Palladium(II)-Catalyzed S_N2' Reactions of α-Allenic Acetates. Stereoconvergent Synthesis of (*Z*,*E*)-2-Bromo-1,3-dienes

Attila Horváth and Jan-E. Bäckvall*

Department of Organic Chemistry, Arrhenius Laboratory, Stockholm University, SE-106 91, Stockholm, Sweden

Jeb@organ.su.se

Received July 19, 2001

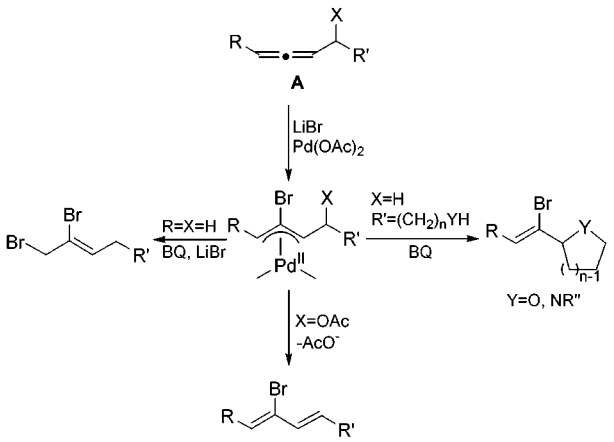
The reaction of acetylated α-allenic alcohols with LiBr in the presence of 1.5 mol % of $Pd(OAc)_2$ provides easy access to substituted (*Z*,*E*)-2-bromo-1,3-dienes in good yields with excellent diastereoselectivity. Both secondary and tertiary acetates as well as terminal and nonterminal allenes were studied to investigate the scope and the limitations of the reaction. A mechanism is proposed to clarify how a diastereomeric mixture of the starting compound is transformed into a single diastereomer of the product.

Introduction

Palladium-catalyzed reactions of allenes represent a large and dynamically growing field of organometallic chemistry.[1,2] Most of these reactions are known to proceed via a (π-allyl)palladium intermediate. We are particularly interested in the chemistry of 2-bromo-substituted (π-allyl)palladium complexes. These complexes can be formed via the reaction of an allene, bromide ion, and palladium(II) (Scheme 1), and in certain cases they are stable enough to be isolated.[3] Depending on the substitution pattern of the allene in the presence of *p*-benzoquinone (BQ), the (π-allyl)palladium complex can react to give either dibrominated[4] or heterocyclic products.[3] During the work on 1,2-oxidations of allenes, we observed that α-acetoxy allenes (**A**, X = OAc, Scheme 1) react without benzoquinone to give substituted 2-bromo-1,3-dienes as elimination products. In this paper we report on a highly stereoselective synthesis of 2-bromo-1,3-dienes from α-acetoxy allenes and lithium bromide via a palladium(II)-catalyzed S_N2' reaction.

2-Bromo-1,3-dienes are useful compounds in organic synthesis. For example, they are viable coupling reagents for introducing a diene moiety into more complex molecules,[5,6] and they have been used in Diels−Alder reactions where the bromide acts as a sterically directing group that can be easily removed or replaced after the reaction.[7−11] A palladium(0)-catalyzed reaction of 2-bromo-1,3-dienes to give optically active allenes was also reported recently.[12]

Scheme 1. Versatile Utilization of the Bromo Substituted (π-Allyl)palladium Complex



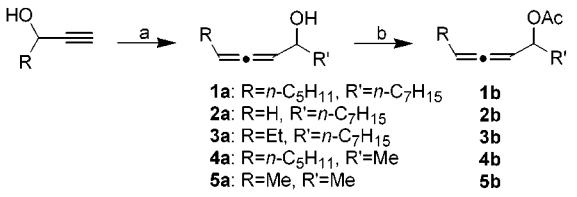
Most previous syntheses of 2-bromo-1,3-dienes have involved coupling reactions.[13−15] Roush et al. reported a synthesis of (*Z*,*E*)-2-bromo-1,3-dienes[13] based on a palladium(0)-catalyzed cross-coupling of 1,1-dibromo olefins and vinylboronic acid derivatives under basic conditions. Dibromo olefins having an allylic alkoxy group afforded the coupling products selectively and in good yields, but olefins lacking the allylic alkoxy group gave the desired products only in moderate (43−61%) yields. Other cross-coupling reactions such as Stille[14] and Negishi[15] couplings were also applied to the synthesis of 2-bromo-1,3-dienes. These reactions, however, proceeded with poor diastereoselectivity or were applied only to the synthesis of dienes with one terminal double bond.

Tsirk et al. prepared tertiary amines containing the (*Z*,*E*)-2-bromo-1,3-diene moiety via an amine-induced

(1) Hashmi, A. S. K. *Angew. Chem., Int. Ed.* **2000**, *39*, 3590.
(2) Zimmer, R.; Dinesh, C. U.; Nandanan, E.; Khan, F. A. *Chem. Rev. (Washington, D.C.)* **2000**, *100*, 3067.
(3) Jonasson, C.; Horváth, A.; Bäckvall, J.-E. *J. Am. Chem. Soc.* **2000**, *122*, 9600.
(4) Bäckvall, J.-E.; Jonasson, C. *Tetrahedron Lett.* **1997**, *38*, 291.
(5) Johnson, W. S.; Telfer, S. J.; Cheng, S.; Schubert, U. *J. Am. Chem. Soc.* **1987**, *109*, 2517.
(6) Schreiber, S. L.; Kiessling, L. L. *J. Am. Chem. Soc.* **1988**, *110*, 631.
(7) Abe, H.; Aoyagi, S.; Kibayashi, C. *J. Am. Chem. Soc.* **2000**, *122*, 4583.
(8) Roush, W. R.; Koyama, K.; Curtin, M. L.; Moriarty, K. J. *J. Am. Chem. Soc.* **1996**, *118*, 7502.
(9) Roush, W. R.; Riva, R. *J. Org. Chem.* **1988**, *53*, 710.
(10) Parker, K. A.; Iqbal, T. *J. Org. Chem.* **1987**, *52*, 4369.
(11) Tsirk, A.; Gronowitz, S.; Hornfeldt, A. B. *Tetrahedron* **1998**, *54*, 9529.
(12) Ogasawara, M.; Ikeda, H.; Nagano, T.; Hayashi, T. *J. Am. Chem. Soc.* **2001**, *123*, 2089.
(13) Roush, W. R.; Moriarty, K. J.; Brown, B. B. *Tetrahedron Lett.* **1990**, *31*, 6509.
(14) Shen, W.; Wang, L. *J. Org. Chem.* **1999**, *64*, 8873.
(15) Ogasawara, M.; Ikeda, H.; Hayashi, T. *Angew. Chem., Int. Ed.* **2000**, *39*, 1042.

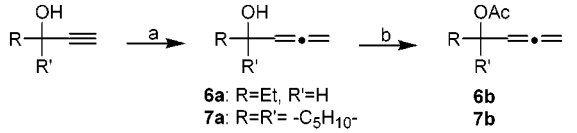
10.1021/jo015950x CCC: $20.00
Published on Web 11/02/2001

Scheme 2[a]



[a] Reagents: (a) 1. 3,4-dihydro-2*H*-pyran; 2. n-BuLi, R′COH; 3. $LiAlH_4$; (b) Ac_2O, pyridine.

Scheme 3[a]



[a] Reagents: (a) 1. Paraformaldehyde, diisopropylamine, CuBr; (b) Ac_2O, pyridine, DMAP.

ring opening of 3-bromo-2,5-dialkylthiophene-1,1-dioxide with either *ω*-unsaturated acyclic amines (28−35% yield) or cyclic amino alcohols (89−91% yield).[11]

Even though several methods exist for the synthesis of substituted 2-bromo-1,3-dienes, as described above, they are either applicable only to a specific group of compounds or give low diastereoselectivity. In this paper we report a more general, simple, and efficient palladium-(II)-catalyzed reaction for the stereoselective synthesis of substituted (*Z*,*E*)-2-bromo-1,3-dienes.

Results and Discussion

Synthesis of Starting Materials. α-Allenic acetates **1b**−**5b** (Scheme 2) were prepared from the corresponding alcohols **1a**−**5a**. The alcohols were synthesized according to a slightly modified procedure reported by Landor et al.[16] (Scheme 2).

Terminal allenes **6b** and **7b** were conveniently prepared via homologation of the corresponding propargyl alcohol according to the procedure reported by Crabbé et al.,[17] followed by acetylation of the α-allenic alcohols (Scheme 3). All the α-acetoxy allenes were stable at room temperature and could be stored for several months without any detectable decomposition.

Palladium-Catalyzed S_N2' Reactions. Acetoxy allene **1b** was added to a solution of lithium bromide and catalytic amount of palladium acetate in a 1:1 mixture of acetic acid and acetone at 40 °C. The initially orange solution of the in situ-formed palladium(II) bromide turns pale yellow after the addition of the allene in a few minutes. When all the allene has reacted, the color changes back to orange due to the reformed palladium-(II) bromide. After workup the bromo-diene **8** was isolated in 85% yield with excellent diastereoselectivity (Table 1, entry 1). Terminal allenes **2b** and **6b** also reacted smoothly and afforded the corresponding dienes **9** and **13**, respectively, in good yields. To determine what steric requirements R and R′ groups have to fulfill, several other acetoxy allenes (**3b**−**5b**) were synthesized and reacted with lithium bromide (Table 1, entries 4−11). Apparently, a methyl group is big enough to induce highly diastereoselective formation of the corresponding product (entry 8, Table 1). The isolated 2-bromo-1,3-dienes could be stored for a couple of days at room temperature, but they polymerized slowly. In a control experiment it was shown that without palladium(II) catalyst there was no conversion of acetoxy allenes **1b**−**6b** to bromo-dienes. For example, when allene **2b** was stirred with lithium bromide in acetic acid at 40 °C, no conversion could be detected after 4 days.

Allenes without an acetoxy group in the α-position are known to undergo oxidative dibromination under similar condition if *p*-benzoquinone is present (Scheme 1).[4] Without benzoquinone and in the presence of a potential leaving group in the allylic position, however, 2-bromo-1,3-dienes are formed (Table 1). To investigate the possibility of dibromination of our substrates, allene **1b** was reacted with lithium bromide in the presence of *p*-benzoquinone and palladium(II) acetate (Scheme 4).

The major product was diene **8** together with its oxidized Diels−Alder adduct with *p*-benzoquinone (**14**), but 12% of the product from the dibromination reaction (**15a**) was also observed. We found that the dibromination is regio- and stereoselective giving rise to a single diastereomer of dibromide **15**. To verify this observation the other, unobserved diastereomer (**15b**) also had to be synthesized. The nonselective reaction of allene **1b** with $CuBr_2$ afforded both *syn*- and *anti*-**15** that could be separated by preparative HPLC. According to the proposed mechanism (Figure 3), the observed diastereomer **15a** should be the anti isomer, but we were unable to make the stereochemical assignment of compounds **15a** and **15b**.

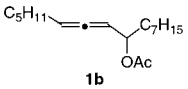
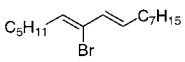
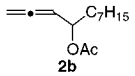
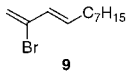
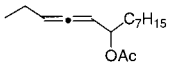
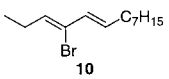
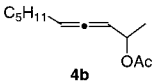
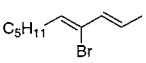
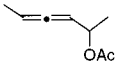
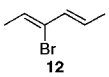
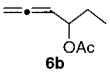
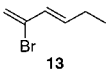
Dienes **12** and **13** were too volatile to be conveniently isolated. Acetoxy allenes **5b** and **6b** were therefore reacted in deuterated solvents, and yields were determined by ^{1}H NMR spectroscopy. During these reactions, we noticed that the reaction times in deuterated solvents (acetic acid-d_4:acetone-d_6 = 1:1 or neat acetic acid-d_4) were about twice as long, indicating a considerable solvent isotope effect. The products could be further reacted in a one-pot Diels−Alder reaction and isolated as their tetracyanoethylene adduct (Scheme 5).

Changing the solvent from a mixture of acetone and acetic acid to neat acetic acid led to a faster but less diastereoselective reaction (method B, Table 1). From the four possible diastereomers, however, only the two shown in Figure 1 are formed. Because the double bond closer to R′ has the *E* stereochemistry in both of the products obtained, the only diastereomer obtained from terminal allenes (R = H) are the *E*-dienes (entries 3, 12, and 13, Table 1). The stereochemistry of the products were assigned on the basis of the coupling constants between protons H_a and H_b (^3J = 14.5−14.7 Hz) clearly indicating a trans relationship and by the NOE measurements (Figure 1). In the case of nonterminal dienes **8** and **10**−**12** the signals of protons H_a and H_b did not separate in deuterated chloroform; therefore, benzene-d_6 was used to determine the coupling constants and the NOE (Figure 1).

Allenes bearing a tertiary acetoxy group also reacted with lithium halides in an S_N2' fashion (Scheme 6). In contrast to the secondary acetoxy compounds these reactions also worked without the palladium catalyst, and only when bromide was used as nucleophile could a 4-fold acceleration with $Pd(OAc)_2$ be detected. The mod-

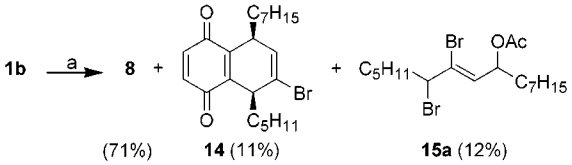
(16) Cowie, J. S.; Landor, P. D.; Landor, S. R. *J. Chem. Soc., Perkin Trans.* **1973**, 720.
(17) Crabbe, P.; Fillion, H.; Andre, D.; Luche, J. L. *J. Chem. Soc., Chem. Commun.* **1979**, 859.

Table 1. Palladium-Catalyzed S_N2' Reaction of α-Allenic Acetates

Entry	α-Allenic-acetate	Product[a]	Method[b]	Yield[c] (%)	Diastereo-selectivity[d]	Reaction time (h)
1	 **1b**	 **8**	A	85	98	25
2			B	85	91	9
3	 **2b**	 **9**	B	79	>99	4
4	 **3b**	 **10**	A	88	98	26
5			B	86	91	13
6	 **4b**	 **11**	A	84	97	25
7			B	84	86	12
8	 **5b**	 **12**	A	n.d.	97	20
9			A[e]	91[d]	96	40
10			B	n.d.	92	19
11			B[e]	94[d]	91	40
12	 **6b**	 **13**	B	n.d.	>99	6
13			B[e]	77[d]	>99	14

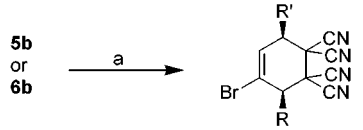
[a] Only the major diastereomer is shown. [b] The reaction was carried out in the presence of 1.5% $Pd(OAc)_2$ and 2.5 equiv of LiBr at 40 °C in acetic acid/acetone 1:1 mixture (method A) or in acetic acid (method B). [c] Isolated yield unless otherwise noted; n.d. = not determined. [d] Determined by ^1H NMR. [e] Reactions were carried out in deuterated solvents.

Scheme 4[a]



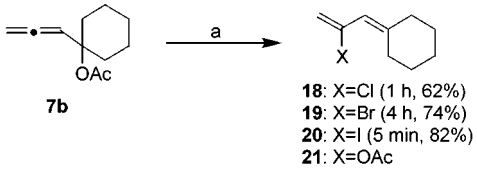
[a] Reagents and condition: (a) 2.5 equiv of LiBr, 2.5 equiv of *p*-benzoquinone, 5% $Pd(OAc)_2$ in acetic acid at 40 °C; yields were determined by HPLC using naphthalene as internal standard.

Scheme 5[a]



[a] Reagents: (a) 1. 2.5 equiv of LiBr, 1.5% $Pd(OAc)_2$ in acetic acid at 40 °C; 2. 2 equiv of tetracyanoethylene; numbers in brackets refer to isolated yields.

Scheme 6[a]



[a] Reagents: (a) 2.5 equiv of lithium halide in acetic acid at 40 °C; numbers in brackets refer to reaction times and isolated yields.

erate yield with chloride as nucleophile is due to the competing acid-catalyzed rearrangement reaction to form diene **21**.[18]

Mechanism and Stereochemistry. The palladium-(II)-catalyzed reactions of allenes with bromide proceed via a 2-bromo-(π-allyl)palladium complex (Figure 2).

First, palladium coordinates to either of the two double bonds and then the bromide attacks the middle allene

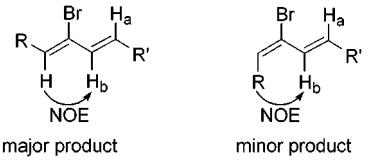


Figure 1. Stereochemical assignments of the products.

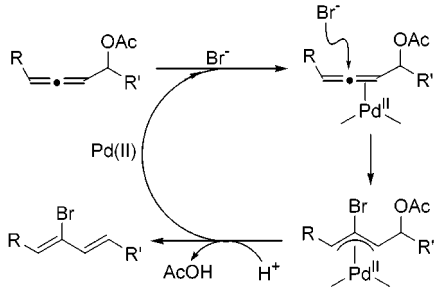


Figure 2. Proposed mechanism for the palladium-catalyzed S_N2' reaction.

carbon. A σ-allyl complex is initially formed, which rapidly equilibrates to the π-allyl complex. Finally, an acid-catalyzed elimination of the acetoxy group and palladium(II) gives the 2-bromo-1,3-diene derivative. To account for the strongly preferred formation of only one diastereomer several possibilities has to be considered.

It was shown that under certain conditions palladium catalyzes the cis−trans isomerization of alkenes.[19−21] In our case the simplest explanation of the observed high diastereoselectivity would be the isomerization of the products to the thermodynamically most stable (*Z*,*E*)-diene. To investigate this possibility (*E*,*E*)-4-bromo-2,4-decadiene (**22**), the minor product from the reaction of

(18) Olsson, L. I.; Claesson, A.; Bogentoft, C. *Acta Chem. Scand.* **1973**, *27*, 1629.
(19) Schwarz, I.; Braun, M. *Chem. Eur. J.* **1999**, *5*, 2300.
(20) Henry, P. M. *J. Am. Chem. Soc.* **1971**, *93*, 3547.
(21) Cramer, R.; Lindsey, R. V., Jr. *J. Am. Chem. Soc.* **1966**, *88*, 3534.

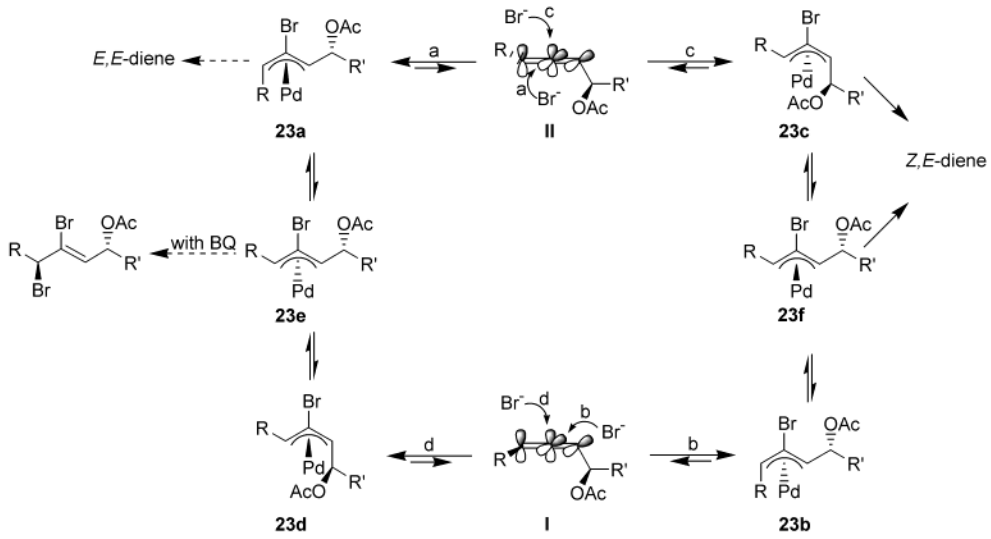


Figure 3. Proposed mechanism for the stereoselective formation of (*Z*,*E*)-2-bromo-1,3-dienes. The coordinated palladium is omitted from the structures of the allenes, and only the enantiomers with (*R*) central chirality are indicated for clarity. In each case palladium is coordinated to the opposite face of the double bond that is attacked by the bromide.

allene **4b**, was isolated and stirred in acetic acid in the presence of lithium bromide and palladium acetate at 40 °C. No isomerization could be detected after 2 days. Furthermore, when the least diastereoselective reaction of allene **5b** was over (entry 11, Table 1) acetone-d_6 was added to the solution. A slight enhancement of the diastereoselectivity was expected because reactions in mixture of acetone and acetic acid show higher preference to the (*Z*,*E*)-diene. No isomerization of the product occurred after 2 days. The possibility of product isomerization was therefore excluded.

All nonterminal allenes (i.e. **1b** and **3b**−**5b**) used as starting materials were mixtures of diastereomers (**I** and **II**, Figure 3). After coordination of palladium to either double bond the middle allenic carbon could be attacked by bromide from four directions. These directions are perpendicular to the plane of the double bond which palladium is coordinated to. Two of these attacks are cis to one of the allylic carbons and therefore kinetically unfavored. The other two possibilities are (1) attack on the double bond closer to the acetoxy group from the direction trans to the R group (routes a and b, Figure 3) and (2) attack on the other double bond from the direction trans to the C(OAc)R′ group (routes c and d, Figure 3).

The formed π-allyl complexes **23a**−**d** (Figure 3) then isomerize to the thermodynamically more stable syn,syn complexes (**23e** and **23f**) via an η^3-η^1-η^3-rearrangement. This isomerization is faster than the product formation because only small amount of (*E*,*E*)-diene is formed in the reaction. The next step is elimination of the acetoxy group and palladium(II) which is only possible if they are in anti position. Only three of the (π-allyl)palladium complexes fulfill this requirement, two of them (**23c** and **23f**) form the product, the third (**23a**) leads to the observed byproduct. The elimination is acid-catalyzed, i.e., the rate is slower in acetic acid−acetone mixture than in pure acetic acid. This was used to inhibit the formation of the nondesired diastereomer. If the final elimination step is slow, then the initially formed (π-allyl)palladium complex (**23a**) has enough time to isomerize to the more stable syn,syn complexes (**23e** and **23f**) and the product is formed with a higher diastereomeric ratio (method A and B, Table 1).

As a consequence, the proposed mechanism requires that the two diastereomers of the allene are in equilibrium during the reaction. To show that this equilibrium exists, the pure diastereomers of α-acetoxy allene **1b** were isolated and reacted separately with lithium bromide according to method B (Table 1). Both diastereomers (**1b′** and **1b″**) isomerized during the reaction and formed about 8% of the other diastereomer.

This result clearly shows that the formation of the (π-allyl)palladium complex from allene, bromide ion, and palladium(II) is reversible. Furthermore we found that one diastereomer (**1b′**) reacted slower than the other diastereomer (**1b′**:**1b″** = 0.6:1). When starting from the faster reacting diastereomer **1b″** after 96% conversion, we observed that the reaction mixture contained more **1b′** than **1b″**, which resulted in a decreased reaction rate toward the end of the reaction. These observations are in good agreement with the different reaction rates and the isomerization of the starting allene.

Knowing about the possibility of starting material isomerization an alternative route would be that the slower reacting diastereomer **1b′** isomerizes to **1b″** and the product is only formed from **1b″**. In this case, however, an induction period would be expected in one of the reactions, but this was not observed. Both diastereomers of the starting allene can therefore form the product without the need for a preceding isomerization. If both routes b and c are possible, then routes a and d (Figure 3) cannot be excluded either because they represent attack of the nucleophile from the same direction as b and c, respectively, but on the other diastereomer. This means that during the reaction a certain amount of catalyst is in the nonreactive syn,syn form **23e**. It has to reform the allene before it can be transformed to the product. If terminal allenes are used (R = H, Figure 3) they do not contain axial chirality and the mechanism is more simple. All the intermediate (π-allyl)palladium complexes can form the (*E*)-diene either directly or after an η^3-η^1-η^3-rearrangement. This results in a faster reaction for terminal allenes (entries 3 and 12, Table 1).

Synthetic Utility. The (*Z*,*E*)-2-bromo-1,3-dienes obtained should be useful for the synthesis of stereodefined products via Diels−Alder and coupling reactions. After

a Diels−Alder cycloaddition the vinylic bromide can be further functionalized via metal-catalyzed cross-coupling reactions. The recent observation that 2-bromo-1,3-dienes can be transformed into optically active allenes also opens up a useful desymmetrization of allenes starting from α-acetoxy allenes.

Conclusions

An efficient palladium(II)-catalyzed synthesis of substituted (*Z*,*E*)-2-bromo-1,3-dienes has been developed. Formally, the reaction is an S_N2' substitution; however, the products are formed with excellent diastereoselectivity even when the substituents on the formed diene are small. The high diastereomeric purity of these bromodienes makes them attractive for stereoselective organic syntheses. A mechanism was proposed that account for the stereoconvergence of the reaction. The following observations are in good agreement with the proposed mechanism: (1) isomerization of the starting allene during the reaction; (2) expected stereochemistry of the product and byproducts; (3) enhanced reaction rate when terminal allenes were used; (4) better selectivity and longer reaction time in less acidic solvent; (5) significant solvent isotope effect. The reaction of the allene containing a tertiary acetoxy group proceeds at comparable rate without catalyst; therefore, it is not expected to be stereoselective.

Experimental Section

General Methods. Diethyl ether and THF were distilled from sodium benzophenone ketyl; dioxane was dried with CaH_2 and then with $LiAlH_4$ and distilled from sodium. All other reagents and solvents were used without further purification. ^{1}H NMR (400 or 300 MHz) and ^{13}C NMR (100 or 75 MHz) were recorded on a Varian Mercury spectrometer using the residual peak of chloroform-*d* (7.26 ppm for ^{1}H and 77 ppm for ^{13}C) as internal standard. IR spectra were recorded on a Perkin-Elmer 1600 FT-IR instrument using neat films or KBr pellets of the samples, and only the strongest or structurally most important peeks are listed. Mass spectra were recorded on a ThermoQuest GCQ plus GLC-MS instrument using electron ionization (EI). Preparative HPLC was performed on a Bischoff liquid chromatograph using Kromasil 100 SIL 5 μm (250 × 20 mm) column. Analytical HPLC was performed on a Waters liquid chromatograph using μ Porasil (300 × 3.9) column. Elemental analysis was performed by Analitische Laboratorien, Lindlar, Germany. Melting points are uncorrected. Merck silica 60 (240−400 mesh) was used for column chromatography, and analytical TLC was performed on Merck precoated silica 60-F_{254} plates.

General Procedure for the Preparation of α-Allenic Alcohols 1a−5a. 3,4-Decadien-2-ol (4a).[22] To a stirred mixture of 1-octyn-3-ol (0.988 g, 7.83 mmol) and 3,4-dihydro-2*H*-pyran (0.659 g, 7.83 mmol) was added a catalytic amount of HCl gas. The reaction mixture was stirred until it cooled to room temperature, 11 mL of dry THF was added, and it was cooled to 0 °C. n-BuLi (7.3 mL, 1.6 M in hexane) was added dropwise, and the resulting yellow solution was stirred for 1.5 h before acetaldehyde (0.345 g, 7.83 mmol) was slowly added. The mixture was stirred for 4 h at 0 °C, quenched with water, and extracted three times with ether. The combined organic solutions were washed with water and brine and dried over Na_2SO_4. Most of the ether was evaporated, and the resulting 5-(tetrahydro-2*H*-2-pyranyloxy)-3-decyn-2-ol was added dropwise to a suspension of $LiAlH_4$ (0.327 g, 8.61 mmol) in diethyl ether (18 mL). The mixture was refluxed for 4 h, quenched with the minimum amount of water, and filtered through Celite. The solid residue was washed four times with ether, and then the solvent was evaporated. Column chromatography (pentane/ethyl acetate 7:1) afforded **4a** (0.708 g, 4.59 mmol) in 59% yield, pale yellow oil. Pure samples of the diastereomers were obtained by preparative HPLC (pentane/ethyl acetate 2:1). IR (neat, cm^{-1}) 3327, 1963. **4a′**: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.27 (m, 2H), 4.31 (br s, 1H), 2.02 (m, 2H), 1.67 (s, 1H), 1.41 (m, 2H), 1.30 (m, 4H), 1.29 (d, *J* = 6.4 Hz, 3H), 0.88 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 201.6, 96.9, 94.6, 65.9, 91.3, 28.8, 28.7, 23.4, 22.4, 14.0. **4a″**: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.27 (m, 2H), 4.32 (app pentet d, *J* = 6.1, 2.5 Hz, 1H), 2.01 (m, 2H), 1.69 (s, 1H), 1.40 (m, 2H), 1.30 (m, 4H), 1.29 (d, *J* = 6.3 Hz, 3H), 0.88 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 201.7, 96.9, 94.4, 66.2, 31.3, 28.75, 28.66, 23.4, 22.4, 14.0.

General Procedure for the Preparation of Acetylated α-Allenic Alcohols 1b−5b. 1-Methyl-2,3-nonadienyl Acetate (4b). Allenic alcohol **4a** (0.650 g, 4.21 mmol), acetic anhydride (0.79 mL, 8.42 mmol), and pyridine (0.32 mL, 3.91 mmol) were stirred overnight. Column chromatography (pentane/diethyl ether 9:1) of the crude reaction mixture afforded **4b** (0.779 g, 3.97 mmol) in 94% yield as colorless oil. Pure samples of the diastereomers were obtained by preparative HPLC (pentane/diethyl ether 98:2). IR (neat, cm^{-1}) 1956, 1741, 1370, 1238, 1044. **4b′**: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.33 (qdd, *J* = 6.4, 5.7, 2.3 Hz, 1H), 5.26 (qd, *J* = 6.5, 2.3 Hz, 1H), 5.23 (app pentet d, *J* = 3.1, 5.7 Hz, 1H), 2.02 (s, 3H), 1.99 (ddd, *J* = 7.7, 6.7, 3.1 Hz, 2H), 1.39 (m, 2H), 1.31 (d, *J* = 6.4 Hz, 3H), 1.28 (m, 4H), 0.87 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 203.7, 170.3, 94.1, 92.6, 68.6, 31.3, 28.6, 28.4, 22.4, 21.3, 19.6, 14.0. **4b″**: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.33 (qdd, *J* = 6.4, 2.3, 0.5, Hz, 1H), 5.28 (qd, *J* = 6.4, 2.3 Hz, 1H), 5.22 (app heptet, *J* = 3.0 Hz, 1H), 2.03 (s, 3H), 1.99 (ddd, *J* = 7.8, 6.7, 3.0 Hz, 2H), 1.39 (m, 2H), 1.31 (d, *J* = 6.4 Hz, 3H), 1.30 (m, 4H), 0.88 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 203.5, 170.4, 94.1, 92.7, 68.7, 31.2, 28.7, 28.4, 22.4, 21.3, 19.8, 14.0. Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. Found: C, 73.63; H, 10.17.

General Procedure for the Preparation of Acetoxy Allenes 6b and 7b. 1-Propadienylcyclohexyl Acetate (7b). Following a slight modification of the procedure of Crabbe et al.,[17] 1-ethynylcyclohexanol (2.97 g, 23.9 mmol), paraformaldehyde (1.15 g, 38.2 mmol), cuprous bromide (1.72 g, 12.0 mmol), and diisopropylamine (4.05 mL, 28.7 mmol) were refluxed in dry dioxane (160 mL) overnight. The dioxane was carefully evaporated, and water was added to the residue. Extraction with diethyl ether and evaporation of the solvent gave 1-propadienylcyclohexanol[23] (**7a**) that was used without further purification. Acetic anhydride (4.51 mL, 47.8 mmol), pyridine (1.79 mL, 22.2 mmol), and DMAP (0.292 g, 2.39 mmol) were added to the alcohol, and the mixture was stirred at 40 °C overnight. Column chromatography (pentane/ether 95:5) of the crude mixture afforded **7b** (3.07 g, 17.0 mmol) in 71% overall yield, colorless oil: IR (neat, cm^{-1}) 1954, 1735, 1367, 1232; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.59 (t, *J* = 6.8 Hz, 1H), 4.80 (d, *J* = 6.8 Hz, 2H), 2.04 (m, 2H), 1.96 (s, 3H), 1.65 (m, 2H), 1.47 (m, 5H), 1.30 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 207.6, 169.8, 95.4, 80.5, 77.5, 35.2 (2H), 25.2 (2H), 22.1, 22.0. Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 73.12; H, 8.93.

General Procedure for the Preparation of Dienes 8−13 and 18−20. (6*Z*,8*E*)-7-Bromo-6,8-hexadecadiene (8). Allene **1b** (94.30 mg, 0.336 mmol) was added to a solution of $Pd(OAc)_2$ (1.13 mg, 0.00504 mmol) and LiBr (72.85 mg, 0.841 mmol) in 3.4 mL of acetic acid/acetone 1:1 mixture (method A) or in acetic acid (method B). The solution was stirred at 40 °C until it turned to orange (9 h in this case). Water and pentane were added, and the aqueous phase was extracted twice with pentane. The combined organic extracts were washed with water, sat. $NaHCO_3$, and brine and dried over Na_2SO_4. Evaporation of the solvent followed by flash chromatography (pentane/ether 9:1) afforded **8** (86.4 mg, 0.287 mmol) in 85% yield, pale yellow liquid: IR (neat, cm^{-1}) 1647, 1612,

(22) Cherkezishvili, K. I.; Gverdtsimeli, I. M.; Taktakishvili, M. O. *Zh. Obshch. Khim.* **1976**, *46*, 1297.

(23) For ^{1}H NMR, see: Claesson, A.; Bogentoft, C. *Acta Chem. Scand.* **1972**, *26*, 2540.

1466, 950; ^{1}H NMR ($CDCl_3$, 400 MHz) δ ^{1}H NMR (C_6D_6, 400 MHz) δ 6.23 (dt, J = 14.6, 7.2 Hz, 1H), 5.97 (d, J = 14.6 Hz, 1H), 5.64 (t, J = 7.1 Hz, 1H), 2.28 (app q, J = 7.1 Hz, 2H), 2.04 (app q, J = 7.2 Hz, 2H), 1.36−1.17 (m, 16H), 0.89 (t, J = 7.1 Hz, 3H), 0.84 (t, J = 6.9 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 134.8, 132.0, 129.1, 125.4, 32.2, 31.8, 31.44, 31.40, 29.3, 29.20, 29.16, 28.1, 22.7, 22.5, 14.1, 14.0. Anal. Calcd for $C_{16}H_{29}$-Br: C, 63.78; H, 9.70. Found: C, 64.01; H, 9.80.

(3*E*)-2-Bromo-1,3-undecadiene (9). Prepared from allene **2b** (101.77 mg, 0.484 mmol) following the general procedure (method B). After flash chromatography (pentane/ether 9:1), the title compound was isolated in 79% yield (88.34 mg, 0.382 mmol), colorless liquid: IR (neat, cm^{-1}) 1647, 1587, 1466, 953, 872; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.10 (dt, J = 14.7, 6.7 Hz, 1H), 6.01 (d, J = 14.7 Hz, 1H), 5.69 (s, 1H), 5.51 (s, 1H), 2.17 (dt, J = 6.7, 7.0 Hz, 2H), 1.43 (m, 2H), 1.29 (m, 8H), 0.89 (t, J = 6.9 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 138.8, 130.2, 128.2, 117.5, 32.1, 31.8, 29.2, 29.1, 29.0, 22.6, 14.1.

(3*Z*,5*E*)-4-Bromo-3,5-tridecadiene (10). Prepared from allene **3b** (84.24 mg, 0.353 mmol) following the general procedure (method A). After flash chromatography (pentane/ether 9:1), the title compound was isolated in 88% yield (80.80 mg, 0.312 mmol), colorless liquid: IR (neat, cm^{-1}) 1648, 1613, 1458, 950; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.02 (m, 2H), 5.83 (t, J = 7.0 Hz, 1H), 2.30 (app pent., J = 7.4 Hz, 2H), 2.15 (m, 2H), 1.42 (m, 2H), 1.29(m, 8H), 1.04 (t, J = 7.6 Hz, 3H), 0.89 (t, J = 6.9 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 134.9, 133.3, 129.0, 124.8, 32.2, 31.8, 29.3, 29.20, 29.16, 24.9, 22.7, 14.1, 12.9. Anal. Calcd for $C_{13}H_{23}Br$: C, 60.23; H, 8.94. Found: C, 60.42; H, 8.93.

(2*E*,4*Z*)-4-Bromo-2,4-decadiene (11). Prepared from allene **4b** (97.97 mg, 0.499 mmol) following the general procedure (method A). After flash chromatography (pentane/ether 9:1) the title compound was isolated in 84% yield (91.44 mg, 0.421 mmol), colorless liquid: IR (neat, cm^{-1}) 1652, 1614, 1447, 948; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.04 (m, 2H), 5.82 (t, J = 7.1 Hz, 1H), 2.28 (app q, J = 7.1 Hz, 2H), 1.82 (m, 3H), 1.43 (m, 2H), 1.32 (m, 4H), 0.90 (t, J = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 131.8, 130.4, 129.2, 125.0, 31.4, 31.3, 28.2, 22.5, 17.4, 14.0.

(2*Z*,4*E*)-3-Bromo-2,4-hexadiene (12). Prepared from allene **5b** following the general procedure (method B). After extraction with pentane and drying with Na_2SO_4, the solvent was carefully evaporated via a distillation column at normal pressure. IR (neat, cm^{-1}) 1744, 1448, 948; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.04 (m, 2H), 5.88 (q, J = 6.7 Hz, 1H), 1.85 (br d, J = 6.7 Hz, 3H), 1.82 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 130.3, 129.1, 126.5, 126.1, 17.5, 17.0.

(3*E*)-2-Bromo-1,3-hexadiene (13).[24] Prepared from allene **6b** following the general procedure (method B). Pure samples of the title compound were obtained after careful distillation. IR (neat, cm^{-1}) 1624, 1459, 842; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.15 (dt, J = 14.8, 6.3 Hz, 1H), 6.01 (br d, J = 14.8 Hz, 1H), 5.70 (br s, 1H), 5.52 (br s, 1H), 2.20 (app br pentet, J = 7.3 Hz, 2H), 1.06 (t, J = 7.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 140.0, 130.2, 127.4, 117.6, 25.1, 13.2.

6-Bromo-5-heptyl-8-pentyl-1,4,5,8-tetrahydro-1,4-naphthalenedione (14). Obtained as a byproduct from the reaction of allene **1b** (23.50 mg, 0.0838 mmol) with LiBr (18.18 mg, 0.209 mmol) and *p*-benzoquinone (22.64 mg, 0.209 mmol) in the presence of $Pd(OAc)_2$ (0.94 mg, 0.0042 mmol) in acetic acid (0.35 mL) at 40 °C. Pure samples of the title compound was obtained by preparative HPLC (pentane/diethyl ether 95:5); yellow liquid: IR (neat, cm^{-1}) 1655, 843; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.72 (s, 2H), 6.28 (d, J = 5.2 Hz, 1H), 3.68 (dt, J = 3.8, 5.0 Hz, 1H), 3.42 (ddt, J = 9.3, 5.2, 3.8 Hz, 1H), 1.77 (m, 2H), 1.44 (m, 2H), 1.27 (m, 16H), 0.88 (t, J = 6.8 Hz, 3H), 0.85 (t, J = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 186.2, 186.0, 143.1, 142.1, 136.5, 136.4, 130.1, 123.7, 42.5, 38.1, 36.8, 33.2, 31.8 (2C), 29.5, 29.1, 27.5, 25.9, 22.6, 22.4, 14.1, 14.0. EIMS *m*/*z* 408 (^{81}Br, 25.7), 406 (^{79}Br, 24.2), 338 (^{81}Br, 36.3), 336 (^{79}Br, 36.4), 327 (70.7), 239 (^{81}Br, 100), 237 (^{79}Br, 83.2). Anal. Calcd for $C_{22}H_{31}BrO_2$: C, 64.86; H, 7.67. Found: C, 65.02; H, 7.70.

(*Z*)-3,4-Dibromo-1-heptyl-2-nonenyl Acetate (15). 15a obtained as a byproduct from the same reaction as compound **14**. **15b** was isolated from the reaction of allene **1b** with 3 equiv of $CuBr_2$ in acetonitrile. Pure samples of **15a** and **15b** were obtained by preparative HPLC (pentane/diethyl ether 95:5), pale yellow liquid: IR (neat, cm^{-1}) 1744, 1370, 1233. **15a**: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.03 (d, J = 7.8 Hz, 1H), 5.52 (dt, J = 6.0, 7.5 Hz, 1H), 4.56 (t, J = 7.3 Hz, 1H), 2.04 (m, 2H), 2.03 (s, 3H), 1.70 (m, 1H), 1.61 (m, 1H), 1.30 (m, 16H), 0.88 (t, J = 6.9 Hz, 3H), 0.87 (t, J = 6.9 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.0, 131.2, 130.4, 73.8, 57.6, 37.8, 33.3, 31.7, 30.9, 29.3, 29.1, 26.9, 24.7, 22.6, 22.3, 21.0, 14.1, 13.9. EIMS *m*/*z* 361 (^{81}Br, 48.0), 359 (^{79}Br, 48.3), 319 (^{81}Br, 98.6), 317 (^{79}Br, 100), 301 (^{81}Br, 17.9), 299 (^{79}Br, 16.5), 237 (35.7), 219 (63.2). **15b**: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.05 (d, J = 7.9 Hz, 1H), 5.56 (dt, J = 7.9, 6.5 Hz, 1H), 4.54 (t, J = 7.4 Hz, 1H), 2.05 (s, 3H), 2.02 (m, 2H), 1.69 (m, 1H), 1.59 (m, 1H), 1.29 (m, 16H), 0.89 (t, J = 6.7 Hz, 3H), 0.87 (t, J = 6.7 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 169.7, 130.9, 130.0, 73.6, 57.3, 38.3, 33.7, 31.8, 31.0, 29.4, 29.2, 27.2, 24.8, 22.7, 22.5, 21.2, 14.2, 14.0. EIMS *m*/*z* 361 (^{81}Br, 50.8), 359 (^{79}Br, 51.0), 319 (^{81}Br, 99.3), 317 (^{79}Br, 100), 301 (^{81}Br, 14.8), 299 (^{79}Br, 15.3), 237 (37.8), 219 (57.7). Anal. Calcd for $C_{18}H_{32}Br_2O_2$: C, 49.11; H, 7.33. Found: C, 49.27; H, 7.42.

General Procedure for the Preparation of Compound 16 and 17. 5-Bromo-3-ethyl-4-cyclohexene-1,1,2,2-tetracarbonitrile (17). Prepared from allene **6b** (89.12 mg, 0.636 mmol) following the general procedure (method B). After the reaction was over, tetracyanoethylene (162.8 mg, 1.27 mmol) was added to the orange solution and stirring was continued overnight. The reaction mixture was extracted with dichloromethane, the combined extracts was washed with sat. $NaHCO_3$ and brine and dried over Na_2SO_4, and the solvent was evaporated. Column chromatography (pentane/ethyl acetate 2:1) afforded **17** (127.4 mg, 0.441 mmol) in 69% yield, white crystal: Mp: 136−139 °C; IR (KBr, cm^{-1}) 3082, 2257, 1657, 1426, 864; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.21 (dd, J = 1.9, 3.7 Hz, 1H), 3.46 (ddd, J = 18.4, 3.3, 2.1 Hz, 1H), 3.38 (ddd, J = 18.4, 2.2, 1.6 Hz, 1H), 2.97 (m, 1H), 2.05 (dqd, J = 13.6, 7.4, 4.2 Hz, 1H), 1.76 (ddq, J = 13.6, 10.5, 7.4 Hz, 1H), 1.24 (t, J = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 126.5, 113.6, 110.6, 109.9, 109.6, 108.3, 44.6, 43.1, 39.43, 39.39, 24.6, 11.0. Anal. Calcd for $C_{12}H_9BrN_4$: C, 49.85; H, 3.14; N, 19.38. Found: C, 49.88; H, 3.29; N, 19.28.

***syn*-4-Bromo-3,6-dimethyl-4-cyclohexene-1,1,2,2-tetracarbonitrile (16).** Prepared from allene **5b** (94.12 mg, 0.671 mmol) following the general procedure. Column chromatography (pentane/ethyl acetate 7:1) followed by crystallization from cyclohexane afforded **16** (133.5 mg, 0.462 mmol) in 69% yield, white crystal: Mp: 90−91 °C; IR (KBr, cm^{-1}) 3081, 2257, 1654, 1449, 867; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.10 (dd, J = 2.7, 1.7 Hz, 1H), 3.37 (qdd, J = 7.4, 1.2, 1.7 Hz, 1H), 3.26 (qdd, J = 7.2, 2.7, 2.1 Hz, 1H), 1.83 (d, J = 7.4 Hz, 3H), 1.61 (d, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 128.2, 120.8, 110.9, 110.7, 109.6, 109.2, 43.4, 43.0, 41.5, 38.8, 17.1, 17.0. Anal. Calcd for $C_{12}H_9BrN_4$: C, 49.85; H, 3.14; N, 19.38. Found: C, 49.95; H, 3.12; N, 19.50.

(1-Chloro-2-propenylidene)cyclohexane (18). Prepared from allene **7b** (107.09 mg, 0.594 mmol) following the general procedure (method B). After flash chromatography (pentane/ether 9:1), the title compound was isolated in 62% yield (57.9 mg, 0.370 mmol), colorless liquid: IR (neat, cm^{-1}) 1647, 1617, 1448, 878, 843; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.64 (app hextett, J = 1.3 Hz, 1H), 5.35 (d, J = 1.1 Hz, 1H), 5.12 (dd, J = 1.3, 1.1 Hz, 1H), 2.39 (m, 2H), 2.15 (m, 2H), 1.63−1.53 (m, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 147.0, 136.7, 120.1, 114.3, 37.0, 29.7, 28.3, 27.2, 26.4. Anal. Calcd for $C_9H_{13}Cl$: C, 69.00; H, 8.36. Found: C, 69.21; H, 8.48.

(1-Bromo-2-propenylidene)cyclohexane (19). Prepared from allene **7b** (117.80 mg, 0.654 mmol) following the general procedure (method B). After flash chromatography (pentane/ether 9:1), the title compound was isolated in 74% yield (96.9 mg, 0.482 mmol), yellow liquid: IR (neat, cm^{-1}) 1645, 1610,

(24) Grimaldi, J.; Cozzone, A.; Bertrand, M. *Bull. Soc. Chim. Fr.* **1967**, 2723.

1447, 884, 843; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.74 (m, 1H), 5.59 (dd, J = 1.4, 0.5 Hz, 1H), 5.51 (app. t, J = 1.4 Hz, 1H), 2.36 (m, 2H), 2.14 (m, 2H), 1.65−150 (m, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 146.5, 127.2, 122.3, 118.6, 36.7, 29.6, 28.3, 27.8, 26.4.

(1-Iodo-2-propenylidene)cyclohexane (20). Prepared from allene **7b** (86.21 mg, 0.478 mmol) following the general procedure. After flash chromatography (pentane/ether 9:1), the title compound was isolated in 82% yield (97.1 mg, 0.391 mmol), violet liquid: IR (neat, cm^{-1}) 1639, 1606, 1446, 892, 843; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.89 (dd, J = 1.7, 1.2 Hz, 1H), 5.86 (app. t, J = 1.2 Hz, 1H), 5.83 (m, 1H), 2.32 (m, 2H), 2.11 (m, 2H), 1.60−1.51 (m, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 144.8, 127.2, 126.7, 103.4, 36.4, 29.4, 28.3, 27.7, 26.5. EIMS *m*/*z* 248 (1.1), 121 (75.1), 93 (100).

1-(Cyclohexylidenmethyl)vinyl Acetate (21). Obtained as a byproduct from the reaction of allene **7b** with LiCl. IR (neat, cm^{-1}) 1758, 1448, 1370, 1019; The ^{1}H NMR spectra is in accordance to that previously reported;[18] ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.0, 151.7, 147.2, 116.0, 104.5, 37.6, 29.9, 28.4, 27.6, 26.4, 21.0.

(2*E*,4*E*)-4-Bromo-2,4-decadiene (22) Prepared from allene **4b** following the general procedure (method B). After flash chromatography (pentane/ether 9:1), the title compound was separated from **11** by preparative HPLC (pentane/ether 98:2), colorless liquid. IR (neat, cm^{-1}) 1647, 1447, 947; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.26 (dm, J = 14.5 Hz, 1H), 6.13 (ddq, J = 14.5, 0.4, 6.6 Hz, 1H), 5.92 (tq, J = 7.8, 0.7 Hz, 1H), 2.19 (app q, J = 7.5 Hz, 2H), 1.86 (ddd, J = 6.6, 1.5, 0.7 Hz, 3H), 1.41 (m, 2H), 1.30 (m, 4H), 0.89 (t, J = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 133.4, 132.7, 124.8, 121.2, 31.3, 29.5, 28.9, 22.5, 17.9, 14.0.

Acknowledgment. Financial support from the Swedish Foundation for Strategic Research and the Swedish Natural Science Research Council is gratefully acknowledged.

Supporting Information Available: A more detailed discussion about the mechanism; characterization of compounds **1a**−**3a**, **5a**, **1b**−**3b**, **5b**, and **6b**; ^{1}H NMR and ^{13}C NMR spectra of compounds **1a**, **1b**, **3a**−**5a**, **3b**−**7b**, **8**−**11**, **13**−**22**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO015950X