Carbon−Carbon Bond Formation in Regio- and Stereoselective Palladium-Catalyzed Cyclization of Allene-Substituted Conjugated Dienes

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Regio- and stereoselective palladium-catalyzed reactions of allene-substituted 1,3-dienes **1** in acetic acid at room temperature lead to cyclization with formation of a carbon−carbon bond between the middle carbon of the allene and the terminal carbon of the 1,3-diene. Two different types of reactions, both that constitute 1,4-carboacetoxylations of the 1,3-diene, have been developed. In one of the reactions, Pd(II) catalyzes the oxidation of **1** to bicyclic compounds **2**, and in the other, Pd(0) catalyzes the transformation of **1** to bicyclic compounds **3**. The products **2** are useful for further synthetic transformations and undergo Diels−Alder reactions with dienophiles to give polycyclic ring systems.

Introduction

Transition metal-catalyzed reactions of allenes have attracted increasing interest during the last two decades.[1] The majority of these reactions involve palladium(0)-catalyzed transformations, but recently palladium(II)-catalyzed oxidations have also been reported.

We have previously been working on palladium(II)-catalyzed oxidations of 1,3-dienes and developed a number of regio- and stereoselective inter- and intramolecular 1,4-addition reactions.[2,3] These palladium(II)-catalyzed oxidations were recently extended to 1,2-additions of 1,2-dienes, that is, allenes.[4]

Most of the oxidation reactions developed so far for 1,3- and 1,2-dienes have involved regioselective formation of new carbon−heteroatom bonds by the use of heteroatom nucleophiles. A more difficult task is to obtain carbon−carbon bond formation in these reactions since carbon nucleophiles are more sensitive to the oxidative reaction conditions. In the intramolecular palladium(II)-catalyzed 1,4-oxidation of 1,3-dienes, carbon−carbon bond formation has been achieved in a few instances.[5−7] In one approach, alkynes were used to generate a vinylpalladium intermediate, which subsequently adds to the diene.[5] In another method, allylsilanes were employed as masked carbon nucleophiles.[6] Finally, the use of highly stabilized carbanions ($pK_A \approx 5$) led to carbon−carbon bond formation in the 1,4-oxidation.[7]

The present work was inspired by the fact that allenes easily can form a vinylpalladium species,[1] which can add to a double bond. If the allene is the only double bond species, this leads to a dimerized product.[8] In the presence of carbon monoxide, allenes are carbonylated.[9] It is also reported in the literature that allenes readily insert into palladium−carbon bonds resulting in the formation of a new carbon−carbon bond.[10]

In this paper, we report on palladium-catalyzed reactions in which an allene in the side chain of a cyclic 1,3-diene is employed to create a carbon−carbon bond via cyclization. The transformations, which formally constitute 1,4-carboacetoxylations of the 1,3-diene, are highly stereoselective (Scheme 1).

Results and Discussion

A. Preparation of Starting Materials. Allene-substituted dienes **1a**−**f** were obtained from the ketones

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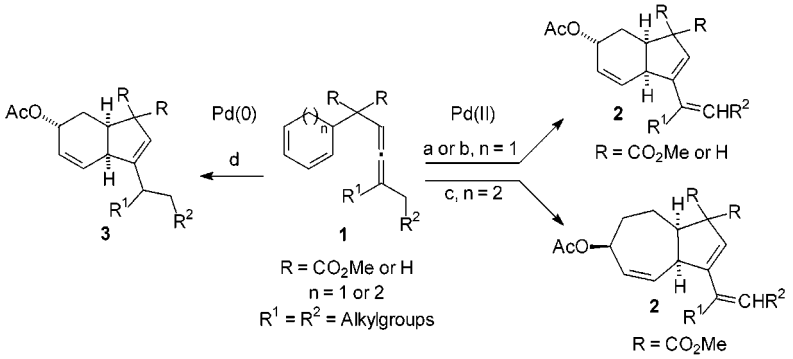
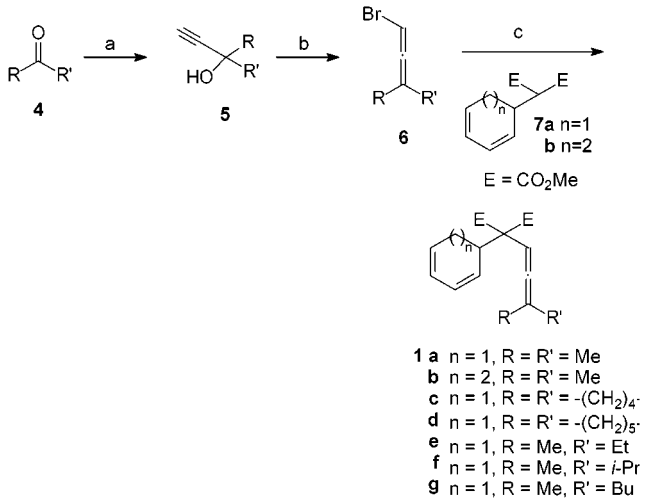
Scheme 1[a]



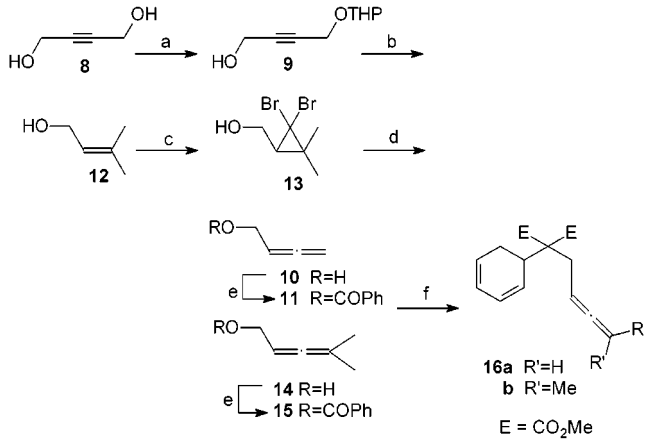
[a] Conditions: (a) 0.1 equiv of $Pd(OAc)_2$, 4 equiv of LiOAc, 2 equiv of *p*-benzoquinone, HOAc, room temperature, 4 h; (b) 0.05 equiv of $Pd(OAc)_2$, 0.3 equiv of *p*-benzoquinone, HOAc, 0.02 equiv of iron phthalocyanine, room temperature, 24 h, O_2; (c) 0.1 equiv of $Pd(OAc)_2$, 4−50 equiv of LiOAc, 2 equiv of *p*-benzoquinone, HOAc, room temperature, 14 h; (d) 0.05 equiv of $Pd(dba)_2$, 4 equiv of LiOAc, HOAc, room temperature, 24 h.

Scheme 2[a]



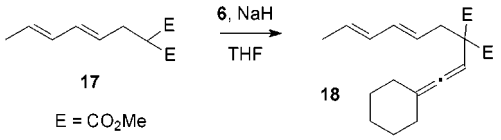
[a] Conditions: (a) lithium acetylide diamine, THF; (b) CuBr, NH_4Br, Cu powder, HBr; (c) **7**, NaH, THF.

Scheme 3[a]



[a] Conditions: (a) DHP, PPTS, THF; (b) $LiAlH_4$, Et_2O, reflux; (c) $CHBr_3$, *t*-BuOK, pentane, 0 °C; (d) MeLi, Et_2O, −78 °C; (e) benzoyl chloride, pyridine, DMAP, CH_2Cl_2; (f) **7a**, NaH, $Pd(PPh_3)_4$, THF.

Scheme 4



4 according to Scheme 2. Reaction of **4** with lithium acetylide gave 1,1-disubstituted propargylic alcohols, which on subsequent treatment with copper bromide in HBr afforded the corresponding bromoallenes **6** in high yields.[11] Using the method of Landor,[12] the latter were converted to **1a**−**g** by reaction with the sodium salt of the appropriate diene malonates **7**.[6a,13]

The allene diene homologues **16** were synthesized either from alkyndiol **8** or from alkenol **12** (Scheme 3). Monoprotection[14] of **8** as the THP derivative **9** followed by reduction with $LiAlH_4$ in ether[15] gave the allenic alcohol **10**. The dimethyl analogue of **10**, allene alcohol **14**, was prepared from **12** by cyclopropanation[16] followed by lithiation of the dibromocyclopropane alcohol **13** and subsequent rearrangement.[17] Allene alcohols **10** and **14** were transformed into the corresponding benzoate esters **11** and **15**, respectively, which in turn were allowed to react with the sodium salt of **7a** in a palladium(0)-catalyzed reaction[18] to give **16**.

The malonate diene **17** was obtained according to a literature procedure.[19] Reaction of the sodium salt of **17** with **6** gave the allene diene **18** (Scheme 4) in 63% yield using the method of Landor.[12]

Allene-substituted dienes **1h**−**k**, without methoxycarbonyl groups, were prepared according to Scheme 5. The malonate diene **7a** was transformed to the Weinreb amide **19** according to a modified literature procedure.[5a,20] Subsequent reaction of **19** with the appropriate lithium acetylide followed by DIBALH-reduction gave alcohols **20** in good to high yields. Mesylation and subsequent copper-

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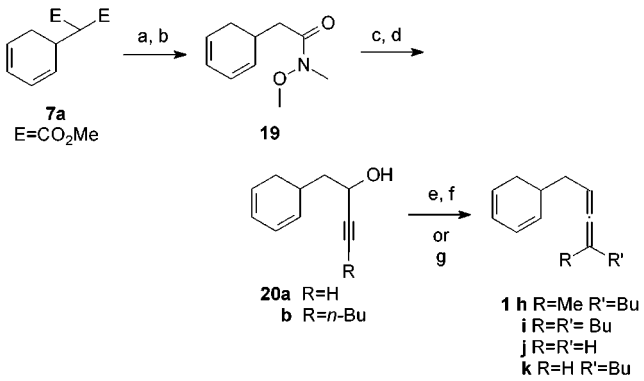
Scheme 5[a]



[a] Conditions: (a) NaCN, H_2O, DMSO; (b) $AlMe_3$, HN(OMe)Me, CH_2Cl_2; (c) LiC≡CR, THF; (d) DIBALH, Et_2O; (e) BuLi, MsCl, THF; (f) R'_2CuLi, Et_2O; (g) DEAD, PPh_3, *o*-nitrobenzezesulfonylhydrazide,[23] THF.

(I)-mediated S_N2' displacement afforded allenes **1h** and **1i** in 52% and 89% yield, respectively.[21] Allenes **1j** and **1k** were obtained by transformation of the alcohols **20a** and **20b** to the corresponding hydrazine derivative under Mitsunobu conditions, which spontaneously decomposed to give the allenes in 54% and 60% yield, respectively.[22]

B1. Palladium-Catalyzed Oxidative Cyclizations of Allene-Substituted Conjugated Dienes. Allene-substituted dienes **1** were transformed into bicyclic compounds **2** in a palladium-catalyzed oxidation reaction. In the reaction, two new stereocenters are created with high stereoselectivity in relation to the stereocenter already present in the starting material. The relative stereochemistry between the three stereocenters is completely controlled in almost all of the cases in this 1,4-carboacetoxylation of the conjugated diene. The cyclohexadiene-allene derivatives **1a** and **1c**−**i** gave a *trans*-1,4-carboacetoxylation, whereas the cycloheptadiene-allene **1b** gave the opposite stereochemistry, that is, *cis*-1,4-carboacetoxylation. It is known from previous work that the cycloheptadiene behaves differently under halide-free conditions[2] (see mechanistic discussion). The reactions were carried out at room temperature in acetic acid with catalytic amounts of palladium acetate and with *p*-benzoquinone as the oxidant. For substrates **1a** and **1c**−**i**, the amount of lithium acetate has a minor influence on the outcome of the oxidation. Most reactions were carried out with 4 equiv of LiOAc (0.3 M LiOAc in HOAc) relative to the starting material. However, the effect of LiOAc was large when the cycloheptadiene-allene (**1b**) was employed as the starting material. In this case, 1,2-addition (**2b′**) and competing 1,4-diacetoxylation were observed (Table 1, entry 2). It was found that 2 M LiOAc in HOAc gave the most selective reaction with respect to formation of **2b** (entry 2c). Interestingly, with the use of 4 M LiOAc in HOAc, formation of the 1,2-addition product **2b′** was completely depressed (entry 2d). However, in the latter case the relative amount of the noncyclized diacetate **2b″** was 38%.

The reaction can also be carried out with a catalytic amount of *p*-benzoquinone (30%), palladium acetate (5%), and iron phthalocyanine (2%) under an oxygen atmosphere.[24] Under these conditions, **1a** gave product **2a** in good yield (entry 1b).

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The starting materials were varied with respect to the diene ring size and allene substituents. Methyl-substituted allene **1a** gave the product **2a** in good yield (Table 1, entry 1). Cyclohexylidene- and cycloheptylidene-substituted allenes **1c** and **1d** afforded products **2c** and **2d**, respectively, in good yields (Table 1, entries 3 and 4). There is a selectivity for the formation of the more substituted alkyl chain, and this thermodynamically more stable product is predominantly formed (Table 1, entries 5−8). The bis-methoxycarbonyl substituents have only a minor effect on the isolated yields (cf. Table 1, entries 7 and 8), but without these substituents, a lower stereoselectivity in the 1,4-carboacetoxylation across the 1,3-diene was obtained (Table 1, entry 8). The size of the alkyl substituents on the allene seems to have a significant effect on the yield with lower yields for larger substituents (cf. Table 1, entries 1 and 7). In addition, it seems to be necessary to have three substituents on the allene. Attempts to use terminal allenes (**1j**, Figure 1) or 1-monosubstituted allenes (**1k**, Figure 1) were unsuccessful and gave complex mixtures of products. Extension of the allene side chain with an extra methylene group (**16a** and **16b**, Figure 1) also gave a complex mixture of products. The acyclic diene (**18**, Figure 1) gave no reaction.

B2. Palladium-Catalyzed Non-Oxidative Cyclizations of Allene-Substituted Cyclodienes. In an attempt to isolate a possible (π-allyl)palladium intermediate in the palladium(II)-catalyzed cyclizations, the reaction of **1a** was carried out without *p*-benzoquinone. The (π-allyl)palladium intermediate could not be isolated, but another product **3a** (Table 2) was formed instead, in a slow reaction. The reaction seems to be catalyzed by Pd(0). Replacement of $Pd(OAc)_2$ with $Pd(dba)_2$ as the palladium source went equally well or better. We also studied the palladium(0)-catalyzed reaction of some additional allene-substituted dienes (**1c**, **1e**, and **1h)** in the absence of oxidant, which also gave bicyclic compounds **3** (Table 2). The reactions were performed using catalytic amounts of palladium dibenzylideneacetone or palladium acetate in the presence of 0.3 M LiOAc in acetic acid. When the reaction of **1a** was carried out in deuterated acetic acid, monodeuterated product d_1-**3a** was formed (Scheme 6). ^1H NMR analysis showed that deuterium had been incorporated at the tertiary carbon of the isopropyl group with high selectivity (>99%).

C1. Mechanism of Oxidative Cyclization in the Presence of *p*-Benzoquinone (BQ). The mechanism for the palladium(II)-catalyzed oxidative cyclization of allene dienes can be explained by Scheme 7a (path A), where the allene acts as a nucleophile and attacks the diene in diene complex **21**, from the face opposite to that of palladium, to give π-allyl complexes **22a** and **22b**. An intramolecular attack (cis migration), where the acetate is delivered from palladium in **22a**, would explain the stereochemistry of the product **2a**.[25] External attack by acetate on π-allyl complex **22b** would give product **2b**. Intramolecular cis migration of acetate is known to be more difficult from a seven-membered ring than from a

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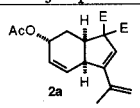
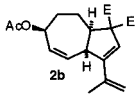
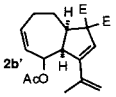
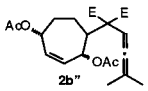
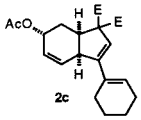
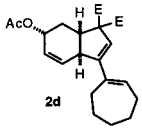
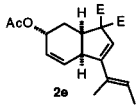
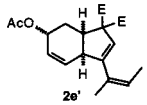
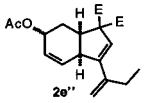
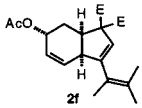
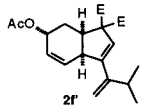
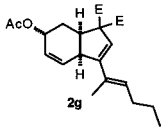
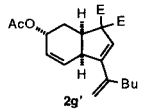
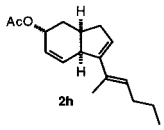
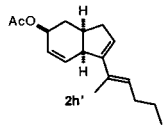
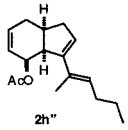
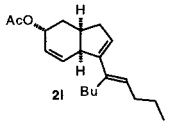
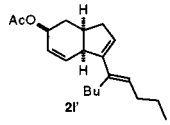
Table 1. Palladium(II)-Catalyzed Carboacetoxylation of Allene-Substituted Dienes[a]

Entry	Reactant	Major product	Minor product	Minor product	Yield[b]	Ratio
1a	**1a**				67	
1b					67[c]	
2a	**1b**				87	60:40:0[d]
2b					71	57:24:19[e]
2c					75	79:12:9[f]
2d					79	62:0:38[g]
3	**1c**				77	
4	**1d**				60	
5	**1e**				67	78:8:14
6	**1f**				60	56:44
7	**1g**				49	76:24
8	**1h**				48	60:30:10
9	**1i**				44	75:25

[a] General procedure: To a stirred solution of 10 mol % of palladium acetate were added 2 equiv of *p*-benzoquinone and 4 equiv of lithium acetate dihydrate in acetic acid (0.3 M) as starting material during 3 h. [b] Total isolated yield after flash chromatography. [c] Alternative procedure: To the starting material were added 5 mol % palladium acetate, 2 mol % iron phthalocyanine, and 30 mol % *p*-benzoquinone. This was dissolved in acetic acid, and the reaction was run under oxygen atmosphere. The reaction was stirred at room temperature for 24 h. [d] Alternative procedure: as method in *a*, but starting material was added during 14 h. [e] Alternative procedure: as method in *a*, but starting material was added during 14 h to 16 equiv of lithium acetate dihydrate in acetic acid (1 M). [f] Alternative procedure: as method in *a*, but starting material was added during 14 h to 50 equiv of lithium acetate dihydrate in acetic acid (2 M). [g] Alternative procedure: as method in *a*, but starting material was added during 14 h to 50 equiv of lithium acetate dihydrate in acetic acid (4 M).

six-membered ring, and this has been explained by conformational differences between the two ring systems.[2] In the oxygen−carbon bond-forming process (**22a** → **2a** and **22b** → **2b**), palladium(0) is formed, which is reoxidized to palladium(II) by *p*-benzoquinone closing the catalytic cycle.[26]

Three other possible mechanisms (path B, C, and D) for the palladium(II)-catalyzed oxidative cyclization of allene dienes were considered and are discussed below (Scheme 7b). Path B starts with a nucleophilic attack on the activated 1,3-diene to give a π-allyl complex which subsequently would add to the allene to give π-allyl complex **23**. This carbon−carbon bond formation is similar to carbopalladation reactions of allenes,[10] in which a vinyl- or arylpalladium species adds to the middle carbon of the allene.[1] Subsequent β-hydride elimination from the π-allyl complex **23** gives the product **2**. In ongoing work in our group, we are studying related insertions in more detail.[27] This route cannot, however, explain the different stereochemistry of **2a** and **2b** (Table 1, entry 2), nor the 1,2-products formed (Table 1, entries 2 and 8). Path C would give a vinyl palladium species from acetoxyoxypalladation of the allene, and subsequent insertion of the diene would give a π-allyl complex. An

(26) Attempts to reverse the stereochemistry on the six-membered ring, thus blocking migration with chloride, have so far been unsuccessful. The reaction gives a mixture of products.

(27) Löfstedt, J.; Franzen, J. Unpublished results.

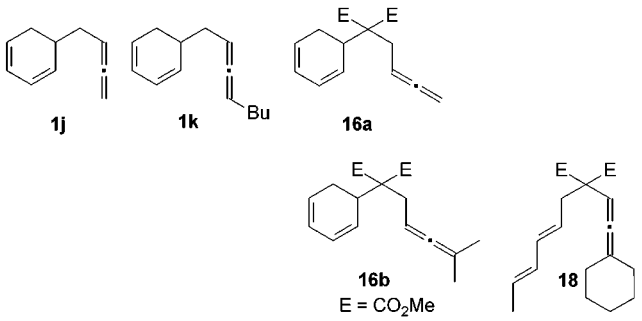
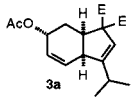
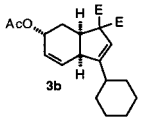
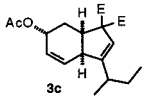
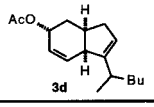


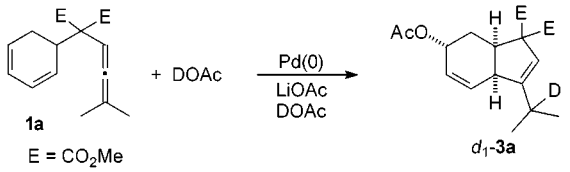
Figure 1. Unsuccessful starting materials.

Table 2. Palladium(0)-Catalyzed Carboacetoxylation of Allene-Substituted Dienes[a]

Entry	Reactant	Product	Catalyst	Yield[b]
1a	**1a**	 **3a**	$Pd(dba)_2$ (10 %)	65
1b			$Pd(dba)_2$ (5 %)	50
2a	**1c**	 **3b**	$Pd(dba)_2$ (10 %)	84
2b			$Pd(OAc)_2$ (5 %)	45
3	**1e**	 **3c**	$Pd(dba)_2$ (5 %)	52
4	**1h**	 **3d**	$Pd(dba)_2$ (10 %)	44

[a] General procedure: To a mixture of starting material, palladium catalyst, and lithium acetate dihydrate (4 equiv) was added acetic acid, and the reaction was stirred at room temperature for 24 h. [b] Total isolated yield after flash chromatography.

Scheme 6



external acetate attack can now give diacetate **24**, which would undergo 1,4-elimination of AcOH via π-allyl complex **23** to give **2**.[28] This route implies that the acetate attack would have to be external for the six-membered ring and intramolecular for the seven-membered ring, which is highly unlikely and against previous observations.[2c] An intramolecular attack would explain the minor 1,2-*cis*-addition product (Table 1, entries 2 and 8) and the 1,4-*cis*-carboacetoxylation product formed in some cases (Table 1, entries 8 and 9). Path D involves an allylic C−H activation[29] of the allene to give an alkylidene π-allyl complex, which should be stabilized in the form of a dienyl palladium species. This dienyl palladium species can in turn add to the diene moiety to give a (π-allyl)-palladium complex. External attack by acetate on this π-allyl complex would give the product. Again, this route implies that the acetate attack would have to be external for the six-membered ring and intramolecular for the seven-membered ring, which is less likely.[2c] However, mechanism D would be consistent with intramolecular delivery of acetate in the 1,2- and 1,4-*cis*-addition products formed as minor products (Table 1, entries 2, 8, and 9). The latter products could also be formed according to mechanism A via an external attack by acetate.

Path A, where the allene acts as a nucleophile, is the mechanism that best explains the experimental data and should be the major pathway. It is consistent with previous observations that an internal attack by acetate is usually faster than an external attack by acetate for six-membered ring π-allyl complexes and that the reactivity order is reversed for the corresponding seven-membered ring complexes. At present, it is difficult to completely exclude the involvement of routes B, C, or D in the palladium(II)-catalyzed oxidative cyclization. In an attempt to detect possible intermediates from Scheme 7a and b, ^{1}H NMR experiments were carried out in deuterated acetic acid. However, no (π-allyl)palladium intermediate could be observed, and the proposed intermediate diacetate **24** could not be detected. With mechanism A, this would suggest that an allene attack on the π-diene-palladium complex is slower than an acetate attack on the intermediate (π-allyl)palladium complex, which is reasonable. A control experiment showed that in the absence of palladium no reaction occurs, and the starting material was recovered after 48 h.

C2. Mechanism of Non-Oxidative Cyclization in the Absence of Benzoquinone. The mechanism of the Pd(0)-catalyzed cyclization can be explained via a palladacycle (Scheme 8) similar to that in a mechanism proposed by Cazes and Gore.[30] In our case, this palladacycle is a bis-allyl complex, and the reactivity of complexes of this type has recently been explored by Szabo[31] and Yamamoto.[32] It is known that one of the allyls, the σ-allyl in σ,π-bis-allyl complexes, is quite reactive toward electrophiles.[31−33]

We believe that the metallacycle **25** initially formed rearranges to σ,π-bis-allyl complex **26** (Scheme 8). The latter complex will react with a proton in the γ position of the σ-allyl ligand to give (π-allyl)palladium complex **27**. This regioselectivity for electrophilic attack on σ,π-allyl palladium complexes is now well established.[31,33] External attack on π-allyl **27** from the exo side would give the product **3**. It is believed that migration of acetate from palladium to carbon is disfavored in this case because palladium is coordinated to the endo face of the bicyclic system. This would make it difficult to form the σ-allyl complex required for cis migration of acetate.[25]

A palladium hydride mechanism for the transformation of **1** to **3** seems less likely since the hydride would be expected to attack the middle carbon of the allene.[1] An

(28) This elimination should proceed via oxidative addition to give a π-allyl intermediate, followed by β-elimination. It is likely that the oxidative addition to **24** would be facilitated by assistance of the double bond of the cyclohexene ring.

(29) Bäckvall, J. E.; Zetterberg, K.; Åkermark B. π-Allylic Complexes from Allylic C−H Bond Cleavage in Olefins by Metal Complexes. In *Inorganic Reactions and Methods*; Zuckerman, J. J., Ed.; Verlag Chemie: Weinheim, Germany, 1991; pp 123−32.

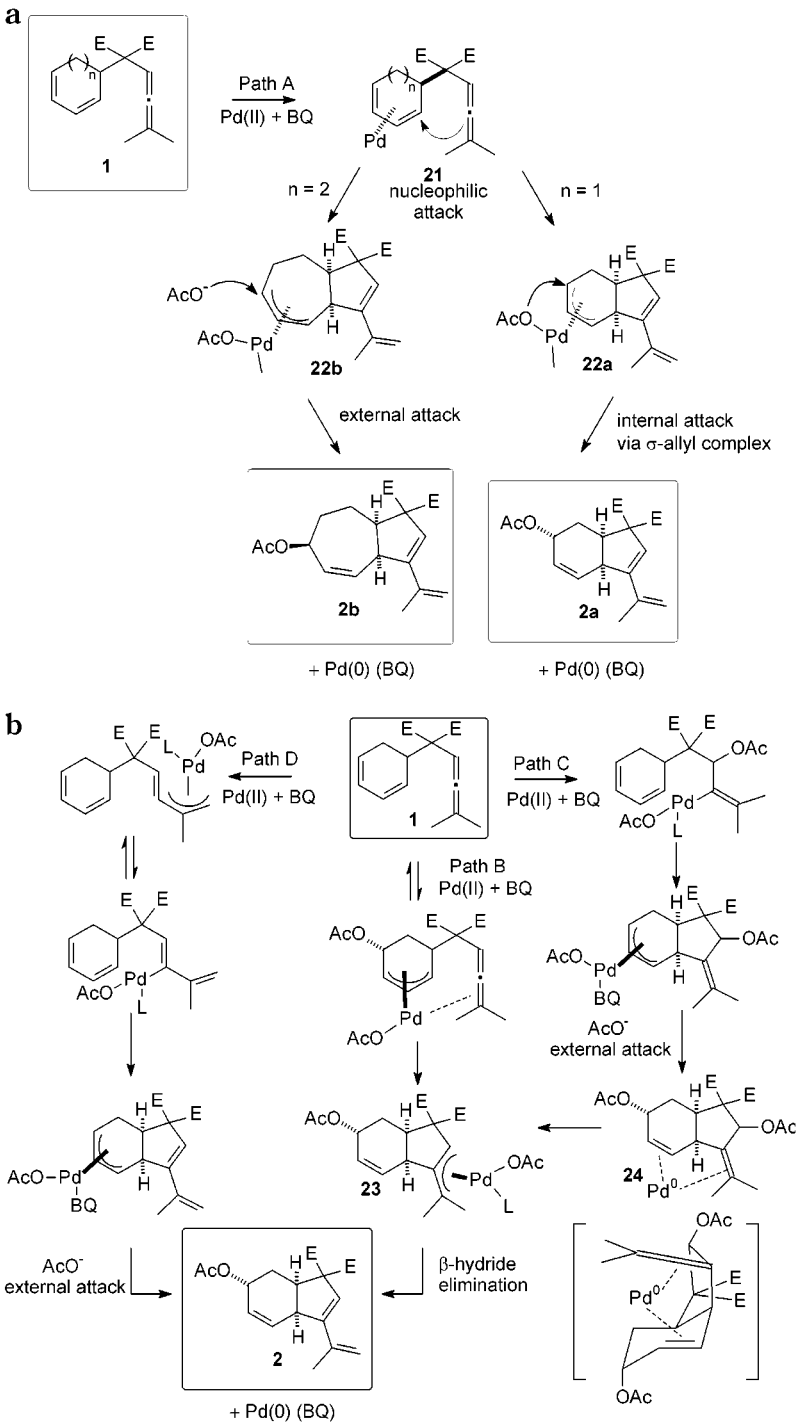
(30) Besson, L.; Gore, J.; Cazes, B. *Tetrahedron Lett.* **1995**, *36*, 3853.

(31) (a) Szabo, K. J. *Chem. Eur. J.* **2000**, *6*, 4413. (b) Solin, N.; Narayan, S.; Szabo, K. J. *J. Org. Chem.* **2001**, *66*, 1686. (c) Solin, N.; Narayan, S.; Szabo, K. J. *Org. Lett.* **2001**, *3*, 909.

(32) Nakamura, H.; Aoyagi, K.; Yamamoto, Y. *J. Am. Chem. Soc.* **2001**, *123*, 372.

(33) (a) Benn, R.; Jolly, P. W.; Mynott, R.; Schenker, G. *Organometallics* **1985**, *4*, 1136. (b) Benn, R.; Jolly, P. W.; Mynott, R.; Raspel, G.; Schenker, G.; Schick, K.-P.; Schroth, G. *Organometallics* **1985**, *4*, 1945. (c) Jolly, P. W.; Mynott, R.; Raspel, G.; Schick, K.-P. *Organometallics* **1986**, *5*, 473.

Scheme 7. Palladium(II)-Catalyzed Oxidative Cyclization Mechanism: (a) Path A and (b) Paths B, C, and D

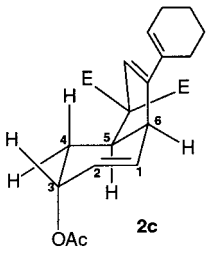


interesting observation is that $Pd(PPh_3)_4$ does not catalyze the reaction.

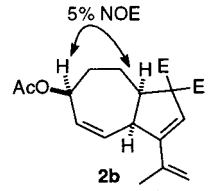
D. Stereochemical Assignment. The stereochemistry of **2c** was assigned by ^1H NMR spectroscopy via analysis of coupling constants (Figure 2). H-3 shows only small couplings to protons H-4 ($^3J_{3,4a} = {}^3J_{3,4e} = 4.5$ Hz), and, as a consequence, H-3 must be equatorial. Furthermore, the large value of $^3J_{4a,5}$ (10.2 Hz) indicates that H-5 is axial and trans to H-4a. The value of $^3J_{5,6}$ (6.8 Hz) confirms the cis junction between the rings. These data imply that the carbons that have added to C-6 and the acetate are trans to one another (*trans*-1,4-carboacetoxylation). In the corresponding seven-membered ring compound **2b**, the stereochemistry was assigned using NOE as indicated in Figure 2. An NOE between the allylic hydrogen in the ring α to acetate and one of the bridge hydrogens shows that the acetate and the carbon that have added are cis to one another (*cis*-1,4-carboacetoxylation).[34]

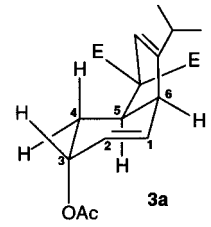
The coupling constants for compound **3a**, given in Figure 2, confirm the stereochemistry assigned. The

(34) For **2b′**, we were not able to assign the stereochemistry of the acetate. A significant NOE (11%) was obtained between the C*H*−OAc and the vicinal bridge proton for **2b′**, but this does not distinguish between cis and trans stereochemistry since the trans isomer may have both vicinal hydrogens equatorial.



$^3J_{3,4a} = {}^3J_{3,4e} = {}^3J_{2,3} = 4.5$ Hz,
$^3J_{4a,5} = 10.2$ Hz, $^2J_{4a,4e} = 14.5$ Hz,
$^3J_{4e,5} = 5.0$ Hz, $^3J_{5,6} = 6.8$ Hz.

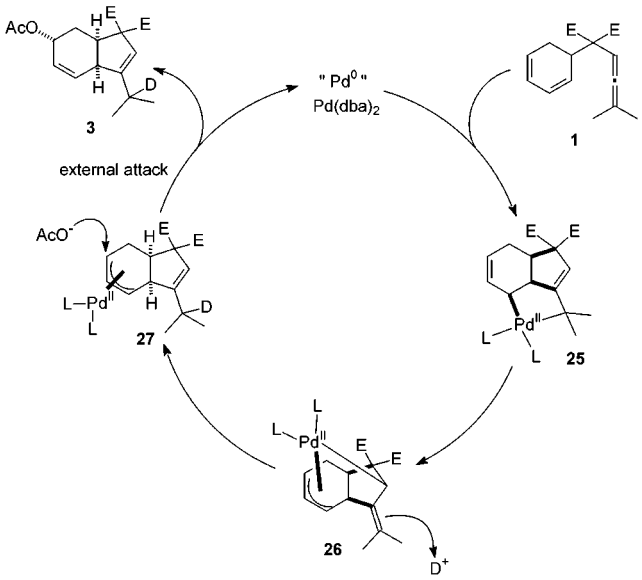




$^3J_{3,4a} = 3.3$ Hz, $^3J_{3,4e} = {}^3J_{2,3} = 5.5$ Hz,
$^3J_{4a,5} = 11.0$ Hz, $^2J_{4a,4e}$ = not determined,
$^3J_{4e,5} = 6.6$ Hz, $^3J_{5,6} = 6.6$ Hz.

Figure 2.

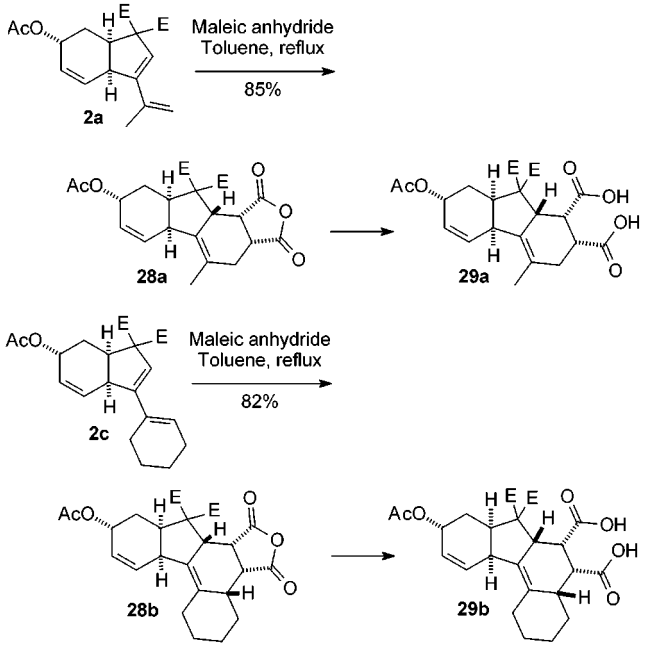
Scheme 8. Palladium(0)-Catalyzed Non-Oxidative Cyclizations of Allene-Substituted Dienes



coupling constants of relevance for the stereochemistry are in the same range as those of **2c** and show that the acetate is on the exo face of the bicyclic system.

E. Synthetic Applications. The products **2** obtained in the palladium(II)-catalyzed oxidative cyclization contain a conjugated diene unit, which can undergo a Diels–Alder [4 + 2] cycloaddition with an appropriate dienophile.[35] This provides a simple, direct route to more complex polycyclic systems. The latter transformation is usually stereoselective, and the synthetic utility of compounds **2** was demonstrated by the reaction of **2a** and

Scheme 9. Diels–Alder Reaction of Compounds 2a and 2c



2c with maleic anhydride in refluxing toluene to give cycloadducts **28a** and **28b**, respectively, as a single diastereoisomer in each case (Scheme 9). The latter compounds were hydrolyzed and characterized as the diacids **29a** and **29b**, respectively. It is interesting to note that in the two transformations **1c** → **2c** → **28b**, the relative stereochemistry between seven stereocenters is completely controlled. NOESY experiments are consistent with the stereochemistry assigned for **29a** and **29b** which is in accordance with the stereochemistry of compounds **2** and the addition of maleic anhydride to the less-hindered face of compounds **2**.

Conclusion

A highly stereoselective palladium(II)-catalyzed oxidation of allene-substituted dienes in acetic acid involving carbon–carbon bond formation has been developed to give highly substituted bicyclic products. Although the detailed mechanism of the reaction is not yet established, a nucleophilic attack by an allene on a diene palladium complex from the face opposite to that of palladium (*trans*-carbopalladation) is a likely pathway for the C–C bond formation. A palladium(0)-catalyzed reaction of the same substrates also led to bicyclic products via carbon–carbon bond formation. The latter reaction is reminiscent of the reaction of two 1,3-dienes and acetic acid (telomerization).[36] In our case, a 1,2-diene replaces one 1,3-diene. The mechanism in our case as well as in telomerization is believed to involve a cyclometalation leading to a bis allyl palladium intermediate.

Experimental Section

^{1}H NMR (400 or 300 MHz) and ^{13}C NMR (100 or 75 MHz) spectra were recorded using chloroform-d_1 (7.26 ppm ^{1}H, 77

(35) (a) Paquette, L. A.; Schaefer, A. G.; Blount, J. F. *J. Am. Chem. Soc.* **1983**, *105*, 3642. (b) Nugent, W. A.; Calabrese, J. C. *J. Am. Chem. Soc.* **1984**, *106*, 6422. (c) Trost, B. M.; Lautens, M. *J. Am. Chem. Soc.* **1985**, *107*, 1781. (d) Trost, B. M.; Tanoury, G. J.; Lautens, M.; Chan, C.; MacPherson, D. T. *J. Am. Chem. Soc.* **1994**, *116*, 4255. (e) Trost, B. M.; Romero, D. L.; Rise, F. *J. Am. Chem. Soc.* **1994**, *116*, 4268.

(36) (a) Tsuji, J. *Palladium Reagents and Catalysts: Innovations in Organic Synthesis*; Wiley: Chichester, 1995. (b) Takacs J. M. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, G. A., Wilkinson, G., Eds.; Pergamon: Elmsford, 1995; Vol. 12 (Hegedus, L. S., Vol. Ed.), p 785. (c) Takacs, J. M.; Chandramouli, S. V. *J. Org. Chem.* **1993**, *58*, 7315.

ppm ^{13}C) as an internal standard. GC-MS (EI) was measured using a Thermo Quest GCQ plus. Elemental analyses were performed by Analytische laboratorien, Lindlar, Germany. All reactions were performed under argon atmosphere, unless otherwise stated.

General Procedure for the Preparation of Diene Allenes 1. Allene 1a. The dienemalonate **7a** (0.25 g, 1.2 mmol) was dissolved in dry THF (6 mL) and cooled to 0 °C. NaH (60% in mineral oil) (0.06 g, 1.5 mmol) was added, and the solution was stirred for 5 min. The cooling bath was then removed, and the slurry was stirred for an additional 60 min. The bromoallene **1a** (0.8 g, 2.4 mmol) was added dropwise as a solution in THF (3 mL). The reaction was followed by GC-MS and stirred until the dienemalonate had disappeared (3 h). Water (30 mL) was added, the aqueous phase was extracted with Et_2O (3 × 30 mL), and the combined organic layers were dried (Na_2SO_4). Careful evaporation (water bath at room temperature) followed by flash chromatography (pentane:Et_2O, 90:10) gave 0.24 g (72% yield) of **1a**. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.94−5.81 (m, 2H), 5.76−5.68 (m, 2H), 5.50 (septet, J = 2.9 Hz, 1H), 3.69 (two s, 6H), 3.29−3.21 (m, 1H), 2.28−2.18 (m, 2H), 1.64 (br s, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 201.8, 170.2, 170.1, 126.8, 125.9, 124.5, 123.5, 99.4, 87.8, 61.6, 52.4, 52.3, 38.8, 24.6, 19.8, 19.7. MS (EI) *m*/*z*: 276 (9) [M^+], 216 (44), 157 (100).

Allene 1b. This was prepared as above in 80% yield. Contains a byproduct that was effectively removed by HPLC purification. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.90−5.65 (m, 4H), 5.50 (septet, J = 2.7 Hz, 1H), 3.69 (s, 6H), 3.06 (br d, J = 9.3 Hz, 1H), 2.5−2.3 (m, 2H), 2.02 (m, 1H), 1.8−1.5 (m, 7H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 202.3, 170.6, 170.5, 134.1, 133.9, 124.6, 123.9, 99.4, 87.8, 62.6, 52.5, 52.4, 45.5, 32.2, 29.8, 20.0, 19.9. MS (EI) *m*/*z*: 290 (5) [M^+], 231 (64), 230 (100).

Allene 1c. This was prepared as above in 55% yield. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.94−5.81 (m, 2H), 5.77−5.69 (m, 2H), 5.50 (quintet, J = 2.9 Hz, 1H), 3.72 (two s, 6H), 3.32−3.21 (m, 1H), 2.30−2.21 (m, 2H), 2.13−2.05 (m, 4H), 1.66−1.44 (m, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 198.5, 170.3 (2C), 127.0, 126.0, 124.6, 123.6, 106.6, 87.7, 61.6, 52.5, 52.4, 38.9, 30.8 (2C), 27.1 (2C), 25.9, 24.7. MS (EI) *m*/*z*: 316 (14) [M^+], 257 (50), 256 (72), 197 (100).

Allene 1d. This was prepared as above in 40% yield (based on recovered starting material). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.96−5.81 (m, 2H), 5.77−5.69 (m, 2H), 5.50 (quintet, J = 2.9 Hz, 1H), 3.72 (two s, 6H), 3.32−3.21 (m, 1H), 2.40−2.20 (m, 6H), 1.70−1.50 (m, 8H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 201.6, 170.3, 170.2, 126.9, 125.9, 124.5, 123.5, 108.6, 87.5, 61.5, 52.4, 52.3, 38.8, 31.7 (2C), 29.2 (2C), 28.0 (2C), 24.6. MS (EI) *m*/*z*: 330 (18) [M^+], 270 (68), 211 (100).

Allene 1e. This was prepared as above in 68% yield (two diastereomers 50:50). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.96−5.79 (m, 2H), 5.77−5.69 (m, 2H), 5.59 (two overlapping sextets, J = 2.9 Hz, 1H), 3.68 (two s, 6H), 3.28−3.13 (m, 1H), 2.33−2.18 (m, 2H), 1.96−1.88 (m, 2H), 1.65 (m, 3H), 0.98 (m, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 200.7 [diastereomer 200.7], 170.0 [dst 170.0], 169.9 [dst 169.9], 126.8 [dst 126.7], 125.9 [dst 125.8], 124.5 [dst 124.4], 123.4 [dst 123.4], 105.8 [dst 105.8], 89.8 [dst 89.7], 61.5 [dst 61.5], 52.3 [dst 52.3] (2C), 39.1 [dst 38.9], 26.9 [dst 26.8], 24.8 [dst 24.7], 18.4 [dst 18.3], 11.9 [dst 11.9]. MS (EI) *m*/*z*: 290 (12) [M^+], 230 (55), 197 (60), 169 (85), 143 (100).

Allene 1f. This was prepared as above in 50% yield (two diasteromers 50:50). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.94−5.81 (m, 2H), 5.77−5.69 (m, 2H), 5.60 (m, 1H), 3.72 (two s, 6H), 3.28−3.13 (m, 1H), 2.40−2.18 (m, 2H), 2.17−2.06 (m, 1H), 1.67−1.64 (m, 3H), 0.98−0.95 (m, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 200.3 [diastereomer 200.1], 170.3 [dst 170.3], 170.2 [dst 170.2], 127.1 [dst 126.9], 126.1 [dst 125.9], 124.7 [dst 124.7], 123.6 [dst 123.5], 110.2 [dst 110.2], 90.1 [dst 90.0], 61.6 [dst 61.5], 52.3 [dst 52.3] (2C), 39.2 [dst 38.9], 32.1 [dst 32.1], 24.8 [dst 24.7], 22.2 [dst 22.2] (2C), 16.2 [dst 18.1]. MS (EI) *m*/*z*: 304 (18) [M^+], 229 (58), 201 (100), 183 (80).

Allene 1g. This was prepared as above in 73% yield (two diasteromers 50:50). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.94−5.81 (m, 2H), 5.77−5.69 (m, 2H), 5.50 (m, 1H), 3.63 (two s, 6H), 3.20−3.10 (m, 1H), 2.30−2.10 (m, 2H), 1.95−1.78 (m, 2H), 1.59 (br s, 3H), 1.35−1.17 (m, 4H), 0.85−0.79 (m, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 201.1 [diastereomer 201.0], 170.0 [dst 170.0], 169.9 [dst 169.8], 126.8 [dst 126.7], 125.8 [dst 125.7], 124.4 [dst 124.4], 123.4 [dst 123.3], 104.0 [dst 104.0], 89.1 [dst 89.0], 61.3 [dst 61.3], 52.1 [dst 52.1], 52.1 [dst 52.1], 38.9 [dst 38.7], 33.2 [dst 33.2], 29.3 [dst 29.3], 24.5 [dst 24.5], 22.2 [dst 22.2], 18.2 [dst 18.1], 13.7 [dst 13.7]. MS (EI) *m*/*z*: 318 (22) [M^+], 258 (50), 198 (87), 157 (75), 143 (100).

Preparation of Allene Ester 11. Compound **10** was obtained according to literature procedures[14,15] and benzoylated by dissolving the allene alcohol (0.5 g, 7.1 mmol) in CH_2Cl_2 (7 mL). The solution was cooled to 0 °C, and pyridine (0.85 mL, 8.6 mmol) and DMAP (0.09 g, 0.7 mmol) were then added. Finally, benzoyl chloride was added dropwise, and the reaction was stirred for 3 h (not full conversion). The organic layer was washed with HCl (2 M) and saturated $NaHCO_3$ and finally dried (Na_2SO_4). Evaporation followed by flash chromatography (pentane:Et_2O, 75:25) gave 0.17 g (48% yield based on recovered starting material) of **11**. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.05 (m, 2H, Ph), 7.53 (m, 1H, Ph), 7.40 (m, 2H, Ph), 5.40 (quintet, J = 6.7 Hz, 1H), 4.82 (m, 4H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 209.5, 166.0, 132.8, 130.0, 129.5, 128.2, 86.4, 76.6, 62.6.

Allene Ester 15. This was prepared as above in 30% yield. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.05 (m, 2H, Ph), 7.55 (m, 1H, Ph), 7.42 (m, 2H, Ph), 5.22 (tsept, J = 6.5, 2.7 Hz, 1H), 4.75 (d, J = 6.5 Hz, 2H), 1.70 (d, J = 2.7 Hz, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 203.5, 166.6, 130.1, 130.7, 129.8, 128.5, 97.7, 85.1, 63.9, 20.5.

General Procedure for the Preparation of Diene-Allenes 16. Diene-Allene 16a. The diene malonate **7a** (0.38 g, 1.8 mmol) was dissolved in dry THF (2 mL) and cooled to 0 °C. NaH (60% in mineral oil) (0.1 g, 2.4 mmol) was added to the solution and stirred for 5 min; the cooling bath was then removed, and the slurry was stirred for additional 30 min. This was added to $Pd(PPh_3)_4$ (0.05 g, 0.04 mmol) in THF (5 mL) via cannula. Finally, a solution of **11** (0.17 g, 0.91 mmol) was added dropwise as a solution in THF (0.5 mL). The reaction was followed by GC-MS and stirred overnight. Water was added, the aqueous phase was extracted with Et_2O (3 × 30 mL), and the combined organic layers were dried (Na_2SO_4). Careful evaporation (water bath at room temperature) followed by flash chromatography (pentane:Et_2O, 90:10) gave 0.08 g (33% yield) of **16a**. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.95 (m, 1H), 5.91 (m, 1H), 5.85 (m, 2H), 4.97 (quint, J = 7.3 Hz, 1H), 4.63 (m, 2H), 3.70 (s, 3H), 3.68 (s, 3H), 3.15 (ddt, J = 12.6, 9.8, 3.6 Hz, 1H), 2.63 (m, 2H), 2.35 (ddd, J = 17.5, 8.9, 4.9 Hz, 1H), 2.19 (dddd, J = 17.5, 13.4, 3.6, 2.5 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 209.8, 170.7 (2C), 126.1, 125.9, 124.9, 123.5, 84.5, 74.6, 60.7, 52.3, 52.2, 36.2, 32.2, 24.4. MS (EI) *m*/*z*: 262 (5) [M^+], 230 (100), 198 (95), 145 (100).

Diene-Allene 16b. This was prepared as above in 36% yield. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.93 (m, 1H), 5.85 (m, 1H), 5.75 (m, 2H), 4.78 (tseptet, J = 7.5, 2.9 Hz, 1H), 3.71 (s, 3H), 3.70 (s, 3H), 3.18 (dddd, J = 12.1, 9.1, 6.3, 3.3 Hz, 1H), 2.64 (dd, J = 14.4, 7.5 Hz, 1H), 2.58 (dd, J = 14.4, 7.5 Hz, 1H), 2.34 (dddd, J = 17.3, 8.8, 5.2, 1.4 Hz, 1H), 2.20 (dddd, J = 17.3, 13.8, 4.0, 2.4 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 203.9, 171.2 (2C), 126.8, 126.3, 125.1, 123.9, 95.5, 83.1, 60.7, 52.5, 52.4, 36.1, 33.3, 24.5, 20.6 (2C). MS (EI) *m*/*z*: 290 (70) [M^+], 230 (48), 226 (56), 133 (68), 132 (100).

Diene-Allene 18. This was prepared as for **1a** in 63% yield. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 5.98 (m, 2H), 5.60 (m, 1H), 5.48 (quintet, J = 2.0 Hz, 1H), 5.37 (m, 1H), 3.71 (s, 6H), 2.74 (d, J = 7.4 Hz, 2H), 2.10 (m, 4H), 1.71 (d, J = 7.1 Hz, 3H), 1.65−1.45 (m, 6H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 198.3, 170.7 (2C), 134.1, 131.3, 128.3, 125.0, 107.1, 88.1, 58.5, 52.6 (2C), 37.7, 32.8, 31.0, 27.3, 25.9, 23.0, 18.0. MS (EI) *m*/*z*: 318 (16) [M^+], 259 (44), 258 (100).

Preparation of Weinreb Amide 19. Water (3.0 mL, 166 mmol) was added at room temperature via a cannula to a solution of **7a** (7.0 g, 33.3 mmol) and NaCN (8.2 g, 166 mmol) in DMSO (98 mL). The reaction mixture was stirred at 75 °C for 30 h. Water was added, followed by extraction of the water

phase with Et_2O (6 × 40 mL). The combined organic phases were washed with water and brine followed by drying (Na_2SO_4). The solvent was removed by distillation at ambient pressure, and the residue was purified by column chromatography (pentane:Et_2O, 90:10). The solvent was again removed by distillation at ambient pressure to give 4.6 g (91%) of the ester.

Trimethylaluminum (2 M in hexane, 13.9 mL, 27.8 mmol) was added dropwise to a solution of *N*,*O*-dimethylhydroxylamine hydrochloride (2.7 g, 27.8 mmol) in CH_2Cl_2 (35 mL) at room temperature. The solution was stirred for 15 min followed by addition of the neat ester (2.1 g, 13.9 mmol) and stirred overnight. The reaction was quenched by very slow addition of 1 M HCl followed by extraction of the water phase with CH_2Cl_2 (3 × 30 mL) and drying of the combined organic phases (Na_2SO_4). The solvent was removed under reduced pressure to give the product (2.3 g, 90%), which was used without further purification. Spectral data were in accordance with those previously reported.[5b]

Acetylene Alcohol 20a. Trimethylsilyl acetylene alcohol was prepared from Weinreb amide **19** (1.20 g, 6.6 mmol) and trimethylsilyl acetylene as described for butyl acetylene alcohol **20b** below. The crude trimethylsilyl acetylene alcohol (1.43 g) was dissolved in MeOH (40 mL), KF (1.50 g, 26.0 mmol) was added, and the mixture was stirred overnight. CH_2Cl_2 (50 mL) and H_2O (50 mL) were added followed by extraction of the water phase with CH_2Cl_2 (3 × 30 mL) and drying of the combined organic phases (Na_2SO_4). The solvent was removed under reduced pressure, and the residue was column-chromatographed (pentane:Et_2O, 80:20) to give 608 mg (62%) of **20a** (diastereomeric mixture (50:50)) as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.90 (m, 2H), 5.75 (m, 2H), 4.46 (m, 1H), 2.57 (m, 1H), 2.48 (apparent dd, J = 4.7, 2.2 Hz, 1H), 2.35 (m, 1H), 2.10−1.70 (m, 4H). ^{13}C NMR ($CDCl_3$, 400 MHz): δ 130.4 [dst 130.3], 125.8 [dst 125.7], 124.5 [dst 124.5], 124.3 [dst 124.3], 85.1, 73.4 [dst 73.3], 60.6 [dst 61.0], 42.2 [dst 42.1], 29.5 [dst 29.4], 28.8 [dst 28.5].

Acetylene Alcohol 20b. *n*-BuLi (1.6 M in hexane, 2.76 mL, 4.42 mmol) was added dropwise to a solution of 1-hexyne (0.63 mL, 5.52 mmol) in THF (2.5 mL) at −78 °C. The mixture was stirred at −78 °C for 20 min and then at 0 °C for 1 h. The lithium-hexyne reagent was transferred via cannula to the Weinreb amide **19** (466 mg, 2.57 mmol) in THF (2.5 mL) at −40 °C. The reaction mixture was warmed to 0 °C for 20 min and then to room temperature for an additional 30 min and poured into ice-cooled 1 M HCl (30 mL). Et_2O (30 mL) and brine were added, and the water phase was extracted with Et_2O:CH_2Cl_2 1:1 (3 × 30 mL). The combined organic phases were dried ($MgSO_4$), and the solvent was removed under reduced pressure. The crude product was dissolved in Et_2O (10 mL) and cooled to −78 °C. DIBALH (1.5 M in toluene, 2.40 mL, 3.60 mmol) was added dropwise to the solution. After 15 min, H_2O (10 mL) was added at ambient temperature, and the mixture was warmed to room temperature and partitioned between Et_2O (10 mL) and 2 M HCl (10 mL). The water phase was extracted with Et_2O (4 × 20 mL), and then the combined organic phases were washed with water and brine followed by drying ($MgSO_4$) and removal of the solvent under reduced pressure. The residue was column-chromatographed (pentane:Et_2O, 85:15) to afford 474 mg (90%) of **20b** (diastereomeric mixture (50:50)) as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.87 (m, 2H), 5.74 (m, 2H), 4.42 (m, 1H), 2.54 (m, 1H), 2.32 (m, 1H), 2.19 (m, 2H), 2.01 (m, 1H), 1.91−1.63 (m, 3H), 1.47 (m, 2H), 1.39 (m, 2H), 0.89 (apparent t, J = 7.3 Hz, 3H). ^{13}C NMR ($CDCl_3$, 400 MHz): δ 130.9 [dst 130.8], 125.8 [dst 125.8], 124.3 [dst 124.2] (2C), 86.0 [dst 85.9], 81.4 [dst 81.3], 61.0 [dst 61.0], 42.9 [dst 42.7], 30.9, 29.7 [dst 29.6], 28.8 [dst 28.6], 22.1, 18.6, 13.8.

Allene 1j. This was prepared from acetylene alcohol **20a** as described for butyl allene **1k** below except for the workup which was done as follows. The reaction mixture was partitioned between pentane and water. The water phase was extracted with pentane (3 × 30 mL), and the combined organic phases were washed with water (2 × 30 mL) and brine (30 mL) followed by drying ($MgSO_4$). The solvent was removed by distillation at ambient pressure, and the residue was column-chromatographed (pentane, 100%). The solvent was again removed by distillation at ambient pressure to give 295 mg (54%) of **1j** as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.92−5.85 (m, 2H), 5.79−5.70 (m, 2H), 5.07 (quintet, J = 6.9 Hz, 1H), 4.67 (dt, J = 6.6, 2.9 Hz, 2H), 2.45−2.35 (m, 1H), 2.29 (dddd, J = 17.2, 8.6, 4.8, 1.5 Hz, 1H), 2.13−2.00 (m, 3H). ^{13}C NMR ($CDCl_3$, 400 MHz): δ 209.4, 130.9, 126.0, 124.2 (2 C), 88.1, 74.7, 33.3, 33.2, 28.4. MS (EI) *m*/*z*: 132 (9) [M^+], 117 (73), 77 (100).

Allene 1k. Diethyl azodicarboxylate (0.28 mL, 1.76 mmol) was added to a solution of PPh_3 (462 mg, 1.76 mmol) in THF (5 mL) at −15 °C. After 10 min, a solution of the acetylene alcohol **20b** (257 mg, 1.26 mmol) in THF (4 mL) was added to the solution. The mixture was stirred for an additional 10 min at ambient temperature before a solution of *o*-nitrobenzenesulfonylhydrazine (387 mg, 1.76 mmol) in THF (5 mL) was added. After 1 h at −15 °C, the mixture was warmed to room temperature and stirred overnight. The solvent was removed under reduced pressure, and the residue was column-chromatographed (pentane, 100%) to give 143 mg (60%) of **1k** as a mixture of diastereomers (50:50). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.88 (m, 2H), 5.75 (m, 2H), 5.11−4.99 (m, 2H), 2.38 (m, 1H), 2.28 (m, 1H), 2.08 (m, 3H), 1.99 (m, 2H), 1.37 (m, 4H), 0.91 (t, J = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$, 400 MHz): δ 204.9 [dst 204.8], 131.2 [dst 131.2], 126.0 [dst 126.0], 124.2 (2C) [dst 124.1 (2C)], 91.0, 88.9, 34.1 [dst 34.1], 33.3 [dst 33.3], 31.6, 28.9, 28.5 [dst 28.4], 22.4, 14.1. MS (EI) *m*/*z*: 188 (22) [M^+], 145 (70), 117 (66).

Preparation of Lithium Dialkylcuprates, General Procedure. MeLi or BuLi (2.05 equiv) in hexane was added dropwise to a slurry of CuI (1.0 equiv) in Et_2O (7.5 mL/mmol) at 0 °C and then cooled to −78 °C for immediate use.

Allene 1h. *n*-BuLi (1.6 M in hexane, 1.9 mL, 3.09 mmol) was added dropwise to a solution of acetylene alcohol **20a** (600 mg, 2.9 mmol) in THF (3 mL) at −78 °C and after 5 min was followed by addition of mesyl chloride (0.25 mL, 3.19 mmol). After an additional 5 min at ambient temperature, the mixture was transferred via cannula to a Et_2O solution of Me_2CuLi (4.35 mmol, prepared as above) at −78 °C. The resulting suspension was stirred at ambient temperature for 0.5 h and then warmed to 0 °C for 10 min and quenched with saturated NH_4Cl (30 mL). Et_2O (20 mL) was added, and the mixture was filtered through Celite. The water phase was extracted with Et_2O (3 × 30 mL), the combined organic phases were dried ($MgSO_4$), and the solvent was removed under reduced pressure. The residue was column-chromatographed (pentane, 100%) to afford 521 mg (89%) of **1h** as a mixture of diastereomers (50:50). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.88 (m, 2H), 5.75 (m, 2H), 4.95 (m, 1H), 2.37 (m, 1H), 2.28 (apparent dddd, J = 17.0, 8.5, 4.8, 1.3 Hz, 1H), 2.10−2.01 (m, 3H), 1.93 (apparent td, J = 7.0, 2.9 Hz, 2H), 1.67 (d, J = 2.9 Hz, 3H), 1.37 (m, 4H), 0.91 (t, J = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$, 400 MHz): δ 202.3, 131.5 [dst 131.4], 126.0, 124.2, 123.9 [dst 123.9], 99.4, 88.1 [dst 88.0], 34.5, 34.0 [dst 34.0], 33.3 [dst 33.3], 30.0 [dst 30.0], 28.5 [dst 28.5], 22.6, 19.4 [dst 19.4], 14.2. MS (EI) *m*/*z*: 202 (100) [M^+], 145 (46).

Allene 1i. This was prepared from butylacetylene alcohol **20b** as described for methylbutyl allene **1h** above in 52% yield (diastereomeric mixture (50:50)). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.88 (m, 2H), 5.75 (m, 2H), 5.01 (t quintet, J = 6.9, 2.9 Hz, 1H), 2.36 (m, 1H), 2.28 (dddd, J = 17, 8.5, 4.8, 1.3 Hz, 1H), 2.07 (m, 3H), 1.92 (td, J = 6.9, 2.8 Hz, 4H), 1.34 (m, 8H), 0.90 (t, J = 7.1 Hz, 6H). ^{13}C NMR ($CDCl_3$, 400 MHz): δ 201.8, 131.5, 126.0, 124.2, 123.9, 104.2, 89.6, 34.7, 33.5, 32.7, 32.6, 30.2 (2 C), 28.5, 22.7 (2 C),14.2 (2 C). MS (EI) *m*/*z*: 244 (100) [M^+], 187 (54), 131 (68), 117 (50).

General Procedure for the Preparation of 2. Compound 2c. To a stirred solution of palladium acetate 0.033 g (0.14 mmol), benzoquinone 0.31 g (2.9 mmol), and lithium acetate dihydrate 0.59 g (5.8 mmol) in acetic acid (15 mL) at room temperature was added 0.46 g (1.46 mmol) of **1c** dissolved in acetic acid (4 mL) during 3 h. The reaction was stirred an additional hour, water was added, and the water layer was extracted with Et_2O (3 × 30 mL). The combined

organic layers were washed with NaOH (2 M) and brine and finally dried (Na_2SO_4). Evaporation followed by flash chromatography (pentane:Et_2O, 75:25) gave 0.42 g (77% yield) of **2c**. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 6.15 (ddd, J = 0.9, 3.9, 10.1 Hz, 1H), 5.85 (m, 1H), 5.80 (ddd, J = 2.3, 4.5, 10.1 Hz, 1H), 5.65 (d, J = 2.3 Hz, 1H) 5.06 (q, J = 4.5 Hz, 1H, C*H*OAc), 3.8−3.7 (overlapping peaks including s at 3.74 and 3.69, total 7H), 3.50 (ddd, J = 10.2, 6.8, 5.0 Hz, 1H), 2.3−2.0 (m, 4H), 2.01 (s, 3H), 1.84 (ddd, J = 14.5, 10.2, 4.5 Hz, 1H), 1.7−1.5 (m, 5H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 170.6, 170.4, 170.2, 131.9, 131.6, 127.3, 125.0, 120.6, 67.8, 65.2, 52.8, 52.6, 43.8, 38.7, 27.1, 26.7, 25.6, 22.1, 21.3. MS (EI) *m*/*z*: 374 (1) [M^+], 254 (90), 196 (100). Anal. Calcd for $C_{21}H_{26}O_6$: C, 67.36; H, 7.00. Found: C, 67.24; H, 7.06.

Compound 2a. This was prepared as above in 67% yield. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.19 (ddd, J = 10.3, 3.8, 0.9 Hz, 1H), 5.84 (ddd, J = 10.0, 4.4, 2.3 Hz, 1H), 5.73 (d, J = 2.6 Hz, 1H), 5.13−5.04 (m, 3H), 3.8−3.7 (overlapping peaks including s at 3.77 and 3.72, total 7H), 3.56 (ddd, J = 12.0, 7.0, 5.3 Hz, 1H), 2.15 (s, 3H), 1.93 (br s, 3H), 1.84 (ddd, J = 13.8, 10.3, 4.4 Hz, 1H), 1.65 (dt, J = 13.8, 5.0 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 170.6, 170.5, 170.1, 148.7, 138.3, 131.3, 125.3, 124.0, 115.2, 68.0, 65.1, 52.8, 52.6, 43.9, 38.7, 27.0, 21.5, 21.2. MS (EI) *m*/*z*: 276 (9), 216 (44), 157 (100). Anal. Calcd for $C_{18}H_{22}O_6$: C, 64.66; H, 6.63. Found: C, 64.92; H, 6.50.

Compounds 2b. These were prepared as above in 71−87% total yield. The reaction gave two to three isomers depending on LiOAc concentration (Table 1), which were separated by flash chromatograhy or HPLC.

2b (major product). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.12 (dd, J = 11.3, 3.8 Hz, 1H), 5.77 (d, J = 2.5 Hz, 1H), 5.70 (ddd, J = 11.0, 4.7, 2.7 Hz, 1H), 5.36 (m, 1H), 5.10 (br s, 1H), 4.94 (br s, 1H), 3.90 (m, 1H), 3.80−3.65 (overlapping peaks including s at 3.77 and 3.72, total 7H), 2.68 (ddd, J = 11.8, 9.9, 4.4 Hz, 1H), 2.15 (m, 1H), 2.06 (s, 3H), 1.92 (br s, 3H), 1.84 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 171.0, 170.2, 170.1, 150.3, 137.6, 136.5, 129.5, 124.9, 115.6, 71.2, 68.2, 52.6, 52.3, 51.1, 47.4, 30.2, 25.0, 21.2, 21.0. MS (EI) *m*/*z*: 288 (15), 229 (100). Anal. Calcd for $C_{19}H_{24}O_6$: C, 65.50; H, 6.94. Found: C, 65.29; H, 6.88.

2b′. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.87 (dd, J = 7.2, 4.7 Hz, 1H), 5.84 (dd, J = 5.8, 1.6 Hz, 1H), 5.78 (d, J = 2.2 Hz, 1H), 5.71 (dd, J = 5.8, 2.5 Hz, 1H, CHOAc), 5.03 (br s, 1H), 4.91 (br s, 1H), 3.81 (s, 3H), 3.70 (s, 3H), 3.25 (dt, J = 9.6, 2.5 Hz, 1H), 3.17 (td, J = 10.7, 3.0 Hz, 1H), 2.42−2.10 (m, 3H), 1.93 (s, 3H), 1.87 (br s, 3H), 1.50 (m, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 171.4, 170.5, 170.3, 149.9, 138.4, 134.2, 127.6, 125.7, 113.9, 71.2, 69.1, 68.1, 52.6, 52.4, 52.3, 46.4, 27.9, 27.3, 21.8, 20.9. MS (EI) *m*/*z*: 348 (2) [M^+], 229 (100), 228 (60), 169 (70).

2b″. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 5.64−5.54 (m, 4H, 2 olefinic + 2 CHOAc), 5.42 (sept, J = 2.9 Hz, 1H), 3.71 (s, 6H), 2.84 (tt, J = 9.5, 5.1 Hz, 1H), 2.07 (s, 6H), 2.00 (m, 4H), 1.68 (s, 3H), 1.67 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 202.3, 170.3 (2C), 170.1 (2C), 130.3 (2C), 99.2, 86.8, 70.5 (2C, CHOAc), 63.1, 52.5 (2C), 33.7 (CH), 32.6 ($2CH_2$), 21.2 (2C, AcO), 19.8 (2C, Me). MS (EI) *m*/*z*: 349 (25), 197 (100).

Compound 2d. This was prepared as above in 60% yield. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.15 (ddd, J = 7.4, 4.4, 0.7 Hz, 1H), 5.97 (t, J = 7.1 Hz, 1H), 5.80 (dddd, J = 7.4, 5.0, 2.5, 0.7 Hz, 1H), 5.58 (d, J = 2.5, 1H), 5.09 (q, J = 4.5 Hz, 1H, C*H*OAc), 3.8−3.7 (overlapping peaks including s at 3.77 and 3.72, total 7H), 3.52 (ddd, J = 11.5, 6.6, 5.0 Hz, 1H), 2.33 (m, 2H), 2.21 (m, 2H), 2.06 (s, 3H), 1.8−1.2 (m, 8H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 170.7 (2C), 170.4, 150.7, 139.4, 131.9, 131.6, 124.9, 120.8, 67.9, 65.2, 52.8, 52.5, 44.1, 38.4, 32.1, 31.4, 29.7, 28.6, 27.0, 26.6, 26.5, 21.3. MS (EI) *m*/*z*: 388 (10), 268 (100), 209 (75).

Compounds 2e. These were prepared as above in 67% total yield. The reaction gave three isomers (Table 1), which were separated by HPLC as **2e** + **2e″** and **2e′**.

2e (major). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.92 (app d, J = 2.7 Hz, 2H), 5.51 (d, J = 2.9 Hz, 1H), 5.43 (qq, J = 6.8, 1.5 Hz, 1H), 5.12 (m, 1H), 3.80−3.69 (overlapping peaks including s at 3.76 and 3.71, total 7H), 3.51 (ddd, J = 12.3, 11.9, 6.4 Hz, 1H), 2.05 (s, 3H), 1.75 (br s, 3H), 1.62−1.54 (m, 5H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 170.7, 170.3, 170.3, 148.2, 131.5, 130.9, 125.0, 123.9, 123.5, 68.5, 65.0, 52.7, 52.4, 45.7, 38.1, 26.9, 23.1, 21.3, 14.6. MS (EI) *m*/*z*: 306 (3) [M^+], 228 (100).

2e′. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.15 (ddd, J = 10.3, 4.1, 1.0 Hz, 1H), 5.83 (ddd, J = 10.3, 4.7, 2.5 Hz, 1H), 5.67 (qq, J = 6.8, 1.4 Hz, 1H), 5.62 (d, J = 2.5 Hz, 1H, olefin), 5.09 (q, J = 4.7 Hz, 1H), 3.80−3.65 (overlapping peaks including s at 3.77 and 3.72, total 7H), 3.53 (dddd, J = 11.8, 10.4, 6.9, 4.9 Hz, 1H), 2.03 (s, 3H), 1.95−1.60 (m including s at 1.81 and d at 1.73, total 8H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 170.8−170.6 (2C), 150.3, 131.7, 125.1, 124.7, 121.4, 100.0, 68.2, 65.2, 52.8, 52.6, 43.8, 38.6, 27.1, 21.3, 14.7, 13.9. MS (EI) *m*/*z*: 306 (3) [M^+], 228 (90), 169 (100).

2e″. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.14 (ddd, J = 0.7, 4.0, 10.1 Hz, 1H), 5.85 (ddd, J = 2.4, 4.8, 10.1 Hz, 1H), 5.72 (d, J = 2.6 Hz, 1H), 5.1−5.0 (m, including s at 5.07 and 5.03, 3H), 3.80−3.45 (overlapping peaks including s at 3.77 and 3.72, total 7H), 2.25 (br q, J = 7.4 Hz, 2H), 2.05 (s, 3H), 1.62−1.54 (m, 2H), 1.05 (t, J = 7.4 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 170.7−170.3 (3C), 144.2, 131.4, 125.2, 123.2, 123.2, 112.8, 68.0, 65.1, 52.8, 52.6, 44.2, 38.5, 27.6, 27.0, 12.5. MS (EI) *m*/*z*: 306 (3) [M^+], 228 (80), 169 (100).

Compounds 2f. These were prepared as above in 60% total yield. The reaction gave two isomers (Table 1), which were not possible to separate by HPLC. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.09 (dd, J = 10.3, 4.3 Hz, 1H), 5.90 (m, 2H + 1H), 5.70 (d, J = 2.6 Hz, 1H), 5.13 (m, 1H + 1H, C*H*OAc), 5.05 (br s, 1H), 4.98 (br s, 1H), 3.80−3.65 (overlapping peaks including s at 3.77, 3.76 and 3.72, 3.71, total 7H + 7H), 3.50 (m, 1H + 1H), 2.53 (septet, J = 7.0 Hz, 1H), 2.05 (s, 3H + 3H), 1.8−1.5 (m including d at 1.69, J = 4.4 Hz, and s at 1.65 and 1.55, 2H + 11H), 1.09 (d, J = 7.0 Hz, 3H), 0.98 (d, J = 7.0 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 170.7−170.2 (3C + 3C), 150.9, 149.7, 149.1, 132.2, 131.7, 130.0, 125.3, 124.9, 123.1, 122.8, 111.0, 68.8, 65.4, 65.3, 53.0, 52.9, 52.8, 52.6, 46.2, 45.0, 38.6, 38.2, 32.1, 29.9, 27.2, 27.1, 22.7, 21.9, 21.5, 21.2, 20.4, 18.2. MS (EI) *m*/*z* (major): 362 (1) [M^+], 330 (10), 183 (100). (minor): 330 (6), 242 (60), 228 (80), 183 (100).

Compounds 2g. These were prepared as above in 49% total yield. The reaction gave two isomers (Table 1), which were separated by HPLC.

Major 2g. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.92 (m, 2H), 5.48 (dd, J = 2.9, 0.7 Hz, 1H), 5.34 (tt, J = 7.6, 1.5 Hz, 1H), 5.12 (m, 1H), 3.80−3.65 (overlapping peaks including s at 3.76 and 3.71, total 7H), 3.50 (ddd, J = 12.0, 6.2, 5.5 Hz, 1H), 2.05 (s, 3H), 1.93 (br q, J = 8.0 Hz, 1H), 1.75 (br s, 3H), 1.60 (m, 2H), 1.30 (m, 2H), 0.83 (br t, J = 8.0 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 170.7, 170.3, 170.2, 148.4, 131.6, 130.2, 129.9, 124.9, 123.1, 68.5, 65.0, 52.7, 52.4, 45.8, 38.1, 30.9, 26.8, 23.1, 21.3, 13.8. MS (EI) *m*/*z*: 376 (3) [M^+], 317 (20), 256 (100), 197 (70).

Minor 2g′. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.14 (ddd, J = 10.2, 4.1, 0.8 Hz, 1H), 5.86 (ddd, J = 10.2, 4.9, 2.5 Hz, 1H), 5.71 (d, J = 2.5 Hz, 1H), 5.10 (q, J = 4.5 Hz, 1H, C*H*OAc), 5.06 (br s, 1H), 5.03 (br s, 1H), 3.80−3.65 (overlapping peaks including s at 3.77 and 3.72, total 7H), 3.53 (m, 1H), 2.3−0.8 including s at 2.05 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 170.6, 170.5 (2C), 148.3, 143.1, 131.4, 125.1, 123.4, 113.7, 68.1, 65.1, 52.8, 52.6, 44.2, 38.5, 34.6, 30.2, 29.7, 27.0, 22.3, 13.9. MS (EI) *m*/*z*: 376 (3) [M^+], 316 (20), 256 (100).

Compounds 2h. These were prepared as above in 48% total yield. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.88 (ddd, J = 10.1, 3.8, 1.1 Hz, 1H), 5.78 (ddd, J = 10.1, 4.0, 2.3 Hz, 1H), 5.38 (dd, J = 2.4, 4.8 Hz, 1H), 5.29 (tq, J = 7.3, 1.5 Hz, 1H), 5.24 (br dd, J = 9.9, 4.6 Hz, 1H), 3.36−3.32 (m, 1H), 2.74−2.66 (m, 1H), 2.54 (ddt, J = 16.3, 8.1, 2.3 Hz, 1H), 2.10 (ddt, J = 16.3, 4.8, 2.4 Hz, 1H), 2.05 (s, 3H), 1.96 (qq, 7.3, 1.1 Hz, 2H), 1.87 (ddd, J = 13.4, 8.8, 4.5 Hz, 1H), 1.78−1.71 (m, 4 H), 1.30 (m, 2H), 0.85 (t, J = 7.4 Hz, 3H). ^{13}C NMR ($CDCl_3$, 400 MHz): δ 171.1, 144.6, 132.5, 131.7, 129.0, 126.0, 125.4, 66.9, 46.3, 37.1, 32.7, 31.4, 31.3, 23.9, 23.6, 21.6, 14.1. MS (EI) *m*/*z*: 260 (5) [M^+], 218 (51), 200 (87), 171 (100), 157 (67), 143 (50), 129 (47).

2h′. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.79 (ddd, J = 10.3, 3.7, 2.2 Hz, 1H), 5.66 (dtd, J = 10.2, 2.2, 1.2 Hz, 1H), 5.35 (dd, J = 5.0, 2.65 Hz, 1H), 5.32−5.25 (m, 2H), 3.28 (m, 1H), 2.65−2.56 (m, 2H), 2.09 (dt, J = 16.8, 2.5 Hz, 1H), 2.05 (s, 3H), 1.98 (qt, J = 7.4, 1.2 Hz, 2H), 1.90 (m, 1H), 1.77 (dd, J = 2.8, 1.3 Hz, 3H), 1.53 (m, 1H), 1.32 (qd, J = 7.5, 1.5 Hz, 2H), 0.87 (t, J = 7.4 Hz, 3H). ^{13}C NMR ($CDCl_3$, 400 MHz): δ 171.1, 144.5, 131.8, 130.3, 128.7, 128.2, 125.0, 69.7, 46.4, 38.1, 34.2, 32.7, 31.4, 23.8, 23.6, 21.6, 14.1. MS (EI) *m/z*: 260 (5) [M^+], 218 (50), 200 (82), 171 (100).

2h″. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.96 (dddd, J = 10.0, 5.0, 3.7, 1.3 Hz, 1H), 5.79 (ddt, J = 9.9, 3.85, 2.0 Hz, 1H, olefinic), 5.43 (q, J = 2.2 Hz, 1H), 5.30 (tq, J = 7.2, 1.4 Hz, 1H), 5.08 (m, 1H, C*H*OAc), 3.01 (m, 1H), 2.56 (m, 1H), 2.50 (dt, J = 7.5, 2.4, 1H), 2.28 (br dt, J = 17.5, 5.7 Hz, 1H), 2.07 (dt, J = 17.5, 2.3 Hz, 1H), 2.01 (s, 3H), 1.93 (overlapping peaks including a br q, J = 7.2 Hz, total 3H), 1.78 (q, J = 1.3 Hz, 3H), 1.29 (m, 2H), 0.85 (t, J = 7.5 Hz, 3H). MS (EI) *m/z*: 200 (22), 171 (100).

Compounds 2i. These were prepared as above in 44% total yield. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.87 (ddd, J = 10.1, 3.6, 0.9 Hz, 1H), 5.78 (ddd, J = 10.1, 4.2, 2.2 Hz, 1H), 5.34 (dd, J = 2.4, 4.8 Hz, 1H), 5.26 (tt, J = 7.3, 1.3 Hz, 1H), 5.23 (br q, J = 4.4 Hz, 1H), 3.30−3.26 (m, 1H), 2.74−2.65 (m, 1H), 2.57 (ddt, J = 16.1, 8.0, 2.4 Hz, 1H), 2.13−1.91 (m, 8H), 1.84 (ddd, J = 13.6, 9.4, 4.4 Hz, 1H), 1.75 (dt, 13.6, 5.1 Hz, 1H), 1.33−1.18 (m, 6H), 0.84 (t, J = 7.32 Hz, 6H). ^{13}C NMR ($CDCl_3$, 400 MHz): δ 171.1, 143.4, 136.6, 132.8, 128.3, 126.6, 125.2, 66.9, 46.5, 37.3, 36.9, 32.5, 31.5, 31.2, 30.9, 23.6, 22.4, 21.6, 14.2, 14.1. MS (EI) *m/z*: 302 (12) [M^+], 260 (65), 242 (100).

2i′. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.77 (ddd, J = 10.3, 3.7, 2.0 Hz, 1H), 5.64 (ddd, J = 10.3, 3.5, 2.0 Hz, 1H), 5.32−5.25 (m, 3H), 3.26−3.20 (m, 1H), 2.66−2.55 (m, 2H), 2.13−2.01 (m, 8H), 1.89 (dddd, J = 11.8, 5.3, 4.4, 1.3 Hz, 1H), 1.53 (td, J = 12.0, 9.7 Hz, 1H), 1.37−1.21 (m, 6H), 0.86 (t, J = 7.3 Hz, 6H). ^{13}C NMR ($CDCl_3$, 400 MHz): δ 171.3, 143.4, 136.6, 130.4, 128.2, 128.1, 125.7, 69.8, 46.6, 38.2, 36.8, 34.3, 32.8, 31.2, 30.8, 23.6, 22.4, 21.6, 14.2, 14.1. MS (EI) *m/z*: 302 (2) [M^+], 242 (91), 199 (86), 143 (100).

Alternative Procedure for the Preparation of 2. To **1a** (90 mg, 0.33 mmol) were added palladium acetate (4 mg, 0.016 mmol), iron phthalocyanine (4 mg, 0.007 mmol), and benzoquinone (10 mg, 0.10 mmol). This was dissolved in acetic acid, and a balloon filled with oxygen was applied. The reaction was stirred at room temperature for 24 h. Water was added and extracted with Et_2O (3 × 30 mL). The combined organic layers were dried (Na_2SO_4); evaporation followed by flash chromatography (pentane:Et_2O, 75:25) gave 73 mg (67% yield) of **2a**.

General Procedure for the Preparation of 3. Compound 3a. To **1a** (0.11 g, 0.41 mmol) were added lithium acetate dihydrate (0.17 g, 1.6 mmol) and $Pd(dba)_2$ (0.023 g, 0.04 mmol), and the mixture was dissolved in 6 mL of HOAc. The reaction mixture was stirred at room temperature for 24 h. H_2O was added, and the water layer was extracted with Et_2O (3 × 30 mL). The combined organic layers were dried (Na_2SO_4), concentrated in vacuo, and subsequent flash chromatography (pentane:Et_2O, 75:25) of the residue gave 0.09 g (65% yield) of **3a**. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 6.09 (dd, J = 9.1, 4.4 Hz, 1H), 5.96 (ddd, J = 10.2, 5.5, 2.2 Hz, 1H), 5.44 (dd, J = 3.0, 1.6 Hz, 1H), 5.11 (td, J = 5.5, 3.3 Hz, 1H), 3.74 (s, 3H), 3.70 (s, 3H), 3.57 (m, 1H), 3.44 (dt, J = 11.0, 6.6, Hz, 1H), 2.31 (tpent, J = 7.1, 1.3), 2.05 (s, 3H), 1.52 (m, including J = 3.3 Hz, 2H), 1.10 (d, J = 6.6 Hz, 3H), 1.02 (d, J = 6.9 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 170.9, 170.7 (2C), 131.7, 125.5, 118.9, 68.1, 65.4, 52.9, 52.6, 45.3, 38.7, 28.1, 26.9, 21.6, 21.5, 20.9. MS (EI) *m/z*: 294 (2) [M^+], 212 (100).

Compound 3b. This was prepared as above in 84% yield. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.08 (dd, J = 10.0, 4.4 Hz, 1H), 5.96 (ddd, J = 10.0, 5.4, 2.2 Hz, 1H), 5.41 (dt, J = 5.4, 3.4 Hz, 1H), 3.74 (s, 3H), 3.70 (s, 3H), 3.57 (m, 1H), 3.42 (dt, J = 11.7, 6.3, Hz, 1H), 2.05 (s, 3H), 2.00−1.64 (m, 6H), 1.53 (m, 2H), 1.40−0.92 (m, 5H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 170.7, 170.6, 170.5, 155.7, 131.6, 125.2 118.8, 67.9, 65.2, 52.7, 52.3, 44.9, 38.3, 37.7, 32.1, 31.1, 26.6, 26.4, 26.1, 21.3. MS (EI) *m/z*: 284 (24) [M^+], 252 (100). Anal. Calcd for $C_{21}H_{28}O_6$: C, 67.00; H, 7.50. Found: C, 67.22; H, 7.34.

Compound 3c. This was prepared as above in 52% yield (diastereomeric mixture (50:50)) using 5 mol % $Pd(dba)_2$ and stirred for 48 h. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 6.07 (dd, J = 10.2, 4.4 Hz, 1H), 5.96 (m, 1H), 5.45 (br s, 1H), 5.12 (m, 1H), 3.74 (s, 3H), 3.70 (s, 3H), 3.55 (m, 1H), 3.43 (dt, J = 11.0, 6.6 Hz, 1H), 2.21 (q, J = 6.8 Hz, 0.5H), 2.07 (m overlapping a s at 2.05, 3.5H), 1.7−1.4 (m, 3H), 1.35 (m, 1H), 1.07 (d, J = 6.9 Hz, 1.5H), 1.01 (d, J = 6.9 Hz, 1.5H), 0.88 (t, J = 7.4 Hz, 1.5H), 0.78 (t, J = 7.2 Hz, 1.5H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 170.9 [2 dst], 170.7 (2C) [2 dst], 154.6 [dst 154.2], 131.8 [2 dst], 125.5 [dst 125.3], 120.3 [dst 119.7], 68.1 [2 dst], 65.4 [dst 65.4], 52.9 [dst 52.9], 52.6 [2 dst], 45.5 [dst 45.4], 38.6 [2 dst], 35.3 [dst 34.1], 27.8 [dst 27.6], 27.0 [dst 26.9], 21.5 [2 dst], 19.3 [17.6 dst], 12.1 [10.5 dst]. MS (EI) *m/z*: 290 (3) [M^+], 229 (100). Anal. Calcd for $C_{19}H_{26}O_6$: C, 65.13; H, 7.48. Found: C, 64.86; H, 7.40.

Compound 3d. This was prepared as above in 44% yield (diastereomeric mixture (50:50)) using 5 mol % $Pd(OAc)_2$ and stirred for 48 h. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.04 (m, 1H), 5.80 (m, 1H), 5.28 (m, 1H), 5.21 (m, 1H), 3.14 (m, 1H), 2.63 (m, 1H), 2.44 (m, 1H), 2.20−2.12 (m, 1H), 2.05 (s, 3H), 1.98 (m, 1H), 1.82 (m, 1H), 1.69 (apparent dt, J = 13.5, 5.1 Hz, 1H), 1.49 (m, 1H), 1.26 (m, 5H), 1.02 (apparent dd, J = 12.5, 6.8 Hz, 3H), 0.88 (apparent td, J = 7.0, 1.4 Hz, 3H). ^{13}C NMR ($CDCl_3$, 400 MHz): δ 171.1, 150.5, 132.7, 125.6, 121.6 [dst 121.2], 67.0 [dst 66.9], 45.9 [dst 45.8], 36.6 [dst 36.6], 35.5 [dst 35.2], 33.6 [dst 33.2], 33.0 [dst 32.9], 31.3 [dst 31.3], 30.0 [dst 29.2], 23.1 [dst 23.1], 21.6 [dst 20.4], 18.8, 14.3. MS (EI) *m/z*: 203 (13), 202 (42), 146 (100).

General Procedure for the Preparation of 28. Compound 28a. To 0.32 g (0.96 mmol) of **2a** dissolved in 12 mL of dry toluene were added maleic anhydride 0.47 g (4.8 mmol) and two crystals of butylated hydroxytoluene (BHT). The reaction was refluxed for 24 h. Evaporation followed by flash chromatography (pentane:Et_2O, 50:50 to 0:100) gave **28a** (0.37 g) in 85% yield. The solid diacid **29a** was formed in the freezer. This solid was washed with CH_2Cl_2 and pentane, and the purified solid was not soluble in $CDCl_3$. ^{1}H NMR ($CO(CD_3)_2$, 400 MHz): δ 6.34 (dd, J = 10.1, 4.8 Hz, 1H), 5.85 (ddd, J = 10.1, 5.3, 2.2 Hz, 1H), 5.11 (dt, J = 5.8, 3.2 Hz, 1H), 3.73 (s, 3H), 3.70−3.56 (m, 3H), 3.53 (s, 3H), 3.06 (m, 2H), 2.30 (m, 1H), 2.17−2.05 (m, 1H), 1.99 (s, 3H), 1.69 (br s, 3H), 1.57 (br td, J = 13.5, 3.1 Hz, 1H), 1.48 (dt, J = 13.5, 3.9 Hz, 1H). ^{13}C NMR ($CO(CD_3)_2$, 75 MHz): δ 173.2, 171.1, 170.4, 169.9, 169.8, 133.1, 130.8, 124.8, 123.4, 65.2, 63.9, 52.2, 50.9, 48.7, 43.6, 41.7, 41.3, 38.5, 31.6, 27.4, 20.4, 19.0.

Compound 28b. This was prepared as above in 82% yield and purified to form the solid diacid **29b**. ^{1}H NMR ($CO(CD_3)_2$, 400 MHz): δ 6.12 (ddd, J = 10.1, 4.4, 1.1 Hz, 1H), 5.68 (ddd, J = 10.1, 3.7, 2.0 Hz, 1H), 5.11 (m, 1H), 4.18 (dd, J = 8.8, 4.1 Hz, 1H), 3.75 (s, 3H), 3.70 (s, 3H), 3.58 (t, J = 8.8 Hz, 1H), 3.49 (m, 2H), 3.33 (m, 1H), 2.61 (m, 1H), 2.39 (m, 1H), 2.28 (m, 1H), 1.99 (s, 3H), 1.95 (m, 1H), 1.88 (m, 1H), 1.76 (m, 1H), 1.69 (m, 2H), 1.56 (m, 2H), 1.43 (m, 1H). ^{13}C NMR ($CO(CD_3)_2$, 75 MHz): δ 173.4, 171.5, 171.4, 170.0, 169.8, 138.2, 131.2, 131.1, 124.8, 65.2, 63.6, 52.7, 52.3, 46.5, 44.9, 44.7, 42.2, 41.6, 36.8, 27.6, 25.6, 24.7, 21.8, 21.7, 20.4.

Supporting Information Available: Characterization spectra for compounds **1a**−**k**, **2d**, **2e** + **2e″**, **2e′**, **2f** + **2f′**, **2g**, **2g′**, **2h**, **2h′**, **2h″**, **2i**, **2i′**, **3a**, **3d**, **11**, **15a**,**b**, **16a**,**b**, **20a**,**b**, **28a**,**b**, **29a**,**b**. This material is available free of charge via the Internet at http://pubs.acs.org.

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