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Palladium-Catalyzed Alkylation of Vinyl Oxiranes with Substituted Allenes. Direct Access to Bifunctionalized Allylic Alcohols

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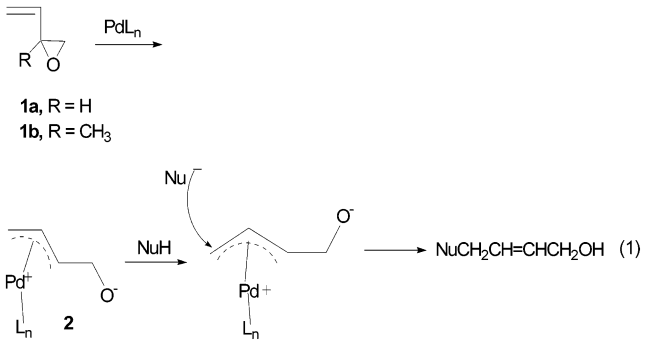
The first palladium-catalyzed alkylation of vinyl oxiranes with substituted allenes to form functionalized allylic alcohols is described. The reaction of activated allenes **5** with vinyl oxiranes **1** in the presence of catalytic amounts of $Pd(PPh_3)_4$ (10 mol %) and 1,3-bis(diphenylphosphino)-propane (dppp) (20 mol %) in THF at 60 °C gave the corresponding allylic alcohols **6** in good to excellent yields. The allylic alcohols were obtained in different ratios of trans/ cis isomers.

A great deal of attention has recently been paid to the palladium-catalyzed ring opening of vinyl oxiranes.[1] A number of publications have appeared on the regio- and stereoselective formation of five-, six-, and seven-membered ring heterocycles by the palladium-catalyzed ring opening and cycloaddition reactions of vinyl oxiranes with heterocumulenes.[2]

It is known that the palladium(0)-catalyzed reaction of vinyl oxiranes with nucleophiles (NuH) gives allylic alcohols via π-allylpalladium intermediates (eq 1). Stable carbon pronucleophiles, such as $CH_2(CO_2Et)_2$, $CH_2(COPh)(CO_2H)$, and $CH_2(CO_2Me)(COCH_3)$, are used as NuH,[3] giving the corresponding carbon chain elongated allylic alcohols in good yields. The ring opening of vinyl oxiranes by organometallic reagents such as $Pd(OAc)_2$,[4] $Pd(PPh_3)_4$,[5] and $Pd_2(dba)_3{\cdot}CHCl_3$[6] to form allylic alcohols is a versatile reaction in organic synthesis.[7] The reactivity of allyllithium compounds with vinyl oxiranes has also been studied as a route to synthesize allylic alcohols.[8] These metal-catalyzed reactions prompted us to explore the synthesis of new functionalized compounds by the palladium complex catalyzed reaction of vinyl oxiranes and allenes.



In this reaction, effected under neutral conditions, nucleophilic attack takes place selectively at the terminal carbon, giving the 1,4-adduct. It has been shown that C−C bond formation proceeds without adding a base since the π-allylpalladium complex **2** behaves as a base to pick up a proton.[9] Although there are several examples for the ring expansion, cycloaddition, and alkylation of vinyl oxiranes with heterocumulenes and a variety of pronucleophiles, no attempt has been made to use allenes. Due to the unique arrangement of the two sets of π-orbitals, the reactivity of electron-deficient 1,2 dienes should be higher than that of the corresponding alkynes. Herein, we wish to report a convenient palladium-catalyzed reaction ($Pd(PPh_3)_4$/dppp) of vinyl oxiranes **1** with allenes possessing different substituents, to form functionalized allylic alcohols **6**, in good to excellent yields. Neutral conditions are used because in situ generated alcoholate is basic enough to deprotonate the pronucleophilic entity (allene). A wide variety of functional groups are tolerated in this reaction.

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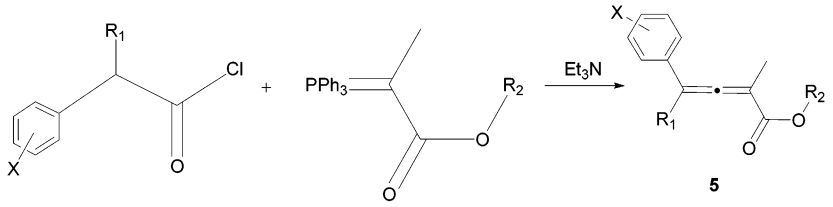
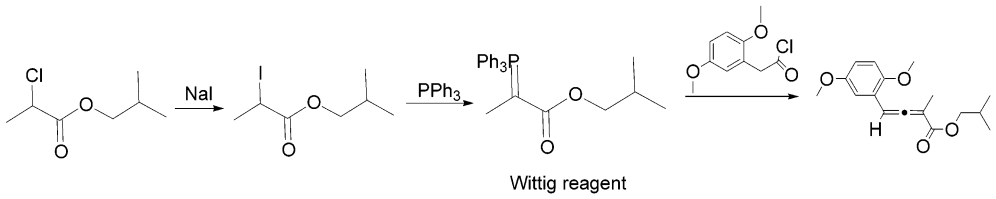
TABLE 1. Preparation of α-Allenic Esters by the Wittig Reaction[a]



entry	X	R_1	R_2	yield[c] (%)
1	Ph	H	C_2H_5	**5a**, 66
2	*o*-Br-Ph	H	C_2H_5	**5b**, 63
3	*p*-Br-Ph[b]	H	C_2H_5	**5c**, 51
4	*p*-Cl-Ph	H	C_2H_5	**5d**, 53
5	*p*-F-Ph	H	C_2H_5	**5e**, 47
6	2-(2-naphthyl)	H	C_2H_5	**5f**, 64
7	*m*,*m*-CF_3-Ph[b]	H	C_2H_5	**5g**, 23
8	*p*-OMe-Ph	H	C_2H_5	**5h**, 65
9	*o*,*m*-OMe-Ph	H	$CH_2CH(CH_3)_2$	**5i**, 83
10	Ph	C_2H_5	C_2H_5	**5j**, 52

[a] Reaction conditions: acid chloride (1 equiv), phosphorane (1 equiv), Et_3N (1 equiv). [b] Prepared from the acid using $SOCl_2$. [c] Isolated yield of the pure product.

SCHEME 1



Results and Discussion

We started this study using commercially available allenes such as 2,3-ethylbutadienoate, and 3-methyl-1,2-butadiene with vinyl oxirane. Absence of the expected products prompted us to use trisubstituted allenes. Although there are a number of methods known for the synthesis of allenes,[10] the requisite substituted allenes used in this study were prepared through the application of a slightly modified procedure to that described by Balme and co-workers (Table 1).[11] The preparation of α-allenic esters was accomplished by the reaction of resonance-stabilized phosphoranes with isolable ketenes,[12] ketene[13] itself, and with acid chlorides in CH_2Cl_2 in the presence of a second equivalent of the phosphoranes. Disadvantages of the above methods have led to the development of the acylation of Wittig reagents to synthesize trisubstituted allenes in good yield. It was found that the acylation of a Wittig reagent provides the most convenient means for the preparation of allenes substituted with various electron-withdrawing substituents in good yields.

The mild reaction conditions used in the modified method avoids the base-catalyzed isomerization of the conjugated allenes to acetylenes. The reaction presumably involves in situ formation of ketene and its capture by the stabilized ylide. To obtain the allene in good purity it was crucial to use freshly distilled acid chlorides, since these decompose on storage. The ready availability of acid chlorides allowed us to prepare a wide range of allenes by this method.

A number of α-allenic esters were synthesized in good yields, and yields were lower when electron-withdrawing substituents were present on the arene ring (Table 1, e.g., entries 4 and 5). This could be due to the fact that electron-withdrawing substituents lower the electron density, which reduces the rate of formation of the intermediates.

Entry 9 was prepared using literature methods outlined in Scheme 1.[14] The formation of the Wittig reagent was best accomplished through the reaction of triphenylphosphine and isobutyl 2-chloropropionate in the presence of triethylamine. Treatment of the intermediate phosphonium salt with aqueous base yielded the Wittig reagent as a pale yellow precipitate, which then reacted with the corresponding acid chloride to form the allene.

The reaction of vinyl oxirane **1a** (1 mmol) with mono- and disubstituted allenes **5** was first investigated by using reaction conditions similar to those described for the reaction of vinyl oxiranes with heterocumulenes. Mono- and disubstituted allenes are not suitable for the present reaction, as the reaction of **1a** with **5** in the presence of different palladium catalysts and ligands in THF under N_2 gave none of the expected products. According to the mechanism, *β*-H is necessary to form the active allene intermediate, which will be stabilized by other three substituents. In the case of mono- and

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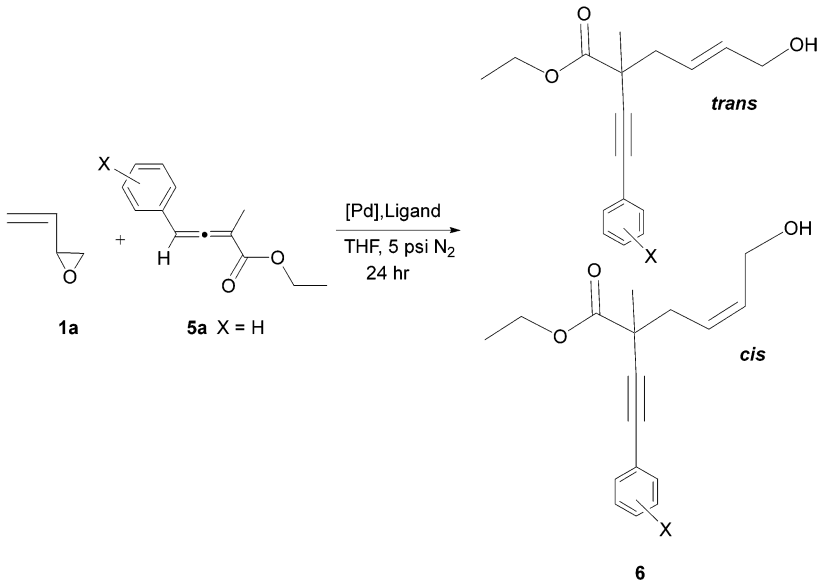
TABLE 2. Optimized Conditions for the Reaction of Vinyl Oxirane 1a with Trisubstituted Allenes, Catalyzed by Palladium[a]



entry	palladium/ligand[a] (mol %)	*T* (°C)	yield of **6**[b] (%)	trans/cis[c]
1	$Pd_2(dba)_3$ (10/20)	60	50	50/50
2	$Pd(PPh_3)_4$ (10/20)	60	74	43/57
3	$Pd(PPh_3)_4$ (10/20)	rt	71	44/56
4	$Pd(PPh_3)_4$ (5/10)	rt	58	44/56
5	$Pd(PPh_3)_4$ (10)[d]	85	–	
6	*e*	60	–	

[a] Palladium catalyst and dppp were premixed for 30 min in 3.0 mL of dry degassed THF followed by addition of **1a** and **5a**. [b] Isolated yield of **6**. [c] Ratio of trans/cis was determined by ^{1}H NMR. [d] In the absence of ligand. [e] In the absence of catalyst and ligand.

disubstituated allenes, stabilization of the negatively charged allene intermediate would be difficult compare to the trisubstituted allenes.

We next examined the reactivity of trisubstituted allenes (Table 2). The reaction of vinyl oxirane with trisubstituted allenes proceeded rapidly under mild conditions with 5−10 mol % of the palladium catalyst. The reaction is totally regioselective giving only the 1,4-adduct. According to similar work done in the past with a variety of heterocumulenes, we expected to see the five-membered ring cycloadduct. The present investigation shows that the product consisted of a mixture of trans and cis isomers of allylic alcohols. We concluded that the trisubstituted allenes are important for the alkylation of vinyl oxiranes.

Next, the effect of the catalyst system was examined. 1,2-Bis(diphenylphosphino)ethane (dppe), 1,2-bis(diphenylphosphino)butane (dppb), and 1,2-bis(diphenylphosphino)ferrocene (dppf) were tested as ligands, in addition to dppp. The use of $Pd_2(dba)_3$ as a catalyst, instead of $Pd(PPh_3)_4$, in THF, gave poor results (entry 1). Other catalyst systems, such as $Pd(PPh_3)_4$−dppe and $Pd(PPh_3)_4$−2dppf, were also tested, but $Pd(PPh_3)_4$−2dppp was the best among the catalyst systems examined. In addition, catalysts such as $Pd(OAc)_2$ and $PdCl_2(PhCN)_2$ were totally ineffective. Based on the above reaction conditions, we concluded that the catalytic system consisting of $Pd(PPh_3)_4$ and dppp is preferred for the present reaction.

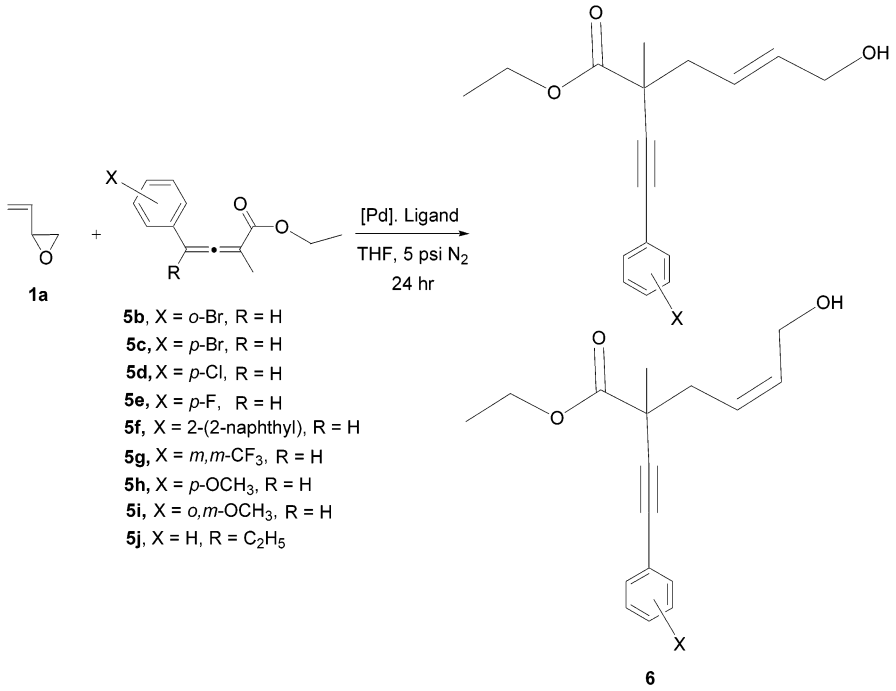
The amount of catalyst-to-ligand ratio was next investigated, and the best results were obtained using $Pd(PPh_3)_4$/dppp in a 10:20 mol % ratio (entry 2). When the amount of catalyst was decreased to 5 mol % the product yield was reduced (entry 4). We also found that the reaction of vinyl oxirane with allene alone in THF at ambient temperature does not proceed to give the allylic alcohol (entry 6). Both catalyst and the ligand are required for the reaction, as the use of catalyst without ligand did not afford the product (entry 5). Also, THF was found to be the best solvent for the alkylation of vinyl oxirane with allenes.

When we examined the temperature effect for the alkylation reaction, 60 °C was found to be the optimum temperature for the present reaction. Alkylation occurs even at room temperature, but the isolated yield is poor compared to the reaction at 60 °C (Table 2, entry 3).

To understand the effect of substituents on the reactivity of allenes, we used electron-withdrawing and -donating substituents as well as bulky substituents present on the arene ring (Table 3). Under the usual reaction conditions, monosubstituted aryl allenes were converted to the corresponding allylic alcohol in higher yields (entry 9). It should be noted that disubstituted aryl allenes gave moderate yields compared to monosubstituted aryl allenes, indicating that the steric bulkiness of the substituents may have a significant effect on the reaction (entry 10).

In all the reactions investigated, allenes with an electron-withdrawing group on the phenyl ring afford the product as a mixture of *E*, *Z* isomers, in good to excellent conversion. It also showed that the stereochemistry of the resultant double bond is predominantly *Z*. This

TABLE 3. Palladium-Catalyzed Reactions of Vinyl Oxirane 1a with Substituted Allenes 5 in THF[a]



entry	allene	*T* (°C)	yield[b] (%)	trans/cis[c]
1	**5b**	70	**6b**, 80	39/61
2	**5b**	rt	**6b**, 72	46/54
3	**5c**	60	**6c**, 73	40/60
4	**5d**	60	**6d**, 69	38/62
5	**5e**	60	**6e**, 71	44/56
6	**5f**	60	**6f**, 62	41/59
7	**5f**	rt	**6f**, 23	45/55
8	**5g**	60	**6g**, 58	31/69
9	**5h**	60	**6h**, 67	51/49
10	**5i**	60	**6i**, 64	54/46
11	**5j**[d]	60		
12	**5j**	100		
13	**5j**	120		

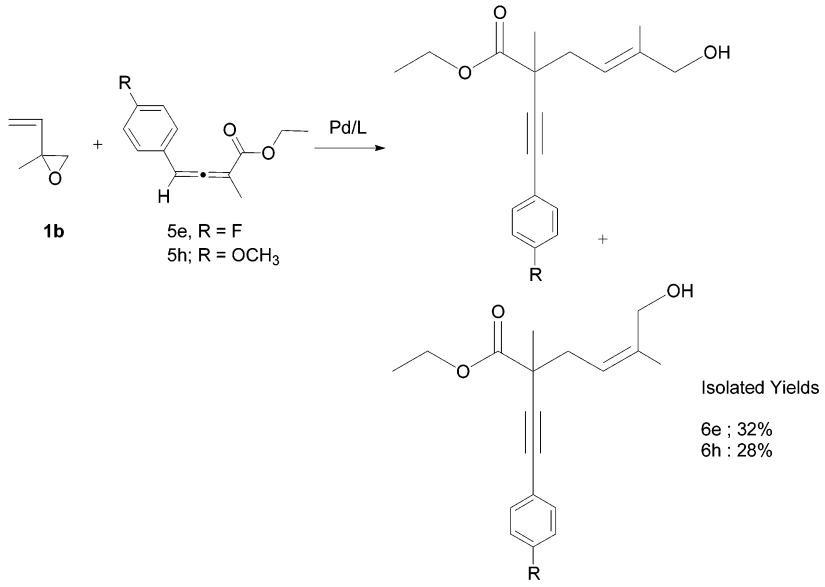
[a] $Pd(PPh_3)_4$ and dppp (10/20 mol %) were premixed for 30 min in 3.0 mL of dry, degassed THF followed by addition of **1a** and **5** under 10 psi of N_2 at the specified temperature in a glass autoclave. [b] Isolated yield is based on the allene **5** used. [c] Ratio of trans/cis was determined based on ^{1}H and GC. [d] Tetrasubstituted allene.

feature reflects the greater stability of the intermediate *syn* complexes compared to the *anti* isomers. Some of the advantages of the present reaction are that it can be carried out in a comparatively shorter time and in some cases at a relative low temperature (entry 2).

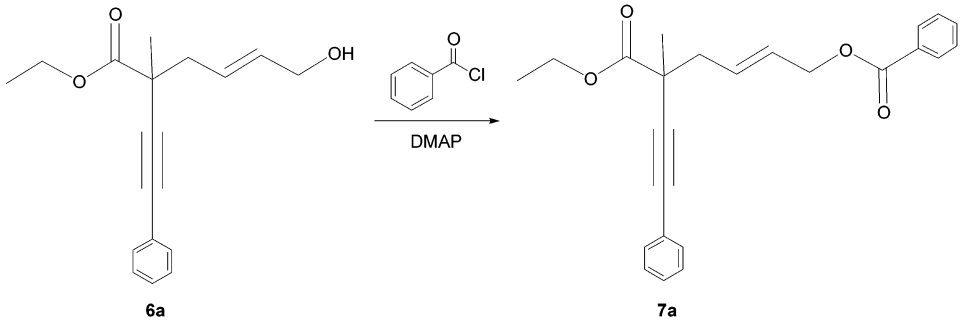
We also examined the reaction of a substituted vinylic oxirane, 2-methyl-2-vinyloxirane (**1b**). The reaction was performed under similar reaction conditions to **5e** and **5h** (Scheme 2). Although the reaction of 2-methyl-2-vinyloxirane **1b** was sluggish in comparison with that of **1a**, presumably due to the steric congestion of the π-allylpalladium intermediate **2**, the alkylation products were obtained in quite good yields.

The structural assignment of the products was made on the basis of NMR and mass spectral results. We also investigated the stereoselectivity of the reaction by using **5c** as the allene. The latter was a mixture of *trans* and *cis* isomers (inseparable by GC and TLC). This led us to use preparative HPLC to separate the two isomers. The data obtained for compound **6c** in $CDCl_3$ are discussed below: (1) The ^{1}H NMR spectrum of the *trans*/*cis* mixture showed aromatic protons at δ 7.53−7.36, two multiplets at δ 5.8 (4H) and δ 4.2 (8H), a dd at δ 2.8, two singlets at δ 1.49 and 1.51 (6H), and a multiplet at δ 1.29−0.122, which integrates to 8H instead of 6H. The integration at δ 1.29−1.22 did not match with the number of protons, which indicated that there could be an OH group underneath the multiplet. The ^{1}H NMR analysis of **6c** in benzene resolved this problem, indicating that the compound has an OH group adjacent to a methylene center. A 2-D COSY experiment showed correlation between that methylene center and the alkene protons. (2) ^{13}C NMR spectrum gave a signal at 172.8 ppm, which corresponds to the ester carbonyl carbon. The two quaternary carbons in the nonaromatic region (80−90 ppm) suggest the presence of an alkyne functional group in the product. (3) Mass spectral data for compound **6c** supported the molecular formula ($C_{17}H_{19}O_3Br_1$) proposed for the estimated value. (4) An intense absorption band at 1732 cm^{-1} region, typical of ester carbonyls, was present in the IR spectrum and the absence of the characteristic allene bond in the 1946 cm^{-1} region was observed after

SCHEME 2



SCHEME 3



the reaction. A weak IR absorption was observed at 2340 and 2358 cm^{-1}, which corresponds to the alkyne bond.

Esterification of **6a** was performed to confirm the presence of the allylic alcohol functionality (Scheme 3). Benzoyl chloride and a catalytic amount of 4-(dimethylamino)pyridine (DMAP) were added to a solution of **6a** in CH_2Cl_2 to give **7a** in 53% yield.

A possible mechanism for the Pd-catalyzed reaction is outlined in Scheme 4. Initial oxidative addition of the Pd(0) catalyst to vinyl oxirane **1** may give the π-allylpalladium intermediate **2**. Addition of the activated allene to the π-allylpalladium intermediate would produce **6** as a mixture of *trans* and *cis* isomers.

In conclusion, we have observed the first regioselective palladium-catalyzed ring opening and alkylation of vinyl oxiranes with substituted allenes. The reaction is catalyzed by 10 mol % of $Pd(PPh_3)_4$ and 20 mol % dppp affording the corresponding funtionalized allylic alcohols in good to excellent yields. The reaction tolerates a wide range of functionality on the arene ring of the allylic alcohols. This reaction provides a convenient new synthetic route to allylic alcohols.

Experimental Section

All reactions and manipulations of chemicals were carried out using standard Schlenk techniques under an atmosphere of nitrogen. 2,3-Butadienoate, $Pd(PPh_3)_4$, and dppp were purchased from commerical suppliers and were used as received. THF was dried over sodium/benzophenone and distilled prior to use. All NMR spectra were recorded using $CDCl_3$ as the solvent with reference to residual $CHCl_3$ (^1H at 7.2 ppm and ^{13}C at 77.0 ppm) except for **6c**.

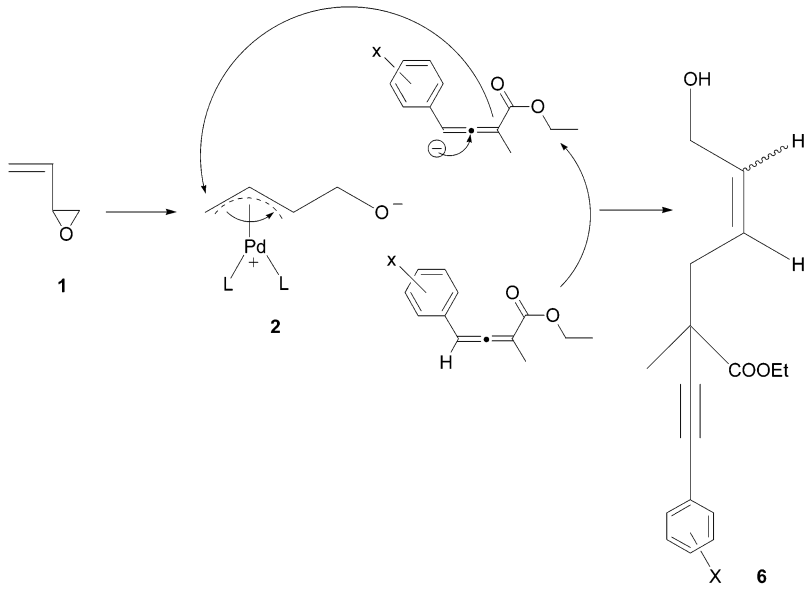
Separation of two isomers of **6c** and **7c** was achieved using a HPLC equipped with a Nova-Pak Silica analytical, Nova-Pak Silica preparative column with hexanes/ethyl acetate as the mobile phase.

Spectral Data. 6-Hydroxy-2-methyl-2-phenylethynyl-4-hexenoic acid ethyl ester (6a) (X = H): light yellow oil; ^1H NMR (300 MHz, $CDCl_3$) δ 7.42−7.25 (m, 10H), 5.83−5.68 (m, 4H), 4.23−4.02 (m, 8H), 2.78−2.47 (m, 4H), 1.54 (s, 3H), 1.51 (s, 3H), 1.39−1.21 (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.8, 172.7, 133.2, 131.7, 131.4, 128.0, 127.9, 127.8, 127.7, 126.6, 126.4, 122.8, 122.7, 89.9, 89.7, 83.2, 62.9, 61.5, 61.3, 58.0, 43.1, 43.0, 42.4, 37.3, 25.1, 24.6, 13.9, 13.8; MS *m*/*e* 272 (M^+); EIHRMS calcd for $C_{17}H_{20}O_3$ 272.1412, found 272.1422.

2-(2-Bromophenylethynyl)-6-hydroxy-2-methyl-4-hexenoic acid ethyl ester (6b) (X = *o*-Br): light yellow oil; ^1H NMR (300 MHz, $CDCl_3$) δ 7.54 (d, J = 8.0 Hz, 2H), 7.44 (d, J = 1.68 Hz, 2H), 7.22−7.10 (m, 4H), 5.91−5.73 (m, 4H), 4.28−4.13 (m, 4H), 4.11 (d, J = 5.1 Hz, 4H), 2.82−2.65 (m, 2H), 2.56−2.03 (m, 2H), 1.54 (s, 3H), 1.52 (s, 3H), 1.44−1.23 (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.7, 172.4, 133.3, 133.1, 133.0, 132.1, 132.0, 131.6, 129.0, 128.9, 126.8, 126.7, 126.6, 126.5, 125.4, 124.9, 124.8, 94.7, 94.5, 81.9, 63.1, 61.6, 61.4, 58.1, 58.0, 43.4, 43.3, 42.3, 37.2, 25.1, 24.5, 14.0, 13.9; MS (*m*/*e*) 350 (M^+); EIHRMS calcd for $C_{17}H_{19}O_3Br_1$ 350.0518, found 350.0514.

2-(4-Bromophenylethynyl)-6-hydroxy-2-methyl-4-hexenoic acid ethyl ester (6c) (X = *p*-Br): yellow oil; ^1H NMR (300 MHz, $CDCl_3$) δ 7.53 (d, J = 8.49 Hz, 4H). 7.36 (d, J = 8.42 Hz, 4H), 5.83−5.27 (m, 4H), 4.22−4.08 (m, 8H), 2.75−

SCHEME 4



2.44 (m, 4H), 1.51 (s, 3H), 1.49 (s, 3H), 1.29−1.22 (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.1, 133.8, 133.1, 132.4, 131.8, 131.4, 128.0, 127.7, 127.3, 126.4, 126.0, 122.3, 122.2, 121.9, 121.1, 91.7, 91.4, 82.5, 62.9, 61.5, 61.3, 58.2, 43.4, 43.2, 42.6, 37.4, 25.1, 24.6, 13.9, 13.8; MS (*m*/*e*) 351 (M^+); EIHRMS calcd for $C_{17}H_{19}O_3Br_1$ 350.0518, found 350.0515.

2-(4-Chlorophenylethynyl)-6-hydroxy-2-methyl-4-hexenoic acid ethyl ester (6d) (X = *p*-Cl): light yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32 (d, J = 8.05 Hz, 4H), 7.24 (d, J = 5.69 Hz, 4H), 5.85−5.59 (m, 4H), 4.27−4.11 (m, 8H), 2.77−2.45 (m, 4H), 1.54 (s, 3H), 1.51 (s, 3H), 1.30−1.25 (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.9, 172.6, 134.2, 134.1, 133.5, 133.0, 132.0, 128.6, 128.5, 127.2, 127.0, 121.7, 121.5, 118.6, 91.3, 91.1, 82.5, 63.4, 61.8, 61.6, 58.5, 43.5, 43.3, 42.8, 42.7, 37.5, 25.4, 24.9, 14.2, 14.1; MS (*m*/*e*) 306 (M^+); EIHRMS calcd for $C_{17}H_{19}O_3Cl$ 306.1023, found 306.0992.

2-(4-Fluorophenylethynyl)-6-hydroxy-2-methyl-4-hexenoic acid ethyl ester (6e) (X = *p*-F): light yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37 (dd, J = 6.5 Hz, 4H), 6.97 (t, J = 8.30 Hz, 4H), 5.85−5.64 (m, 4H), 4.26−4.04 (m, 8H), 2.77−2.45 (m, 4H), 1.51 (s, 3H), 1.49 (s, 3H), 1.39−1.21 (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.0, 172.8, 164.0, 163.9, 160.6, 160.5, 133.5, 133.47, 133.4, 131.9, 126.9, 126.6, 119.1, 119.05, 119.0, 118.9, 115.5, 115.4, 115.2, 115.1, 89.7, 89.6, 82.4, 63.2, 61.7, 61.6, 58.3, 43.3, 43.2, 42.6, 37.4, 25.3, 24.8, 14.1, 14.0; MS (*m*/*e*) 290 (M^+); EIHRMS calcd for $C_{17}H_{19}O_3F$ 290.1318 found 290.1307.

6-Hydroxy-2-methyl-2-naphthalen-2-ylethynyl-4-hexenoic acid ethyl ester (6f) (X = naphthyl): light yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.93 (s, 2H), 7.79−7.72 (m, 6H), 7.47−7.42 (m, 6H), 5.88−5.69 (m, 4H), 4.29−4.08 (m, 8H), 2.83−2.519 (m, 4H), 1.58 (s, 3H), 1.56 (s, 3H), 1.32−1.27 (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.1, 172.9, 133.5, 132.8, 131.9, 131.4, 131.3, 128.5, 128.4, 127.8, 127.7, 127.6, 127.5, 126.8, 126.5, 126.43, 126.4, 126.3, 120.3, 120.2, 90.5, 90.3, 83.8, 63.2, 61.8, 61.6, 58.3, 43.4, 43.3, 42.7, 37.5, 25.4, 24.9, 14.1, 14.0; MS (*m*/*e*) 322 (M^+); EIHRMS calcd for $C_{21}H_{22}O_3$ 322.1569, found 322.1545.

2-(3,5-Bis(trifluoromethyl)phenylethynyl)-6-hydroxy-2-methyl-4-hexenoic acid ethyl ester (6g) (X = *m,m*-CF_3): light yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.83 (s, 4H), 7.76 (s, 2H), 5.84−5.62 (m, 4H), 4.28−4.05 (m, 8H), 2.79−2.48 (m, 4H), 1.55 (s, 3H), 1.53 (s, 3H), 1.31−1.22 (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.4, 172.2, 135.0, 133.8, 132.4, 132.2, 132.0, 131.6, 131.5, 131.1, 126.7, 126.3, 125.4, 125.3, 124.7, 121.5, 121.1, 94.0, 93.8, 80.9, 63.3, 62.1, 61.9, 58.4, 43.6, 43.5, 42.5, 37.4, 25.3, 24.8, 14.2, 14.1; MS (*m*/*e*) 408 (M^+); EIHRMS calcd for $C_{19}H_{18}O_3F_6$ 408.1160 found 408.1156.

6-Hydroxy-2-(4-methoxyphenylethynyl)-2-methyl-4-hexenoic acid ethyl ester (6h) (X = *o*-OMe): light yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33 (d, J = 8.59 Hz, 4H), 6.78 (d, J = 8.48 Hz, 4H), 5.80−5.66 (m, 4H), 4.21−4.08 (m, 8h), 3.77 (s, 6H), 2.74−2.44 (m, 4H), 1.50 (s, 3H), 1.48 (s, 3H), 1.29−1.22 (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.0, 172.8, 159.2, 159.1, 133.1, 132.8, 131.6, 127.1, 126.8, 115.0, 114.8, 113.6, 113.5, 88.4, 88.3, 83.0, 63.1, 61.5, 61.3, 58.1, 43.1, 43.0, 42.5, 37.3, 25.3, 24.7, 13.9, 13.8; MS (*m*/*e*) 302 (M^+); EIHRMS calcd for $C_{18}H_{22}O_4$ 302.1518, found 302.1607.

2-(2,5-Dimethoxyphenylethynyl)-6-hydroxy-2-methyl-4-hexenoic acid isobutyl ester (6i) (X = *o,o*-OMe): light yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.89 (s, 2H), 6.77 (dd, J = 3.77 Hz, 4H), 5.90−5.67 (m, 4H), 4.09 (d, J = 5.18 Hz, 4H), 3.91 (d, J = 6.84 Hz, 4H), 3.75 (d, J = 17.87 Hz, 6H), 2.79−2.46 (m, 4H), 2.04−1.90 (m, 2H), 1.54 (s, 3H), 1.52 (s, 3H), 1.2−0.94 (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.2, 173.0, 154.6, 154.4, 153.2, 153.1, 133.3, 131.9, 127.5, 127.3, 118.3, 118.2, 115.4, 115.3, 113.1, 112.9, 112.5, 112.4, 94.1, 94.0, 79.8, 79.7, 71.6, 71.5, 63.6, 58.4, 56.6, 56.5, 55.8, 43.9, 43.7, 42.7, 37.5, 27.8, 25.7, 25.0, 19.0; MS (*m*/*e*) 360 (M^+); EIHRMS calcd for $C_{21}H_{28}O_5$ 360.1937, found 360.1959.

Benzoic acid 5-ethoxycarbonyl-5-methyl-7-phenylhept-2-en-6-ynyl ester (7a) (X = H): light yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.16−7.24 (m, 20H), 6.03−5.78 (m, 4H), 4.92 (d, J = 5.09 Hz, 2H), 4.79 (d, J = 5.86 Hz, 2H), 4.21 (m, 4H), 2.84−2.49 (m, 4H), 1.55 (s, 3H), 1.52 (s, 3H), 1.31−1.25 (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.8, 172.7, 166.4, 166.3, 133.7, 132.9, 131.7, 130.3, 130.2, 129.6, 129.5, 128.4, 128.3, 128.2, 128.1, 128.0, 126.9, 123.0, 122.9, 89.9, 89.8, 83.6, 83.5, 65.1, 61.7, 61.6, 60.9, 43.2, 43.1, 42.7, 37.7, 25.2, 25.0, 14.1, 14.0; MS (*m*/*e*) 376 (M^+); EIHRMS calcd for $C_{24}H_{24}O_4$, 376.1675 found 376.1695.

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Supporting Information Available: ^{1}H and ^{13}C NMR spectra of compounds **6a**−**i** and **7a**; ^{1}H COSY spectra of compounds **6c** (*cis*) in C_6D_6, **7a** (*cis*), and **7a** (*trans*); ^{1}H−^{13}C HMQC spectra of compound **7a** (*cis*). This material is available free of charge via the Internet at http://pubs.acs.org.

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