Allylic Carboxylations and Lactonization Using Benzoquinone and Hydrogen Peroxide or *tert*-Butyl Hydroperoxide as Oxidants

Björn Åkermark,* E. Magnus Larsson,* and Johan D. Oslob
Department of Organic Chemistry, Royal Institute of Technology, S-100 44 Stockholm, Sweden

Received March 2, 1994®

Two new systems have been developed for catalytic carboxylation of alkenes. Both use palladium(II) as catalyst and benzoquinone as cocatalyst. In the first hydrogen peroxide was used as oxidant in acetic acid solution. Alkenes such as cyclohexene and 5-decene were converted cleanly to allylic acetates, but with 1-decene mainly the methyl ketone was formed. A diene such as 1,3-cyclohexadiene gave the diacetate while *cis*-1,2-divinylcyclohexane gave the cyclized monoacetate. In the second system, *tert*-butyl hydroperoxide was used as oxidant, permitting a wider choice of solvents and nucleophiles. Intramolecular reaction to lactones was possible in addition to allylic addition of acids such as benzoic, pivalic, and (*S*)-*O*-acetylmandelic acid.

Introduction

Allylic acetates have become important intermediates in organic synthesis, in particular after it was realized that metal-catalyzed replacement of the acetoxy group by nucleophiles is a facile and efficient reaction.[1] In the course of our investigations on reoxidation systems for palladium-catalyzed allylic acetoxylation of olefins, using oxygen[2] as final oxidant, we found evidence that hydrogen peroxide is formed as a very active intermediate oxidant.[3] Because hydrogen peroxide has previously been used as the reoxidant in Wacker-type reactions,[4,5] we decided to investigate if it also could be used in allylic acetoxylation and related reactions, provided the reaction conditions were modified. With solvents other than acetic acid there is a potential to use nucleophiles other than acetate. The possibility is also opened for intramolecular reactions, lactonizations, for reactions with dienes and for chiral induction by the use of acids from the chiral pool.

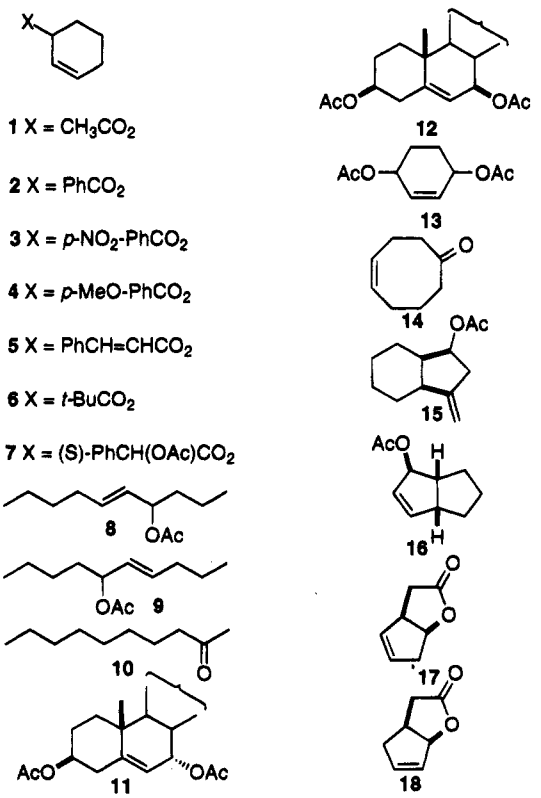
Results and Discussion

The acetoxylation reactions were performed essentially according to the procedure described earlier[6] except that hydrogen peroxide or *tert*-butyl hydroperoxide was used as oxidant in place of MnO_2. In a typical reaction, palladium acetate (5 mol %) was used as catalyst in combination with hydroquinone or benzoquinone (10 mol %) as cocatalyst, hydrogen peroxide (35%, 150 mol %) as oxidant, and acetic acid as solvent at temperatures between 25 and 70 °C. The optimized reaction conditions were determined using an internal standard and by monitoring the reactions by GLC. Acetoxylation of cyclohexene gave ca. 80% isolated yield of **1** (ca. 90% GLC yield, Table 1) in a reaction that was approximately eight times faster than when manganese dioxide was used as oxidant.

Table 1. Oxidation of Olefins with Palladium Acetate Using Hydrogen Peroxide and Benzoquinone as Oxidant in Acetic Acid[a]

entry	substrate	product	yield[b] (%)	time (h)/ *T* (°C)
1	cyclohexene	**1**	77	2/50
2	*trans*-5-decene	**8** and **9**	71 (1:1 mixture)	16/25
3	1-decene	**10**	46	16/70
4	cholest-5-en-3β-yl acetate	**11** and **12**	20 (1:1 mixture)	15/70
5	1,3-cyclohexadiene	**13**	67[c]	24/25
6	1,5-cyclooctadiene	**14**	42	22/25
7	*cis*-1,2-divinylcyclohexene	**15**	60	20/25

[a] Reactions run with 5 mol % $Pd(OAc)_2$, 10 mol % benzoquinone, and 150 mol % hydrogen peroxide. [b] Isolated yields. [c] Reaction run in a two-phase system of pentane and acetic acid and 110 mol % LiOAc added.



When the amount of hydrogen peroxide was increased from 1.5 equiv to 2.5, the initial reaction rate increased somewhat but a slight decrease in yield could be observed. A similar decrease in yield was observed when dilute (35%) hydrogen peroxide was substituted by concentrated (85%) hydrogen peroxide. The lower yield

® Abstract published in *Advance ACS Abstracts,* August 1, 1994.

(1) (a) Tsuji, J. *Organic Synthesis with Palladium Compounds*; Springer Verlag: Heidelberg, 1980. (b) Trost, B. M.; Verhoeven, T. R. In *Comprehensive Organometallic Chemistry*; Wilkinson, G., Stone, F. G. A., Abel, E. W., Eds.; Pergamon: Oxford, 1982; Vol. 8, pp 799–938. (c) Heck, R. F. *Palladium Reagents in Organic Synthesis*; Academic Press: New York, 1985. (d) Magid, R. M. *Tetrahedron* **1980**, *36*, 1902–30. (e) Collman, J. P.; Hegedus, L. S.; Norton, J. R.; Finke, R. G. *Principles and Applications of Organotransition Metal Chemistry*; University Science Books: Mill Valley, 1987. (f) Godleski, S. A. *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, 1991; Vol. 4, Chapter 3.3, pp 585–661. (g) Harrington, J. P. *Transition Metals in Total Synthesis*; John Wiley & Sons: New York, 1990.

(2) Byström, S. E.; Larsson, E. M.; Akermark, B. *J. Org. Chem.* **1990**, *55*, 5674–5675.

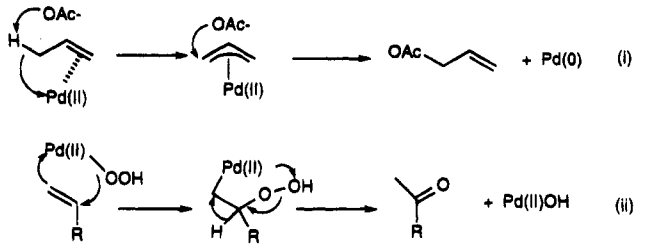
(3) Larsson. E. M.; Akermark, B. Manuscript in preparation.

0022-3263/94/1959-5729$04.50/0

could be explained by byproduct formation due to epoxidation by peroxyacetic acid which should be formed more efficiently from concentrated hydrogen peroxide than from dilute hydrogen peroxide.[7] In a separate experiment it could be shown that *trans*-2-acetoxycyclohexanol is the major product if palladium acetate is excluded. Furthermore, *trans*-2-acetoxycyclohexanol, presumably formed via epoxidation and solvolysis, is the major product even in the presence of palladium acetate if peroxyacetic acid is used as oxidant in place of hydrogen peroxide. Addition of benzoquinone to the reaction is necessary for obtaining high yields. In acetoxylations where benzoquinone was excluded, only ca. 25% cyclohexenyl acetate was obtained, corresponding to five turnovers. One reason for the low turnover number is clearly palladium-catalyzed decomposition of hydrogen peroxide,[8] as indicated by the formation of gas bubbles.[9] When the reaction temperature was lowered from 50 to 25 °C the yield was increased by approximately 5% to 94% (GLC) with a simultaneous increase in reaction time from 2 to 26 h. Finally it may be noted that in all reactions run with cyclohexene, only minute quantities of cyclohexanone could be detected.

Acetoxylation of *trans*-5-decene gave the expected[6] mixture of (*E*)-5-decen-4-yl acetate, **8**, and (*E*)-6-decen-5-yl acetate, **9**, in equal amounts (GLC and ^{1}H-NMR) in a decent yield. A terminal alkene, 1-decene gave mainly the methyl ketone **10** in accordance with results from the literature.[4] Several isomeric acetates were also formed in low yields (GLC). Cyclooctene (15 h/70 °C) gave only a low conversion and a low yield of the desired product, together with a number of different unidentified products. It is known that this olefin is unusually difficult to get to react in the allylic acetoxylation.[6] Also, 3-carene was tried but gave a disappointingly low conversion. Finally, cholest-5-en-3β-yl acetate was studied as an example of a complex substrate where selective acetoxylation would be of great interest. A mixture[10] of cholest-5-ene-3β,7α-diyl diacetate, **11**, and cholest-5-ene-3β,7β-diyl diacetate, **12**, was formed in a rather low yield (ca. 20%) and low conversion.[11] The results may be explained by the operation of two competing reactions (Scheme 1), allylic acetoxylation by palladium(II) (i)[6,12,13] and oxidation to ketone by a hydrogen peroxide–palladium complex (ii).[4]

Scheme 1



In order to investigate if hydrogen peroxide and quinone could be used as a general reoxidant in palladium-catalyzed reactions we have tested this system in 1,4-diacetoxylation of 1,3-dienes[14] and ring closure of 1,5-dienes[15,16] (Table 1). The trans-stereoselectivity for 1,4-diacetoxylation using hydrogen peroxide as reoxidant was quite low[17] (trans/cis 62:38) compared to when manganese dioxide was used (95:5).[14] This is probably due to competiton between hydrogen peroxide anion and acetate for the coordination to palladium(II) which makes the cis migration of coordinated acetate from palladium to the η^3-allyl less important.[14] Increasing the amount of benzoquinone (to 25 mol %) increased the trans/cis ratio to 72:28 while a decrease to 5 mol % decreased the ratio to approximately 1:1 (the product was not as pure as when larger amounts of benzoquinone were used). With acetone[18] as the solvent, the stereoselectivity was increased to 86:14. When benzoquinone was substituted by tetrachlorobenzoquinone, a lower yield of diacetoxylated product was obtained (24%). In this case the isomer in excess was surprisingly the cis isomer as shown by the trans/cis ratio 38:62. Reaction with 1,5-cyclooctadiene gave exclusively cyclooct-4-enone, **14**, with a conversion of ca. 60%. However, *cis*-1,2-divinylcyclohexane was cyclized in good yield to the bicyclic compound **15** (Table 1).

The hydrogen peroxide/benzoquinone/$Pd(OAc)_2$ system proved to be slower in solvents other than acetic acid, and the best yield (in acetone) was only ca. 25% with acetic acid as the nucleophile. In less polar solvents such as dichloromethane, the low reactivity could be due to the low solubility of the hydrogen peroxide. Attempts to use hexafluoroacetone as a more soluble carrier for hydrogen peroxide failed due to extensive decomposition of the peroxide. However, with the less polar peroxide *tert*-butyl hydroperoxide (TBHP), the acetoxylation of cyclohexene worked quite well in dichloromethane (entry 1, Table 2).[19] With this system, a series of other acids could also be added to cyclohexene, giving good to excellent yields of cyclohexenyl carboxylates (Table 2). A bicyclic alkene, *cis*-bicyclo[3.3.0]-2-octene, was also tried with acetate as nucleophile. Excellent yield of the

(4) Roussel, M.; Mimoun, H. *J. Org. Chem.* **1980**, *45*, 5387–5390.
(5) Antonson, T.; Hansson, S.; Moberg, C. *Acta. Chem. Scand. Ser. B* **1985**, *39*, 593–596.
(6) Hansson, S.; Heumann, A.; Rein, T.; Akermark, B. *J. Org. Chem.* **1990**, *55*, 975–984.
(7) Swern, D. Organic Peroxy Acids-Preparation, Properties, and Structure. In *Organic Peroxides*; Swern, D., Ed.; Wiley-Interscience: New York, 1970; Vol. I, Chapter 6.
(8) Hydrogen peroxide is rapidly decomposed in the presence of transition metals. Greenwood, N. N.; Earnshaw, A. *Chemistry of the Elements*; Pergamon Press: Oxford, 1984; p 745.
(9) By measuring the amount of liberated oxygen as a function of time it could be shown that at a concentration of ca. 0.4 M, hydrogen peroxide has a half-life of 1 h at 60 °C in acetic acid in the presence of palladium acetate (20 mM).
(10) The stereoids epimerize in hot acetic acid. Stefanoić, M; Jokić, A.; Lorenc, L.; Mihailović, M. L. *Helv. Chim. Acta* **1970**, *53*, 1895–1902.
(11) A number of other oxidation systems (manganese dioxide/benzoquinone, oxygen/copper acetate, hydroquinone/iron(III) nitrate) have been tried for acetoxylation of cholest-5-en-3β-yl acetate but low yield and conversion were obtained with all of the oxidation systems.
(12) The attack of acetate on η^3-allylpalladium complexes can be either external or internal (by a cis migration of acetate coordinated to palladium). Grennberg, H.; Lagner, V.; Bäckvall, J.-E. *J. Chem. Soc., Chem. Commun.* **1991**, 1190–1192.
(13) Accumulating evidence points to a η^3-allyl intermediate. Grennberg, H.; Simon V.; Bäckvall, J.-E. *J. Chem. Soc., Chem. Commun.* **1994**, 265–266.
(14) Bäckvall, J.-E.; Byström, S. E.; Nordberg, R. E. *J. Org. Chem.* **1984**, *49*, 4619–4631.
(15) Henry, P. M.; Davis, M.; Ferguson, G.; Philips, S.; Restivo, R. *J. Chem. Soc., Chem. Commun.* **1974**, 112–113.
(16) Antonsson, T.; Moberg, C.; Tottie, L.; Heuman, A. *J. Org. Chem.* **1989**, *54*, 4914–4929.
(17) The use of urea–hydrogen peroxide in the oxidation of 1,3-cyclohexadiene to 1,4-diacetoxy-2-cyclohexene has been reported.[15] Also in this case a low stereoselectivity was observed.
(18) Bäckvall, J.-E.; Granberg, K. L.; Hopkins, R. B. *J. Acta Chem. Scand.* **1990**, *44*, 492–499.
(19) To make sure no radical reactions were involved a control experiment with Cu(I)Cl, a compound known to initiate radical reactions, present instead of the palladium salt, was performed. No products were observed. Rawlinson, R. G.; Sonovsky, G. *Synthesis* **1972**, 1.

Table 2. Allylic Carboxylations with the Pd(II)/Benzoquinone/TBHP System[a]

entry	substrate	carboxylic acid	product	time (h)	isolated yield (%) (GLC yield)
1	cyclohexene	AcOH	**1**	24	76[b,c] (87%)
2	cyclohexene	PhCOOH	**2**	13	77[d,e] (90%)
3	cyclohexene	*p*-NO_2PhCOOH	**3**	12	82[d] (87%)
4	cyclohexene	*p*-MeOPhCOOH	**4**	48	85[b,f] (>95%)
5	cyclohexene	cinnamic acid	**5**	14	89[d]
6	cyclohexene	t-BuCOOH	**6**	64	65[b,f]
7	cyclohexene	PhCH(OAc)COOH	**7**	14	82,[b,f] de = 21%[g]
8	*cis*-bicyclo[3.3.0]oct-2-ene	AcOH	**16**	60	79[b,f] (90%)
9	2-cyclopentene-1-acetic acid		**17** and **18**	1.5	73[d] (85%), mixture 15:85[g]

[a] 5 mol % Pd(II), 10 mol % benzoquinone, 110 mol % TBHP, and 200 mol % carboxylic acid in CH_2Cl_2 at 40 °C. [b] With $Pd(OAc)_2$ as catalyst. [c] 240 mol % TBHP was used. [d] With $Pd(OTFA)_2$ as catalyst. [e] 20 mol % benzoquinone was used. [f] A few percent of **1** was formed. [g] Determined by GLC and NMR.

Table 3. Allylic Benzoxylation of Cyclohexene with the Pd(II)/Benzoquinone/TBHP System[a]

entry	quinone (mol %)	TBHP (mol %)	benzoic acid (mol %)	yield[b] (%)	time (h)
1	5	120	100	60	13
2	10	120	100	65	13
3	20	120	100	78	11.5
4	50	120	100	79	8
5	110		100	52	10
6		120	100	7	12
7	20	120	200	90	13
8	20	120	500	94	13
9	20	240	100	70	13
10	20	480	100	49	8
11	5	120	100	38[c,d]	12
12	5	120	100	50[e]	10
13	5	120	100	60[d,f]	14

[a] Benzoquinone, TBHP, benzoic acid, and 5 mol % $Pd(OTFA)_2$ in 6 mL of CH_2Cl_2 at 40 °C. [b] GLC yield. [c] At room temperature. [d] The reaction was not run to completion. [e] Only 3 mL of CH_2Cl_2. [f] With $Pd(OAc)_2$ as catalyst.

acetate **16** (entry 8) was obtained, which is the same product as when manganese dioxide was used as oxidant.[6]

Optimizations of temperature, volume of solvent, equivalents of acid, TBHP, and benzoquinone were carried out with the intermolecular reaction with benzoic acid as nucleophile and cyclohexene as substrate (Table 3). The reactions were run in dichloromethane, but acetone also worked as solvent although the rates and the yields were lower. The rate of the reaction was quite dependent of the amount of benzoquinone (entries 1–4, Table 3), and in the absence of benzoquinone the yield (GLC) was very low, about 5% (entry 6). The rate of the reaction was quite temperature dependent (entry 11). Increasing the amount of acid from 100 mol % to 200 mol % increased the yield about 10%; however, a further increase of the amount of acid had little effect on the yield (entries 3, 7, and 8). Use of more than 1.2 equiv of TBHP increased the initial rate but lowered the final yield (entries 3, 9, and 10) markedly, probably due to slow destruction of the product. The rate could also be increased by using less solvent, but then the final yield was lowered (entries 1 and 12).

Several differently substituted benzoquinones were tested (Table 4), both more and less electron rich than unsubstituted benzoquinone. However, the parent benzoquinone proved to be the most efficient.

Among the aromatic acids, *p*-nitro and *p*-methoxybenzoic acid both worked excellently (entries 3 and 4, Table 2). Unsaturation implies no problem as shown by the high yield with cinnamic acid (entry 5). Even a hindered aliphatic acid such as pivalic acid worked quite well (entry 6).

Table 4. Yields for Benzoxylation of Cyclohexene with Different Benzoquinones[a]

entry	quinone	yield[b] (%)
1	2,3-bis(methylthio)naphthoquinone	0
2	2,5-di-*tert*-butylbenzoquinone	13[c]
3	2,6-dimethoxybenzoquinone	7[c]
4	2,5-diaminobenzoquinone	2
5	benzoquinone	65
6	tetrachlorobenzoquinone	0

[a] 5 mol % $Pd(OTFA)_2$, 10 mol % quinone, 110 mol % TBHP, and 100 mol % benzoic acid in CH_2Cl_2 at 40 °C. [b] GLC yield after 13 h. [c] The reaction was not completed.

The rate dependence of pK_a of the carboxylic acid was investigated using differently para-substituted benzoic acids. These reactions were performed in acetone since the *p*-methoxy- and *p*-nitro-substituted benzoic acids were not completely soluble in dichloromethane. The carboxylic acid with the lower pK_a reacted faster. When 0.5 equiv of *p*-methoxybenzoic acid and 0.5 equiv *p*-nitrobenzoic acid were used at the same time the more acidic *p*-nitrobenzoic acid still reacted faster. Thus, the rate difference seems to be the result of different degrees of dissociation of the acids rather than the different availabilities of protons; i.e., the carboxylate seems to be the actual nucleophile.

With palladium acetate as catalyst,[20] small amounts of allylic acetates (4–6%) were generally formed when carboxylates other than acetate were used as nucleophiles. Palladium trifluoroacetate was therefore also tried as catalyst. In some cases, e.g., with *p*-nitrobenzoate as nucleophile, this catalyst gave both cleaner reactions and higher yields.

One lactonization was also performed (Table 2, entry 9).[21] A mixture of two lactones, **17** and **18**, was obtained. This reaction was much faster than the intermolecular reactions (85% GLC yield after 1.5 h), and the final yield was good (73% isolated).

Finally, it is interesting to note that it is possible to obtain some stereoselectivity (de = 21%) by using a chiral carboxylic acid such as (*S*)-*O*-acetylmandelic acid (entry 7, Table 2). The chemical shift differences of diastereomeric *O*-acetylmandelate esters seem to follow the same trend as those of diastereomeric *O*-methylmandelate esters,[22] which have proven to be useful in determining the absolute configuration of many chiral secondary

(20) The quality of the palladium catalyst was important. Recrystallization from acetic acid prior to use often increased the conversions about 10%.

(21) Similar palladium-catalyzed lactonizations have been perfomed with good yields by using oxygen as reoxidant for palladium in DMSO at room temperature. Larock, R. C.; Hightower, T. R. *J. Org. Chem.* **1993**, *58*, 5298–5300.

(22) Dale, J. A.; Mosher, H. S. *J. Am. Chem. Soc.* **1973**, *58*, 512–519.

alcohols.[23] Using the same arguments as for the *O*-methylmandelate esters that the oxygen-containing α-substituent and the carbonyl oxygen preferably are eclipsed[23] the (*R*,*S*)-configuration can be assigned to the major diastereomer by NMR.

(*S*)-Mandelic acid was also used and gave a somewhat higher de (32%), but the yield was low (about 15%).

Conclusions

Hydrogen peroxide and TBHP, in combination with a quinone, effect rapid inter- and intramolecular allylic carboxylation of cyclic and internal alkenes. Both oxidants induce faster reaction than oxidants used previously.[6] With TBHP solvents other than acetic acid can be used, which leads to facilitated workup. It becomes possible to use nucleophiles other than acetate, such as *p*-nitrobenzoate which is a better leaving group in, e.g., palladium(0)-catalyzed allylic substitution. Lactonization can also be perfomed under mild reaction conditions.

Experimental Section

General. All solvents and reagents were purchased from commercial sources (Aldrich, Engelhardt, Fluka, Labasco, Merck) and used as received, unless otherwise indicated. $Pd(OAc)_2$ was purchased from Aldrich and Engelhardt and recrystallized from acetic acid prior to use. $Pd(OTFA)_2$ was prepared from $Pd(OAc)_2$ using a literature procedure.[24] Bulb-to-bulb distillation refers to distillation with a Büchi GKR-50 Kugelrohr apparatus. Purification by medium-pressure liquid chromatography (MPLC) was performed as described by Baeckström *et al.*[25] Flash chromatography was performed as described by Still *et al.*[26] The gel used was Merck silica gel 60. TLC analyses were performed on Merck aluminum plates coated with silica using UV light and 5% phosphomolybdic acid in ethanol for visualization. ^1H NMR and ^{13}C NMR spectra were recorded on a 400-MHz NMR (Bruker Model AM 400) and a 250-MHz NMR (Bruker Model ACF 250). ^1H NMR chemical shifts are reported in δ (ppm) relative to Me_4Si as internal standard. ^{13}C chemical shifts are given in δ values relative to the solvent ($CDCl_3$ 77.00 ppm or C_6D_6 128.0 ppm). The abbreviation app = apparent is used in descriptions of NMR multiplicities. ^1H NMR integrations are reported as relative number of hydrogens (H). NMR data are reported only if they are more detailed than data in the literature. GLC analyses were performed on a Varian 3700 instrument fitted with a BP-1 (methylsilicone, 25 m) capillary column. C_8–C_{16} *n*-alkanes were used as internal standards for GLC analyses. Elemental analyses were performed by Analytische Laboratorien, Engelskirchen, Germany.

Oxidations with Hydrogen Peroxide as Oxidant. Oxidation of Olefins.[27] Palladium acetate (22.4 mg, 0.1 mmol) and benzoquinone (22 mg, 0.2 mmol) were dissolved in glacial acetic acid (10 mL) in a test tube, and the atmospere was changed to argon. Internal standard, 2 mmol of the olefin, and 35% hydrogen peroxide (3 mmol, 0.25 mL) were added. The optimizations were done by following the reactions by capillary GLC by using internal standards. The mixture was stirred for the reported time at the reported temperature. After the mixture was cooled to room temperature, 50 mL of pentane–ether (1:1) was added and the resulting mixture was successively washed with 50 mL of water and with 50 mL of 2 M NaOH three times. The combined aqueous phases were extracted three times with 50 mL of pentane–ether (1:1), and the combined organic phases were finally dried over anhydrous $MgSO_4$. After evaporation of the solvent, the product was purified either by distillation or by flash chromatography, eluent hexane–ether, 95:5.

2-Cyclohexen-1-yl Acetate (1). Reaction time 2 h, temperature 50 °C. A 216-mg (77%; distillation) sample was isolated. ^1H NMR[28] and ^{13}C NMR[29] spectra were in full accordance with those reported in the literature.

(*E*)-5-Decen-4-yl Acetate (8) and (*E*)-6-Decen-5-yl Acetate (9). Reaction time 16 h, temperature 25 °C. A 282-mg (71%; flash chromatography) sample of a 1:1 mixture (from NMR and GLC) of **8** and **9** was isolated. ^1H NMR and ^{13}C NMR spectra[6] were in full accordance with those reported in the literature.

Oxidation of 1-Decene. Reaction time 16 h, temperature 70 °C. A 144-mg (46%; distillation) sample of 2-decanone, **10**, was isolated. ^1H NMR spectrum[30] was in full accordance with that reported in the literature.

Cholest-5-ene-3β,7α-diyl Diacetate (11) and Cholest-5-ene-3β,7β-diyl Diacetate (12). Reaction time 15 h, temperature 70 °C. A 194-mg (20%; flash chromatography) sample of a mixture of **11** and **12** was isolated. ^1H NMR data[31] were in full accordance with those reported in the literature.

1,4-Diacetoxy-2-cyclohexene (13). The reaction was run in a two-phase system of pentane and acetic acid.[14] Reaction time 24 h, temperature 25 °C. A 266-mg (67%; recrystallization from hexane) sample of a mixture (62:38) of *trans*- and *cis*-**13** was isolated. ^1H NMR spectrum[14] was in full accordance with that reported in the literature.

Oxidation of 1,5-Cyclooctadiene. Reaction time 22 h, temperature 25 °C. A 104-mg (42%; flash chromatography) sample of cyclooct-4-enone (**14**) was isolated. ^1H NMR[32] and ^{13}C NMR[33] spectra were in full accordance with those reported in the literature.

7-Acetoxy-9-methylenebicyclo[3.3.0]nonane (15). Reaction time 20 h, temperature 25 °C. A 233-mg (60%; flash chromatography) sample of **15** was isolated. ^1H NMR and ^{13}C NMR spectra[16] were in full accordance with those reported in the literature.

Carboxylations with TBHP as Oxidant. General Workup Procedure A. This is a very simple and non-time-consuming procedure which can be applied when the product is nonvolatile. After the reaction mixture had cooled to room temperature, 10 g of silica gel was added to the reaction mixture and the solvent was evaporated in vacuo. **CAUTION.**[34] Purification was performed by MPLC. The solvent gradient was a mixture of hexane and ethylacetate.

General Workup Procedure B. This procedure was performed with the more volatile products. When the reaction mixture had reached room temperature, it was poured onto 100 mL of a freshly prepared solution of 30 g of ferrous sulfate heptahydrate in 100 mL of distilled water, the resulting two-phase mixture stirred for 15–20 min and then transferred to a separatory funnel, and the phases were separated. The aqueous phase was extracted twice with 100 mL of ether. To make sure that the organic phase was peroxide free, Merck

(23) Trost, B. M.; Belletire, J. L.; Godleski, S.; McDougal, P. G.; Baldwin, J. J.; Christy, M. E.; Ponticello, G. S.; Varga, S. L.; Springer, J. P. *J. Org. Chem.* **1986**, *51*, 2370–2374.

(24) Stephenson, T. A.; Morehouse, S. M.; Powell, A. R.; Heffer, J. P.; Wilkinson, G. *J. Chem. Soc.* **1965**, 3632.

(25) Baeckström, P.; Stridh, K.; Li, L.; Norin, T. *Acta Chem. Scand.* **1987**, *B41*, 442–447.

(26) Still, W. C.; Kahn, M.; Mitra, A. J. *Org. Chem.* **1978**, *43*, 2923–5.

(27) The same procedure was used for oxidation of all olefins if not otherwise indicated.

(28) Pearson, A. J.; Hsu, S. Y. *J. Org. Chem.* **1986**, *51*, 2505–11.

(29) Chow, Y. L.; Buono-Core, G. E. *J. Am. Chem. Soc.* **1986**, *108*, 1234–9.

(30) Bäckvall, J.-E.: Hopkins, R. B.; Grennberg, H.; Mader, M. M.; Awasthi, A. K. *J. Am. Chem. Soc.* **1990**, *112*, 5160–5166.

(31) Shoppee, C. W.; Newman, B. C. *J. Chem. Soc. C* **1968**, 981–983.

(32) Zakharkin, L. I. Guseva, V. V.; Kamernitskii, D. A. *J. Org. Chem., USSR* **1989**, 99–102.

(33) Bloodworth, A. J.; Courtneidge, J. L. Curtis, R. J.; Spencer, M. D. *J. Chem. Soc., Perkin Trans. 1* **1990**, 2951–2955.

(34) This procedure has been carried out several times without incident. However, precautions should be taken and the evaporation should be performed behind an adequate blast shield. TBHP is one of the most stable peroxides, and it is known to be safely removed by, e.g., chromatography. Workup procedure B is general and can be applied in all cases where procedure A has been performed if there is a need to remove the peroxide first.

peroxide test strips were used. The combined organic phases were then extracted with two 100-mL portions of saturated K_2CO_3 solution. If emulsions were a problem, the mixture was filtered through a plug of Celite. The water phase was extracted twice with 100 mL of ether. The combined organic phases were then dried with $MgSO_4$, the solvent was distilled off, and the resulting crude oil was subjected to flash chromatography with a mixture of pentane and ether as eluent. The solvent was distilled off, and the product was purified by bulb-to-bulb distillation.

Preparation of a Stock Solution of TBHP in CH_2Cl_2. A 220-mL sample of 70% TBHP in water was added to 500 mL of CH_2Cl_2. The resulting mixture was dried with $MgSO_4$, and the concentration of TBHP was determined by iodometric tiration according to a literature procedure.[35] The concenteration was about 2.0 M. The stock solutions were stored in high-density polyethylene bottles at 0−8 °C. The concentration was constant for several weeks; however, the solution should be dried with $MgSO_4$ and retitrated every 2 weeks for reproducibility of the results.

Oxidation of Olefins.[27] The palladium catalyst (0.5 mmol, 5 mol %), benzoquinone (108 mg, 1.0 mmol, 10 mol %), and the carboxylic acid (200 mol %) were dissolved in 45 mL of CH_2Cl_2 in a 100-mL round-bottomed flask fitted with a reflux condenser. The mixture was stirred at room temperature for 15 min, and then the temperature was raised to 40 °C, TPHB/CH_2Cl_2 stock solution (corresponding to 110 mol % TBHP) and 10 mmol of the olefin were added, and the mixture was stirred and refluxed for the reported time. The optimizations were done by following the reactions by capillary GLC using calibrated internal standards.

2-Cyclohexen-1-yl Acetate (1). $Pd(OAc)_2$ and 220 mol % TBHP were used. Reaction time 24 h. Optimized yield (GLC) 87%. Workup procedure B was performed, yielding 1.04 g (76%). ^1H NMR[28] and ^{13}C NMR[29] spectra were in full accordance with those reported in the literature.

***exo*-Bicyclo[3.3.0]oct-3-en-2-yl Acetate (16).** $Pd(OAc)_2$ was used. Reaction time 60 h. Optimized yield (GLC) 90%. Workup procedure A was performed, yielding 1.31 g (79%). ^1H NMR and ^{13}C NMR spectra[6] were in full accordance with those reported in the literature.

2-Cyclohexen-1-yl Benzoate (2). $Pd(OTFA)_2$ and 20 mol % benzoquinone were used. Reaction time 13 h. Optimized yield (GLC) 90%. Workup procedure A was performed, yielding 1.56 g (77%). ^1H NMR[36] spectrum was in full accordance with that reported in the literature: ^1H NMR (250 MHz, $CDCl_3$) δ 8.06 (m, 2 H), 7.54 (m, 1 H), 7.43 (m, 2 H), 6.02 (dtd, J_1 = 10.0 Hz, J_2 = 4.8 Hz, J_3 = 0.8 Hz, 1 H), 5.84 (ddt, J_1 = 10.0 Hz, J_2 = 3.5 Hz, J_3 = 2.1 Hz, 1 H), 5.51 (td, J = 5.0 Hz, J_2 = 4.8 Hz, 1 H), 2.21−1.62 (m, 6 H); ^{13}C NMR (250 MHz, $CDCl_3$) δ 166.2, 132.9, 132.8, 130.8, 129.6, 128.3, 125.7, 66.6, 28.4, 25.0, 19.0.

2-Cyclohexen-1-yl *p*-Nitrobenzoate (3). $Pd(OTFA)_2$ was used. Reaction time 12 h. Optimized yield (GLC) 87%. Workup procedure A was performed, yielding 2.03 g (82%). ^1H NMR[37] data were in full accordance with those reported in the literature: ^1H NMR (250 MHz, $CDCl_3$) δ 8.28 (AB app d, J = 9.0 Hz, 2 H), 8.21 (AB app d, J = 9.0 Hz, 2 H), 6.07 (dtd, J_1 = 10.1 Hz, J_2 = 3.2 Hz, J_3 = 2.1 Hz, 1 H), 5.83 (dt, J_1 = 10.1 Hz, J_2 = 3.3 Hz, J_3 = 2.1 Hz, 1 H), 5.54 (dd, J_1 = 3.3 Hz, J_2 = 1.5 Hz, 1 H), 2.22−1.67 (m, 6 H); ^{13}C NMR (250 MHz, $CDCl_3$) δ 164.3, 150.5, 136.2, 133.6, 130.7, 125.0, 123.5, 69.8, 28.3, 24.9, 18.8.

2-Cyclohexen-1-yl *p*-Methoxybenzoate (4). $Pd(OAc)_2$ was used. Reaction time 48 h. Optimized yield (GLC) >95%. Capillary GLC indicated a small amount (≤4%) of **1**. Workup procedure A was performed, yielding 1.97 g (85%). ^1H NMR[36] spectrum was in full accordance with that reported in the literature: ^1H NMR (250 MHz, $CDCl_3$) δ 8.01 (AB app d, J = 8.9 Hz, 2 H), 6.91 (AB app d, J = 8.9 Hz, 2 H), 5.99 (dt, J_1 = 10.1 Hz, J_2 = 3.2 Hz, 1 H), 5.82 (ddt, J_1 = 10.1 Hz, J_2 = 3.3 Hz, J_3 = 2.0 Hz,1 H), 5.48 (dd, J_1 = 3.3 Hz, J_2 = 1.7 Hz, 1 H), 3.85 (s, 3 H), 2.14−1.67 (m, 6 H); ^{13}C NMR (250 MHz, $CDCl_3$) δ 166.0, 163.2, 132.6, 131.6, 126.0, 125.7, 123.2, 68.2, 55.4, 28.5, 26.5, 19.0.

2-Cyclohexen-1-yl Cinnamate (5). $Pd(OTFA)_2$ was used. Reaction time 14 h. Workup procedure A was performed, yielding 1.97 g (89%: bp 159 °C/0.1 mmHg) of a colorless oil; ^1H NMR (250 MHz, $CDCl_3$) δ 7.69 (d, J = 16.0 Hz, 1 H), 7.54−7.49 (m, 2 H), 7.39−7.35 (m, 2 H), 6.45 (d, J = 16.0 Hz, 1 H), 6.00 (dtd, J_1 = 10.0 Hz, J_2 = 3.7 Hz, J_3 = 0.9 Hz, 1 H), 5.78 (ddt, J_1 = 10.0 Hz, J_2 = 2.1 Hz, J_3 = 1.7 Hz, 1 H), 5.41 (dt, J_1 = 3.0 Hz, J_2 = 1.7 Hz, 1 H), 2.19−1.61 (m, 6 H); ^{13}C NMR (250 MHz, $CDCl_3$) δ 166.6, 144.5, 134.5, 132.6, 130.2, 128.8, 128.8, 125.8, 118.6, 68.2, 28.4, 24.9, 18.9. Anal. Calcd for $C_{15}H_{16}O_2$: C, 78.92; H, 7.06. Found: C, 78.76; H, 6.93.

2-Cyclohexen-1-yl Pivalate (6). $Pd(OAc)_2$ was used. Capillary GLC indicated a small amount (≤5%) of **1**. Reaction time 64 h. Workup procedure B was performed, yielding 1.20 g (65%). ^1H NMR and ^{13}C NMR spectra[38] were in full accordance with those reported in the literature.

2-Cyclohexen-1-yl *O*-Acetylmandelate (7). $Pd(OAc)_2$ and (*S*)-(+)-*O*-acetylmandelic acid was used. Reaction time 14 h. Workup procedure A was performed, yielding 2.25 g (82%) of a 1.6:1 (from ^1H NMR) mixture of the diastereomers as a colorless oil: ^1H NMR (250 MHz, $CDCl_3$; 1.6:1 mixture of diastereomers) δ 7.49−7.42 (m, 4 H), 7.40−7.35 (m, 6 H (major and minor **7**)), 5.99 (dtd, J_1 = 10.0 Hz, J_2 = 4.3 Hz, J_3 = 0.9 Hz, 1 H (major **7**)), 5.90 (s, 1 H (major **7**)), 5.89 (s, 1 H (minor **7**)), 5.88 (m, 1 H (minor **7**)), 5.72 (ddt, J_1 = 10.0 Hz, J_2 = 3.7 Hz, J_3 = 2.1 Hz, 1 H (major **7**)), 5.52 (ddt, J_1 = 10.1 Hz, J_2 = 3.5 Hz, J_3 = 2.1 Hz, 1 H (minor **7**)), 5.28 (br s, 2 H (major and minor **7**)), 2.20 (s, 6 H (major and minor **7**)), 2.11−1.50 (m, 12 H (major and minor **7**)); ^{13}C NMR (250 MHz, $CDCl_3$; mixture of diastereomers) δ 170.3, 168.5, 134.0, 139.9, 133.4, 133.2, 129.1, 128.7, 127.6, 124.9, 124.8, 74.7, 69.7, 69.4, 28.1, 27.8, 24.8, 20.8, 18.7, 18.5. Anal. Calcd for $C_{16}H_{18}O_4$: C, 70.06; H, 6.61. Found: C, 69.95; H, 6.72.

2-Oxabicyclo[3.3.0]oct-6-en-3-one (17) and 2-Oxabicyclo-[3.3.0]oct-7-en-3-one (18). $Pd(OTFA)_2$ was used. 2-Cyclopentene-1-acetic acid was added last. Reaction time 1.5 h. Optimized yield (GLC) 85%. Workup procedure A was performed, yielding 0.91 g (73%) of a mixture consisting of 15% of **17** and 85% of **18**. ^1H NMR spectra of **17**[39] and **18**[40] were in full accordance with those reported in the literature. **17:** ^1H NMR (400 MHz, $CDCl_3$; mixture of **17** and **18**) δ 5.80 (d app q, J_1 = 5.7 Hz, J_2 = 2.3 Hz, 1 H), 5.59 (d app q, J_1 = 5.7 Hz, J_2 = 1.9 Hz, 1 H), 5.14 (ddd, J_1 = 9.3 Hz, J_2 = 4.5 Hz, J_3 = 3.2 Hz, 1 H), 3.51 (d app q, J_1 = 9.3 Hz, J_2 = 1.9 Hz, 1 H), 2.45 (dd, J_1 = 17.9 Hz, J_2 = 1.9 Hz, 1 H); ^{13}C NMR (400 MHz, C_6D_6; mixture of 17 and 18) δ 175.2, 129.1, 129.0, 81.9, 45.3, 39,4, 32.2. **18:** ^1H NMR (400 MHz, $CDCl_3$; mixture of **17** and **18**) δ 6.09 (dtd J_1 = 5.7 Hz, J_2 = 4.8 Hz, J_3 = 0.8 Hz, 1 H), 5.89 (d app q, J_1 = 5.7 Hz, J_2 = 2.1 Hz, 1 H), 5.53 (br d, J = 8.2 Hz, 1 H), 3.14 (d app q, J_1 = 8.2 Hz, J_2 = 5.7 Hz, J_3 = 2.7 Hz,1 H), 2.84 (dd, J_1 = 18.3 Hz, J_2 = 10.4 Hz, 1 H), 2.33 (dd, J_1 = 18.3 Hz, J_2 = 5.9 Hz, 1 H); ^{13}C NMR (400 MHz, C_6D_6; mixture of 17 and 18) δ 175.7, 136.2, 128.1, 88.5, 39.1, 35.5, 34.7.

Acknowledgment. We thank the Swedish Research Council for Engineering Sciences for financial support, and J.D.O. thanks the Royal Institute of Technology for a research scholarship. We also thank Dr. Tobias Rein for advice and fruitful discussions.

(35) Gao, Y; Hanson, R. M.; Klunder, J. M.; Ko, S. Y.; Masamune, H.; Sharpless, B. K. *J. Am. Chem. Soc.* **1987**, *109*, 5765−5780.
(36) Bellucci, G.; Bianchini, R.; Vecchiani, S. *J. Org. Chem.* **1986**, *51*, 4224−32.
(37) Kantner, S. S.; Humski, K.; Goering, H. L. *J. Am. Chem. Soc.* **1982**, *104*, 1693−7.
(38) Tseng, C. C.; Paisley, S. D.; Goering, H. L. *J. Org. Chem.* **1986**, *51*, 2884−91.
(39) Kitahara, T.; Nishi, T.; Mori, K. *Tetrahedron* **1991**, *47*, 6999−7006.
(40) Tiecco, M.; Testaferri, L.; Tingoli, M.; Bartoli, D. *Tetrahedron* **1990**, *46*, 7139−50.