-carbonylation giving a thioester.[37] Analysis of the reaction mixture by NMR indicated that lactone **6b** was formed in 52% yield (eq 7). The formation



of lactone **6b** can be rationalized as **6b** being derived from an initially produced thioester which is formed via an S_H2 type reaction of an acyl radical at sulfur.[38]

Since LTA-induced δ-carbonylation could not be applied to δ-lactone synthesis from tertiary alcohols, the future work would make the photolytic δ-carbonylation of alkyl 4-nitrobenzenesulfenates be complementary to the LTA-oxidation system.[39]

Conclusion

The remote carbonylation of saturated alcohols with CO has been achieved using LTA as a one-electron oxidant. Remote carbonylation which takes place at the δ-position of alcohols provides a convenient one-step synthesis of δ-lactones from cheap and readily available feedstocks, namely saturated alcohols and CO. The LTA-induced system works well in the carbonylation of primary and secondary alcohols having primary or secondary δ-carbon atoms. The mechanism of this remote carbonylation may involve the sequential generation of an alkoxyl radical, a 1,5-hydrogen-transfer reaction, CO trapping, and the oxidation/cyclization to give a δ-lactone. In the second one-electron oxidation step of saturated alcohols with LTA, our results suggest that coordination of the hydroxyl group to Pb(III or IV) center (in **G**) or intervention of cyclic intermediate **H** would be essential.

Carbonylation of tertiary alcohols, although unsuccessful with the LTA-induced system, can be achieved via photolysis of alkyl 4-nitrobenzenesulfenates. There is a great possibility that the photolytic approach would be an efficient alternative to the LTA-induced δ-carbonylation. The synthesis of δ-lactones is important in view of the numerous important natural products and

(34) For examples of the generation of alkoxyl radicals from nitrate esters, see: (a) Vite, G. D.; Fraser-Reid, B. *Synth. Commun.* **1988**, *18*, 1339. (b) Fraser-Reid, B.; Vite, G. D.; Yeung, B. A.; Tsang, R. *Tetrahedron Lett.* **1988**, *29*, 1645. Also see ref 12a.

(35) For examples of the generation of alkoxyl radicals from *N*-alkoxypyridinethiones and their derivatives, see: (a) Beckwith, A. L. J.: Hay, B. P. *J. Am. Chem. Soc.* **1988**, *110*, 4415. (b) Hartung, J.; Gallou, F. *J. Org. Chem.* **1995**, *60*, 6706. (c) Hartung, J.; Hiller, M.; Schmidt, P. *Chem. Eur. J.* **1996**, *2*, 1014. (d) Hartung, J.; Hiller, M.; Schmidt, P. *Liebigs Ann.* **1996**, 1425. (e) Hartung, J.; Schwarz, M. *Synlett* **1997**, 848.

(36) (a) Beckwith, A. L. J.; Hay, B. P.; Wolliams, G. M. *J. Chem. Soc., Chem. Commun.* **1989**, 1202. (b) Pasto, D. J.; L'Hermine, G. *J. Org. Chem.* **1990**, *55*, 5815. (c) Pasto, D. J.; L'Hermine, G. *Tetrahedron* **1993**, *49*, 3259. Also see refs 8 and 12c.

(37) Photolysis was carried out using a stainless autoclave with quartz glass. Schematic photoirradiation apparatus is given in the Supporting Information in ref 15b.

(38) For atom and group transfer reactions to acyl radicals, see: (a) Walling, C.; Basedow, O. H.; Savas, E. S. *J. Am. Chem. Soc.* **1960**, *82*, 2181. (b) Coveney, D. J.; Patel, V. F.; Pattenden, G.; Thompson, D. M. *J. Chem. Soc., Perkin Trans. 1* **1990**, 2721. (c) Crich, D.; Chen, C.; Hwang, J.-T.; Yuan, H.; Papadatos, A.; Walter, R. I. *J. Am. Chem. Soc.* **1994**, *116*, 8937. Also see refs 15a, b, h, and j.

(39) The detailed results of δ-carbonylation using photolysis of alkyl benzenesulfenates will be reported in a separate paper.

biologically active compounds containing the δ-valerolactone unit.[40] Carbonylation approaches can contribute to this, and indeed, a considerable amount of work has been reported on the transition-metal mediated carbonylation of unsaturated alcohols to yield lactones thus far.[41] However, the synthesis of δ-lactones from saturated alcohols and CO with the use of transition metal catalysts has yet to be realized. The present work clearly demonstrates the validity of free-radical methodology for the carbonylation of unactivated C−H bonds.

Experimental Section

All carbonylation reactions were carried out using a stainless steel autoclave lined with a glass liner. Photoinduced carbonylation of an alkyl 4-nitrobenzenesulfenate was carried out using a 500-W xenon lamp and a stainless steel autoclave with quartz glass windows lined with a standard Pyrex glass liner. Alcohols, **1g**, **1o**, and **1p**, were prepared by the hydrogenation of the corresponding aromatic alcohols, 2-phenyl-1-propanol, 1-phenyl-2-propanol, and *trans*-2-phenyl-1-cyclohexanol with 5% Rh/C.[42] Other alcohols and LTA (90% purity, wet with acetic acid) were obtained from commercial sources and were used as they were. Alkyl 4-nitrobenzenesulfenate **5b** was prepared from the reaction of the corresponding lithium alkoxide with 4-nitrobenzenesulfenyl chloride. C_6H_6 was distilled from CaH_2. ^1H and ^{13}C NMR spectra were recorded at 270 or 400 MHz or 600 MHz (^1H) using $CDCl_3$ with TMS as the internal standard. Flash chromatography was performed with use of silica gel (Fuji Silysia Chemical, Ltd. BW-820MH, 70−200 mesh). Preparative HPLC was performed on GPC columns (JAIGEL 1H and 2H) using $CHCl_3$ as an eluent. Gas chromatography was carried out on capillary column Supelco SPB5 (0.2 mm × 30 m).

General Procedure for Synthesis of δ-Lactones. Carbonylation of 1-adamantaneethanol. To a solution of 1-adamantaneethanol (**1h**) (72 mg, 0.4 mmol) in benzene (40 mL) placed in a 100-mL stainless steel autoclave lined with a glass liner was added LTA (295 mg, 0.6 mmol). The autoclave was sealed, purged twice with 10 atm of carbon monoxide, and then pressurized with 80 atm of CO, with stirring, at 40 °C. After 3 days, the residual CO was ventilated, and the mixture was poured into 0.4 N aqueous hydrogen chloride, extracted with ether (3 × 20 mL), and dried ($MgSO_4$). Rotary evaporation of the solvents followed by flash chromatography on silica gel (hexane, then 10% EtOAc−hexane eluent) afforded adamantano[2,1-*c*]tetrahydro-2*H*-pyran-2-one (**2h**) (55 mg, 67% yield) as a colorless liquid: ^1H NMR ($CDCl_3$, 600 MHz) δ 1.50 (ddd, 1H, J = 2.2, 5.0, 12.8 Hz), 1.55 (dt, 1H, J = 5.2, 14.0 Hz), 1.58−1.80 (m, 8H), 1.83 (d of quintet-like, 1H, J = 13.1(d), 2.6 Hz), 1.90 (dddd, 1H, J = 12.7, 0.7, 5.2, 3.1 Hz), 1.99 (quintet-like, 1H, $J \approx$ 3.0 Hz), 2.01 (quintet-like, 1H, $J \approx$ 3.0 Hz), 2.40 (br s, 1H), 2.49 (q-like, 1H, $J \approx$ 2.8 Hz), 4.33 (ddd, 1H, J = 5.3, 6.2, 11.7 Hz), 4.42 (ddd, 1H, J = 5.3, 9.3, 11.7 Hz); ^{13}C NMR ($CDCl_3$, 68 MHz) δ 27.73 (d), 27.92 (d), 28.06 (d), 31.55 (s), 32.15 (t), 36.33 (t), 36.37 (t), 37.62 (t), 39.30 (t), 44.84 (t), 50.76 (d), 65.52 (t), 173.03 (s); IR neat 1736 cm^{-1}; HREIMS calcd for $C_{13}H_{18}O_2$ *m*/*z* 206.1307, found 206.1291.

Tetrahydro-3-(3-methylbutyl)-4-methyl-2*H*-pyran-2-one (2c). Obtained as a cis/trans-isomer mixture in a 54/46 ratio. These isomers were separated by preparative HPLC. ***cis*-2c**, a yellow liquid: ^1H NMR ($CDCl_3$, 270 MHz) δ 0.90 (d, 3H, J = 6.4 Hz), 0.91 (d, 3H, J = 6.8 Hz), 0.94 (d, 3H, J = 7.3 Hz), 1.12−1.47 (m, 3H), 1.50−1.75 (m, 2H), 1.80−1.96 (m, 1H), 2.08−2.20 (m, 1H), 2.28−2.42 (m, 1H), 2.44−2.52 (q-like, 1H, $J \approx$ 6.4 Hz), 4.20−4.39 (m, 2H); ^{13}C NMR ($CDCl_3$, 68 MHz) δ 16.91 (q), 22.34 (q), 22.65 (q), 24.60 (t), 27.68 (d), 28.10 (d), 30.30 (t), 36.40 (t), 44.23 (d), 65.78 (t), 174.77 (s); IR neat 1744 cm^{-1}; HREIMS calcd for $C_{11}H_{20}O_2$ *m*/*z* 184.1458, found 184.1485. ***trans*-2c**, a yellow liquid: ^1H NMR ($CDCl_3$, 270 MHz) δ 0.90 (d, 3H, J = 6.8 Hz), 0.90 (d, 3H, J = 6.8 Hz), 1.09 (d, 3H, J = 6.4 Hz), 1.14−1.37 (m, 2H), 1.43−1.98 (complex m, 6H), 2.10−2.17 (m, 1H), 4.19−4.39 (m, 2H); ^{13}C NMR ($CDCl_3$, 68 MHz) δ 20.63 (q), 22.33 (q), 22.57 (q), 27.64 (t), 28.23 (d), 30.29 (d), 30.89 (t), 35.68 (t), 48.09 (d), 67.22 (t), 173.97 (s); IR neat 1736 cm^{-1}; HREIMS calcd for $C_{11}H_{20}O_2$ *m*/*z* 184.1458, found 184.1478. In comparison with the spectral data for **2f**,[43] the major isomer is assigned as a cis isomer.

***cis*- and *trans*-Tetrahydro-3-methyl-5-propyl-2*H*-pyran-2-one (2d).** Obtained as a cis/trans-isomer mixture in a 50/50 ratio, a colorless liquid: ^1H NMR ($CDCl_3$, 270 MHz) δ 0.93 (t, 6H, J = 6.8 Hz), 1.15−1.42 (complex m, 15H including 1.23 (d, 3H, J = 6.8 Hz) and 1.27 (d, 3H, J = 6.8 Hz)), 1.61−1.82 (complex m, 2H), 1.95−2.17 (complex m, 3H), 2.45−2.68 (complex m, 2H), 3.93 (dd, 1H, J = 10.7, 3.9 Hz), 3.97 (dd, 1H, J = 9.8, 2.5 Hz), 4.26 (dd, 1H, J = 10.7, 4.9 Hz), 4.34 (dd, 1H, J = 10.7, 4.9, 2.0 Hz); ^{13}C NMR ($CDCl_3$, 68 MHz) δ 13.99 (q, two superimposed lines), 16.54 (q), 16.87 (q), 19.76 (t), 19.96 (t), 31.67 (d), 32.20 (d), 32.96 (t), 33.21 (d), 34.11 (t), 34.60 (t), 34.74 (t), 35.15 (d), 71.82 (t), 73.43 (t), 174.85 (s), 175.97 (s); IR neat 1740 cm^{-1}; HREIMS for first eluted isomer with GC calcd for $C_9H_{16}O_2$ *m*/*z* 156.1150, found 156.1132; HREIMS for second eluted isomer with GC calcd for $C_9H_{16}O_2$ *m*/*z* 156.1150, found 156.1172.

***cis*- and *trans*-Hexahydro-cyclopenta[*c*]pyran-1(3*H*)-one (2e).** Obtained as a cis/trans-isomer mixture in a 77/23 ratio, a colorless liquid: ^1H NMR ($CDCl_3$, 270 MHz) δ 1.20−2.30 (m, cis 8H and trans 10H), 2.49 (m, cis 1H), 2.89 (td-like, cis 1H, $J \approx$ 8.4, 9.9 Hz, α-CH), 4.20 (td-like, cis 1H, $J \approx$ 10.5, 2.5 Hz), 4.28−4.42 (m, cis 1H and trans 2H); ^{13}C NMR ($CDCl_3$, 68 MHz) δ 22.07 (t, cis), 23.39 (t, cis), 25.13 (t, trans), 28.07 (t, cis), 29.17 (t, trans), 29.83 (t, trans), 31.62 (t, cis), 33.61 (t, trans), 36.31 (d, trans), 40.19 (d, cis), 42.88 (d, trans), 47.46 (d, cis), 67.37 (t, cis), 68.57 (t, trans), 174.75 (s, trans), 175.14 (s, cis); IR neat 1736 cm^{-1}; HREIMS calcd for $C_8H_{12}O_2$ *m*/*z* 140.0837, found 140.0838. In comparison with the spectral data for **2f**,[43] the major isomer is assigned as a cis isomer.

Octahydro-4-methyl-1*H*-2-benzopyran-1-one (2g). Obtained as a mixture of four diastereomers in a 27/45/14/14 ratio. The major isomer was isolated in pure form by preparative HPLC, a slightly yellow liquid: ^1H NMR ($CDCl_3$, 270 MHz) δ 0.97 (d, 3H, J = 6.4 Hz), 1.03 (m, 1H), 1.13−1.33 (m, 4H), 1.70−1.87 (m, 3H), 1.96−2.06 (m, 2H), 2.24−2.31 (m, 1H), 3.89 (dd, 1H, J = 11.4, 8.4 Hz), 4.32 (dd, 1H, J = 11.4, 5.4 Hz); ^{13}C NMR ($CDCl_3$, 68 MHz) δ 15.45 (q), 25.33 (t), 25.59 (t), 27.05 (t), 30.89 (t), 34.13 (d), 43.17 (d), 44.62 (d), 73.46 (t), 173.81 (s); IR neat 1728 cm^{-1}; HREIMS calcd for $C_{10}H_{16}O_2$ *m*/*z* 168.1150, found 168.1155. [Partial data was obtained for the other three isomers.] The first eluted isomer with GC: ^1H NMR ($CDCl_3$, 270 MHz) δ 1.01 (d, 3H, J = 6.8 Hz), 3.87 (t-like, 1H, $J \approx$ 11.0 Hz), 4.22 (dd, 1H, J = 11.7, 5.9 Hz); ^{13}C NMR ($CDCl_3$, 68 MHz) δ 16.17 (q), 22.39 (t), 24.70 (t), 25.46 (t), 31.47 (t), 33.83 (d), 38.01 (d), 39.93 (d), 71.99 (t), 174.79 (s); HREIMS calcd for $C_{10}H_{16}O_2$ *m*/*z* 168.1150, found 168.1160. The third eluted isomer with GC: ^1H NMR ($CDCl_3$, 270 MHz) δ 0.94 (d, 3H, J = 6.8 Hz), 4.07 (t-like, 1H, $J \approx$ 11.8 Hz), 4.26 (dd, 1H, J = 11.3, 6.4 Hz); ^{13}C NMR ($CDCl_3$, 68 MHz) δ 13.45 (q), 22.62 (t), 22.94 (t), 25.32 (t), 27.20 (t), 32.72 (d), 38.59 (d), 43.35 (d), 71.90 (t), 172.94 (s); HREIMS calcd for $C_{10}H_{16}O_2$ *m*/*z* 168.1150, found 168.1157. The fourth eluted isomer with GC: ^1H NMR ($CDCl_3$, 270 MHz) δ 1.03 (d, 3H, J = 7.4 Hz), 4.08 (dd, 1H, J = 10.9, 4.0 Hz), 4.36 (dd, 1H, J = 10.9, 4.5 Hz); ^{13}C NMR ($CDCl_3$, 68 MHz) δ 11.28 (q), 25.59 (t), 25.92 (t), 27.43 (t), 29.72 (t), 30.98 (d), 40.02 (d), 40.79 (d), 74.71 (t), 173.54 (s); HREIMS calcd for $C_{10}H_{16}O_2$ *m*/*z* 168.1150, found 168.1153.

(40) For leading references, see: (a) Endo, A.; Kurodo, M.; Tsujita, Y. *J. Antibiot.* **1976**, *29*, 1346. (b) Ranieri, R. L.; Calton, G. J. *Tetrahedron Lett.* **1978**, 499. (c) Wovkulich, P. M.; Tang, P. C.; Chadha, N. K.; Batcho, A. D.; Barrish, J. C.; Uskokovic, M. R. *J. Am. Chem. Soc*. **1989**, *111*, 2596. (d) Danishefsky, S. J.; Simoneau, B. *J. Am. Chem. Soc*. **1989**, *111*, 2599. (e) Liu, Z.-Y.; He, L.; Zheng, H. *Synlett* **1993**, 191. (f) Shin, I.; Zhou, H.-Q.; Que, N. L. S.; Liu, H.-W.; Swedenborg, P. D.; Jones, R. L. *J. Org. Chem.* **1993**, *58*, 2923. Also see a review: (g) Nangia, A.; Prasuna, G.; Rao, P. B. *Tetrahedron* **1997**, *53*, 14507.

(41) For selected examples of metal-mediated carbonylation of unsaturated alcohols to lead to δ-lactones, see: (a) Murray, T. F.; Varma, V.; Norton, J. R. *J. Org. Chem.* **1978**, *43*, 353. (b) Alper, H.; Leonard, D. *J. Chem. Soc., Chem. Commun*. **1985**, 511. (c) Chenal, T.; Naigre, R.; Ciprés, I.; Kalck, P.; Daran, J.-C.; Vaissermann, J. *J. Chem. Soc., Chem. Commun*. **1993**, 747. (d) Naigre, R.; Chenal, T.; Ciprés, I.; Kalck, P.; Daran, J.-C.; Vaissermann, J. *J. Organomet. Chem*. **1994**, *480*, 91. (e) Chow, Y. L.; Huang, Y.-J.; Dragojlovic, V. *Can. J. Chem.* **1995**, *73*, 740.

(42) The general procedure for hydrogenation is given in the Supporting Information.

(43) Fujiwara, Y.; Okamoto, M. *Chem. Pharm. Bull.* **1989**, *37*, 1458.

Tetrahydro-3-(2-phenylethyl)-2*H*-pyran-2-one (2i). Obtained as a colorless liquid: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.59 (m, 1H), 1.77 (d of quintet-like, 1H, J = 9.0 (d), 6.9 Hz), 1.88 (m, 1H), 1.92 (sextet-like, 1H, $J \approx$ 6.8 Hz), 2.13 (sextet-like, 1H, $J \approx$ 6.8 Hz), 2.26 (d of quintet-like, 1H, J = 9.3 (d), 6.8 Hz), 2.44 (ddt, 1H, J = 5.9, 11.0, 7.4 Hz), 2.73 (t, 2H, J = 7.3 Hz), 4.28 (t, 2H, J = 5.9 Hz), 7.15−7.31 (m, 5H); ^{13}C NMR ($CDCl_3$, 68 MHz) δ 21.90 (t), 24.67 (t), 32.77 (t), 32.86 (t), 38.57 (d), 68.08 (t), 125.93 (d), 128.34 (d, two superimposed lines), 141.31 (s), 174.36 (s); IR neat 1736 cm^{-1}; HREIMS calcd for $C_{13}H_{16}O_2$ *m*/*z* 204.1150, found 204.1156.

Tetrahydro-2-oxo-2*H*-pyran-3-acetic acid ethyl ester (2j). Obtained as a colorless liquid: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.27 (t, 3H, J = 7.1 Hz), 1.68 (m, 1H), 1.94 (quintet-like, 2H, $J \approx$ 6.5 Hz), 2.14 (m, 1H), 2.61 (dd, 1H, J = 6.7, 17.0 Hz), 2.81 (dd, 1H, J = 5.3, 17.0 Hz), 2.88−2.99 (m, 1H), 4.16 (q, 2H, J = 7.1 Hz), 4.33−4.42 (9 line m, 2H); ^{13}C NMR ($CDCl_3$, 68 MHz) δ 14.05 (q), 22.19 (t), 24.76 (t), 35.73 (t), 36.33 (d), 60.68 (t), 68.51 (t), 171.54 (s), 173.34 (s); IR neat 1732 cm^{-1}; HREIMS calcd for $C_9H_{14}O_4$ *m*/*z* 186.0888, found 186.0873.

Tetrahydro-6-methyl-3-propyl-2*H*-pyran-2-one (2k). Obtained as a cis/trans-isomer mixture in a 55/45 ratio. These isomers were separated by preparative HPLC. ***cis*-2k**, a colorless liquid: ^{1}H NMR ($CDCl_3$, 270 MHz) δ 0.93 (t, 3H, J = 7.1 Hz), 1.35 (d, 3H, J = 5.9 Hz), 1.39−1.68 (m, 5H), 1.75−2.09 (m, 3H), 2.37−2.52 (m, 1H), 4.38−4.53 (m, 1H); ^{13}C NMR ($CDCl_3$, 68 MHz) δ 13.91 (q), 20.08 (t), 21.00 (q), 23.26 (t), 28.33 (t), 32.89 (t), 37.67 (d), 74.22 (d), 175.62 (s); IR neat 1736 cm^{-1}; HREIMS calcd for $C_9H_{16}O_2$ *m*/*z* 156.1150, found 156.1136. ***trans*-2k**, a colorless liquid: ^{1}H NMR ($CDCl_3$, 270 MHz) δ 0.93 (t, 3H, J = 7.1 Hz), 1.36 (d, 3H, J = 6.4 Hz), 1.42−1.62 (m, 5H), 1.86−2.06 (m, 3H), 2.30−2.45 (m, 1H), 4.39−4.48 (m, 1H); ^{13}C NMR ($CDCl_3$, 68 MHz) δ 13.88 (q), 19.79 (t), 22.10 (q), 25.49 (t), 30.69 (t), 33.94 (t), 40.22 (d), 77.60 (d), 173.95 (s); IR neat 1719 cm^{-1}; HREIMS calcd for $C_9H_{16}O_2$ *m*/*z* 156.1150, found 156.1165. In comparison with the spectral data for **2n**,[44] the major isomer is assigned as a cis isomer.

Tetrahydro-6-ethyl-3-propyl-2*H*-pyran-2-one (2l). Obtained as a cis/trans-isomer mixture in a 55/45 ratio. These isomers were separated by preparative HPLC. ***cis*-2l**, a yellow liquid: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 0.94 (t, 3H, J = 7.2 Hz), 1.00 (t, 3H, J = 7.5 Hz), 1.35−1.46 (m, 3H), 1.49−1.65 (m, 3H), 1.73 (m, 1H), 1.82−1.88 (m, 1H), 1.88−1.96 (m, 1H), 2.03 (ddd, 1H, J = 7.8, 13.4, 16.6 Hz), 2.45 (m, 1H), 4.20 (m, 1H); ^{13}C NMR ($CDCl_3$, 68 MHz) δ 9.51 (q), 13.86 (q), 20.14 (t), 23.25 (t), 26.15 (t), 28.23 (t), 32.90 (t), 37.88 (d), 79.23 (d), 175.83 (s); IR neat 1736 cm^{-1}; HREIMS calcd for $C_{10}H_{18}O_2$ *m*/*z* 170.1307, found 170.1292. ***trans*-2l**, a yellow liquid: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 0.94 (t, 3H, J = 7.3 Hz), 0.99 (t, 3H, J = 7.5 Hz), 1.32−1.47 (m, 2H), 1.55 (m, 3H), 1.60−1.67 (m, 1H), 1.72 (m, 1H), 1.89−1.96 (m, 2H), 2.03 (ddd, 1H, J = 3.2, 6.7, 13.4 Hz), 2.39 (m, 1H), 4.20 (m, 1H); ^{13}C NMR ($CDCl_3$, 68 MHz) δ 9.21 (q), 13.91 (q), 19.83 (t), 25.42 (t), 28.30 (t), 29.11 (t), 34.02 (t), 40.60 (d), 82.46 (d), 174.07 (s); IR neat 1728 cm^{-1}; HREIMS calcd for $C_{10}H_{18}O_2$ *m*/*z* 170.1307, found 170.1310. In comparison with the spectral data for **2n**,[44] the major isomer is assigned as a cis isomer.

Dodecahydro-6*H*-dibenzo[*b*,*d*]pyran-6-one (2p). Obtained as a mixture of eight diastereomers in a 55/15/12/6/4/3/3/2 ratio (600 MHz ^{1}H NMR). Four major isomers were assigned to the retention products (trans) because of the relative larger J value of its C*H*O signal, and four minor isomers to the inversion products (cis). The ratio of retention and inversion was 88/12. After purification by HPLC, the major isomer was obtained in a pure form, a white solid: mp. 106−107 °C; ^{1}H NMR ($CDCl_3$) δ 0.80−0.92 (m, 2H), 1.15−1.35 (m, 7H), 1.44 (dq-like, 1H, J = 3.9, 12.0 Hz), 1.70−1.88 (m, 4H), 1.90−2.00 (m, 3H), 2.06−2.09 (m, 1H), 2.33−2.40 (m, 1H), 3.87 (ddd, 1H, J = 4.1, 9.9, 11.3 Hz); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 24.37 (t), 25.15 (t), 25.24 (t), 25.96 (t), 26.97 (t), 27.34 (t), 28.85 (t), 32.61 (t), 42.30 (d), 44.85 (d), 47.08 (d), 84.34 (d), 172.97 (s); IR neat 1724 cm^{-1}; HREIMS calcd for $C_{13}H_{20}O_2$ *m*/*z* 208.1463, found 208.1461. [Partial data was obtained for the other isomers.] Isomer of 15% content: ^{1}H NMR ($CDCl_3$) δ 3.96 (td, 1H, J = 10.7, 4.2 Hz); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 78.90 (d). Isomer of 12% content: ^{1}H NMR ($CDCl_3$) δ 3.93 (td, 1H, J = 10.6, 4.2 Hz); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 80.00 (d). Isomer of 6% content: ^{1}H NMR ($CDCl_3$) δ 4.16 (td, 1H, J = 11.3, 4.3 Hz); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 79.94 (d). Isomer of 4% content: ^{1}H NMR ($CDCl_3$) δ 4.70 (q-like, 1H, $J \approx$ 3.3 Hz); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 76.06 (d). Isomer of 3% content: ^{1}H NMR ($CDCl_3$) δ 4.51 (q-like, 1H, $J \approx$ 3.3 Hz); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 75.55 (d). Isomer of 3% content: ^{1}H NMR ($CDCl_3$) δ 4.46 (q-like, 1H, $J \approx$ 3.3 Hz); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 74.51 (d). Isomer of 2% content: ^{1}H NMR ($CDCl_3$) δ 4.47 (q-like, 1H, $J \approx$ 3.3 Hz); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 80.09 (d).

***cis*- and *trans*-Tetrahydro-6-ethyl-4-methyl-2*H*-pyran-2-one (2t).** Obtained as a cis/trans-isomer mixture in a 55/45 ratio, a slightly yellow liquid: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.00 (t, cis 3H, J = 7.5 Hz), 1.00 (t, trans 3H, J = 7.4 Hz), 1.04 (d, cis 3H, J = 6.3 Hz), 1.10 (d, trans 3H, J = 6.6 Hz), 1.12−1.27 (m, cis 1H), 1.55−1.81 (complex m, cis 2H and trans 4H), 1.89−1.93 (m, cis 1H), 2.00−2.08 (complex m, cis 2H), 2.14−2.22 (complex m, trans 2H), 2.57 (dd, trans 1H, J = 20.3, 9.4 Hz), 2.67 (ddd, cis 1H, J = 21.3, 10.4, 2.0 Hz), 4.22 (m, cis 1H), 4.32 (m, trans 1H); ^{13}C NMR ($CDCl_3$, 68 MHz) δ 9.11 (q, cis), 9.52 (q, trans), 21.27 (q, trans), 21.57 (q, cis), 23.70 (d, trans), 26.59 (d, cis), 28.38 (t), 28.81 (t), 34.42 (t), 36.34 (t), 37.36 (t), 37.99 (t), 78.50 (d, trans), 81.77 (d, cis), 171.58 (s, cis), 172.53 (s, trans); IR neat 1732 cm^{-1}; HREIMS for the cis isomer calcd for $C_8H_{14}O_2$ *m*/*z* 142.0994, found 142.1002; HREIMS for the trans isomer calcd for $C_8H_{14}O_2$ *m*/*z* 142.0994, found 142.0982. In comparison with the spectral data for **2s**,[45] the major isomer is assigned as a cis isomer.

5,7-Dimethyl-2-oxabicyclo[3.3.1]nonan-3-one (2v). Obtained as a slightly yellow liquid: ^{1}H NMR ($CDCl_3$, 270 MHz) δ 0.93 (d, 3H, J = 6.4 Hz), 1.00 (s, 3H), 1.02 (td-like, 1H, $J \approx$ 13.4, 1.5 Hz), 1.13 (td-like, 1H, $J \approx$ 13.9, 2.0 Hz), 1.47 (td-like, 1H, $J \approx$ 13.6, 2.0 Hz), 1.57 (dm, 1H, J_{doublet} = 13.4 Hz), 1.72 (m, 1H), 1.81 (dm, 1H, J_{doublet} = 13.6 Hz), 2.09 (dm, 1H, J_{doublet} = 13.9 Hz), 2.29 (dd, 1H, J = 1.5, 18.6 Hz), 2.43 (dd, 1H, J = 2.5, 18.6 Hz), 4.79 (septet, 1H, J = 2.0 Hz); ^{13}C NMR ($CDCl_3$, 68 MHz) δ 21.55 (q), 23.90 (d), 30.13 (q), 30.56 (s), 37.14 (t), 38.97 (t), 43.06 (t), 47.39 (t), 76.10 (d), 171.85 (s); IR neat 1732 cm^{-1}; HREIMS calcd for $C_{10}H_{16}O_2$ *m*/*z* 168.1151, found 168.1140.

Tetrahydro-3,6-dipropyl-2*H*-pyran-2-one (2w). GC analysis of the crude extract showed the ratio of **2w**/**2w′** was 24/1. Rotary evaporation of the solvent followed by flash chromatography on silica gel (hexane, then 10% EtOAc−hexane eluent) afforded pure **2w** in 61% yield as a cis/trans-isomer mixture in a 41/59 ratio. The cis/trans isomers of **2w** were separated by preparative HPLC. ***cis*-2w**, a slightly yellow liquid: ^{1}H NMR ($CDCl_3$, 270 MHz) δ 0.93 (t, 6H, J = 6.8 Hz), 1.33−1.73 (m, 9H), 1.86−2.05 (m, 3H), 2.30−2.45 (m, 1H), 4.20−4.32 (m, 1H); ^{13}C NMR ($CDCl_3$, 68 MHz) δ 13.85 (q), 13.91 (q), 18.08 (t), 19.85 (t), 25.51 (t), 28.87 (t), 34.05 (t), 38.36 (t), 40.60 (d), 81.02 (d), 174.03 (s); IR neat 1728 cm^{-1}; HREIMS calcd for $C_{11}H_{20}O_2$ *m*/*z* 184.1463, found 184.1474. ***trans*-2w**, a slightly yellow liquid: ^{1}H NMR ($CDCl_3$, 270 MHz) δ 0.93 (t, 6H, J = 6.8 Hz), 1.31−1.75 (m, 9H), 1.80−1.96 (m, 2H), 1.99−2.11 (m, 1H), 2.40−2.51 (m, 1H), 4.23−4.31 (m, 1H); ^{13}C NMR ($CDCl_3$, 68 MHz) δ 13.83 (q), 13.98 (q), 18.36 (t), 20.18 (t), 23.35 (t), 26.69 (t), 32.96 (t), 37.41 (t), 37.95 (d), 77.75 (d), 175.81 (s); IR neat 1736 cm^{-1}; HREIMS calcd for $C_{11}H_{20}O_2$ *m*/*z* 184.1463, found 184.1437. In comparison with the spectral data for **2n**,[44] the major isomer is assigned as a cis isomer.

Carbonylation of an Alkyl 4-Nitrobenzenesulfenate under Irradiation Conditions. Benzene (25 mL) and sulfenate **5b** (169 mg, 0.5 mmol) were placed in a 50-mL stainless steel autoclave used for irradiation and lined with a Pyrex glass tube. The autoclave was closed, purged twice with 10 atm of CO, and then charged with 60 atm of CO and irradiated with stirring for 1 h using a 500-W xenon lamp (>300 nm) placed 30 cm from the solution. After excess CO was discharged, the benzene was evaporated. The residue was found by ^{1}H NMR to contain a 52% yield of tetrahydro-6,6-dimethyl-3-hexyl-2*H*-pyran-2-one (**6b**) (vs trioxane internal standard). The spectroscopic data of **6b**

(44) Pirkle, W. H.; Adams, P. E. *J. Org. Chem.* **1979**, *44*, 2169. Also see refs 20 and 21c and d.

(45) (a) Carroll, F. I.; Mitchell, G. N.; Blackwell, J. T.; Sobti, A.; Meck, R. *J. Org. Chem.* **1974**, *39*, 3890. (b) Pirkle, W. H.; Adams, P. E. *J. Org. Chem.* **1980**, *45*, 4117.

purified by flash chromatography and preparative HPLC (GPC column) is listed below: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.88 (t, 3H, J = 6.6 Hz), 1.22−1.45 (m, 14H including 1.41 (s, 3H) and 1.37 (s, 3H)), 1.52−1.60 (m, 1H), 1.63−1.98 (complex m, 5H), 2.30−2.38 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.02, 22.47, 22.55, 26.64, 28.00, 29.12, 29.74, 31.61, 31.68, 33.69, 39.56, 81.57, 173.65; IR neat 1727 cm^{-1}; HREIMS calcd for $C_{13}H_{24}O_2$ m/z 212.1776, found 212.1785.

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Supporting Information Available: General procedure for hydrogenation of aromatic alcohols, procedure for control experiments (Tables 1 and 4), characterization data for **2a**−**b**, **2f, 2m**−**o**, **2q**−**s**, **2u, 2x**−**y**, **3a**, and **3z**, procedure for synthesis of **3z**, and cis/trans assignments of 2,5-disubstituted δ-lactones (9 pages, print/PDF). See any current masthead page for ordering information and Web access instructions.

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