Synthesis of Monoprotected 2-Alkylidene-1,3-propanediols by an Unusual S_N2' Mitsunobu Reaction

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A simple and efficient route to monoprotected (*E*)- and (*Z*)-2-alkylidene-1,3-propanediols is described. The key step involves an unusual regio- and stereoselective S_N2' Mitsunobu reaction of substituted 3-hydroxy-2-methylenealkanoates which are readily available from a Baylis–Hillman reaction between methyl acrylate and an aldehyde. These allylic alcohols, when treated with PPh_3, a carboxylic acid, and DEAD in THF at temperatures ranging from −40 °C to 22 °C, produced the corresponding 2-alkylidene-3-hydroxypropanoate derivatives (or (*E*)-2-(hydroxymethyl)-3-substituted-2-alkenoate derivatives) in >70% with S_N2':S_N2 ratio of 22:1 to >50:1. It was found that weak and bulky carboxylic acids and low temperatures favor S_N2' addition. The reaction conditions were effective for alkyl substituted derivatives, but the addition of Et_3N to the Mitsunobu conditions was necessary to improve the S_N2':S_N2 ratios for the vinyl **19** and phenyl **20** derivatives. The monoprotected (*Z*)- and (*E*)-2-alkylidene-1,3-propanediols can be efficiently synthesized by a three-step sequence involving either a transesterification, protection, and DIBAL-H reduction (>80% overall yield) or by the chemoselective reduction, protection, and ester cleavage (67% overall yield).

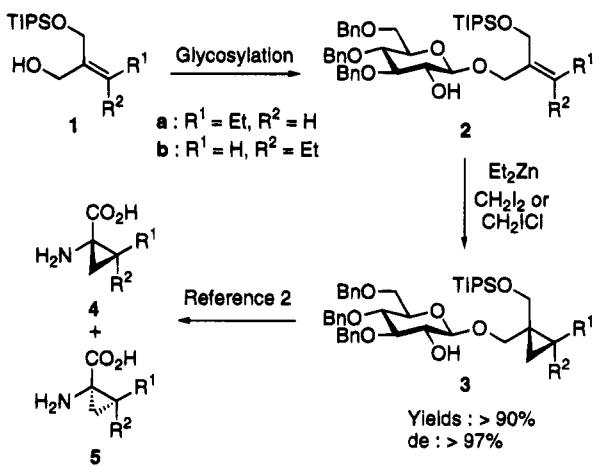
Introduction

We recently reported that 3,4,6-tri-*O*-benzyl-D-glucose could be used as an efficient and practical chiral auxiliary for the asymmetric cyclopropanation of a variety of substituted allylic alcohols.[1] This methodology was then applied to the stereoselective synthesis of all four stereoisomers of coronamic acid (Scheme 1).[2] The key step featured a highly diastereoselective cyclopropanation (>97% de) of the glycosides **2a** and **2b** derived from the allylic alcohol **1a** and **1b**.[3] The viability of this general approach not only relied on the key cyclopropanation step, but also on the availability of the starting monoprotected 2-alkylidene-1,3-propanediol. Although these derivatives are structurally quite simple, we were surprised to see that very little synthetic work, aimed at the synthesis of this general class of compounds, could be found in literature.[4,5]

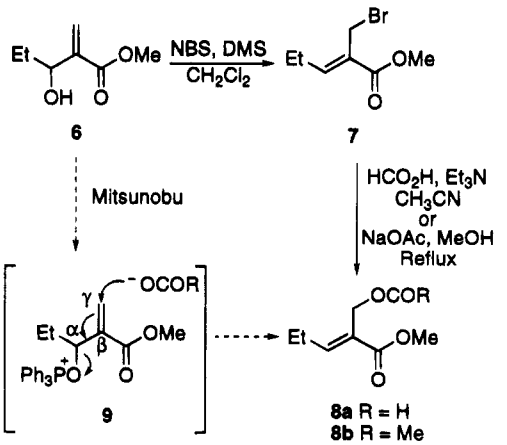
Furthermore, the few approaches available do not address the issues of the full stereochemical control of the olefin and of the differentiation of the oxygenated positions. The efficiency of our approach directed toward the cyclopropane α-amino acids depends highly on these two important issues.

The first approach that was investigated was based on Hoffmann's protocol[6] that produces methyl (*E*)-2-(bromomethyl)-2-pentenoate (**7**) from allylic alcohol **6**[7] (Scheme 2). Treatment of the bromide **7** with ammonium formate[8] or NaOAc[9] produced either ester **8a** or **8b** as single olefinic isomers. These two compounds are suitable

Scheme 1



Scheme 2



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(1) (a) Charette, A. B.; Côté, B.; Marcoux, J.-F. *J. Am. Chem. Soc.* **1991**, *113*, 8166–8167. (b) Charette, A. B.; Marcoux, J.-F.; Côté, B. *Tetrahedron Lett.* **1991**, *32*, 7215–7218. (c) Charette, A. B.; Côté, B. *J. Org. Chem.* **1993**, *58*, 933–936. (d) Charette, A. B.; Turcotte, N.; Côté, B. *J. Carbohydr. Chem.* **1994**, *13*, 421–432. (e) Charette, A. B.; Turcotte, N.; Marcoux, J.-F. *Tetrahedron Lett.* **1994**, *35*, 513–516.

(2) Charette, A. B.; Côté, B. *J. Am. Chem. Soc.*, in press.

(3) Charette, A. B.; Côté, B. *Tetrahedron Lett.* **1993**, *34*, 6833–6836.

(4) (a) Cereda, E.; Bellora, E.; Donetti, A. *Tetrahedron Lett.* **1980**, *21*, 4977–4980. (b) Weiss, F.; Isard, A.; Bensa, R. *Bull. Soc. Chim. Fr.* **1965**, 1355–1358. (c) For a efficient approach to 2-arylidene-1,3-propanediols, see: Foucaud, A.; Guemmout, F. E. *Bull. Soc. Chim. Fr.* **1989**, 403–408. Numerous side products and partially recovered starting material were observed when this procedure was applied to alkyl-substituted systems.

(5) For a cuprate addition/trapping sequence on the propargylic ester, see: Hall, D. G.; Chapdelaine, D.; Préville, P.; Deslongchamps, P. *Synlett* **1994**, 660–662.

(6) Hoffmann, H. M. R.; Rabe, J. *J. Org. Chem.* **1985**, *50*, 3849–3859.

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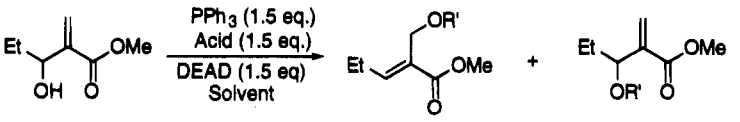
Table 1



6 8 9

entry	acid	solvent	T, °C (time)	ratio[a]	% yield	major product
1	benzoic	THF	0 (15 min)	30:1	90[b]	**8c**, R′ = Bz
2	benzoic	THF	−30 (2 h)	>50:1	80[c]	**8c**, R′ = Bz
3	*p*-nitrobenzoic	THF	0 (15 min)	10:1	86[b]	**8d**, R′ = PNBz[d]
4[e]	*p*-nitrobenzoic	THF	−40 (2 h)	25:1	85[b]	**8d**, R′ = PNBz
5	*p*-nitrobenzoic	CH_2Cl_2	0 (5 h)	5:1	60[c]	**8d**, R′ = PNBz
6	*p*-nitrobenzoic	toluene	0 (15 min)	9:1	60[c]	**8d**, R′ = PNBz
7	acetic	THF	0 (4 h)	>50:1	50[c]	**8b**, R′ = Ac
8	mesitoic[f]	THF	0 (15 min)	>50:1	76[b]	**8e**, R′ = Mes[g]
9	mesitoic	THF	−40 (1 h)	>50:1	75[c]	**8e**, R′ = Mes

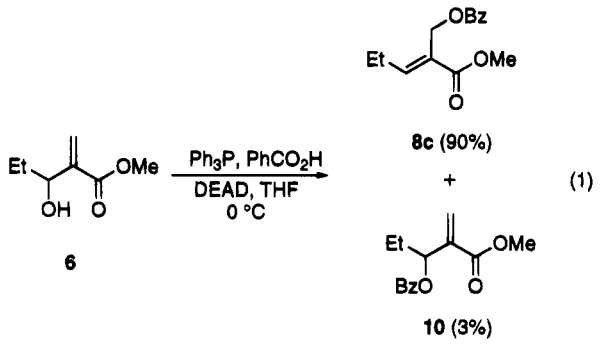
[a] S_N2':S_N2 ratio was determined by 400 MHz ^1H NMR of the crude product. [b] Isolated yield of analytically pure product. [c] Yield was evaluated by ^1H NMR. [d] PNBz:*p*-nitrobenzoyl. [e] The reaction was run on 10 g scale. This reaction was also carried out with diisopropyl azodicarboxylate instead of DEAD without any change in yield and ratio. [f] Mesitoic: 2,4,6-trimethylbenzoic. [g] Mes: 2,4,6-trimethylbenzoyl.

precursors to diols **1**.[10] The regioselectivity and stereoselectivity of the bromination reaction in this system led us to postulate that compounds **8** might be directly available when **6** was submitted to the Mitsunobu conditions.[11] The Michael acceptorlike nature of the oxophosphonium salt **9** derived from **6** should be increased, and the propensity for S_N2' addition on these systems should overwhelm competitive S_N2 attack.[12] This would allow expedient preparation of a variety of derivatives of type **8** directly from **6**.

Although extremely rare, minor products arising from S_N2' attack have been observed in the Mitsunobu reaction of allylic systems.[13,14] On the basis of labeling experiments, Farina[13a] has proposed that these products are generated by nucleophilic attack on the corresponding allylic cation formed via a S_N1 mechanism. To the best of our knowledge, no Mitsunobu reaction has been reported for an acyclic allylic alcohol bearing an ester group at the β-position.[15]

Results and Discussion

When ester **6** was subjected to standard Mitsunobu conditions, the S_N2' attack product **8c** was isolated in 90% yield along with only 3% of the S_N2 attack product **10** (eq 1). Furthermore, 400 MHz ^1H NMR analysis of the crude reaction mixture showed that the (*E*)-isomer was formed exclusively.[16]



(1)

This result prompted us to optimize the reaction conditions by testing various carboxylic acids, solvents, and temperatures in order to improve S_N2' selectivities. These results are summarized in Table 1. In all the cases, the (*E*)-isomer was the only double bond isomer observed. The next important thing to note is that stronger carboxylic acids favor normal Mitsunobu substitution. For example, the S_N2':S_N2 ratio decreases from 30:1 to 10:1 when going from benzoic acid to *p*-nitrobenzoic acid (entry 1 and 3). This observation is consistent with Martin's and Bessodes' conclusion[17] regarding the effect of stronger carboxylic acids on the rate of the Mitsunobu inversion of hindered alcohols. Acetic acid produced a very high S_N2':S_N2 ratio, but a low conversion was obtained due to the autodestruction of the reagents under the reaction conditions (entry 7).[18] Even though the pK_a value of the bulky mesitoic acid is similar to that of *p*-nitrobenzoic acid, very high S_N2' selectivities were observed. This could be explained by the preferential attack of the sterically hindered acid at the most acces-

(7) Obtained on 50 g scale from methyl acrylate and propionaldehyde under Baylis–Hillman condition (cat. DABCO, neat, room temp, 5 days): Baylis, A. B.; Hillman, N. E. *German Patent* 2 155 113, 1972; *Chem. Abstr.* **1972**, *77*, 34174. See also: (a) ref 6. (b) Drewes, S. E.; Freese, S. D.; Emslie, N. D.; Roos, G. H. P. *Synth. Commun.* **1988**, *18*, 1565–1572.

(8) (a) Alpegiani, M.; Zarini, F.; Perrone, E. *Synth. Commun.* **1992**, *22*, 1277–1282. (b) Ravindranath, B.; Gurudutt. K. N.; Srinivas, P. *Tetrahedron* **1982**, *38*, 1843–1846.

(9) Roush, W. R.; Brown, B. B. *J. Org. Chem.* **1993**, *58*, 2151–2161.

(10) A 2:1 mixture of regioisomers resulting from S_N2 and S_N2' attack was obtained if **7** was treated with Cu2O in H2O and DMSO at 50 °C: Yoshioka, M. et al. *Tetrahedron Lett.* **1980**, *21*, 351–354.

(11) (a) Mitsunobu, O. *Synthesis*, **1981**, 1–28. (b) Hughes, D. L. *Org. React.* **1992**, *42*, 335–656.

(12) The S_N2' and S_N2 denomination are used only to describe the regiochemistry of the addition since no mechanistic investigation has been undertaken to determine the stereoselective outcome of this reaction.

(13) (a) Farina, V. *Tetrahedron Lett.* **1989**, *30*, 6645–6648. (b) Danishefsky, S.; Berman, E. M.; Ciufolini, M.; Etheredge, S. J.; Segmuller, B. E. *J. Am. Chem. Soc.* **1985**, *107*, 3891–3898. (c) Lumin, S.; Yadagiri, P.; Falck, J. R. *Tetrahedron Lett.* **1988**, *29*, 4237–4240. (d) Sobti, A.; Sulikowski, G. A. *Tetrahedron Lett.* **1994**, *35*, 3661–3664. (e) Ramesh, N. G.; Balasubramanian, K. K. *Tetrahedron* **1995**, *51*, 255–272. (f) Mulzer, J.; Funk, G. *Synthesis* **1995**, 101–112.

(14) The palladium-catalyzed Mitsunobu reaction of allylic alcohols has also been reported: (a) Stary, I.; Stara, I. G.; Kocovsky, P. *Tetrahedron Lett.* **1993**, *34*, 179–182. (b) Lumin, S.; Falk, J. R.; Capdevila, J.; Karara, A. *Tetrahedron Lett.* **1992**, *33*, 2091–2094.

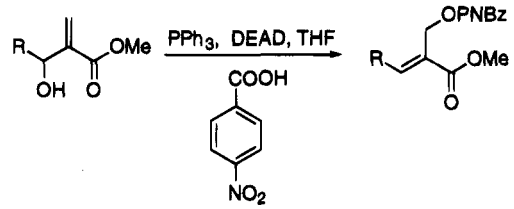
(15) For an exemple of S_N2' Mitsunobu reaction on a cyclic system see: Burke, S. D.; Pacofsky, G. J.; *Tetrahedron Lett.* **1986**, *27*, 445–448.

(16) The geometry of the olefin was unambiguously established by X-ray crystallographic analysis of the *p*-nitrobenzoate analog **8d**. The ORTEP structure is included in the supporting information.

(17) (a) Martin, S. F.; Dodge, J. A. *Tetrahedron Lett.* **1991**, *32*, 3017–3020. (b) Saïah, M.; Bessodes, M.; Antonakis, K. *Tetrahedron Lett.* **1992**, *33*, 4317–4320 and references cited in both publications.

(18) Hughes, D. L.; Reamer, R. A.; Bergan, J. J.; Grabowski, E. J. J. *J. Am. Chem. Soc.* **1988**, *110*, 6487–6491.

Table 2

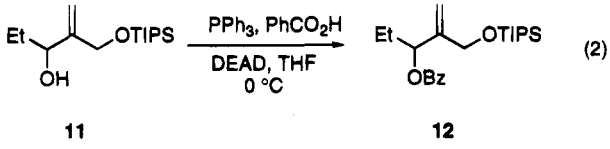


entry	R	temp, °C	% yield[a]	ratio[b]	product
1	Me (**13**)	−40	>80	22:1	**16**
2	Et (**6**)	−40	85	25:1	**8d**
3	*i*-Pr (**14**)	−40	0	–	**17**
4	*i*-Pr (**14**)	0	70	>50:1	**17**
5[c]	*t*-Bu (**15**)	22	20[d]	>50:1	**18**

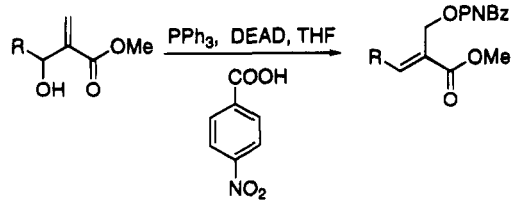
[a] Isolated yield of analytically pure product. [b] S_N2':S_N2 ratio was determined by 400 MHz ^1H NMR of the crude product. [c] Reaction was performed with 5 equiv of triphenylphosphine, 5 equiv of *p*-nitrobenzoic acid, and 5 equiv of DEAD. [d] Yield determined by 400 MHz ^1H NMR of the crude product.

sible position (entry 8, 9). In all cases, the yields and the selectivities were generally superior when THF was used as the solvent (entry 3, 5, 6). Yields or selectivities were not diminished when the reaction was carried out with diisopropyl azodicarboxylate (DIAD), which is considered to be a cheaper and safer reagent than DEAD for large scale applications (entry 4).[18] Despite the fact that *p*-nitrobenzoic acid did not provide the highest S_N2':S_N2 ratio, we found that the products were easier to purify (crystallization). Furthermore, compound **8d** proved to be a more convenient precursor for the subsequent transformations (*vide infra*) leading to monoprotected 1,3-propanediols.

Two additional control experiments clearly showed that both the oxophosphonium moiety *and* the ester group were essential for obtaining high yield of the product resulting from S_N2' attack. Treatment of allylic alcohol **6** with *p*-nitrobenzoic acid in THF at 25 °C *without* DEAD and Ph_3P led to a complete recovery of starting material. Furthermore, replacement of the methyl ester by a protected primary alcohol produced only the Mitsunobu inversion product **12** with no trace of the desired allylic transposition product (eq 2).



(2)



After this exhaustive study with the ethyl derivative **6**, the optimized conditions were applied to different substrates for which R = Me, *i*-Pr, and *t*-Bu (Table 2). As shown previously, the reaction was found to be very stereoselective and only the (*E*)-isomers were formed. These examples clearly show that the size of the R group has a strong effect on the rate of the reaction. With the less hindered methyl substituent (entry 1), the S_N2 site of addition is more accessible and we observed a slight

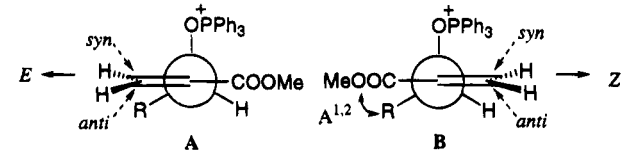
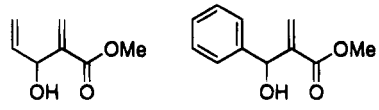


Figure 1. Proposed transition state models leading to the (*E*)- or (*Z*)-isomers.

decrease of selectivity. Interestingly, increasing the steric bulk of the R group not only completely suppressed S_N2 attack, but it also slowed down the rate of the S_N2' attack considerably (entry 2 and 3). In the case of *tert*-butyl substituent, it was impossible to obtain quantitative conversion even when stirring at room temperature for 2 h with 5 equiv of the reagents. In contrast to the less hindered ethyl analog (entry 2), the product resulting from S_N2 attack could not be detected in the last 2 cases even when *p*-nitrobenzoic acid was used as the nucleophile (entry 4 and 5).

Based on the regioselectivity, stereoselectivity, and reactivity of the S_N2' Mitsunobu reaction, all the results presented above could be rationalized by the transition state model proposed in Figure 1. We believe that the oxophosphonium leaving group is oriented parallel to the π system to maximize the overlap $\pi \rightarrow \sigma^*$ upon nucleophilic attack. The preferred model (A), in which the $A^{1,2}$ strain interaction between the R and the ester group is minimized (A vs B), is consistent with the observed stereochemistry of the major products. It is postulated that the nucleophilic attack occurs *anti* to the oxophosphonium leaving group. This model also accounts for the decrease of the reaction rate upon increasing the steric bulk of the R group. We should also point out that the rate difference might also be due to the developing $A^{1,3}$ strain interaction between the ester and the R group upon nucleophilic attack.

As previously illustrated, this synthetic methodology is very effective for controlling the geometry of trisubstituted olefins bearing alkyl groups (compounds **6**, **13**, **14**). In order to increase the scope of the reaction, vinyl and phenyl substituted derivatives **19** and **20** were submitted to the previously optimized conditions.[19]

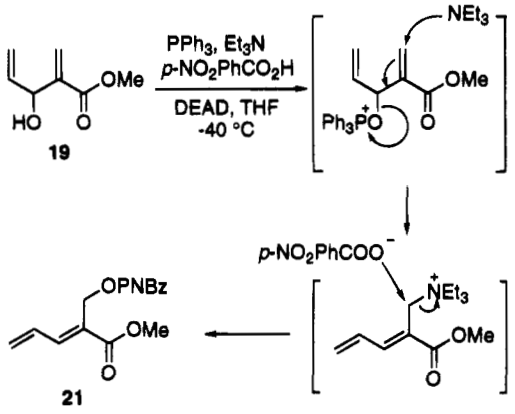


19 **20**

Unfortunately, the Mitsunobu adducts were obtained in less than 50% yield with disappointingly low S_N2':S_N2 ratios (2:1). These results are not very surprising since **19** and **20** are more prone to react via a S_n1 mechanism since they can generate a stable allylic or benzylic cation by elimination of triphenylphosphine oxide prior to nucleophilic attack. Furthermore, we should note that there are three potential electrophilic sites for nucleophilic addition to the vinyl derivative **19**. It was also found that varying the temperature, the carboxylic acid, or the solvent did not lead to any improvement in the yield of the desired product. Interestingly, Walker and Jenkins have pointed out that the order of addition of the reagents in the Mitsunobu reaction could have a

(19) Substrate, PPh_3 (1.5 equiv), *p*-nitrobenzoic acid (1.5 equiv), in THF at −40 °C, and then DEAD (1.5 equiv).

Scheme 3



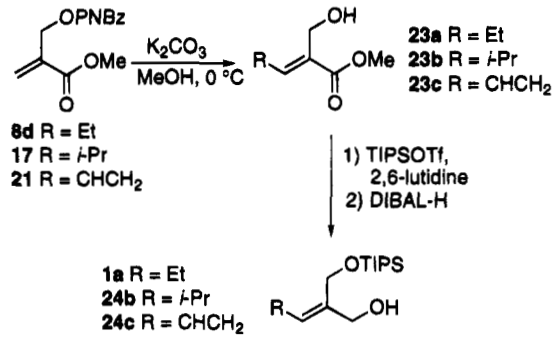
strong impact on the mechanistic pathway.[20] In our system, addition of all the reagents prior to the substrate led not only to a much cleaner reaction (>80% yield), but also to a slight improvement of the $S_N2':S_N2$ ratio (3:1).

In order to accelerate the S_N2' addition process over the postulated competitive S_N1 pathway, we decided to test the idea of using a better nucleophile than a carboxylate ion that would add reversibly at the terminal position and then be subsequently displaced by the carboxylate ion. Foucaud has shown that DABCO can add on a similar aryl-substituted acrylate system and then be displaced by another nucleophile to produce allylic amines.[4c] The allylic transposition reaction on alcohol **19** was therefore carried out in the presence of a stoichiometric amount of triethylamine (Scheme 3). Gratifyingly, the *p*-nitrobenzoate **21** was obtained in >80% yield with a very good $S_N2':S_N2$ ratio (11:1) when this unusual procedure was used. The postulated mechanism involves S_N2' addition of Et_3N on the oxophosphonium moiety followed by displacement of the amine by the carboxylate ion.

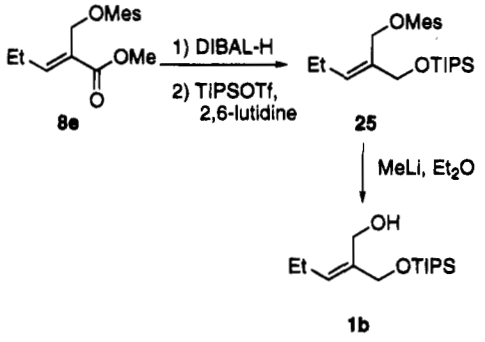
After optimization of the reaction conditions, the Mitsunobu products **21** and **22** were obtained in good yields and excellent $S_N2':S_N2$ ratios (≥30:1) (eqs 3, 4). The geometry of the olefin was confirmed by X-ray crystallographic analysis of the *p*-nitrobenzoate **22**.[21] Given that this procedure using triethylamine proved to be highly selective, we were interested in applying these conditions to the ethyl substituted derivative **6** in order to increase the $S_N2':S_N2$ ratio. Unfortunately, no major improvement of regioselectivity was observed and it appears that this procedure is effective only when new conjugated systems, such as those in **21** and **22**, are generated. In the case of the *tert*-butyl derivative **15**, however, the addition of triethylamine improved the yield to 60% when 5 equiv of the reagents were used.

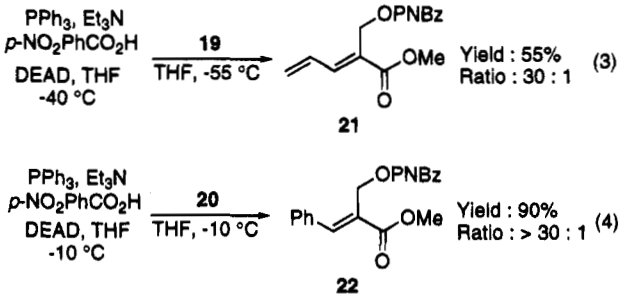
The postulated mechanism illustrated in Scheme 3 indicates that triethylamine could potentially be used in catalytic amounts. The Mitsunobu reaction on the alcohol **20**, when carried out in the presence of only 0.2 equiv of triethylamine, afforded the desired compound **22** in 90% yield and a 30:1 $S_N2':S_N2$ ratio. Finally, the replacement of triethylamine by DABCO was found to completely inhibit the reaction. The starting material was recovered unchanged when alcohol **20** was submitted to the Mitsunobu conditions in the presence of 1 equiv of DABCO.

Scheme 4



Scheme 5





With the Mitsunobu adducts in hand, the syntheses of the (*Z*)-monoprotected diols **1a** and **24** were completed as described in Scheme 4. The preferred starting materials for the sequence were the *p*-nitrobenzoate derivatives since transesterification of the corresponding benzoate produced ca. 25% of methyl ether resulting from S_N2' displacement of the benzoate by the methoxide ion upon treatment with K_2CO_3 in CH_3OH at 0 °C. In contrast, the corresponding *p*-nitrobenzoates **8d**, **17**, and **21** were smoothly cleaved under these conditions to produce alcohols **23a–c**. Subsequent protection and reduction afforded the desired (*Z*)-isomers **1a**, **24**, and **25** in excellent overall yields (81–88%) for the three steps.[22]

Since this strategy ensures differentiation of the two oxygenated positions, the formation of the related (*E*)-isomers could be accomplished by the appropriate standard manipulation of functional groups. An alternative approach that starts with the readily available mesitoate **8e**, is presented in Scheme 5. Chemoselective reduction of the methyl ester followed by silylation and cleavage of the mesitoate ester produced the (*E*)-isomer **1b** in 67% overall yield for the three steps.

(20) (a) Varasi, M.; Walker, K. A. M.; Maddox, M. *J. Org. Chem.* **1987**, *52*, 4235–4238. (b) Camp, D.; Jenkins, I. D. *J. Org. Chem.* **1989**, *54*, 3045–3049.

(21) ORTEP structure of **22** is included in the supporting information.

(22) A similar sequence that produces the monoprotected (*Z*)-TBDMS ether in 85% overall yield on a 15 g-scale has been reported by Roush (ref 9).

Summary

We have shown that allylic alcohols derived from the Baylis–Hillman reaction between aromatic and aliphatic aldehydes and methyl acrylate can served as excellent precursors to (*E*)-trisubstituted olefins under the Mitsunobu conditions. The addition of a carboxylate ion to an allylic alcohol under the these conditions could be completely regio- and stereoselective when this olefin is activated by an ester function. This S_N2' addition proved to be sensitive to carboxylic acid pK_a, temperature, steric effects, and the order in which reagents are added. The methodology was applied to different alkyl substituted derivatives for which the geometry of the olefin was found to be exclusively (*E*) as determined by ^{1}H-NMR and X-ray analysis. For phenyl and vinyl substituted derivatives, we have reported the first Mitsunobu procedure in which Et_3N was used as a nucleophile on the oxophosphonium salt instead of the usual carboxylate. This modification led to higher S_N2':S_N2 ratios (30:1) than those obtained with the standard procedure (3:1). Finally, the *p*-nitrobenzoates resulting from S_N2' Mitsunobu reaction were converted to monoprotected (*Z*)-2-alkylidene-1,3-propanediols in >80% yield using standard transformations (three steps). The (*E*)-isomer was obtained starting from the corresponding mesitoate ester instead of the *p*-nitrobenzoate.

Experimental Section

General. Unless otherwise noted, all nonaqueous reactions were performed under an oxygen-free atmosphere of nitrogen with rigid exclusion of moisture from reagents and glassware. ^{1}H NMR (and ^{13}C NMR) spectra were recorded in deuteriochloroform, unless otherwise noted, at 300 or 400 MHz (75 or 100 MHz). When necessary, solvents and reagents were dried prior to use as follows: ether, tetrahydrofuran, benzene, and toluene were stored over and distilled from sodium benzophenone ketyl; dichloromethane, triethylamine, pyridine, and hexane were distilled over calcium hydride. Unless otherwise stated, the reagents were purchased from Aldrich Chemical Co. and used as received.

Methyl (*E*)-2-[(Benzoyloxy)methyl]-2-pentenoate (8c). To a solution of allylic alcohol **6**[7] (200 mg, 1.39 mmol) in THF (14 mL) were added Ph_3P (548 mg, 2.09 mmol) and benzoic acid (255 mg, 2.09 mmol). The clear solution was cooled to 0 °C, and DEAD (329 μL, 2.09 mmol) was added over a period of 10 min. The reaction was stirred at 0 °C until TLC analysis showed the complete consumption of starting material (15 min). The solution was diluted with ether (50 mL) and H_2O (1 mL). The layers were separated, and the organic layer was washed with H_2O (10 mL) and 2 portions of aqueous NaOH (10 mL, 1.0 N). The aqueous layer was extracted twice with ether (10 mL), and the combined organic layers were washed with saturated aqueous $NaHCO_3$ (10 mL) and with saturated aqueous NaCl (10 mL), dried over $MgSO_4$, and concentrated under reduced pressure. The residue was triturated[23] in a 5% ether/hexane solution and then filtered to eliminate Ph_3PO. The volatiles were evaporated under reduced pressure, and the residue was purified by flash chromatography (5% EtOAc/hexane) to afford the desired benzoate **8c** (312 mg, 90%) as a clear oil and ca. 10 mg of **10**.[24] **8c**: R_f 0.34 (10% EtOAc/hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.97 (m, 2H), 7.49 (m, 1H), 7.36 (m, *J* = 8 Hz, 2H), 7.07 (t, *J* = 8 Hz, 1H), 5.07 (s, 2H), 3.74 (s, 3H), 2.35 (qn, *J* = 8 Hz, 2H), 1.05 (t, *J* = 8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.7, 166.0, 151.0, 132.7, 129.9, 129.4, 128.1, 126.4, 58.2, 51.7, 22.0, 13.0; IR (neat) 2960, 1720, 1650, 1600, 1450, 1260, 1140, 1100, 1020, 950, 700 cm^{-1}; HRMS calcd for $C_{14}H_{16}O_4$ + H 249.1127, found 249.1132.

Methyl (*E*)-2-[[(4-Nitrobenzoyl)oxy]methyl]-2-pentenoate (8d). To a solution of allylic alcohol **6** (8.42 g, 58.4 mmol) in anhydrous THF (500 mL) were added Ph_3P (20 g, 76 mmol) and *p*-nitrobenzoic acid (12.7 g, 76 mmol). The resulting clear solution was placed at −40 °C, and DEAD (12 mL, 76 mmol) was added over a period of 10 min. The reaction was then slowly warmed to −30 °C over 1 h and maintained at this temperature until TLC analysis showed the complete consumption of starting material (1 h). The bath at −30 °C was replaced by an ice bath and after 15 min at 0 °C the solution was concentrated under reduced pressure with a bath temperature of 30 °C. The residue was poured into ether (300 mL), and the organic layer was washed with H_2O (20 mL) and 2 portions of aqueous NaOH (20 mL, 1.0 M). The aqueous layer was extracted twice with ether (50 mL), and the combined organic layers were washed with saturated aqueous $NaHCO_3$ (20 mL) and saturated aqueous NaCl (20 mL), dried over $MgSO_4$, and concentrated under reduced pressure. Subsequent preadsorption of the residue on silica gel and flash chromatography (7% to 20% EtOAc/hexane) produced the desired *p*-nitrobenzoate (14.4 g, 84%) as a slightly yellow solid that can be crystallized from MeOH at 0 °C or in ether/hexane: mp 53–54.5 °C; R_f 0.2 (10% EtOAc/hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.20 (dt, *J* = 9, 2 Hz, 2H), 8.11 (dt, *J* = 9, 2 Hz, 2H), 7.09 (t, *J* = 8 Hz, 1H), 5.09 (s, 2H), 3.74 (s, 3H), 2.36 (qn, *J* = 8 Hz, 2H), 1.06 (t, *J* = 8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.5, 164.2, 151.6, 150.4, 135.3, 130.6, 125.8, 123.3, 59.1, 51.8, 22.1, 13.0; IR (KBr) 2970, 1720, 1610, 1525, 1265, 1100, 950, 710 cm^{-1}; HRMS calcd for $C_{14}H_{15}NO_6$ + H 294.0978, found 294.0946.

Methyl (*E*)-2-[[(2,4,6-Trimethylbenzoyl)oxy]methyl]-2-pentenoate (8e). Mesitoate **8e** was obtained in 76% isolated yield following the procedure described for the benzoate **8c** except that mesitoic acid was used instead of benzoic acid and the reaction was run at 0 °C (200 mg-scale): R_f 0.4 (10% EtOAc/hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.09 (t, *J* = 8 Hz, 1H), 6.83 (s, 2H), 5.09 (s, 2H), 3.76 (s, 3H), 2.40 (qn, *J* = 8 Hz, 2H), 2.28 (s, 6H), 2.26 (s, 3H), 1.10 (t, *J* = 8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.7, 166.8, 151.0, 139.1, 135.0, 130.7, 128.2, 126.2, 58.1, 51.8, 22.1, 20.9, 19.5, 13.0; IR (neat) 2960, 1720, 1650, 1610, 1430, 1255, 1160, 1070, 950, 840 cm^{-1}; HRMS calcd for $C_{17}H_{22}O_4$ + H 291.1597, found 291.1596.

3-(Benzoyloxy)-2-methylene-1-pentanol Triisopropylsilyl Ether (12). Alcohol **11**[25] (49 mg, 0.18 mmol) was submitted to conditions described for **8c** to produce benzoate **12** as the only one product as determined from crude ^{1}H NMR: R_f 0.5 (5% EtOAc/hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.07 (m, 2H), 7.56 (m, 1H), 7.45 (m, 2H), 5.46 (t, *J* = 7 Hz, 1H), 5.33 (m, *J* = 2 Hz, 1H), 5.21 (m, *J* = 1 Hz, 1H), 4.35 (m, *J* = 1 Hz, 2H), 1.85 (m, 2H), 1.08 (m, 21H), 0.99 (t, *J* = 7 Hz, 3H).

Methyl 4,4-Dimethyl-3-hydroxy-2-methylene-1-pentanoate (15). Alcohol **15** (670 mg, 53%) was prepared from pivalaldehyde and methyl 3-(dimethylamino)propionate (1.61 g, 7.42 mmol) according to the general procedure described by Drewes.[26] We have found, however, that the aldol reaction should be carried out at 0 °C for 3 h instead of −78 °C: R_f 0.5 (20% EtOAc/hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.29 (d, *J* = 1 Hz, 1H), 5.77 (t, *J* = 1 Hz, 1H), 4.29 (d, *J* = 1 Hz, 1H), 3.77 (s, 3H), 2.93 (s(br), 1H), 0.90 (s, 9H).

Methyl (*E*)-2-[[(4-Nitrobenzoyl)oxy]methyl]-2-butenoate (16). Ester **16** (284 mg, 88%) was prepared from alcohol **13**[26] (150 mg, 1.15 mmol) according to the procedure described for **8d**: mp 116–117 °C; R_f 0.3 (12% EtOAc/hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (d, *J* = 9 Hz, 2H), 8.15 (d, *J* = 9 Hz, 2H), 7.22 (q, *J* = 7 Hz, 1H), 5.14 (s, 2H), 3.76 (s, 3H), 1.99 (d, *J* = 7 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 164.2, 150.4,

(23) The trituration was done only after triphenylphosphine oxide had crystallized. The solid should be finely pulverized by stirring vigorously in the 5% ether/hexane solution. This purification procedure should not be used with *p*-nitrobenzoate derivative because of their strong propensity to crystallize under these conditions.

(24) Benzoate **10** was compared to authentic material made from alcohol **6** (BzCl, pyr, DMAP in CH_2Cl_2).

(25) Prepared from **6** (DIBAL-H, CH_2Cl_2; TIPSOTf, 2,6-lutidine, CH_2Cl_2).

(26) Brand, M.; Drewes, S. E.; Roos, G. H. P. *Synth. Commun.* **1986**, *16*, 883–889.

145.1, 135.3, 130.6, 127.4, 123.3, 58.9, 51.8, 14.5; IR (neat) 3110, 3000, 2950, 2840, 1710, 1650, 1600, 1510, 1430, 1290, 1115, 1065, 950, 710 cm^{-1}; HRMS calcd for $C_{13}H_{13}NO_6$ + H 280.0821, found 280.0830.

Methyl (*E*)-4-Methyl-2-[[(4-nitrobenzoyl)oxy]methyl]-2-pentenoate (17). Ester **17** (1.36 g, 70%) was prepared from alcohol **14** (1.0 g, 6.32 mmol) according to the procedure described for **8d** except that the reaction was run at 0 °C: R_f 0.25 (10% EtOAc/hexane); ^1H NMR (300 MHz, $CDCl_3$) δ 8.20 (dt, J = 9, 2 Hz, 2H), 8.11 (dt, J = 9, 2 Hz, 2H), 6.90 (d, J = 11 Hz, 1H), 5.09 (s, 2H), 3.73 (s, 3H) 2.83 (m, 1H), 1.02 (d, J = 7 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.7, 164.2, 156.3, 150.4, 135.3, 130.5, 124.1, 123.3, 59.3, 51.8, 28.2, 22.0; IR (neat) 3100, 2960, 1720, 1650, 1605, 1520, 1260, 1100, 950, 710 cm^{-1}; HRMS calcd for $C_{15}H_{17}NO_6$ + H 308.1134, found 308.1134.

Methyl (*E*)-4,4-Dimethyl-2-[[(4-nitrobenzoyl)oxy]methyl]-2-pentenoate (18). Compound **18** was prepared from alcohol **15** (50 mg, 0.29 mmol) according to the procedure described for **22** at 22 °C and using 5 equiv of Ph_3P, 5 equiv of *p*-nitrobenzoic acid, and 5 equiv of DEAD. The *p*-nitrobenzoate derivative was purified by flash chromatography (5% EtOAc/hexane) to produce the desired compound **18** (55 mg, 60% yield): R_f 0.3 (5% EtOAc/hexane); ^1H NMR (300 MHz, $CDCl_3$) δ 8.29–8.25 (m, 2H), 8.20–8.16 (m, 2H), 7.21 (s, 1H), 5.24 (s, 2H), 3.78 (s, 3H), 1.25 (s, 9H).

Methyl (*E*)-2-[[(4-Nitrobenzoyl)oxy]methyl]-2,4-pentadienoate (21). The ester **21** was prepared from alcohol **19**[26] (39 mg, 0.28 mmol) according to the procedure described for **22**. We have found that washing the organic layer with aqueous 10% HCl after the 1.0 M NaOH solution produced a higher yield of the desired compound (57 mg, 55%). The resulting *p*-nitrobenzoate could be crystallized from 10% EtOAc/hexane: mp 86–88 °C; R_f 0.3 (10% EtOAc/hexane); ^1H NMR (400 MHz, $CDCl_3$) δ 8.22 (dt, J = 9, 2 Hz, 2H), 8.14 (dt, J = 9, 2 Hz, 2H), 7.43 (d, J = 12 Hz, 1H), 6.86 (m, 1H), 5.74 (ddd, J = 17, 1, 1 Hz, 1H), 5.65 (ddd, J = 10, 1, 1 Hz, 1H), 5.21 (s, 2H), 3.79 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.6, 164.2, 150.3, 144.6, 135.1, 130.9, 130.6, 128.3, 125.2, 123.3, 59.0, 52.0; IR (KBr) 3120, 2950, 1710, 1630, 1600, 1520, 1435, 1345, 1280, 1230, 1100, 985, 940, 715 cm^{-1}.

Methyl (*E*)-3-Phenyl-2-[[(4-nitrobenzoyl)oxy]methyl]-2-propenoate (22). To a solution of Ph_3P (818 mg, 3.12 mmol) and *p*-nitrobenzoic acid (521 mg, 3.12 mmol) in THF (20 mL) was added of Et_3N (430 μL, 3.12 mmol). The resulting clear solution was cooled at −10 °C, and DEAD (490 μL, 3.12 mmol) was added over a period of 5 min. To this solution was added methyl 3-phenyl-3-hydroxy-2-methylene-1-propanoate (**20**)[27] (400 mg, 2.08 mmol) in THF (1 mL) over a period of 15 min. When TLC analysis showed the complete consumption of starting material (3 h), the reaction was placed at 0 °C (15 min) and then diluted with ether (120 mL) and H_2O (10 mL). The organic phase was washed with H_2O (20 mL) and 1.0 M NaOH (2 × 20 mL). The aqueous layer was extracted with ether (2 × 20 mL), and combined organic layers were washed with saturated aqueous $NaHCO_3$ (20 mL) and saturated aqueous NaCl (20 mL). The organic layer was dried over $MgSO_4$, and concentrated under reduced pressure. The residue was preadsorbed on silica gel and purified by flash chromatography (15% EtOAc/hexane) to afford of *p*-nitrobenzoate **22** (642 mg, 90%) as a slightly yellow solid which could be crystallized from 5% EtOAc/hexane: mp 116–118 °C; R_f 0.3 (12% EtOAc/hexane); ^1H NMR (400 MHz, $CDCl_3$) δ 8.26 (dt, J = 9, 2 Hz, 2H), 8.18 (dt, J = 9, 2 Hz, 2H), 8.08 (s, 1H), 7.43–7.38 (m, 5H), 5.27 (s, 2H), 3.86 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.9, 164.2, 150.4, 146.0, 135.2, 133.9, 130.6, 129.6, 129.2, 128.7, 125.9, 123.4, 60.5, 52.2; IR (KBr) 3100, 3040, 2950, 1710, 1625, 1600, 1510, 1430, 1390, 1340, 1280, 1100, 930, 865, 760, 710 cm^{-1}.

Methyl (*E*)-2-(Hydroxymethyl)-2-pentenoate (23a). The *p*-nitrobenzoate **8d** (3.5 g, 11.9 mmol) was dissolved in methanol (120 mL) and cooled to 0 °C. After 15 min of stirring, K_2CO_3 (3.3 g, 24 mmol) was added in one portion and the reaction was kept at 0 °C until the TLC analysis showed the complete consumption of the starting material (1 h). The solution was poured in ether (300 mL) and saturated aqueous NaCl (50 mL). The minimum amount of H_2O was then added to dissolve solid K_2CO_3. The aqueous layer was extracted with CH_2Cl_2 (50 mL), and the combined organic layers were washed with saturated aqueous NaCl (3 × 50 mL). The organic layer was dried over $MgSO_4$ and concentrated using a rotary evaporator at *atmospheric pressure* in a bath at 50–60 °C. The residue was purified by flash chromatography (20–30% EtOAc/hexane) to produce of the alcohol **23a** (1.5 g, 87%) as a volatile colorless liquid: R_f 0.2 (20% EtOAc/hexane); ^1H NMR (300 MHz, $CDCl_3$) δ 6.81 (t, J = 8 Hz, 1H), 4.27 (s, 2H), 3.71 (s, 3H), 2.79 (s, 1H), 2.24 (qn, J = 8 Hz, 2H), 1.01 (t, J = 8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.9, 147.2, 130.3, 56.7, 51.6, 21.5, 13.1; IR (neat) 3440 (v. br), 2990, 2970, 2890, 1710, 1640, 1430, 1305, 1275, 1220, 1140, 1075, 1005, 745 cm^{-1}; HRMS calcd for $C_7H_{12}O_3$ 144.0787, found 144.0773.

Methyl (*E*)-4-Methyl-2-(hydroxymethyl)-2-pentenoate (23b). The title compound (0.68 g, 97%) was prepared from ester **17** (1.36 g, 4.45 mmol) according to the procedure described for **23a**: R_f 0.3 (30% EtOAc/hexane); ^1H NMR (300 MHz, $CDCl_3$) δ 6.69 (d, J = 10 Hz, 1H), 4.33 (s, 2H), 3.77 (s, 3H), 2.78 (m, 1H), 2.54 (s(br), 1H), 1.05 (d, J = 7 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.1, 152.1, 128.6, 57.1, 51.6, 27.5, 22.2; IR (neat) 3500 (br), 2970, 2880, 1720, 1650, 1470, 1440, 1325, 1270, 1155, 1080, 1020, 750 cm^{-1}; HRMS calcd for $C_8H_{14}O_3$ + H 159.1021, found: 159.1011.

Methyl (*E*)-2-(Hydroxymethyl)-2,4-pentadienoate (23c). The title compound (300 mg, 73%) was prepared from ester **21** (840 mg, 2.89 mmol) according to the procedure described for **23a** except that K_2CO_3 was added at −40 °C and slowly warmed to −20 °C: R_f 0.3 (10% EtOAc/hexane); ^1H NMR (400 MHz, $CDCl_3$) δ 7.15 (d, J = 12 Hz, 1H), 6.71 (d, J = 17, 12, 10 Hz, 1H), 5.59 (dq, J = 17, 1 Hz, 1H), 5.47 (dq, J = 10, 1 Hz, 1H), 4.33 (s, 2H), 3.70 (s, 3H), 2.95 (s(br), 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.0, 141.2, 131.1, 130.2, 126.7, 56.6, 51.8; IR (neat) 3450 (br), 2940, 1695, 1625, 1585, 1430, 1330, 1260, 1080, 1010, 820, 760 cm^{-1}.

(*Z*)-2-[[(Triisopropylsilyl)oxy]methyl]-2-pentenol (1a). Alcohol **23a** (2.0 g, 13.8 mmol) was dissolved in CH_2Cl_2 (150 mL) and cooled to 0 °C. To this clear solution was added 2,6-lutidine (2.4 mL, 20.7 mmol) followed by TIPSOTf (4.5 mL, 16.6 mmol). The ice bath was removed and when TLC analysis showed the complete consumption of the starting material, the reaction was diluted with ether (150 mL) and quenched with water (5 mL). The organic layer was washed with 10% aqueous HCl (3 × 30 mL), saturated aqueous $NaHCO_3$ (30 mL), and saturated aqueous NaCl (30 mL). The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. The residue was filtered on a short plug of silica gel (2% EtOAc/hexane) to remove methyl *p*-nitrobenzoate. The resulting colorless oil was dissolved in CH_2Cl_2 (150 mL) and cooled to −78 °C, and a 1.0 M solution of DIBAL-H in hexane (41 mL, 41 mmol) was added over a period of 15 min. The solution was stirred at −78 °C until TLC analysis showed the complete consumption of starting material. The reaction was then carefully quenched with 0.5 M aqueous Rochelle's salt and diluted with ether (100 mL). The solution was allowed to warmed to room temperature and was diluted with 0.5 M aqueous Rochelle's salt (150 mL). The heterogeneous solution was vigorously stirred until the two layers became clear and completely separated. The organic layer was washed saturated aqueous NaCl (30 mL), dried over $MgSO_4$, and concentrated under reduced pressure. The residue can be purified either by distillation using Kugelrohr (0.5 mmHg/90 °C) or by flash chromatography (6% EtOAc/hexane) to produce the desired alcohol **1a** (3.5 g, 93%): R_f 0.3 (10% EtOAc/hexane); ^1H NMR (300 MHz, $CDCl_3$) δ 5.44 (t, J = 7 Hz, 1H), 4.42 (s, 2H), 4.15 (s, 2H), 2.67 (s (br), 1H), 2.01 (qt, J = 8 Hz, 2H), 1.06 (m, 21H), 0.96 (t, J = 8 Hz, 3H); ^{13}C NMR(75 MHz, $CDCl_3$) δ 136.4, 130.4, 67.1, 61.3, 20.7, 17.9, 14.0, 11.8; IR (neat) 3350 (br), 2940, 2860, 1460, 1070, 870, 790, 670 cm^{-1}; HRMS calcd for $C_{15}H_{32}O_2Si$ + H 273.2251, found 273.2250.

(*Z*)-4-Methyl-2-[[(triisopropylsilyl)oxy]methyl]-2-pentenol (24b). The title compound (687 mg, 95%) was prepared from alcohol **23b** (362 mg, 2.29 mmol) according to procedure

(27) Janecki, T.; Bodalski, R. *Synthesis* **1990**, 799–801.

described for **1a**: R_f 0.3 (6% EtOAc/hexane); ^1H NMR (300 MHz, $CDCl_3$) δ 5.28 (d, J = 10 Hz, 1H), 4.45 (s, 2H), 4.14 (s, 2H), 2.66 (s(br), 1H), 2.49 (m, 1H), 1.11 (m, 21 H), 0.95 (d, J = 7 Hz, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.2, 134.5, 67.3, 61.5, 26.7, 22.9, 17.8, 11.7; IR (neat) 3350 (br), 2940, 2850, 1450, 1370, 1050 (br), 870, 780, 665 cm^{-1}; HRMS calcd for $C_{16}H_{34}O_2Si$ + H 287.2406, found 287.2380.

(*Z*)-2-[[(Triisopropylsilyl)oxy]methyl]-2,4-pentadienol (24c). The title compound (225 mg, 90%) was prepared from alcohol **23c** (131 mg, 0.92 mmol) according to procedure described for **1a**: R_f 0.3 (10% EtOAc/hexane); ^1H NMR (400 MHz, $CDCl_3$) δ 6.52 (ddd, J = 17, 11, 10 Hz, 1H), 6.06 (d, J = 11 Hz, 1H), 5.24 (dd, J = 17, 1 Hz, 1H), 5.15 (d, J = 10 Hz, 1H), 4.54 (s, 2H), 4.23 (s, 2H), 2.67 (s(br), 1H), 1.12 (m, 21H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.1, 131.2, 127.0, 118.7, 66.3, 61.2, 17.8, 11.7; IR (neat) 3350 (br), 2960, 2880, 1600, 1465, 1385, 1070, 885, 800, 690 cm^{-1}.

(*E*)-2-[[(Triisopropylsilyl)oxy]methyl]-2-pentenol (1b). To a solution of mesitoate **8e** (842 mg, 2.9 mmol) in CH_2Cl_2 (30 mL) at −78 °C was added a 1.0 M solution of DIBAL-H in hexane (5.8 mL, 5.8 mmol) over a period of 2 h. The reaction was stirred at −78 °C until TLC analysis showed the complete consumption of starting material.[28] The solution was diluted with ether (20 mL) and with 0.5 M Rochelle's salt (50 mL). The resulting mixture was stirred vigorously until the complete separation of phases (1 h). The organic layer was washed with saturated aqueous NaCl (10 mL), dried over $MgSO_4$, and concentrated under reduced pressure. The residue was filtered on a short plug of silica gel (15% EtOAc/hexane) and concentrated under reduced pressure to afford the desired primary alcohol (640 mg, 84%). This clear oil was dissolved in CH_2Cl_2 (25 mL) and cooled to 0 °C, and 2,6-lutidine (400 μL, 3.66 mmol) and TIPSOTf (787 μL, 2.93 mmol) were added. The ice bath was removed, and when TLC analysis showed the complete consumption of starting material the reaction was diluted with ether (30 mL) and H_2O (2 mL). The organic layer was washed with 10% aqueous HCl (3 × 10 mL), saturated aqueous $NaHCO_3$ (10 mL), and saturated aqueous NaCl (10 mL). The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure The residue was chromatographed on silica gel (2% EtOAc/hexane) to afford the desired silyl ether **26** (1.02 g, 100%) as a clear oil. The silyl ether **26** (116.7 mg, 0.28 mmol) was dissolved in ether (2.8 mL), and the solution was cooled at 0 °C. A 1.4 M solution of MeLi in ether (800 μL, 1.12 mmol) was added over a period of 8 h (1 equiv/2 h). When TLC analysis showed the complete consumption of starting material the reaction was diluted with ether (5 mL) and quenched with saturated aqueous NH_4Cl (1 mL). The resulting mixture was poured into ether (10 mL) and H_2O (10 mL). The aqueous layer was extracted with ether (2 × 5 mL), and the combined organic layers were washed with saturated aqueous NaCl (10 mL), dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by flash chromatography (6% EtOAc/hexane) to afford the monoprotected diol **1b** (61.2 mg, 80%): R_f 0.3 (10% EtOAc/hexane); ^1H NMR (300 MHz, $CDCl_3$) δ 5.48 (t, J = 7 Hz, 1H), 4.31 (s, 2H), 4.25 (s, 2H), 2.55 (s (br), 1H), 2.11 (qn, J = 8 Hz, 2H), 1.09 (m, 21H), 0.98 (t, J = 8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.1, 131.0, 68.6, 60.0, 20.6, 17.9, 14.2, 11.8; IR (neat) 3400 (br), 2940, 2860, 1460, 1110, 1050, 1000, 870, 670 cm^{-1}; HRMS calcd for $C_{15}H_{32}O_2Si$ + H 273.2251, found 273.2250.

(28) The addition of an excess of DIBAL-H may result in the cleavage of mesitoate ester. However, if TLC analysis showed no more progress of the reaction *without* any trace of diol, an extra amount of DIBAL-H could be added by carefully monitoring for the appearance of the diol.

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Supporting Information Available: Copies of the ^1H and ^{13}C NMR spectra of new compounds and the ORTEP structures of compounds **8d** and **22** (32 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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