Carbonylation of Alkynyl Epoxides: Synthesis of 5-Hydroxy-2,3-dienoate Esters and 2,3-Dihydrofuran-3-ol Derivatives

Marcelo E. Piotti and Howard Alper*

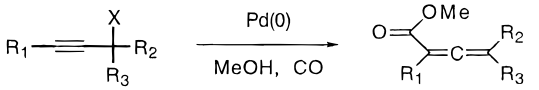
Department of Chemistry, University of Ottawa, 10 Marie Curie, Ottawa, Ontario, Canada K1N 6N5

Received July 15, 1997[⊗]

The carbonylation of alkynyl oxiranes catalyzed by $(MePh_2)_4Pd$ in the presence of 20 atm of carbon monoxide in methanol gives methyl 5-hydroxy-2,3-pentadienoates in good yields. When the reaction is performed on alkynyl oxiranemethanol derivatives, 4,5-dihydrofuran-3-ol derivatives are obtained stereoselectively. These products arise from the spontaneous cyclization of a dihydroxyallenyl ester intermediate.

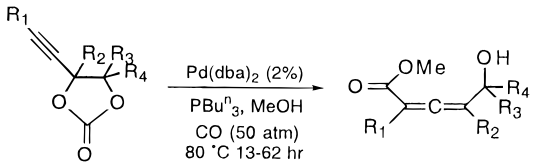
Alkynes containing a leaving group in the propargylic position are frequently used as substrates for reactions catalyzed by Pd(0) complexes.[1] These reactions involve the formation of σ-allenyl palladium (II) intermediates, compounds that have been isolated and characterized.[2] Such intermediates can undergo insertion of molecules such as olefins and carbon monoxide into the C−Pd bond, or can react with nucleophiles at the central carbon of the allene moiety (Scheme 1). In this way, several C−C coupling carbonylation and other reactions of propargylic compounds have been reported.[1]

Carbon monoxide inserts readily into the palladium−carbon bond of a σ-complex, giving an acyl palladium intermediate, which reacts with an alcohol to form an allenic carboxylic ester and liberates the Pd(0) complex. Carbonylation of propargylic carbonates,[3] acetates,[4a] phosphates,[4b] mesylates,[5] bromides,[6a] and amines[6b] catalyzed by palladium(0) complexes have been carried out in this manner (eq 1).



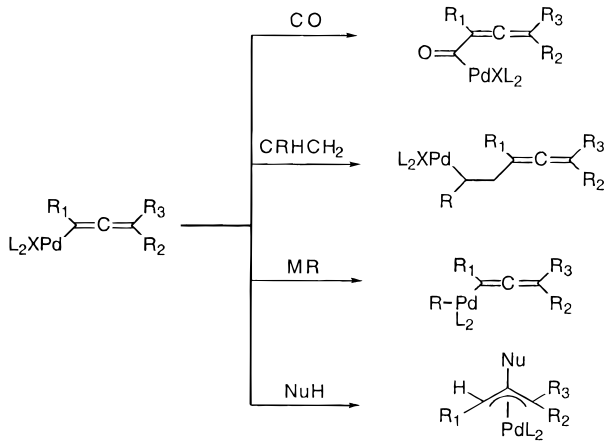
Eq 1

X= OCOOR, OCOR, $PO(OR)_2$, Br, Ms, NR_2



Eq 2

Scheme 1



One strategy to obtain more functionalized allenic esters is by using propargylic compounds in which the leaving group is part of a cyclic structure. In this way, cyclic alkynyl carbonates can be carbonylated to afford 5-hydroxy-2,3-pentadienoates[7] (eq 2). Alkynyl epoxides fall into this category of compounds. Although these compounds have been used in C−C coupling reactions with Pd(0) complexes as catalysts,[8] to our knowledge they have not been reacted with carbon monoxide. In this paper we report the synthesis of 5-hydroxy-2,3-pentadienoates by carbonylation of epoxyalkynes under mild conditions. In addition, oxygen heterocycles can be obtained by carbonylation of hydroxy derivatives of epoxyalkynes. Depending on the reaction conditions, dihydrofuranol or their dehydrated products can be isolated.

Results and Discussion

The carbonylation of alkynyl epoxide **1a** catalyzed by tetrakis(methyldiphenylphosphine)palladium afforded methyl 5-hydroxy-4-methyl-2,3-pentadienoate (**2a**) in 70% yield. The allenyl product can be easily identified by its IR and ^{13}C NMR spectra. The IR spectrum shows absorption bands at 3417 cm^{-1} (OH), 1965 cm^{-1} (C=C=C stretching), and 1712 cm^{-1} (C=O). Signals in the ^{13}C

[⊗] Abstract published in *Advance ACS Abstracts,* October 1, 1997.

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(2) (a) Elsevier, C. J.; Kleijn, H.; Ruitenberg, K.; Vermeer, P. *J. Chem. Soc., Chem. Commun.* **1983**, 1529. (b) Elsevier, C. J.; Kleijn, H.; Boersma, J.; Vermeer, P. *Organometallics* **1986**, *5*, 716.

(3) Tsuji, J.; Mandai, T. *J. Organomet. Chem.* **1993**, *451*, 15 and references therein.

(4) (a) Arzoumanian, H.; Choukrad, M.; Nuel, D., *J. Mol. Catal.* **1993**, *85*, 287. (b) Murahashi, S. I.; Imada, Y.; Mori, T.; Kitamura, T. *Abstr. Jpn. Chem. Soc. Annual Meeting II*, **1993**, 345.

(5) (a) Marshall, J. A.; Wolf, M. A.; Wallace, E. M., *J. Org. Chem.* **1997**, *62*, 367. (b) Marshall, J. A.; Wolf, M. A., *J. Org. Chem.* **1996**, *61*, 3238.

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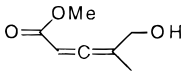
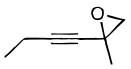
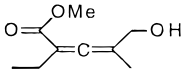
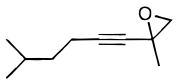
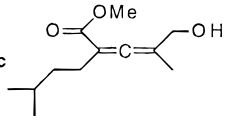
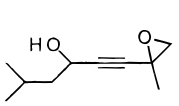
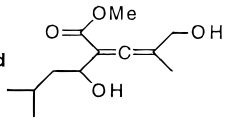
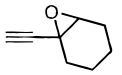
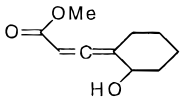
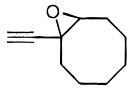
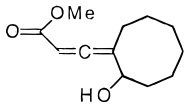
(7) Darcel, C.; Buneau, C.; Dixneuf, P. H. *Synlett* **1996**, 218.

(8) (a) Kleojn, H.; Meijer, J.; Overbeek, G. C.; Vermeer, P. *Recl. Trav. Chim. Pays-Bas* **1982**, *101*, 97. (b) Minami, I.; Masami, Y.; Watanabe, H.; Tsuji, J. *J. Organomet. Chem.* **1987**, *334*, 225.

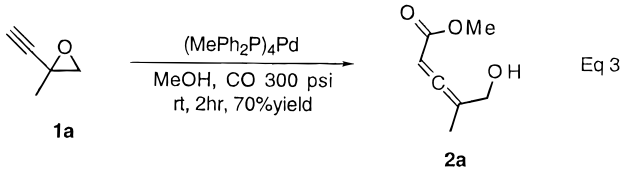
S0022-3263(97)01303-0 CCC: $14.00

Table 1. Carbonylation of Alkynyl Oxiranes Catalyzed by $(MePh_2P)_4Pd$[a]

	substrate		product	yield (%)
1a		2a		70
1b		2b		74
1c		2c		78
1d		2d		55
1e		2e		90
1f		2f		94

a) Reaction conditions: alkynyl epoxide, 0.8 mmol; $(MePh_2P)_4Pd$, 1 mol %; methanol, 10 ml; CO, 300 psi; rt, 2hr.

NMR spectrum appeared at 209.5 ppm for the central allenyl carbon and at 167 ppm for the carbonyl group.



After optimization of the reaction conditions, we were glad to know that the carbonylation reaction takes place under very mild conditions: 0.8 mmol of the alkynyl epoxide, 1 mol % of $(MePh_2P)_4Pd$, 10 mL of methanol, 300 psi of carbon monoxide, room temperature, 2 h. Two hours are sufficient to achieve full conversion of the epoxide, although longer reaction times do not affect the chemical yields. Methanol is the best solvent for the reaction. When benzene or THF was used, in the presence of 0.5 mL of methanol, the conversion was very low, and the desired allene was not detected in the reaction mixture, even when the reaction was carried out at 100 °C. Carbon monoxide pressure above 300 psi does not improve the product yields. A decrease in the conversion occurred when the reaction was effected at less than 200 psi of carbon monoxide.

Table 1 shows the results for the carbonylation of a series of alkynyl epoxides. Linear substrates (**1a**−**c**) give fine yields of hydroxymethyl allenyl esters. The yields are quite high for fused bicyclic epoxides (**1e**−**f**). A hydroxy derivative of an alkynyl epoxide (**1d**) affords a highly oxygenated allene in lower yield.

The mechanism of the reaction is probably the same as that proposed for the carbonylation of cyclic alkynyl carbonates,[12] where a zwitterionic palladium intermediate was involved as a key intermediate. In that case, the driving force of the reaction might be the liberation of CO_2, while in the carbonylation of alkynyl oxiranes the driving force is the release of ring strain by opening the epoxide ring (Scheme 2). A noteworthy feature of the carbonylation of alkynyl oxiranes is that the reaction conditions are much milder than those for the carbonylation of cyclic carbonates.

Scheme 2

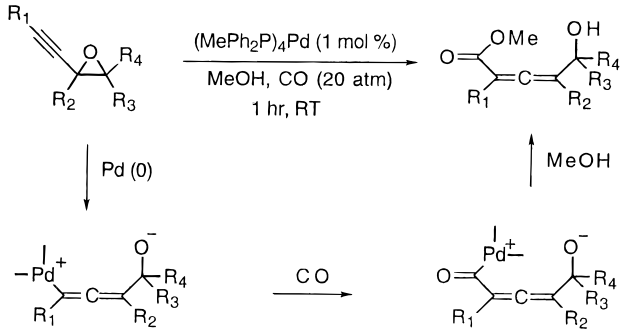
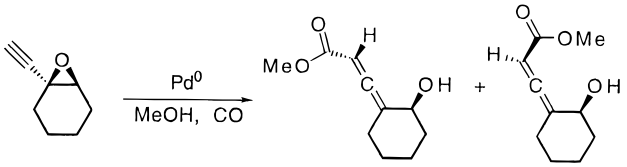


Table 2. Variation of the Diastereomeric Ratio of 1e Depending on the Catalytic System[a]



ligand or catalyst	yield (%)	*anti/syn*
–	0	–
DPPP	78	97/3
DPPB	89	93/7
Ph_3P[b]	88	82/18
DPPPentane	84	97/3
$(Ph_3P)_4Pd$[c]	84	88/12
$(MePh_2P)_4Pd$[c]	90	93/7

[a] Reaction conditions: **1a**, 0.8 mmol; $Pd_2(dba)_3{\cdot}CHCl_3$, 0.004 mmol; ligand, 0.008 mmol; MeOH, 10 mL; 24 h, rt. [b] Using 0.016 mmol of Ph_3P. [c] 0.008 mmol of catalyst and no added ligand.

The effect of different catalytic systems on the carbonylation of **1e** is presented in Table 2. Note that not only is the yield of the reaction affected, but also the diastereomeric ratio of the product. The highest yield is obtained by using commercially available $(MePh_2P)_4Pd^0$. Bidentate phosphine ligands improve the diastereoselectivity. 1,4-Bis(diphenylphosphino)butane (dppb) and 1,5-bis(diphenylphosphino)pentane both give a 97/3 *anti/syn* ratio.

Although we did not determine the configuration of the major diastereomer, we can assume that the formation of the anti isomer is favored. Studies on the carbonylation of chiral mesylates[5] and phosphates[4b] show that the Pd^0 complex reacts with the triple bond in a S_N2' manner. Any loss in stereoselectivity may be due to a racemization induced by the same Pd^0 catalyst. Nucleophilic attack of free Pd^0L_n at the σ-allenyl-Pd intermediate **3** in anti

(9) Baldwin, J. E. *J. Chem. Soc., Chem. Commun.* **1976**, 734.
(10) Baldwin, J. E.; Thomas, R. C.; Kruse, L. I.; Silberman, L. *J. Org. Chem.* **1977**, *42*, 3846.
(11) (a) Cristau, H. J.; Viala, J.; Christol, H., *Tetrahedron Lett.* **1982**, *23*, 1569. (b) Stirling, C. J. M. *J. Chem. Soc.* **1964**, 5856 and 5863.
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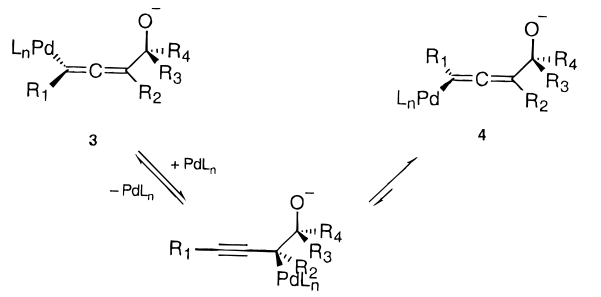
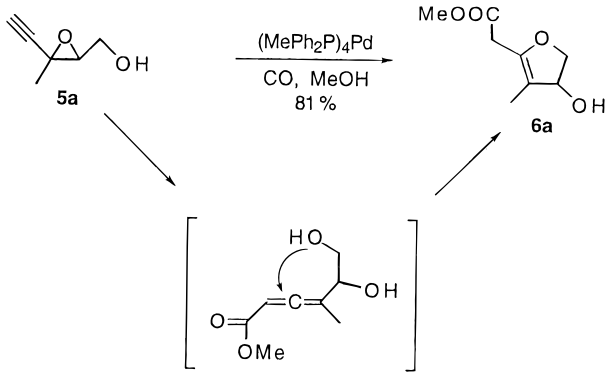
Scheme 3



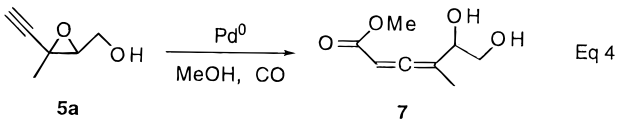
Scheme 4



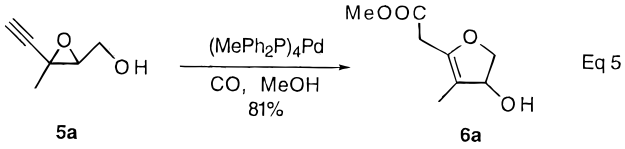
S_N2'fashion, followed by allenyl−propargyl rearrangement in the same plane, would give the intermediate **4** (Scheme 3). This racemization could be minimized by decreasing the amount of catalyst and by using larger diphosphine ligands.

Carbonylation of Alkynyl Oxiranemethanol Derivatives

Following the mechanism proposed above, the carbonylation of alkynyl oxiranemethanol derivative **5a** should lead to the formation of allenyl diol **7** (eq 4).

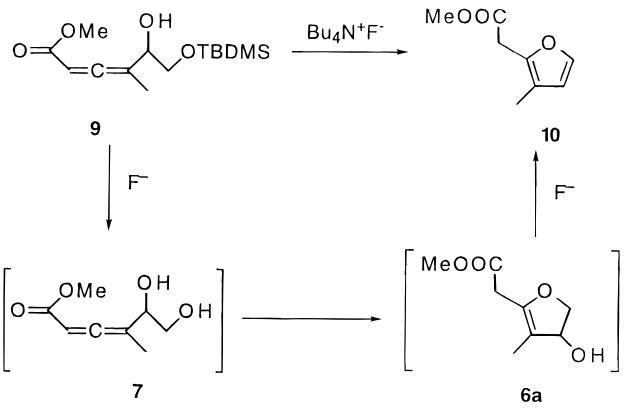


When the alkynyloxirane **5a** is reacted under the standard conditions, the conversion is complete, but product **7** was not detected in the reaction mixture. Instead, the oxygen heterocycle **6a** was isolated in 81% yield (eq 5).

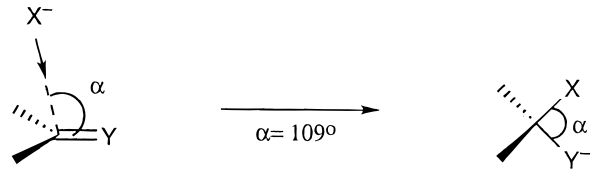


This result can be rationalized as a consequence of a 5-exo cyclization of the expected allenyl diol product under the reaction conditions (Scheme 4). Since the carbonylation reaction is carried out under neutral conditions, we can rule out acid or basic catalysis. The formation of **6a** could be due to a Pd-catalyzed cyclization of the diol or to a noncatalyzed process.

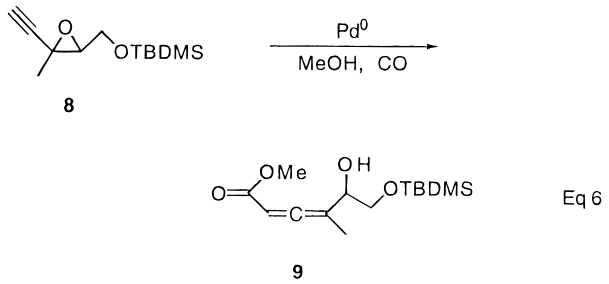
Scheme 5



Scheme 6



We attempted to isolate the diol intermediate by reacting the protected substrate as a silyl ether (**8**). The carbonylation reaction gave 47% yield of the allene **9** (eq 6).



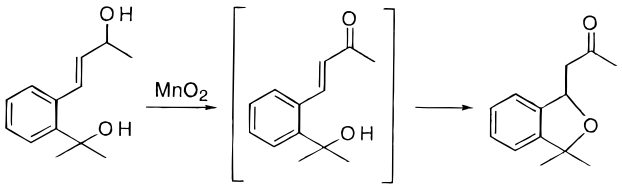
Deprotection of **9** with $Bu_4N^+F^-$ did not afford the expected diol, nor the dihydrofuranol derivative **6a**. Instead, the dehydration product of **6a** was isolated. The basicity of F^- might induce the dehydration of **6a** to form the more stable aromatic compound **10** in 79% yield (Scheme 5).

This result suggests that the cyclization of the diol **7** during the carbonylation reaction occurs spontaneously, following Baldwin's rules for cyclization reactions.[9] For a trigonal ring closure to be favored, the three reacting atoms must maintain an angle of $\alpha = 109°$ during the reaction pathway. This angle is maintained between these atoms in the product (Scheme 6).

The case of conjugate addition of oxygen nucleophiles has been studied in some detail.[10] The cyclization is highly favored for 5-*exo*-*trig* systems. When the secondary hydroxy group in **11** is selectively oxidized, the hydroxy ketone **12** is not observed, since it cyclizes spontaneously to **13** (Scheme 7).

Although compounds containing allenic carboxylic esters have not been studied, molecular models suggest that compound **7** can adopt a conformation favorable for the interaction of the hydroxy group with the π system of the α,β-unsaturation, making for a very facile cyclization reaction (Scheme 8).

Scheme 7



11 12 13

Scheme 8

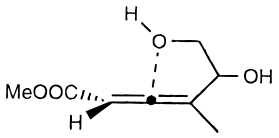
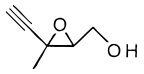
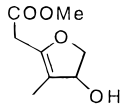
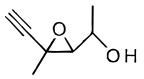
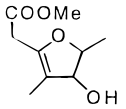
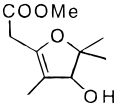
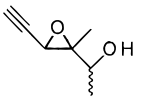
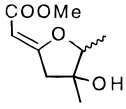
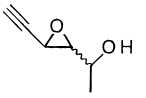
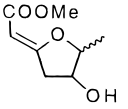
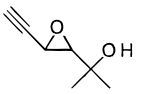
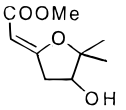


Table 3. Carbonylation of Alkynyl Oxiranemethanol Derivatives[a]

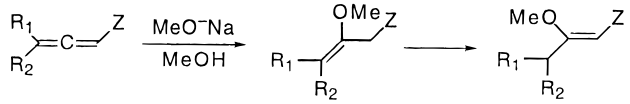
	Substrate		Product	Yield (%)
5a		6a		81 %
5b		6b		49%
5c		6c		91%
5d		6d		74%
5e		6e		30%
5f		6f		91%

a) Reaction conditions: alkynyl epoxide, 0.8 mmol; $(MePh_2P)_4Pd$, 1 mol %; methanol, 10 ml; CO, 300 psi; rt, 2h.

Table 3 shows the results for the carbonylation of a number of alkynyl oxiranemethanol derivatives. Note that, depending on the substitution pattern of the starting material, heterocycles containing *endo* or *exo* double bonds are obtained.

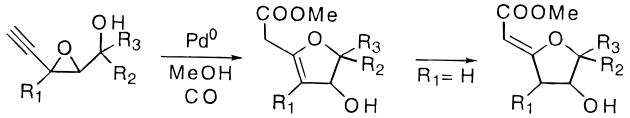
The preference for the formation of the *exo* or *endo* unsaturated products is likely related to their thermodynamic stability. In fact, the intermolecular addition of oxygen nucleophiles to allenic compounds containing an electron acceptor group is well-known.[11] The addition of MeOH to compound **14** gives **15** as the first product. But depending on the substitution pattern, this compound may isomerize to a more stable conjugated system **16** (Scheme 9).

Scheme 9



14 15 16

Scheme 10



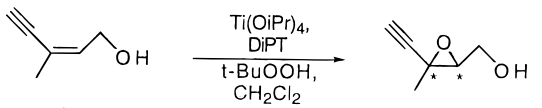
17 18

In the carbonylation of alkynyl oxiranemethanol derivatives, the dihydrofuranol **17** is formed by a normal intramolecular Michael type addition (Scheme 10). When R_1 = Me the product is stable and can be isolated. For R_1 = H isomerization occurs to give a more stable α,β-unsaturated ester **18**.

The formation of one or the other isomer is very selective. The synthesis of the starting epoxides gave mixtures of diastereomers in the cases of **5d** and **5e**, and this ratio is reflected in the *cis*−*trans* distribution in the heterocyclic product (**6e**: 64/36 cis/trans. **6d**: 59/41. We could not determine which one corresponds to cis or trans.)

Preparation of Chiral Heterocycles

The transformation of alkynyl oxiranemethanol compounds to 3,4-dihydrofuran-3-ol derivatives proceeds with loss of stereochemistry at C_3 of the starting material. According to the mechanism of the reaction, the stereochemistry at C_1 and C_2 should not be affected during the course of the reaction. The easy synthesis of chiral alkynyl oxiranemethanol derivatives by Sharpless epoxidation[12] makes this carbonylation reaction a potential route for the preparation of chiral oxygen heterocycles. The asymmetric epoxidation of **19** to **20** was examined as a model system (eq 7).



19 20 Eq 7

60 % ee

Unfortunately, the enantiomeric excess of **20**, measured by chiral GC (Figure 1), was only 47%. The reaction was repeated two times with the same result. After one recrystallization of **20** the ee improved to 60%, and further recrystallizations did not increase the % ee. A literature search shows that there is only one paper where the ee of the same compound obtained by Sharpless epoxidation is reported.[13] In that case, the enantiomeric excess is 60%, the same value that we obtained.

Carbonylation of **20** gave **21** in 79% yield (eq 8). The ee was 55%, as determined by the use of an NMR chiral

(13) Pale, P.; Chuche, J. *Tetrahedron Lett.* **1987**, *28*, 6447.

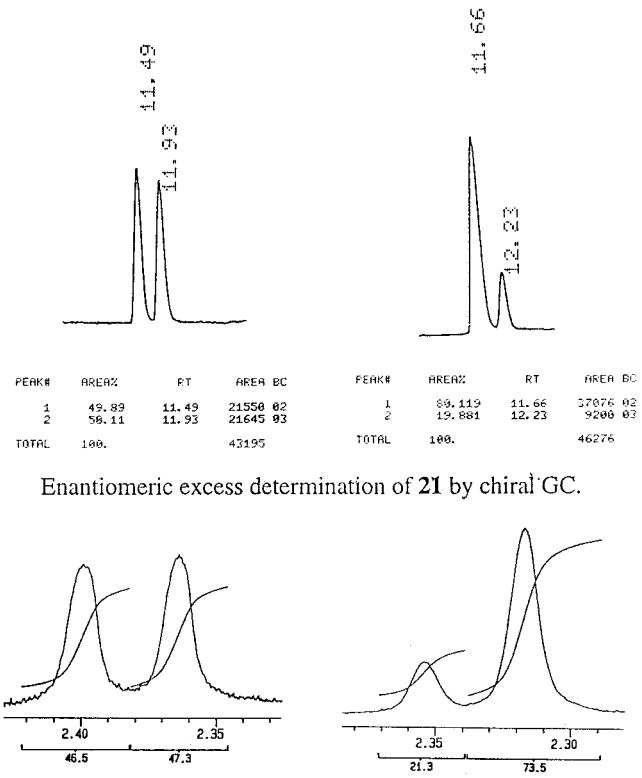
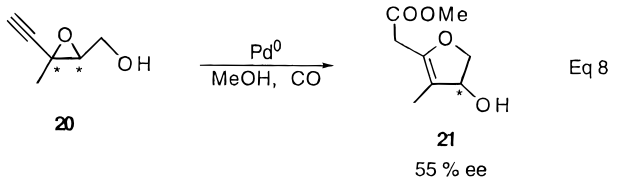


Figure 1. Determination of enantiomeric excess of **20** and **21** (The racemates are shown on the left side).

shift reagent (Figure 1). Chiral GC could not be used because **21** dehydrates upon injection into the column.



This result shows that the stereocenter at C_2 is basically unaffected by the reaction, and therefore different chiral oxygen heterocycles derivatives can be synthesized in this way. It is well-known that compounds of the type **21** can undergo very diastereoselective hydrogenation[14] or epoxidation[15] reactions, since the OH group can act as a directing group. This would allow the preparation of tetrahydrofuran derivatives containing three chiral centers, the only chiral source being the Sharpless epoxidation reaction.

Conclusions

The Pd(0)-catalyzed carbonylation of alkynyl oxiranes affords 5-hydroxy-2,3-pentadienoates derivatives in good yields. The reaction may start with a S_N2' attack on the triple bond by a palladium(0) complex, forming a zwitterionic σ-allenylpalladium intermediate, which after carbon monoxide insertion and attack by methanol leads to the formation of the product. The diastereomeric ratio of the product is affected by the nature of the phosphine ligand, with larger bidentate ligands favoring the formation of the anti products.

The carbonylation of alkynyl oxiranemethanol derivatives afford oxygen heterocyclic compounds. These compounds are formed by spontaneous intramolecular Michael type addition of the diol allenic intermediate, following Baldwin's cyclization rules. Depending on the substitution pattern of the starting epoxide, the heterocycle will contain an *endo* or *exo* carbon−carbon double bond. The use of enantiomerically enriched alkynyl oxiranemethanol leads to the preparation of an optically active 4,5-dihydrofuran-3-ol derivative.

Experimental Section

Synthesis of Alkynyl Oxiranes 1a−f. The synthesis of alkynyl oxiranes was carried out by epoxidation of the corresponding enynes.[16] These precursors were purchased from Aldrich or Lancaster and were used as received. The enyne precursor of **1f** was prepared by dehydration of 1-ethynyl-1-cyclooctanol with $POCl_3$ in pyridine.[16]

General Procedure. To a solution of the enyne (26.2 mmol) in CH_2Cl_2 (17 mL) at 0 °C was added, in portions, 33 mmol of *m*-chloroperbenzoic acid. The reaction mixture was stirred for 15 min at 0 °C, the ice bath was removed, and the mixture was then stirred for 2 h at room temperature. 10% Sodium sulfite solution was slowly added until the mixture gave a negative test with starch−iodide paper. Saturated sodium bicarbonate solution was added, the aqueous phase was discarded, and the organic phase was washed twice with sodium bicarbonate solution, with distilled water (two times), and finally with brine. The organic phase was dried (magnesium sulfate) and filtered, and the solvent was removed using a rotatory evaporator. The residue was distilled under vacuum, unless otherwise noted, to yield the desired alkynyl oxirane.

1-Ethynyl-1-methyloxirane[8a] (1a): 12% yield. The low yield is probably due to the moderate solubility of **1a** in water. ^{1}H NMR (200 MHz) δ = 1.53 (3H, s), 2.27 (1H, s), 2.72 (1H, d, J = 5.6 Hz) and 3.01 (1H, d, J = 5.6 Hz). ^{13}C NMR: 22.6, 46.8, 55.1, 70.3, 83.1 ppm. IR (neat): 3277, 2119 cm^{-1}. MS: 82 (M^+).

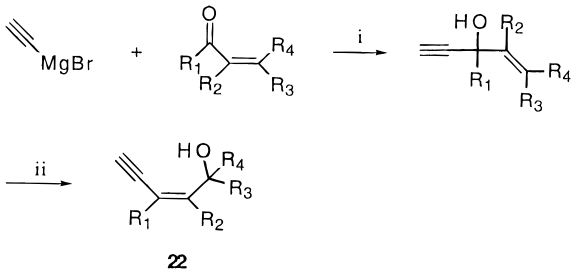
Carbonylation of Alkynyl Oxiranes 1a−f Catalyzed by $(MePh_2P)_4Pd$. In a 45 mL stainless steel autoclave equipped with a magnetic stirring bar, 0.8 mmol of the alkynyl oxirane was mixed with 10 mL of dry, oxygen-free methanol. To this solution was added 0.008 mmol of the catalyst. The autoclave was closed, purged twice with carbon monoxide, and then pressurized to 300 psi of carbon monoxide. The mixture was stirred for 2 h at room temperature, the reaction was stopped, the gas was released, and the solution was filtered through a short Florisil column (silica gel and aluminum oxide slowly decompose the allene product). The solvent was removed by rotatory evaporation. Column chromatography of the crude mixture was performed by using Florisil as the stationary phase and hexane/EtOAc 95/5 as the eluant. After 60 mL of the eluant was used, 80 mL of hexane/EtOAc 60/40 was passed through the column. Evaporation of this last fraction gave the desired product.

Carbonylation of 1a Catalyzed by Other Systems. General procedure: 0.8 mmol of **1a**, 0.004 mmol of $Pd_2(dba)_3{\cdot}CHCl_3$, 0.008 mmol of a bidentate phosphine ligand or 0.016 mmol of Ph_3P, and 10 mL of methanol were placed in an autoclave. The autoclave was pressurized to 300 psi of carbon monoxide, and the mixture was stirred for 24 h. The reaction was worked up as described before.

Methyl 5-hydroxy-4-methyl-2,3-pentadienoate (2a): 70% yield. ^{1}H NMR (200 MHz) δ = 1.78 (3H, d, J = 2.75 Hz), 3.30 (1H, br), 3.67 (3H, s), 4.08 (2H, d J = 2.75 Hz), 5.59 (1H, sext, J = 2.75 Hz). ^{13}C NMR: 14.4, 52.0, 63.0, 88.4, 105.5, 167.1, 209.5 ppm. IR (neat): 1712, 1965, 3417 cm^{-1}. MS: 142 (M^+). HRMS calcd for $C_7H_{10}O_3$: 142.0630. Found: 142.0639.

(14) Crabtree, R. H.; Davis, M. W. *J. Org. Chem.* **1986**, *51*, 2655.
(15) Sharpless, K. B.; Michelson, R. C. *J. Am. Chem. Soc.* **1973**, *95*, 6163.
(16) Alexakis, A.; Marek, I.; Mangeney, P.; Normant, J. F. *Tetrahedron* **1991**, *47*(9), 1667.

Scheme 11



22

i) 1) ether 2) NH_4Cl
ii) H_2SO_4 (50%), ether

Synthesis of Alkynyl Oxiranemethanol Derivatives 5a−f. The preparation of **5a−f** was carried out by epoxidation of the corresponding alk-2-en-4-yn-1-ol precursors **22** by the same procedure used for the epoxidation of enynes. With the exception of the precursor of **5a**, which was purchased from Aldrich, the unsaturated alcohols were prepared following Scheme 11.[18]

The *cis*−*trans* ratio could be determined by measuring the coupling constant between R_1 and R_2 for $R_1 = R_2 = H$, the chemical shift of the proton attached to the *sp* carbon and the proton chemical shift when $R_3 = H$.

2-Ethynyl-2-methyloxiranemethanol[13] (5a): 40% yield. ^{1}H NMR (200 MHz) $\delta = 1.60$ (3H, s), 2.15 (1H, br), 2.43 (1H, s,), 3.13 (1H, dd, $J = 6.0$ and 4.8 Hz), 3.81 (1H, dd, $J = 13.0$ and 5.9 Hz), 3.93 (1H, dd, $J = 13.0$ and 4.9 Hz). ^{13}C NMR: 23.0, 51.5, 62.3, 63.7, 73.1, 80.7 ppm. IR (neat): 3214, 2118 cm^{-1}. MS: 112 (M^+).

Carbonylation of Alkynyl Oxiranemethanol Derivatives 5a−f. The carbonylation of **5a−f** and purification of the products were carried out using the same procedure as that described for the carbonylation of alkynyl oxiranes.

Methyl (4-hydroxy-3-methyl-4,5-dihydrofuran-2-yl)acetate (6a): 81% yield. ^{1}H NMR (200 MHz) $\delta = 1.72$ (3H, s), 3.14 (1H, d, $J = 8$ Hz), 3.21 (2H, s), 3.72 (3H, s), 4.18 (1H, dd, $J = 10.5$ and 3.0 Hz), 4.26 (1H, dd, $J = 10.5$ and 6.9 Hz), 4.71 (1H, m). ^{13}C NMR: 8.8, 32.0, 52.2, 76.2, 77.4, 109.5, 147.5, 170.0 ppm. IR (neat): 3400, 1727 cm^{-1}. MS: 154 (M^+). Anal. Calcd for $C_8H_{12}0_4$: C, 55.81; H, 7.02. Found: C, 55.94; H, 6.69.

Methyl (4-hydroxy-5,5-dimethyltetrahydrofuran-2-ylidene)acetate (6f): 91% yield. ^{1}H NMR (200 MHz) $\delta = 1.24$ (3H, s), 1.36 (3H, s), 2.92 (1H, d, $J = 4.8$ Hz), 3.29 (2H, m), 3.60 (3H, s), 4.06 (1H, q, $J = 3.7$ Hz), 5.22 (1H, t, $J = 1.8$ Hz). ^{13}C NMR: 20.7, 25.6, 40.1, 50.8, 74.7, 89.6, 90.0, 169.4, 174.1 ppm. IR (neat): 3436, 1695, 1637 cm^{-1}. MS: 186 (M^+). HRMS calcd for $C_9H_{14}O_4$: 186.0892. Found: 186.0872.

Synthesis and Carbonylation of Protected Alkynyl Oxiranemethanol 8. The preparation of **8** was carried out by protection of *trans*-3-methylpent-2-en-4-yn-1-ol (**11**) with *tert*-butyldimethylsilyl chloride and epoxidation of the silyl ether.

1-(2-Ethynyl-2-methyloxirane)ethanol, *tert*-butyldimethylsilyl ether[17] (8): 67% yield. ^{1}H NMR (200 MHz) $\delta = 0.09$ (3H, s), 0.89 (9H, s), 1.55 (3H, s), 2.35 (1H, s), 3.01 (1H, t, $J = 15.0$ Hz), 3.78 (1H, dd, $J = 11.2$ and 5.0 Hz), 3.89 (1H, dd, $J = 11.2$ and 5.0 Hz). ^{13}C NMR: −5.2, 18.3, 23.0, 25.9, 51.4, 62.9, 64.2, 72.8, 81.2 ppm. IR (neat): 3287, 2123 cm^{-1}. MS: 211 ($M^+ - 15$).

Carbonylation of 8. The carbonylation of **8** and reaction workup was effected using the same procedure as for **5** to form **9** in 47% yield.

Deprotection of 9.[19] A 250 mg amount of **9** (0.78 mmol) was dissolved in 5 mL of THF and treated at 0 °C with tetra-*n*-butylammonium fluoride (2 equiv) for 5 min. The mixture was stirred at room temperature for 40 min. The solvent was evaporated, and the residue was subjected to column chromathography on Florisil using hexane/EtOAc 95/5 as eluant, affording **10** in 79% yield.

Methyl 5-hydroxy-6-[(*tert*-butyldimethylsilyl)oxy]-4-methyl-2,3-hexadienoate (9): 47% yield. ^{1}H NMR (200 MHz) $\delta = 0.06$ (3H, s), 0.88 (9H, s), 1.83 (3H, d, $J = 2.6$ Hz), 2.70 (1H, br), 3.58 (1H, dd, $J = 10.0$ and 6.8 Hz), 3.73 (1H, dd, $J = 10.0$ and 3.9 Hz), 3.70 (3H, s), 4.18 (1H, m), 5.62 (1H, quint, $J = 2.6$ Hz). ^{13}C NMR: −5.2, 14.6, 18.2, 25.8, 51.9, 65.3, 71.7, 88.8, 104.6, 166.5, 209.6 ppm. IR (neat): 3433, 1964, 1715 cm^{-1}. MS: 286 (M^+). HRMS calcd for $C_{14}H_{26}O_4Si$: 286.16002. Found: 286.15683.

Methyl 3-methyl-2-furanacetate[20] (10): ^{1}H NMR (200 MHz) $\delta = 1.97$ (3H, s), 3.60 (2H, s), 3.69 (3H, s), 6.19 (1H, d, $J = 2.0$ Hz), 7.26 (1H, d, $J = 2.0$ Hz). ^{13}C NMR: 9.7, 32.0, 52.2, 113.0, 116.9, 141.1, 143.1, 170.1 ppm. IR (neat): 1741 cm^{-1}. MS: 154 (M^+).

Synthesis of (−) 20.[12] An oven-dried 500 mL round-bottom flask was equipped with a magnetic stirring bar, fitted with a rubber septum, and flushed with nitrogen. The flask was charged with 400 mL of methylene chloride and 4 g of activated powdered molecular sieves (4 Å). The flask was cooled to −23 °C using a CCl_4/dry ice bath. The following liquids were added in sequence by syringe while stirring at −23 °C: 11.88 mL (40 mmol) of titanium isopropoxide, 8.4 mL (40 mmol) of L-diisopropyltartrate; after stirring during 5 min, 4.16 mL (40 mmol) of *trans*-3-methylpent-2-en-4-yn-1-ol and 14.6 mL (ca. 80 mmol) of an anhydrous decane solution of TBHP (5−6 M) were added. The resulting solution was stored overnight in a freezer at −21 °C. Then the reaction flask was placed in a CCl_4/dry ice bath, and 100 mL of 10% aqueous tartaric acid solution was added while stirring. The aqueous phase solidified. The cooling bath was removed after 30 min, and the mixture was stirred for 2 h. The aqueous phase was separated, and the organic phase was treated with 10% sodium sulfite until a negative test with starch/iodide paper was obtained. The organic phase was washed with water and then with brine and dried with magnesium sulfate. After filtration and evaporation of the solvent, the residue was passed through a short silica gel column using hexane as eluant to separate the remaining decane. The epoxide was eluted from the column with ethyl acetate. After evaporation of the solvent, the product **20** was distilled in a Kügelrohr apparatus and was collected as a white solid [1.47 gr (40% yield)]. The enantiomeric excess was 47%. The enantiomeric excess was determined by capillary chiral GC, using a Lipodex E column, isothermal run at 90 °C, and 20 psi of the carrier gas (He) (see Figure 1). A small amount of hexane was added to the product, and benzene was added dropwise until all the solid dissolved. The flask was stored in a refrigerator for a few hours and the solid formed was filtered. The ee of the solid was 60%. After a second recrystallization, the enantiomeric excess remained unchanged.

Enantiomeric Excess Determination of 21. 21 dehydrates upon injection in the GC. Therefore the % ee was determined by using the NMR chiral shift reagent (+)-Eu(hfc)$_3$, by examining the splitting of the singlet at 1.72 ppm corresponding to the vinylic methyl group (see Figure 1).

Acknowledgment. We are grateful to the Natural Sciences and Engineering Research Council of Canada for support of this research.

Supporting Information Available: ^{1}H and ^{13}C NMR spectra of compounds **1b**, **2a−f**, **5d**, **6b−d**, and **9**. Spectral data of compunds **1b−f**, **2b−f**, **5b−f**, and **6b−e** (30 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

JO971303N

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