Carboindation of Carbon−Carbon Triple Bonds: Regioselective Indium-Mediated Allylation of Functionalized Alkynes and Transformation into Halogen-Substituted 1,4-Dienes

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By examining the allylindation of a series of substituted alkynes, the relationships between allylindation reactivity and alkyne structure were systematically investigated. While terminal alkynes with protected hydroxyl groups gave the corresponding allylated branched 1,4-dienes (Markovnikov products) within 5−6 h, the unprotected alkynols reacted markedly faster, requiring only 2−4 h of ultrasonication in THF to produce the 1,4-dienols in good yields. In the latter reactions, the regioisomeric outcome was found to depend on the distance between the hydroxyl group and the alkyne moiety: propargylic substrates gave linear 1,4-dienes (anti-Markovnikov products), suggesting the involvement of bicyclic "chelation-controlled" transition state, while 4-pentynol and higher homologues exclusively afforded the branched 1,4-dienes. Moreover, the proposed vinylic α,α-bis-indium intermediates from both protected and unprotected substrates were successfully quenched with *N*-bromosuccinimide (NBS) and *N*-iodosuccinimide (NIS) to form tri- and tetrasubstituted dienes in good yields. Taken as a whole, these results illustrate the remarkable stability of the allylindium and vinylindium intermediates despite the presence of protic functionalities in the reaction mixture.

Introduction

Indium-mediated reactions have gained increasing popularity over the past decade as a useful tool in organic synthesis under environmentally benign conditions.[1,2] A particularly important synthetic development involves the stereoselective reaction of allylindium reagents with functionalized carbonyl compounds under aqueous conditions.[3] Using this approach, carbon−carbon bonds can be formed with high stereocontrol via the intermediacy of cyclic chelated transition states that deserve particular consideration when unprotected heterosubstituted aldehydes or ketones (e.g., carbohydrates) are employed as substrates.[2−4]

Other beneficial uses of allylindium reagents have been described.[5] The reactivity of allylindium reagents toward carbon−carbon triple bonds, however, has garnered comparably little attention. It has been demonstrated, for example, that the indium-mediated allylation of alkynes ("carboindation") offers useful advantages over analogous carbometalations.[6] In particular, unprotected terminal alkynols serve as useful substrates for allylindiation reactions as long as the supporting hydroxyl functionality is positioned sufficiently near the alkyne moiety (i.e., in the α- or *β*-position).[7] Furthermore, unfunctionalized terminal alkynes or protected alkynols undergo efficient allylindation under mild conditions.[8]

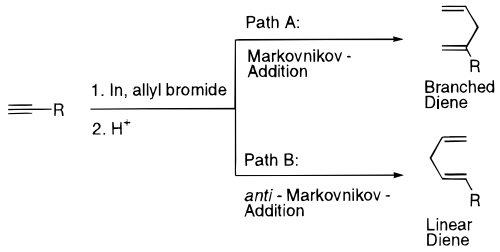

Figure 1. Regiocontrolled allylindation reactions result in the formation of either linear (L) or branched (B) 1,4-dienes. Markovnikow/*anti*-Markovnikow regioselectivity is due to steric, electronic, or chelation control.

The regioselective outcome is dictated by the structure of the alkyne, where the presence of a neighboring coordinating functional group can lead to the formation of linear rather than branched 1,4-dienes (see Figure 1). In these reactions, only *E* isomers are formed, which is consistent with a pathway involving syn addition. A plausible rationalization for these observations was provided by Araki and co-workers,[9] who proposed a bicyclic chelated transition state in which the indium

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(1) (a) Li, C.-J. *Chem. Rev.* **1993**, *93*, 2023. (b) Li, C.-J. *Tetrahedron* **1996**, *52*, 5643. (c) Paquette, L. A. In *Green Chemistry: Frontiers in Benign Chemical Synthesis and Processing*; Anastas, P., Williamson, T., Eds.; Oxford University Press: New York, 1998.

(2) For the regeneration of indium metal by electrolysis, see: Prenner, R. H.; Binder, W. H.; Schmid, W. *Liebigs Ann. Chem.* **1994**, 73.

(3) (a) Li, C.-J.; Chan, T. H. *Tetrahedron Lett.* **1991**, *32*, 7017. (b) Kim, E.; Gordon, D. M.; Schmid, W.; Whitesides, G. M. *J. Org. Chem.* **1993**, *58*, 5500. (c) Chan, T.-H.; Lee, M.-C. *J. Org. Chem.* **1995**, *60*, 4228. (d) Marshall, J. A. *Chemtracts−Org. Chem.* **1997**, *10*, 481.

(4) (a) Binder, W. H.; Prenner, R. H.; Schmid, W. *Tetrahedron* **1994**, *50*, 749. (b) Paquette, L. A.; Mitzel, T. M. *Tetrahedron Lett.* **1995**, *36*, 6863. (c) Paquette, L. A.; Mitzel, T. M. *J. Am. Chem. Soc.* **1996**, *118*, 1931.

(5) (a) Cintas, P. *Synlett* **1995**, 1087. (b) Hashmi, A. S. *J. Prakt. Chem.* **1998**, *340*, 84. (c) Araki, S.; Nakano, H.; Subburaj, K.; Hirashita, T.; Shibutani, K.; Yamamura, H.; Kawai, M.; Butsugan, Y. *Tetrahedron Lett.* **1998**, *39*, 6327 and references cited therein.

(6) For reviews, see: (a) Normant, J. F.; Alexakis, A. *Synthesis* **1981**, 841. (b) Oppolzer, W. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 38. (c) Knochel, P. Carbometalation of Alkenes and Alkynes. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: New York, 1991; Vol. 4, pp 865−911.

(7) Araki, S.; Imai, A.; Shimizu, K.; Butsugan, Y. *Tetrahedron Lett.* **1992**, *33*, 2581.

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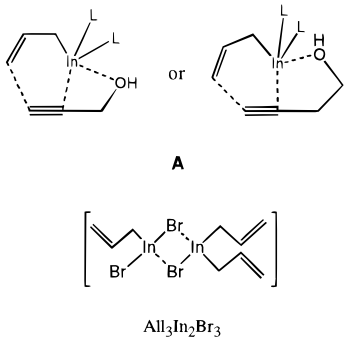
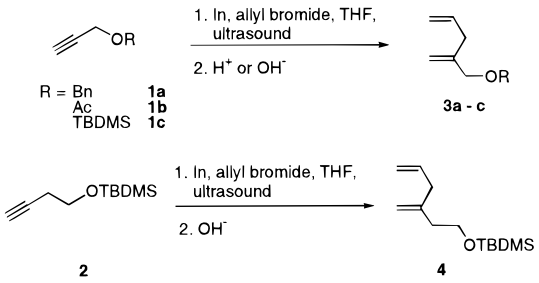


Figure 2. (A) Proposed bicyclic transition state for the chelation-controlled allylindation of propargylic alcohol. The indium atom would be accommodated into a four- or five-membered ring. (B) In situ formed allylindium compound ("indium sesquibromide") under Barbier conditions.

Scheme 1



atom occupies a bridgehead position (Figure 2A). Consequently, the addition reaction proceeds with an orientation that gives anti-Markovnikov allylation products. In the absence of a chelated transition state, however, the allylindation proceeds with Markovnikov regioselectivity to form branched rather than linear 1,4-dienes (Figure 1). Due to specific electronic factors, an exception has been observed with TMS-substituted alkynes.[10]

We report here a systematic exploration of the relationships between alkyne structure and regiocontrol in a series of allylindation reactions. Our studies provide new insight into the mechanistic details of the allylindation process, which offers alternative access to 1,4-dienes in a synthetically useful manner. We further demonstrate that the reaction of vinylic indium intermediates with electrophilic halogen reagents can be used as a versatile method for the preparation of vinylic halides and α,α-dihaloalkenes.

Results and Discussion

To provide a general measure of the efficiency of the allylindation reaction, differently protected alkynols (**1a**−**c**, **2**) were prepared and used for allylation under Barbier-type conditions (Scheme 1), which involve the in situ formed indium sesquihalide (Figure 2B).[11] In a standard procedure, 2 mmol of the alkyne and 16 mmol of allyl bromide were dissolved in 2 mL of dry THF. Indium (shot) was freshly cut into small pieces (3 mmol) and added to the solution, followed by sonication for several hours. The use of excess allyl bromide (5−8 equiv) led to optimized yields and short reaction times.[8] Aqueous workup was conducted either under acidic or basic conditions (concentrated or dilute HCl or 1 M NaOH, respectively). For efficient acidic quenching of the allylindiation product, the addition of TMSCl prior to extraction with dilute HCl proved to be beneficial.[12]

Table 1. Allylindation of Protected Terminal Alkynols (Quenching with H^+)[a]

entry	alkyne	time, h	conditions	product (yield, %)[b]	ratio B:L − diene
1[c]	**1a**	6	ultrasound	**3a** (100)	100:0
2[d]	**1a**	28	rt	**3a** (25)	100:0
3	**1b**	6	ultrasound	**3b** (67)	95:5
4[d]	**1b**	24	rt	**3b** (64)	88:12
5	**1c**	6	ultrasound	**3c** (84)	100:0
6[d,e]	**1c**	24	rt	**3c** (66)	100:0
7[e]	**2**	5	ultrasound	**4** (100)	100:0

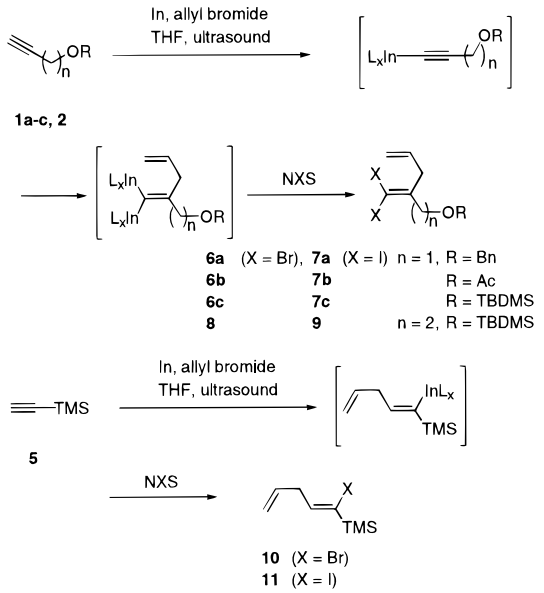
[a] The reactions were performed with 2 mmol of alkyne, 3 mmol In, and 16 mmol of allyl bromide in 2 mL of THF. Acidic workup was done by addition of aqueous HCl. [b] After isolation by silica gel chromatography; combined yield branched (B) + linear (L) − 1,4-diene. [c] Quenching with Me_3SiCl, followed by addition of dilute HCl. [d] 1 mmol of alkyne, 1 mmol In, and 8 mmol of allyl bromide in 2 mL of THF. [e] Basic workup by addition of 1 M NaOH.

The use of ultrasound treatment during the allylindation reactions led to substantially higher yields and shorter reaction times.[13] The results of these experiments are summarized in Table 1. As expected, the exclusive formation of branched 1,4-dienes was observed with a single exception in the case of the acetate-protected substrate **1b** (entries 3 and 4). In the transition state for this reaction, the acetoxy group apparently coordinates weakly to the indium atom (i.e., path B in Figure 1). For the allylindation of benzyl- or TBDMS-protected substrates, however, the reaction proceeds without "chelation control" (i.e., via path A in Figure 1).[14]

While 1,4-dienes can be prepared in fair to excellent yields with allyl bromide as the precursor to the allylindium reagent, we examined the use of substituted allylic bromides to further explore the scope of the reaction. We found that neither prenyl bromide nor 1,3-dibromopropene exhibited any detectable allylindation activity toward the protected alkynols and that 2-substituted allylic systems such as 2,3-dibromoprop-1-ene and ethyl-α-bromomethacrylate afforded only poor yields (3−8%) of the corresponding allylated branched alkenes. Moreover, the latter products contained an additional Br atom attached to the terminal carbon of the newly generated double bond. Along with other side products, such as an α-allylated THF species, these observations suggest the participation of a competing radical mechanism.[15] To summarize these studies, the allylindation of protected terminal alkynols can tolerate a wide variation in the

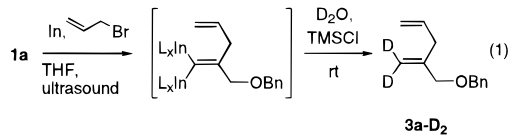
(8) Ranu, B. C.; Majee, A. *J. Chem. Soc., Chem. Commun.* **1997**, 1225.
(9) Araki, S.; Imai, A.; Shimizu, K.; Yamada, M.; Mori, A.; Butsugan, Y. *J. Org. Chem.* **1995**, *60*, 1841.
(10) (a) Fujiwara, N.; Yamamoto, Y. *J. Org. Chem.* **1997**, *62*, 2318. After this paper was submitted, an addional report was published: (b) Fujiwara, N.; Yamamoto, Y. *J. Org. Chem.* **1999**, *64*, 4095.
(11) Araki, S.; Ito, H.; Butsugan, Y. *J. Org. Chem.* **1988**, *53*, 1831.
(12) We interpret the beneficial yields to arise from a loss of chelation upon the addition of TMSCl, which destabilizes the vinylic indium intermediate and thereby facilitates the subsequent aqueous workup. No In−Si interchange was observed.
(13) *Ultrasound: Its Chemical, Physical and Biological Effects*; Suslik, K. S., Ed.; VCH Publishers: New York, 1988.
(14) 1,2-Isopropylidenedioxybut-3-yne was also tested to give 63% of the allylindation product, which was exclusively the branched alkene (characterized by ^1H NMR spectroscopy).
(15) The observation of probable radical pathways in carboindation reactions has been described; see ref 9.

Scheme 2



structure of the alkynol, but the reaction appears limited to allyl bromide as the sole species that can be reliably used to generate a reactive allylindium reagent.

To probe the mechanism of the allylindation of carbon−carbon triple bonds, the reaction of propargyl benzyl ether **1a** was quenched with D_2O (eq 1). The dideuterated diene



3a−d_2 (70% D_2) was isolated, which might suggest the involvement of a vinylic α,α-bis-indium intermediate. It is possible that this intermediate arises via initial indium acetylide formation followed by the addition of 1 equiv of allylindium across the triple bond (compare Scheme 2 for the discussion below).[10] The proposed pathway can be used to rationalize the unique reactivity of terminal alkynes in other related carboindation reactions.[8,9]

The latter results led us to examine the potential reactivity of the proposed vinylic α,α-bis-indium intermediate toward various electrophilic reagents. Indeed, the apparent double substitution of In by Br or I in the allylindation intermediates proceeds in moderate to good yields giving direct access to α,α-dihalo-1,4-dienes **6**−**9** (Scheme 2, Table 2). We found that optimum yields were obtained by adding 2 equiv of N-halosuccinimide at 0 °C; otherwise, the formation of byproducts (e.g., halogenation of the remaining double bond) substantially lowers the yield. Monohalogenated 1,4-dienes were formed in only trace amounts. When adding a substoichiometric quantity (0.95 equiv) of NIS to the allylindated product of **1a**, again double iodination occurred to give the corresponding diiododiene **7a**, but no monoiodination was observed. A small amount of unsubstituted product **3a** was, however, isolated.[16] The examination of other electrophiles (carbon- and silicon-centered) failed to give any substitution products.

(16) The double substitution of carboindation products might proceed by a fast consecutive exchange, possibly via intermediacy of a sterically less crowded haloindium carbenoid.

Table 2. NXS Quenching of Allylindation Products.[a] Synthesis of *gem*-Dihalodienes

entry	alkyne	reaction time, h	X, time of quenching, h	product (yield %)[b]
1	**1a**	6	Br, 0.5	**6a** (75)
2	**1a**	6	I, 17	**7a** (64)
3	**1b**	6	Br, 0.5	**6b** (35)
4	**1b**	6	I, 1	**7b** (48)
5	**1c**	6	Br, 1.5	**6c** (78)
6	**1c**	6	I, 1	**7c** (76)
7	**2**	5	Br, 3	**8** (72)
8	**2**	5	I, 1.5	**9** (60)
9	**5**	5	Br, 1	**10** (67)
10	**5**	5	I, 1	**11** (68)

[a] Standard conditions were applied (2 mmol scale). NXS quenching was done by addition of 4 mmol of NXS and stirring without ultrasound. [b] After purification by column chromatography.

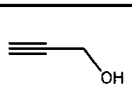
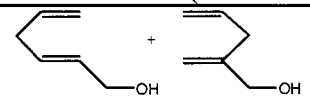
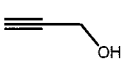
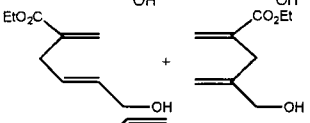
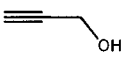
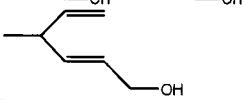
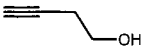
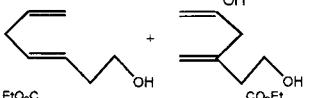
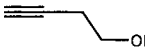
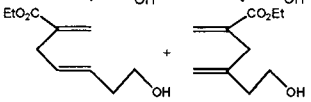
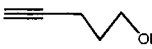
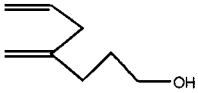
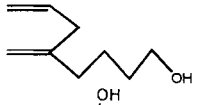
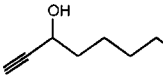
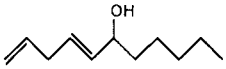
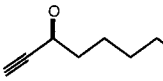
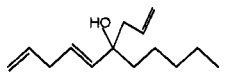
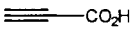
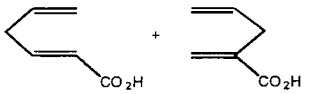
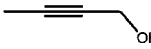
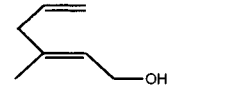
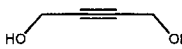
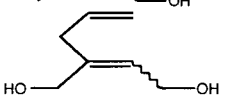
In contrast, the allylindation of TMS-acetylene followed by quenching with NXS afforded the monohalogenated products **10** and **11** (entries 9 and 10 in Table 2). In this reaction, the regioselectivity appears to be governed by electronic factors to give only a monoindated intermediate. There was no halogen quenching found on the β-position, so it is probable that the electron-rich character of the alkyne permits the direct addition of allylindium across the triple bond without requiring initial indium acetylide formation.

Characteristic of indium chemistry is the extraordinary stability of the in situ formed organoindium sesquihalides. In protic media, these stable species are highly reactive and stereoselective in carbonyl addition reactions.[3,4] To make use of these unique features of allylindium compounds, we examined their coupling with alkynes bearing protic functional groups (**12**−**16**, see Table 3). These studies were designed to evaluate the degree of regiocontrol afforded by the presence of functional groups capable of chelating to the indium atom during the allylindation reaction. Since the basicity of the solvent will probably also influence the degree of regiocontrol, we explored the use of solvent mixtures in these studies.[17] The reactions (summarized in Table 3) were carried out as described above using THF as the solvent of choice. Applying water as a cosolvent did not result in product formation, but the use of 10% ethanol in THF was well tolerated. In general, the rates of allylindation were substantially faster with the hydroxyl group of the alkynols left unprotected.[4c] Furthermore, besides allyl bromide (**17a**), substituted allylic bromides can be used in these reactions to give synthetically acceptable yields, i.e., ethyl α-bromomethacrylate (**17b**) and crotyl bromide (**17c**). Table 3 provides an overview of the yields and the regioselectivities obtained. These data show that the principal structural feature governing regioselectivity in the allylindation of alkynols is the distance of the hydroxyl group from the carbon−carbon triple bond (eq 2).[9]

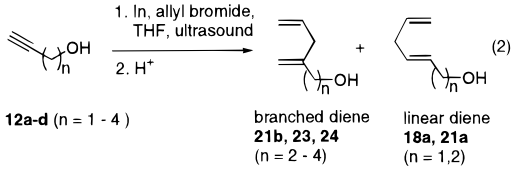
Although the rates of reaction appear relatively unchanged throughout this series, the participation of at least two separate mechanistic pathways is required to rationalize the structures of the products formed. The predominance of the linear 1,4-diene in the case of propargylic alcohol **12a** (entries 1−3 in Table 3) suggests

(17) See, for example, in carbocuprations: Alexakis, A.; Commerçon, A.; Coulentianos, C.; Normant, J. F. *Tetrahedron* **1984**, *40*, 715.

Table 3. Allylindation of Unprotected Alkynols, H^+ Quenching. Synthesis of Branched (B) and Linear (L) 1,4-Dienols[a]

entry	alkyne		Allylic Bromide	time h	products (yield %)[b] : L + B – 1,4-diene (ratio L : B[c])
1		**12a**	**17a**	3.5	 **18a+18b** (97) (> 97 : 3[d])
2[e]		**12a**	**17b**	6.5	 **19a+19b** (79) (95 : 5[f])
3		**12a**	**17c**	5	 **20** (77) (100 : 0[g])
4		**12b**	**17a**	4	 **21a+21b** (92) (39 : 61[h])
5[i]		**12b**	**17b**	6	 **22a+22b** (55) (13 : 87)
6		**12c**	**17a**	4.5	 **23** (75) (0 : 100)
7		**12d**	**17a**	4.5	 **24** (85) (0 : 100)
8[j]		**13a**	**17a**	4	 **25** (85) (100 : 0)
9[k,j]		**13b**	**17a**	6	 **26** (68) (100 : 0)
10		**14**	**17a**	5.5	 **27a+27b** (44) (50 : 50)
11		**15**	**17a**	6	 **28** (53) (100 : 0)
12		**16**	**17a**	6	 **29** (29[l])

[a] Standard conditions were 2 mmol of alkyne, 16 mmol of allylic bromide, 3 mmol In, and 2 mL of THF. Acidic workup by addition of 32% HCl. [b] After isolation by silica gel chromatography. [c] Determined by ^{1}H NMR of the crude product. [d] L:B = 93:7 in 10% EtOH/THF (87% yield). [e] 10 mmol scale of alkyne, 50 mmol bromomethacrylate, 30 mmol In, 20 mL of THF. [f] L:B = 50:50 in ethanolic THF (19% yield). [g] Exclusively γ-addition. [h] Same ratio in 10% EtOH/THF [i] with excess of alkyne: 5 mmol, 1 mmol of bromomethacrylate, 1 mmol In. [j] Basic workup by addition of 1 N NaOH. [k] 2 mmol of alkyne, 18 mmol of allyl bromide, 4 mmol In. [l] *Z*:*E* = 79:21.

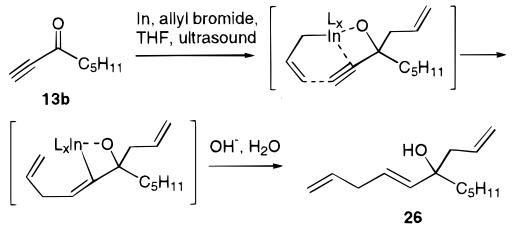


the intermediacy of a bicyclic chelated transition state that affords anti-Markovnikov regiochemistry (see Figures 1 and 2).[18] When the hydroxyl group is positioned far from the alkyne moiety (e.g., γ or more; entries 6 and 7), branched 1,4-dienes were produced in good yields. We propose that these latter reactions also proceed via initial metalation at the acetylenic position followed by allylindation (see the discussion below).

The use of 3-butynol (**12b**) represents the approximate crossover point in the regiocontrol, affording mixtures of regioisomers **21a** and **21b** (entry 4 in Table 3). Comparison of these data to those in entries 1−3 demonstrates that the indium atom can be most readily accommodated into a four-membered rather than a five-membered ring in the bicyclic chelated transition state (Figure 2 A). The carboindation with ethyl α-bromomethacrylate (**17b**, entries 2 and 5) shows both reduced reactivity and reduced regioselectively compared to that with unsubstituted allyl bromide **17a** (entries 1 and 4, respectively). These observations can be rationalized by asserting that chelation in the bicyclic transition state for **17b** is weaker than that for **17a**. Support for this assertion was gained by experiments carried out in 10% ethanolic THF solution: the regioselectivity in the case of indium-mediated addition of **17b** to **12a** (entry 2) drops substantially from a ratio of linear/branched of 95:5 in pure THF to a ratio of 50:50 in the mixed solvent system. These results suggest that ethanol competes effectively with the alkynol for coordination to the indium atom during the reaction. In contrast, the use of a 10% ethanolic THF solvent

(18) Linear 1,4-dienes were found to have the *E* configuration, as a result of syn addition of the organoindium reagent. No *Z*-dienes were detected; see ref 9.

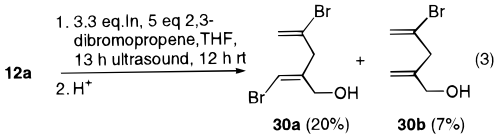
Scheme 3



system in the indium-mediated addition of **17a** to **12a** or **12b** (entries 1 and 4) fails to influence the regiochemical outcome.[19]

Propiolic acid **14** can be subjected to allylindation to give a mixture of regioisomers **27a** and **27b** (entry 10 in Table 3). While the carboxylic acid functionality was tolerated in this reaction, the yield was moderate. The lack of regioselectivity observed here can be interpreted to indicate that "chelation control" versus electronic effects are of the same order of magnitude for this substrate.[20] We further broadened the scope of alkyne carboindation reactions by demonstrating the successful allylindation of internal alkynols (entries 11 and 12). In contrast to previous reports,[8,9] we also find that internal carbon−carbon triple bonds are susceptible to addition of the allylindium reagent,[10b] albeit with low to moderate yields. Allylation of 2-butynol **15** affords exclusively the linear 2,5-dienol **28**, indicating that "chelation control" is also operative in this case. Entry 9 reveals a combination of carbonyl addition and carboindation. Double allylation of the acetylenic ketone **13b** leads to the formation of the tertiary bisallylic alcohol **26** in a "one pot" synthesis, most likely via tandem allylation (see Scheme 3), where the carbonyl moiety reacts prior to the carbon−carbon triple bond, affording "chelation control" and thus formation of the linear 1,4-diene. Basic workup allows isolation of this highly acid-labile compound in good yields.

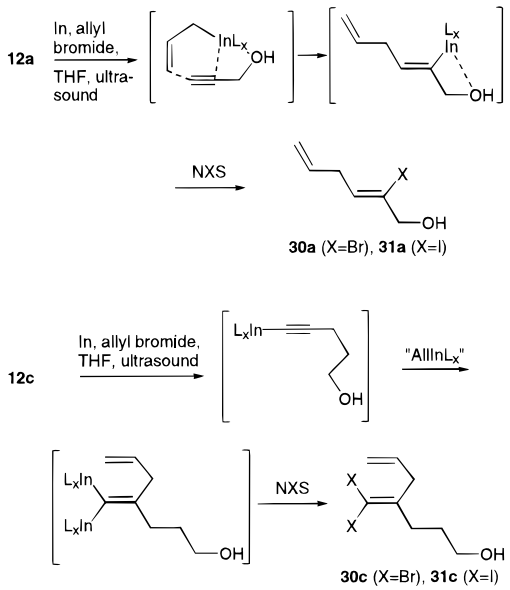
As observed in our studies of the carboindation of protected terminal alkynols described above, the carboindation of protic alkynes also permits little structural variation of the allylic bromide. Although ethyl α-bromomethacrylate (**17b**) as well as crotyl bromide (**17c**) proved to be useful substrates, the use of other electronically (dibromopropenes) or sterically (prenylbromide) demanding substrates gave low yields. When 2,3-dibromo-1-propene, for example, was used in the carboindation of **12a**, addition products were obtained in 27% yield (eq 3). Moreover, isolation of the branched 1,4-diene



(3)

30b as well as the dibrominated product **30a** (up to 20% yield via the anti addition of the allylic bromide with

Scheme 4



Markovnikov regioselectivity) suggests the participation of radical pathways rather than the exclusive action of a concerted metallo-ene pathway (which would be expected to proceed with anti-Markovnikov "chelation-controlled" orientation). No linear 1,4-dienes were detected.

As with the allylindation of protected terminal alkynols, the proposed vinylic indium intermediates appear to be stable during the allylindation of protic alkynes. Quenching of the reaction with NXS gave mono- and dihalogenated allylindation products (see Table 4). This strategy affords a short and efficient "one-pot" preparation of unsaturated bromo- and iodo alcohols bearing a tri- or tetrasubstituted carbon−carbon double bond without having to protect the hydroxyl group. Entries 5−8 in Table 4 demonstrate the convenient preparation of α,α-dibromoalkenes (**31c** and **31d**) and α,α-diiodoalkenes (**32c** and **32d**) in moderate to good yields. Since these carboindations exhibit Markovnikov regiocontrol with dihalogenation as the dominant product, the reaction mechanism is consistent with indium acetylide formation followed by allylindation across the triple bond (Scheme 4) despite the presence of the hydroxyl group in the reaction mixture.

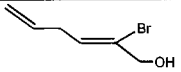
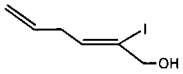
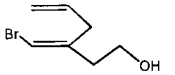
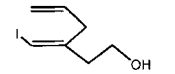
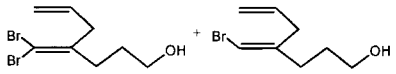
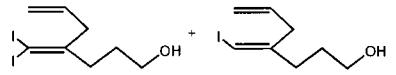
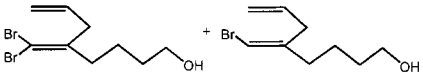
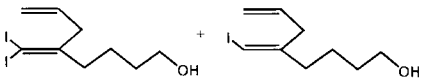
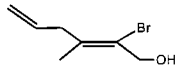
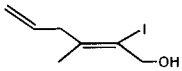
To gain further insight into the mechanistic details, we varied the stoichiometry in the reaction of 4-pentynol **12c** with allyl bromide, which was then quenched by the addition of NBS (see entry 5 in Table 4). When this reaction was repeated using a substoichiometric portion of indium (0.67 equiv, which affords a maximum of 1 equiv of available allyl moieties[21]), allylindation products in 30% combined yield were isolated. Furthermore, all products were either mono- or dibrominated, with the α,α-dibromide **31c** predominating (**31c**, 23%; **33c**, 7%). Assuming that these reactions proceed through indium acetylide intermediates (see Scheme 4), the present results can be interpreted to indicate that the basicity of the indium acetylide intermediates is less than that of any alkoxides that might form during the reaction (via deprotonation of the hydroxyl groups). The results thus provide indirect support for the proposed nonbasic nature of allylindium reagents.[22]

(19) The origin of the differences for **17a** and **17b** might arise from enhanced steric crowding in the bicyclic chelated transition state for **17b** relative to that for **17a**. Alternatively, chelation in the bicyclic transition state for **17b** might be destabilized relative to that for **17a** due to the presence of the electron-withdrawing ester group in **17b**.

(20) Therefore, the carboxylic acid moiety is not as strongly chelating as the hydroxyl moiety in this case, which contrasts the findings in carbonyl addition reactions; see: Bernardelli, P.; Paquette, L. A. *J. Org. Chem.* **1997**, *62*, 8284.

(21) In carbonyl addition reactions only two of three ligands typically react; see ref 11.

Table 4. Allylation of Alkynols. Quenching with NXS:Synthesis of Halogenated Dienols[a]

entry	alkynol	X	products (yield %)[b]
1	**12a**	Br	 **31a** (66)
2	**12a**	I	 **32a** (64)
3	**12b**	Br	 **31b** (47[c])
4	**12b**	I	 **32b** (52[d])
5	**12c**	Br	 **31c+33c** (68 + 9)
6	**12c**	I	 **32c+34c** (64 + 32)
7	**12d**	Br	 **31d+33d** (59 + 33)
8[e]	**12d**	I	 **32d+34d** (46 + 50)
9	**15**	Br	 **35** (46)
10	**15**	I	 **36** (41)

[a] General conditions were as follows: 2 mmol of alkynol, 16 mmol of allyl bromide, 3−4 mmol of In, 2−3 mL of THF, 2−4 h. Quenching was carried out by addition of 2−5 mmol of NXS at 0 °C or room temperature for 0.5−2.5 h. [b] Isolated yields. [c] Smaller amounts of the corresponding geminal dihalogenated B-diene (7%) as well as of the monohalogenated L-diene (10%) were also isolated. [d] Dihalogenated B-diene (6%) and monohalogenated L-diene (6%) also isolated. [e] The products were separated and fully characterized as their corresponding acetates (obtained by standard acetylation of the mixture).

The data in Table 4 also show that substantial monohalogenated allylation products having Markovnikov orientation were isolated (entries 3−8), where the halogen atom is syn to the allyl group. Moreover, while the allylindation and halogenation of propargylic alcohol **12a** (entries 1 and 2) yield the anti-Markovnikov vinylic monohalides **31a** and **32a** as the major products, the analoguous reaction of 3-butynol **12b** (entries 3 and 4) yields the Markovnikov vinylic monohalides **31b** and **32b** as the major products (with the respective monohalogenated linear diene and α,α-dihalodiene as side products).[23] Both substrates exhibit syn addition of allylindium. The fact that no dihalogenated products were found in the allylation of propargylic alcohol **12a** suggests that this "chelation-controlled" allylindation takes place without initial metalation of the terminal acetylenic carbon atom (Scheme 4). This hypothesis is supported by the allylindation of the internal alkyne 2-butynol **15** (entries 9 and 10) in which initial indium acetylide formation is prohibited, but the 1,4-dienes **35** and **36** containing one tetrasubstituted C−C double bond are obtained in yields comparable to those from the analogous allylindation of **12a**.

Conclusion

Our studies of the carboindation of substituted alkynes have further defined the scope and mechanism(s) of this important carbon−carbon bond-forming methodology. Our new facile route for the preparation of 1,4-dienols as well as their halogenated analogues should offer alternative strategies for the preparation of synthetically versatile compounds. Both the presence and position of the hydroxyl group play a central role in governing the yields and distributions of the products (e.g., branched versus linear dienes). Two strategies can be used to strongly influence the nature of the addition of the allylindium reagent to the alkyne moiety: use of a terminal alkyne (which might lead to initial indium acetylide formation) and use of a chelating moiety near the carbon−carbon triple bond. The results strongly suggest that stable vinylic indium intermediates can be generated in these reactions. Moreover, facile halogen substitution can be carried out under mild conditions without having to protect the hydroxyl group. Additionally, the tolerance of alcohols as cosolvents offers new applications for the carboindation reaction. Further studies to clarify the mechanistic principles of this powerful synthetic method are underway.

Experimental Section

General Methods. IR spectra were recorded neat on single-crystal silica plates.[24] ^{1}H and ^{13}C NMR spectra were recorded at 250 or 400 MHz using $CDCl_3$ as internal standard. HRMS experiments were done in the EI mode (70 eV) ($\sigma = \pm 5$ ppm). For analytical HPLC, a 250 × 4 mm Nucleosil column was used, with 2 mL/min flow and UV or RI detection. GC−MS analysis was carried out applying following temperature programm: injection at 40 °C, heating to 70 °C with 10 °C/

(22) Paquette, L. A.; Rothhaar, R. R.; Isaac, M.; Rogers, L.; Rogers, R. D. *J. Org. Chem.* **1998**, *63*, 5463.

(23) A possible fast intramolecular proton transfer (via a six-membered ring) from the hydroxy group to the In-centered carbon would result in "quenching" of the In atom in syn orientation to the hydroxy group.

(24) Mikenda, W. *Vibr. Spectrosc.* **1992**, *3*, 327.

min and to 200 °C with 6 °C/min; a 25 m DB 5 fused silica capillary column was used, with EI detection (70 eV). Ultrasonication was performed in an ultrasound bath. TLC monitoring was done on Merck plates (silica gel F_{254}), compounds were visualized by treatment with a solution of 3% $Ce(SO_4)_2$ in 1 M H_2SO_4, followed by heating. Flash chromatography was performed using Merck silica gel 60 (230−400 mesh). The glassware for the reactions was usually flame dried, and THF was distilled from potassium/benzophenone ketyl under an argon atmosphere. Chemicals and starting materials (alkynols, allylic bromides) as well as Indium (shot, 2−5 mm; 99.9%) were purchased from Aldrich Chemical Co. and were distilled, if necessary, before use. Ethyl α-bromomethacrylate **17b** was prepared following a literature procedure.[25] The protected alkynols **1a**−**c** and **2** were prepared utilizing standard procedures or according to the literature.[26] *N*-Iodosuccinimide was freshly prepared[27] before addition to the reaction mixture and used as a suspension in THF; for NIS quenching and the following workup procedure the exclusion of light was necessary due to the sensibility of the *gem*-diiododiene products.

For the following compounds prepared by different methods as described here analytical data are reported in the literature: **3b**,[28] **10**,[29] **20**,[30] **21a**,[31] **21b**, [32] **27a**,[33] **27b**,[34] and **29**.[35] Compounds **3a** and **18a** were prepared by others applying the indium methodology.[8]

Standard Conditions for Allylindation. Typical Procedure Followed by Acidic Workup (Method A): 5-Methylene-oct-7-en-1-ol (24). To a solution of 2 mmol (196 mg) of 5-hexyn-1-ol (**12d**) in 2 mL of dry THF were added 16 mmol of allyl bromide and 3 mmol of indium (345 mg, freshly cut into small pieces), and the Erlenmeyer flask was put into an ultrasound cleaning bath. TLC monitoring (hexanes/ethyl acetate 3:1, $R_f = 0.31$) showed product formation after 0.5 h, while the metal was rapidly consumed. After 4.5 h of sonication, 1.1 mL of 32% aqueous HCl was added at room temperature (rt), followed by extraction with ether after 30 min. The organic layer was washed with brine, dried over Na_2SO_4, filtered, and evaporated. Silica gel column chromatography (hexanes/ethyl acetate = 6:1) yielded 239 mg (1.71 mmol, 85%) of **24** as a colorless oil. Only the branched diene was detected as allylindation product: IR (neat) 3353, 3078, 2935, 1644, 1434 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.79 (ddt, $J = 17.1$, 10.0, 6.8 Hz, 1H), 5.04 (dq, $J = 17.1$, 1.5 Hz, 1H), 5.02 (dq, $J = 10.0$, 1.0 Hz, 1H), 4.75 (br s, 2H), 3.64 (t, $J = 6.0$ Hz, 2H), 2.74 (d, $J = 7.0$ Hz, 2H), 2.03 (t, $J = 7.3$ Hz, 2H), 1.45−1.62 (m, 4H), 1.29 (br s, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 147.9, 136.4, 116.0, 110.1, 62.9, 40.7, 35.6, 32.4, 23.7; HRMS calcd for $C_9H_{16}O$ (M^+) 140.1201, found 140.1201. Anal. Calcd ($C_9H_{16}O$): C, 77.09; H, 11.50. Found: C, 76.73; H, 11.44.

Typical Procedure Followed by Basic Workup (Method B): 1-(*tert*-Butyldimethylsilyloxy)-3-methylenehex-5-ene (4). To a solution of 2 mmol of TBDMS ether **2** (368 mg) in 2 mL of dry THF were added 16 mmol of allyl bromide and 3 mmol of indium, and the mixture was sonicated for 5 h. TLC (hexanes) showed complete consumption of starting material and clean product formation ($R_f = 0.29$). The reaction mixture was quenched with 1 M aqueous NaOH for 15 min at room temperature, followed by centrifugation of the precipitated In salts. Ether extraction of the residual aqueous phase, washing with brine, drying, and evaporation of the solvent afforded the crude product, which was purified by silica gel chromatography (hexanes) to yield 452 mg (2.0 mmol, 100%) of **4** as a colorless oil: IR (neat) 3080, 2928, 1637 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.79 (ddt, $J = 16.8$, 10.3, 6.8 Hz, 1H), 5.00−5.07 (m, 2H), 4.78 (d, $J = 4.5$ Hz, 2H), 3.69 (t, $J = 7.0$ Hz, 2H), 2.76 (d, $J = 6.5$ Hz, 2H), 2.23 (t, $J = 7.0$ Hz, 2H), 0.87 (s, 9H), 0.03 (s, 6H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 145.3, 136.3, 116.2, 111.7, 62.3, 41.2, 39.2, 25.9, 18.3, −5.3; HRMS calcd for $C_9H_{17}OSi$ ($M^+ - t$-Bu) 169.1048, found 169.1053. Anal. Calcd ($C_{13}H_{26}OSi$): C, 68.96; H, 11.57. Found: C, 68.78; H, 11.62.

Standard Conditions for Allylindation with Subsequent NXS Quenching (Method C). Typical Procedure for Preparation of Geminal Dibromides: 1,1-Dibromo-2-(*tert*-butyldimethylsilyloxymethyl)-penta-1,4-diene (6c). Propargyl *tert*-butyldimethylsilyl ether (**1c**) (2 mmol; 340 mg) was allylindated under standard conditions (see above) by sonication for 6 h. Subsequently, 4 mmol (712 mg) of NBS and 5 mL of THF were added at room temperature. After 90 min (TLC (hexanes) showed clean formation of the product, $R_f = 0.33$), the reaction mixture was diluted with 1 M aqueous HCl, and the product formed was extracted with ether. The organic layer was washed with 10% $KHCO_3$ and concentrated. Silica gel chromatography (hexanes) yielded 577 mg (1.56 mmol, 78%) of pure **6c** as a colorless liquid: IR (neat) 3081, 2955, 1640, 1472 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.75 (ddt, $J = 17.1$, 10.5, 6.5 Hz, 1H), 5.10 (dq, $J = 17.1$, 1.5 Hz, 1H), 5.06 (dq, $J = 10.0$, 1.5 Hz, 1H), 4.26 (s, 2H), 3.12 (dt, $J = 6.5$, 1.3 Hz, 2H), 0.89 (s, 9H), 0.07 (s, 6H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 143.0, 132.8, 116.8, 87.4, 64.4, 37.6, 25.8, 18.3, −5.4; FI-MS $m/z = 369.9$ (M^+); EI-HRMS calcd for ($M^+ - t$-Bu), 310.9103, found 310.9100. Anal. Calcd ($C_{12}H_{22}Br_2OSi$): C, 38.93; H, 5.99, Br, 43.17. Found: C, 39.27, H, 5.81; Br, 42.88.

2-(*tert*-Butyldimethylsilyloxymethyl)penta-1,4-diene (3c). Method B was applied for allylindation of **1c** (2 mmol; 340 mg). The raw material was purified by column chromatography on silica gel (hexanes, 2% ethyl acetate) to yield 356 mg (1.68 mmol, 84%) of **3c** as a colorless, volatile oil: IR 2921, 1654, 1560 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 5.86 (ddt, $J = 16.9$, 10.1, 6.9 Hz, 1H), 5.11 (qt = dtt, $J = 1.8$, 0.9 Hz, 1H), 5.10 (dq, $J = 16.9$, 1.6 Hz, 1H), 5.07 (dq, $J = 10.1$, 1.1 Hz, 1H), 4.89 (dquint = dtt, $J = 2.1$, 1.4 Hz, 1H), 4.10 (ddt, $J = 1.7$, 1.3, 0.5 Hz, 2H), 2.80 (dqq, $J = 6.9$, 1.4, 0.7 Hz, 2H), 0.95 (s, 9H), 0.10 (s, 6H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 147.0, 136.0, 116.2, 109.6, 65.6, 37.3, 25.9, 18.4, −5.4; FD-MS $m/z = 212.2$ (M^+). Anal. Calcd ($C_{12}H_{24}OSi$): C, 67.86; H, 11.39. Found: C, 67.49; H, 11.52.

2-(Benzyloxymethyl)-1,1-dibromopenta-1,4-diene (6a). Method C was applied for allylindation of 2 mmol of **1a**. After 6 h, the reaction mixture was quenched with 4 mmol of NBS at room temperature for 30 min. Dilution with 1 M aqueous HCl and extraction with ether afforded the crude product containing small amounts of monobromo- and unsubstituted allylindation products. Separation by silica gel chromatography (hexanes, 1% ethyl acetate) yielded 522 mg (1.51 mmol, 75%) of pure *gem*-dibromide **6a** as a colorless oil: IR 3030, 2858, 1639, 1454, 1074 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.26−7.37 (m, 5H), 5.76 (ddt, $J = 17.1$, 10.0, 6.8 Hz, 1H), 5.11 (dq, $J = 17.1$, 1.5 Hz, 1H), 5.08 (dq, $J = 10.0$, 1.5 Hz, 1H), 4.48 (s, 2H), 4.17 (s, 2H), 3.14 (dt, $J = 6.7$, 1.5 Hz, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 140.7, 137.8, 132.5, 128.4, 127.8 (2C), 117.3, 90.5, 72.3, 70.7, 38.3; EI-HRMS calcd for M^+ ($C_{13}H_{14}Br_2O$) 343.9412, found 343.9426. Anal. Calcd ($C_{13}H_{14}Br_2O$): C, 45.12; H, 4.09. Found: C, 45.17; H, 4.21.

2-(Benzyloxymethyl)-1,1-diiodopenta-1,4-diene (7a). Method C was applied for allylindation of 1 mmol of **1a**. After 6 h, the reaction mixture was quenched with 2 mmol of NIS (as a suspension in THF) at room temperature, and stirring was continued for 17 h (TLC (hexanes/ethyl acetate = 9:1) showed product formation after already 30 min, $R_f = 0.83$). Extraction and separation by silica gel chromatography (hex-

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anes, 2% ethyl acetate) yielded 281 mg (0.64 mmol, 64%) of the *gem*-diiodide **7a** as a colorless, light-sensitive oil: IR 3028, 2854, 1637, 1453, 1063 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.26−7.37 (m, 5H), 5.74 (ddt, J = 17.1, 10.0, 6.5 Hz, 1H), 5.11 (dq, J = 17.1, 1.5 Hz, 1H), 5.08 (dq, J = 10.0, 1.5 Hz, 1H), 4.49 (s, 2H), 4.13 (s, 2H), 3.15 (dt, J = 6.5, 1.3 Hz, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 150.2, 137.7, 132.5, 128.4, 127.8 (2C), 117.3, 74.1, 72.4, 42.6, 16.6; EI-HRMS calcd for M^+ ($C_{13}H_{14}OI_2$) 439.9134, found 439.9149. Anal. Calcd ($C_{13}H_{14}I_2O$): C, 35.48; H, 3.21. Found: C, 35.35; H, 3.09.

2-(Acetoxymethyl)-1,1-dibromopenta-1,4-diene (6b). Method C was applied for allylindation of 2 mmol (196 mg) of **1b**. After 6 h, the reaction mixture was quenched with 4 mmol of NBS (suspension in THF) at room temperature. Silica gel chromatography (hexanes/ethyl acetate = 10:1) gave 206 mg (0.69 mmol, 35%) of **6b** as a colorless oil: IR 3081, 2930, 1746, 1639, 1437 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.71 (ddt, J = 16.9, 10.4, 6.5 Hz, 1H), 5.10 (dq, J = 17.6, 1.5 Hz, 1H), 5.09 (dq, J = 10.0, 1.5 Hz, 1H), 4.70 (s, 2H), 3.07 (dt, J = 6.5, 1.5 Hz, 2H), 2.06 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 170.4, 138.2, 132.0, 117.5, 92.7, 65.1, 38.8, 20.7; EI-HRMS calcd for M^+ ($C_8H_{10}Br_2O_2$) 295.9048, found 295.9031.

2-(Acetoxymethyl)-1,1-diiodopenta-1,4-diene (7b). Method C was applied for allylindation of 2 mmol of **1b**. After 6 h, 4 mmol of NIS (THF suspension) were added at room temperature. Extraction and silica gel chromatography (hexanes: ethyl acetate = 10:1) afforded 377 mg (0.96 mmol, 48%) of *gem*-diiodide **7b** as a colorless, light-sensitive oil containing small amounts of the corresponding monoiodo-substituted product.: IR 3079, 2978, 1743, 1638, 1432, 1223 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.68 (ddt, J = 16.8, 10.3, 6.5 Hz, 1H), 5.10 (dq, J = 17.1, 1.5 Hz, 1H), 5.09 (dq, J = 10.3, 1.5 Hz, 1H), 4.65 (s, 2H), 3.08 (dt, J = 6.5, 1.5 Hz, 2H), 2.05 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 170.2, 147.5, 131.9, 117.5, 68.3, 43.1, 20.7, 18.8; EI-HRMS calcd for M^+ ($C_8H_{10}I_2O_2$) 391.8770, found 391.8758.

2-(*tert*-Butyldimethylsilyloxymethyl)-1,1-diiodopenta-1,4-diene (7c). Method C was applied for allylindation of 2 mmol of **1c**. After 6 h, 4 mmol of NIS was added at room temperature. Silica gel chromatography (hexanes) of the crude orange oil yielded 701 mg (1.51 mmol, 76%) of pure **7c** as a colorless liquid (light sensitive): IR 3080, 2954, 1638, 1471 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.72 (ddt, J = 17.1, 10.0, 6.5 Hz, 1H), 5.11 (dq, J = 17.1, 1.5 Hz, 1H), 5.07 (dq, J = 10.0, 1.5 Hz, 1H), 4.21 (s, 2H), 3.13 (dt, J = 6.5, 1.5 Hz, 2H), 0.89 (s, 9H), 0.08 (s, 6H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 152.3, 132.8, 116.9, 68.3, 41.9, 25.9, 18.3, 12.7, −5.3; FI-MS: m/z = 463.8 (M^+); EI-HRMS calcd for (M^+ − *t*-Bu), 406.8825, found 406.8820. Anal. Calcd ($C_{12}H_{22}I_2OSi$): C, 31.05; H, 4.78. Found: C, 31.30; H, 4.74.

1-(*tert*-Butyldimethylsilyloxy)-3-(dibromomethylene)-hex-5-ene (8). Method C was applied for allylindation of 2 mmol of **2** (5 h, then addition of 6 mmol of NBS to the reaction mixture at 0 °C). The crude product was purified by silica gel chromatography (hexanes) to yield 553 mg (1.44 mmol, 72%) of **8** as a colorless oil: IR 3082, 2929, 1639, 1472 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.71 (ddt, J = 17.1, 10.0, 6.5 Hz, 1H), 5.09 (dq, J = 17.1, 1.5 Hz, 1H), 5.07 (dq, J = 10.0, 1.5 Hz, 1H), 3.71 (t, J = 6.8 Hz, 2H), 3.05 (dt, J = 6.5, 1.5 Hz, 2H), 2.48 (t, J = 7.0 Hz, 2H), 0.87 (s, 9H), 0.04 (s, 6H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 141.2, 132.8, 117.1, 88.1, 60.4, 41.4, 39.1, 25.9, 18.3, −5.3; HRMS calcd for $C_9H_{15}Br_2OSi$ (M^+ − *t*-Bu) 324.9259, found 324.9260. Anal. Calcd ($C_{13}H_{24}Br_2OSi$): C, 40.64; H, 6.30; Br, 41.59. Found: C, 40.68; H, 6.28; Br, 41.85.

1-(*tert*-Butyldimethylsilyloxy)-3-(diiodomethylene)-hex-5-ene (9). Method C was applied for allylindation of 0.94 mmol of **2** (1.5 mmol of In, 7.5 mmol of allyl bromide, 2 mL of THF). After 5 h, 3.0 equiv of NIS was added to the reaction mixture at 0 °C, and after 30 min the mixture was brought to room temperature. The usual workup procedure (method C), followed by silica gel chromatography (hexanes), afforded derivative **9** together with the *E*- and *Z*-monoiodo compounds and unsubstituted **4**. To purify **9**, a HPLC separation was performed to yield 269 mg (0.56 mmol, 60%; colorless oil): IR 2952, 2932, 2842, 1636 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.69 (ddt, J = 17.1, 10.0, 6.5 Hz, 1H), 5.10 (H-6Z, dq, J = 17.1, 1.5 Hz, 1H), 5.08 (H-6E, dq, J = 10.0, 1.5 Hz, 1H), 3.70 (t, J = 7.0 Hz, 2H), 3.10 (dt, J = 6.0, 1.3 Hz, 2H), 2.53 (t, J = 7.0 Hz, 2H), 0.87 (s, 9H), 0.05 (s, 6H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 151.2, 132.8, 117.2, 60.5, 45.4, 42.8, 26.0, 18.3, 14.3, −5.2; HRMS calcd for $C_9H_{15}I_2OSi$ (M^+ − *t*-Bu) 420.8982, found 420.8970.

1-Iodo-1-trimethylsilylpenta-1(*Z*),4-diene (11). Method C was applied for allylindation of 2 mmol (196 mg) of **5** (4 mmol of In and addition of 1.2 equiv (2.4 mmol) of NIS at 0 °C after 5 h). Purification by silica gel chromatography (hexanes) yielded 363 mg (1.36 mmol, 68%) of **11** as a colorless, light sensitive oil. Only the syn adduct was isolated (determined by NOE experiments): IR 3081, 2958, 1639, 1600 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.13 (t, J = 6.3 Hz, 1H), 5.82 (ddt, J = 17.1, 10.0, 6.5 Hz, 1H), 5.10 (ddt, J = 17.1, 1.5, 1.5 Hz, 1H), 5.05 (dd, J = 10.5, 1.5 Hz, 1H), 2.98 (tt, J = 6.5, 1.5 Hz, 2H), 0.15 (s, 9H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 144.5, 134.2, 116.1, 114.6, 43.2, −1.4; HRMS calcd for $C_8H_{15}ISi$ (M^+) 265.9988, found 265.9990. Anal. Calcd ($C_8H_{15}ISi$): C, 36.10; H, 5.68. Found: C, 36.26; H, 5.57.

Ethyl 6-Hydroxy-2-methylene-hex-4 (*E*)-enoate (19a). A mixture of 10 mmol (560 mg) of **12a**, 50 mmol (9.65 g) of **17b**, and 30 mmol (3.45 g) of indium in 20 mL of THF was sonicated for 6.5 h. Workup followed method A. Silica gel chromatography (hexanes/ethyl acetate = 4:1) yielded 1.27 g (7.44 mmol, 74%) of pure **19a** as a colorless oil. Small amounts of the regioisomeric branched diene **19b** (69 mg, 0.41 mmol, 4%) were also isolated. Data for **19a**: IR 3456, 2984, 1716, 1632 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.16 (s, 1H), 5.74 (dt, J = 15.6, 5.5 Hz, 1H), 5.67 (dt, J = 15.6, 4.5 Hz, 1H), 5.53 (d, J = 1.0 Hz, 1H), 4.19 (q, J = 7.0 Hz, 2H), 4.09 (d, J = 4.0 Hz, 2H), 3.03 (d, J = 5.0 Hz, 2H), 1.52 (br s, 1H), 1.28 (t, J = 7.0 Hz, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 166.9, 139.2, 131.3, 129.1, 125.3, 63.4, 60.7, 34.5, 14.2; EI-HRMS calcd for (M^+) 170.0943, found 170.0950. Anal. Calcd ($C_9H_{14}O_3$): C, 63.51; H, 8.29. Found: C, 63.27; H, 8.07.

Ethyl 2,4-Dimethylene-6-hydroxyhexanoate (22b). A mixture of 1 mmol (193 mg) of **17b**, 5 mmol (350 mg) of **12b**, and 1 mmol (115 mg) of indium in 20 mL of THF was sonicated for 6 h. Workup followed method A. The crude material was purified by silica gel chromatography (hexanes/ethyl acetate = 6:1). A 101 mg (0.55 mmol) portion of the allylindation product was obtained as a mixture of regioisomeres (83:17 in favor to the branched 1,4-diene; not separated) in 55% total yield (colorless oil). **22b**: IR 3401, 2936, 1718, 1631 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.24 (d, J = 1.0 Hz, 1H), 5.58 (d, J = 1.0 Hz, 1H), 4.91 (s, 1H), 4.84 (s, 1H), 4.17 (q, J = 7.0 Hz, 2H), 3.73 (q, J = 5.5 Hz, 2H), 3.01 (s, 2H), 2.29 (t, J = 6.0 Hz, 2H), 1.96 (t, J = 5.0 Hz, 1H), 1.27 (t, J = 7.0 Hz, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 167.1, 143.6, 138.4, 126.7, 113.7, 60.9, 60.4, 39.4, 37.6, 14.1; HRMS calcd for $C_{10}H_{16}O_3$ (M^+) 184.1099, found 184.1104. Data for the minor regioisomer **ethyl 7-hydroxy-2-methylenehept-4(*E*)-enoate (22a)**: determined from the mixture; ^1H NMR (400 MHz, $CDCl_3$) δ 6.14 (s, 1H), 5.55 (m, 1H), 5.53 (d, J = 1.5 Hz, 1H), 5.46 (dt, J = 15.1, 7.5 Hz, 1H), 4.18 (q, J = 7.0 Hz, 2H), 3.62 (t, J = 5.6 Hz, 2H), 3.00 (s, 2H), 2.27 (m, 2H), 1.51 (br s, 1H), 1.27 (t, J = 7.0 Hz, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 130.1, 128.6, 125.1, 61.9, 60.7, 35.9, 35.0, 14.2.

4-Methylenehept-6-en-1-ol (23). Method A was applied for allylindation of 2 mmol (168 mg) of **12c**. Silica gel chromatography (hexanes/ethyl acetate = 6:1) yielded 189 mg (1.50 mmol, 75%) of **23** as a colorless oil: IR 3380, 3079, 2936, 1643, 1434 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.79 (ddt, J = 17.1, 10.0, 6.9 Hz, 1H), 5.03 (dq, J = 17.1, 2.0 Hz, 1H), 5.02 (dq, J = 9.0, 1.0 Hz, 1H), 4.78 (s, 1H), 4.76 (s, 1H), 3.64 (t, J = 6.5 Hz, 2H), 2.76 (d, J = 7.0 Hz, 2H), 2.09 (t, J = 7.5 Hz, 2H), 1.70 (quintett, J = 6.9 Hz, 2H), 1.45 (br s, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 147.7, 136.3, 116.2, 110.3, 62.7, 40.7, 32.1, 30.5; HRMS calcd for $C_8H_{14}O$ (M^+) 126.1044, found 126.1044. Anal. Calcd ($C_8H_{14}O$): C, 76.14; H, 11.18. Found: C, 75.80; H, 11.13.

Undeca-1,4(*E*)-dien-6-ol (25). Method B was applied for allylindation of 2 mmol (252 mg) of oct-1-yn-3-ol (**13a**). Silica gel chromatography (hexanes/ethyl acetate = 20:1) yielded 285

mg (1.70 mmol, 85%) of **25** as a colorless oil: IR 3355, 3080, 2930, 1638 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.78 (ddt, J = 17.1, 10.0, 6.5 Hz, 1H), 5.61 (dt, J = 15.6, 6.5 Hz, 1H), 5.46 (ddt, J = 15.6, 7.0, 1.5 Hz, 1H), 5.00 (dq, J = 17.1, 1.5 Hz, 1H), 4.97 (dq, J = 10.0, 1.5 Hz, 1H), 4.02 (q, J = 6.5 Hz, 1H), 2.75 (dt, J = 6.5, 1.2 Hz, 2H), 1.69 (s, 1H), 1.38−1.56 (m, 2H), 1.20−1.38 (m, 6H), 0.85 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 136.4, 134.3, 129.1, 115.4, 72.9, 37.2, 36.2, 31.7, 25.1, 22.5, 13.9; HRMS calcd for $C_{11}H_{20}O$ (M^+) 168.1514, found 168.1514. Anal. Calcd ($C_{11}H_{20}O$): C, 78.51; H, 11.98. Found: C, 78.48; H, 12.16.

6-(Prop-2-enyl)undeca-1,4(*E*)-dien-6-ol (26). A mixture of 2 mmol (248 mg) of oct-1-yn-3-one (**13b**), 4 mmol of In, and 18 mmol of allyl bromide in 2.5 mL of THF was sonicated for 6 h. Workup was performed following method B. The bis-allylated product **26** was isolated by silica gel chromatography (hexanes, 10% ethyl acetate) yielding 281 mg (1.35 mmol, 68%) as a colorless oil: IR 3448, 3078, 2933, 1639 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.80 (ddt, J = 17.1, 10.5, 6.3 Hz, 1H), 5.70−5.80 (m, 1H), 5.60 (dt, J = 15.6, 6.3 Hz, 1H), 5.45 (dt, J = 15.6, 1.3 Hz, 1H), 5.05−5.13 (m, 2H), 5.01 (dq, J = 17.1, 1.8 Hz, 1H), 4.98 (dq, J = 10.3, 1.5 Hz, 1H), 2.78 (dt, J = 6.3, 1.3 Hz, 2H), 2.29 (dd, J = 13.6, 6.5 Hz, 1H), 2.22 (dd, J = 13.6, 8.5 Hz, 1H), 1.58 (s, 1H), 1.43−1.52 (m, 2H), 1.18−1.35 (m, 6H), 0.85 (t, J = 7.0 Hz, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 136.9, 136.6, 133.8, 126.4, 118.8, 115.2, 74.1, 45.7, 40.9, 36.2, 32.2, 23.1, 22.6, 14.0; HRMS calcd for $C_{14}H_{22}$ ($M^+ - H_2O$) 190.1722, found 190.1722. Anal. Calcd ($C_{14}H_{24}O$): C, 80.71; H, 11.61. Found: C, 80.92; H, 11.68.

Hexa-2(*E*),5-dienoic Acid (27a) and 2-Methylenepent-4-enoic Acid (27b). A mixture of 4 mmol (280 mg) of **14**, 6 mmol (690 mg) of In, and 32 mmol of allyl bromide in 4 mL of THF was sonicated for 5.5 h, quenched with 1 M aqueous HCl, and extracted with ether. The product mixture was separated from less polar byproducts by dissolving in a $NaHCO_3$ solution and washing with ether. After acidification with 1 M HCl and $CHCl_3$ extraction, a 50:50 mixture of pure **27a** and **27b** was obtained as a colorless liquid, 196 mg (1.75 mmol), 44% yield. NMR spectra are in accordance with literature data.[28]

3-Methylhexa-2(*E*),5-dien-1-ol (28). Method A was applied to 4 mmol of **15**. Silica gel chromatography (hexanes/ethyl acetate = 6:1) yielded 238 mg (2.13 mmol, 53%) of **28** as a colorless oil. The assignment of the double-bond geometry was achieved by performing NOE experiments. The compound was obtained in >99% purity, as determined by GC−MS analysis: EI-MS m/z = 112 (M^+); IR 3319, 2940, 1650 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.74 (ddt, J = 17.1, 10.0, 6.8 Hz, 1H), 5.38 (tq, J = 6.8, 1.5 Hz, 1H), 4.97−5.04 (m, 2H), 4.10 (d, J = 7.0 Hz, 2H), 2.70 (d, J = 6.5 Hz, 2H), 1.91 (br s, 1H), 1.62 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 137.8, 136.0, 124.3, 116.2, 59.1, 43.8, 16.1.

2-Bromohexa-2(*Z*),5-dien-1-ol (31a). Method C was applied to 2 mmol of **12a**. A 2 mmol (1 equiv) portion of NBS was added at room temperature after 2 h, which dissolved within 15 min in an exothermic reaction. After 30 min, the resulting pale yellow solution treated as described for method C. The brominated product **31a** was obtained by silica gel chromatography (hexanes/ethyl acetate = 6:1), followed by semipreparative HPLC (hexane, 12% ethyl acetate), to yield 234 mg (1.32 mmol, 66%) as a colorless oil: IR 3351, 3080, 2917, 1640, 1428 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 6.03 (tt, J = 7.0, 1.1 Hz, 1H), 5.78 (ddt, J = 17.1, 10.1, 6.4 Hz, 1H), 5.08 (dq, J = 17.1, 1.7 Hz, 1H), 5.02 (dq, J = 10.1, 1.5 Hz, 1H), 4.24 (br s, 2H), 2.94 (tm, J = 6.6 Hz, 2H), 2.06 (br s, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 134.2, 127.6, 127.5, 116.1, 68.3, 35.0; the Z configuration was determined by performing a NOESY experiment; FI-MS m/z = 175.9 (M^+). Anal. Calcd (C_6H_9BrO): C, 40.71; H, 5.12. Found: C, 40.63; H, 4.93.

2-Iodohexa-2(*Z*),5-dien-1-ol (32a). Method C was applied for 2 mmol of **12a** (after 2 h of sonication, 2 mmol (1 equiv) of NIS was added at room temperature). Silica gel chromatography (hexanes/ethyl acetate = 6:1), followed by semipreparative HPLC (hexane, 7% ethyl acetate) yielded 287 mg (1.28 mmol, 64%) of **32a** as a colorless oil (>99% purity, determined by GC−MS): IR 3350, 3080, 2860, 1638, 1427 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 5.93 (tt, J = 6.9, 1.3 Hz, 1H), 5.78 (ddt, J = 17.1, 10.1, 6.3 Hz, 1H), 5.10 (dq, J = 17.1, 1.7 Hz, 1H), 5.04 (dq, J = 10.1, 1.5 Hz, 1H), 4.25 (d, J = 3.4 Hz, 2H), 2.92 (tm, J = 6.6 Hz, 2H), 1.97 (br t, 1H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 134.0, 133.4, 116.2, 109.2, 71.6, 39.9; the Z configuration was determined by NOE experiments; FI-MS m/e = 223.9 (M^+).

3-((*E*)-Bromomethylene)hex-5-en-1-ol (31b). Method C was applied for allylindation of 2 mmol of **12b** (quenching after 4 h of sonication with 3 mmol of NBS at room temperature). Separation by silica gel chromatography and subsequent HPLC chromatography (hexanes, 20% ethyl acetate) afforded the pure monobrominated product **31b** (minor amounts of the corresponding dibromide (0.14 mmol, 7%) together with the monobrominated linear diene (0.19 mmol, 10%) were also obtained as an unseparable mixture; determined by NMR): 179 mg (0.93 mmol, 47%); colorless oil (HPLC analysis: >99% purity). The E configuration was assigned unambiguously by NOE experiments: IR 3350, 3079, 2930, 1639, 1623, 1434, 1042 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.06 (s, 1H), 5.74 (ddt, J = 17.1, 10.0, 6.5 Hz, 1H), 5.11 (dq, J = 17.1, 1.5 Hz, 1H), 5.07 (dq, J = 10.0, 1.5 Hz, 1H), 3.68 (t, J = 6.3 Hz, 2H), 2.99 (d, J = 6.5 Hz, 2H), 2.35 (td, J = 6.3, 1.0 Hz, 2H), 1.58 (br s, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 139.9, 133.5, 116.9, 104.2, 60.0, 39.0, 37.3; HRMS calcd for $C_7H_{11}BrO$ (M^+) 189.9993, found 189.9990.

3-((*E*)-Iodomethylene)hex-5-en-1-ol (32b). Method C was applied for allylindation of 2 mmol of **12b** (after 4 h of sonication 3 mmol of NIS was added at room temperature). The complex product mixture was separated by silica gel chromatography (hexanes/ethyl acetate/dichloromethane = 4:1:5). The monoiodide **32b** as main product was purified by HPLC chromatography (hexanes, 20% ethyl acetate) to afford 250 mg (1.05 mmol, 52%) as a colorless oil. The E configuration was assigned by NOE experiments: IR 3338, 3078, 2929, 1638, 1608, 1432, 1043 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 6.10 (t, J = 1.1 Hz, 1H), 5.73 (ddt, J = 17.1, 10.1, 6.6 Hz, 1H), 5.13 (dq, J = 17.1, 1.7 Hz, 1H), 5.09 (dq, J = 10.1, 1.5 Hz, 1H), 3.68 (t, J = 6.3 Hz, 2H), 2.99 (dt, J = 6.6, 1.3 Hz, 2H), 2.44 (td, J = 6.3, 1.1 Hz, 2H), 1.53 (br s, 1H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 145.9, 133.5, 117.0, 77.9, 60.2, 41.7, 40.2; HRMS calcd for $C_7H_{11}IO$ (M^+) 237.9854, found 237.9850. Anal. Calcd ($C_7H_{11}IO$): C, 35.32; H, 4.66; I, 53.31. Found: C, 35.38; H, 4.54; I, 53.22.

4-(Dibromomethylene)hept-6-en-1-ol (31c) and 4-((*Z*)-Bromomethylene)hept-6-en-1-ol (33c). Method C was applied to 2 mmol of **12c** (3 h of sonication, followed by addition of 4 mmol (2 equiv) of NBS at room temperature). Silica gel chromatography yielded 385 mg (1.36 mmol, 68%) of the *gem*-dibromide **31c** as a colorless oil: IR 3356, 2938, 1639, 1435 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.72 (ddt, J = 17.1, 10.0, 6.5 Hz, 1H), 5.10 (dq, J = 17.1, 1.5 Hz, 1H), 5.07 (dq, J = 10.0, 1.5 Hz, 1H), 3.63 (t, J = 6.3 Hz, 2H), 3.01 (dt, J = 6.5, 1.5 Hz, 2H), 2.33 (m, 2H), 1.66−1.74 (m, 2H), 1.50 (br s, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 143.1, 132.8, 117.2, 87.1, 62.2, 40.5, 32.5, 29.9; HRMS calcd for $C_8H_{12}Br_2O$ (M^+) 281.9255, found 281.9243. Anal. Calcd ($C_8H_{12}Br_2O$): C, 33.84; H, 4.26; Br, 56.27. Found: C, 34.02; H, 4.18; Br, 56.60. The monobromoproduct **33c** was obtained in minor amounts: 39 mg (0.19 mmol), 9%, colorless oil: ^1H NMR (250 MHz, $CDCl_3$) δ 5.98 (quintet, J = 0.7 Hz, 1H), 5.73 (ddt, J = 17.0, 9.9, 6.6 Hz, 1H), 5.02−5.14 (m, 2H), 3.61 (t, J = 6.4 Hz, 2H), 2.98 (dt, J = 6.6, 1.1 Hz, 2H), 2.19 (dt, J = 7.7, 1.1 Hz, 2H), 1.61−1.73 (m, 2H), 1.48 (br s, 1H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 142.7, 133.7, 116.7, 102.4, 62.1, 37.3, 32.2, 30.3; FI-MS $C_8H_{13}BrO$, found m/z = 204 (M^+); the stereochemical assignment was done by NOE experiments.

4-(Diiodomethylene)hept-6-en-1-ol (32c) and 4-((*Z*)-Iodomethylene)hept-6-en-1-ol (34c). Method C was applied to 2 mmol (168 mg) of **12c** (sonication for 3 h was followed by the addition of 5 mmol of NIS (suspension in THF) at 0 °C and stirring for a further 30 min). The reaction mixture was allowed to reach rt and extracted after a further 2 h. The obtained mixture of the di- and the monobromo compound was separated by silica gel chromatography (hexanes/ethyl acetate = 6:1). **32c**: 482 mg (1.27 mol), 64%; colorless, light-sensitive

oil; IR 3290, 2920, 1634 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.70 (ddt, J = 17.1, 10.0, 6.5 Hz, 1H), 5.11 (dq, J = 17.1, 1.5 Hz, 1H), 5.09 (dq, J = 10.0, 1.5 Hz, 1H), 3.64 (t, J = 6.3 Hz, 2H), 3.07 (dt, J = 6.5, 1.3 Hz, 2H), 2.38 (m, 2H), 1.66−1.74 (m, 2H), 1.57 (br s, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 153.1, 132.8, 117.3, 62.2, 44.4, 36.5, 30.1, 13.2; HRMS calcd for $C_8H_{12}I_2O$ (M^+) 377.8978, found 377.8991. Anal. Calcd ($C_8H_{12}I_2O$): C, 25.42; H, 3.20; I, 67.15. Found: C, 25.58; H, 3.07; I, 67.05. Data for the monosubstituted product **34c**: 164 mg (0.65 mmol), 32%; colorless oil (containing small amounts of **32c**); ^1H NMR (250 MHz, $CDCl_3$) δ 5.99 (br s, 1H), 5.63−5.80 (m, 1H), 5.03−5.15 (m, 2H), 3.60 (t, J = 6.4 Hz, 2H), 2.97 (dt, J = 6.6, 1.4 Hz, 2H), 2.26 (dt, J = 7.8, 1.1 Hz, 2H), 1.61−1.71 (m, 2H), 1.54 (br s, 1H); the stereochemistry was assigned by comparison with the ^1H NMR − data of the homologous hexynol products (**34d** and its corresponding *E* isomer. Diagnostic ^1H shifts are of the bisallylic protons and the halomethyleneproton).

5-(Dibromomethylene)oct-7-en-1-ol (31d) and 5-((*Z*)-Bromomethylene)oct-7-en-1-ol (33d). Method C was applied for allylindation of 2 mmol of **12d**. The obtained mixture of di- and monobromo compounds was separated by silica gel chromatography (hexanes/ethyl acetate = 6:1). **31d**: 354 mg (1.19 mmol, 59%); colorless oil; IR 3353, 3092, 2932, 1645, 1437 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.71 (ddt, J = 16.8, 10.0, 6.5 Hz, 1H), 5.09 (dq, J = 17.1, 1.5 Hz, 1H), 5.07 (dq, J = 10.0, 1.5 Hz, 1H), 3.63 (t, J = 6.3 Hz, 2H), 3.00 (dt, J = 6.5, 1.5 Hz, 2H), 2.27 (t, J = 7.5 Hz, 2H), 1.47−1.62 (m, 4H), 1.42 (br s, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 143.5, 132.9, 117.1, 87.0, 62.5, 40.4, 35.7, 32.2, 23.2; HRMS calcd for $C_9H_{14}Br_2O$ (M^+) 295.9411, found 295.9423. Anal. Calcd ($C_9H_{14}Br_2O$): C, 36.27; H, 4.74; Br, 53.62. Found: C, 35.91; H, 4.77; Br, 53.50. Data for the monobromoproduct **33d**: 145 mg (0.66 mmol, 33%); colorless oil; IR 3360, 3072, 2942, 1649, 1441 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.95 (s, 1H), 5.73 (ddt, J = 17.1, 10.0, 6.5 Hz, 1H), 5.09 (dq, J = 17.1, 1.5 Hz, 1H), 5.04 (dq, J = 10.0, 1.5 Hz, 1H), 3.62 (t, J = 6.0 Hz, 2H), 2.96 (d, J = 6.5 Hz, 2H), 2.12 (t, J = 6.8 Hz, 2H), 1.44−1.57 (m, 4H), 1.35 (br s, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 143.1, 133.8, 116.5, 102.3, 62.6, 37.3, 35.7, 32.1, 23.6; FI-MS $C_9H_{15}BrO$, found m/z = 218.1 (M^+). The stereochemistry of the vinyl bromide was assigned by NOE experiments.

5-(Diiodomethylene)oct-7-en-1-ol (32d) and 5-((*Z*)-Iodomethylene)oct-7-en-1-ol (34d). Method C was applied for allylindation of 2 mmol (196 mg) of **12d** (quenching with 5 mmol NIS at 0 °C). After silica gel chromatography, a mixture of 357 mg (0.91 mmol, 46%) of **32d** and 266 mg (1.00 mmol, 50%) of the monoiodocompound **34d** was obtained as a colorless, light-sensitive oil. Separation of the products was achieved after acetylation (Ac_2O in pyridine, DMAP; rt, 16 h; 85% yield) and semipreparative HPLC (hexanes, 5% ethyl acetate), which afforded the corresponding acetates **32d-Ac** and **34d-Ac** in pure form (>99% by HPLC analysis). **32d-Ac**: IR 2951, 1738, 1637 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.68 (ddt, J = 16.8, 10.3, 6.5 Hz, 1H), 5.09 (dq, J = 17.1, 1.5 Hz, 1H), 5.08 (dq, J = 9.5, 1.5 Hz, 1H), 4.05 (t, J = 6.5 Hz, 2H), 3.04 (dt, J = 6.5, 1.5 Hz, 2H), 2.29 (t, J = 8.0 Hz, 2H), 2.02 (s, 3H), 1.64 (quint, J = 7.0 Hz, 2H), 1.45−1.53 (m, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 171.1, 153.1, 132.8, 117.2, 64.0, 44.3, 39.5, 28.2, 23.6, 21.0, 13.3; HRMS calcd for $C_{11}H_{16}I_2O_2$ (M^+) 433.9240, found 433.9221. **34d-Ac**: IR 3079, 2942, 1740, 1638 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.96 (s, 1H), 5.70 (ddt, J = 17.1, 10.0, 6.5 Hz, 1H), 5.10 (dq, J = 17.1, 1.5 Hz, 1H), 5.06 (dq, J = 10.0, 1.5 Hz, 1H), 4.02 (t, J = 6.5 Hz, 2H), 2.95 (dt, J = 6.5, 1.5 Hz, 2H), 2.19 (dt, J = 7.5, 1.0 Hz, 2H), 2.02 (s, 3H), 1.54−1.62 (m, 2H), 1.43−1.52 (m, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 171.1, 148.7, 133.7, 116.7, 76.0, 64.1, 41.7, 36.6, 28.0, 23.9, 20.9; EI-MS ($C_{11}H_{17}IO_2$), m/z = 181 (M^+ − I).

The free alcohols were partly separated in order to obtain the respective analytical data. **32d**: ^1H NMR (250 MHz, $CDCl_3$) δ 5.61−5.77 (m, 1H), 5.02−5.15 (m, 2H), 3.64 (t, J = 6.4 Hz, 2H), 3.05 (dt, J = 6.4, 1.4 Hz, 2H), 2.30 (t, J = 7.7 Hz, 2H), 1.43−1.62 (m, 4H), 1.40 (br s, 1H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 153.4, 132.9, 117.1, 62.4, 44.2, 39.7, 32.2, 23.4, 13.1; EI-MS ($C_9H_{14}I_2O$), found m/z = 392 (M^+). **34d**: IR 3350, 3078, 2936, 1638, 1433 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.96 (s, 1H), 5.71 (ddt, J = 17.1, 10.0, 6.5 Hz, 1H), 5.10 (dq, J = 17.1, 1.5 Hz, 1H), 5.06 (dq, J = 10.0, 1.5 Hz, 1H), 3.62 (t, J = 6.0 Hz, 2H), 2.96 (dt, J = 6.5, 1.5 Hz, 2H), 2.20 (t, J = 6.5 Hz, 2H), 1.44−1.57 (m, 4H), 1.36 (br s, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 149.0, 133.8, 116.7, 75.8, 62.6, 41.7, 36.8, 32.1, 23.8; EI-MS ($C_9H_{15}IO$), found m/z = 139 (M^+ − I); the *Z* stereochemistry of the vinyl iodide was assigned by NOE experiments.

2-Bromo-3-methylhexa-2(*Z*),5-dien-1-ol (35). Method C was applied for allylindation of 2 mmol of **15** (4 mmol of In and 3 mL of THF; sonication (4 h) was followed by addition of 4 mmol of NBS at 0 °C). After 30 min the formed colorless suspension was warmed to room temperature, and stirring was continued for 30 min. After dilution with 1 M HCl and extraction with ether, the organic solvent was removed in a vacuum and the residue was purified by silica gel chromatography (hexanes/ethyl acetate = 4:1) to yield 176 mg (0.92 mmol, 46%) of the brominated allylindation product **35** as a colorless oil in >97% purity (GC−MS analysis). The *Z* stereochemistry was assigned by NOE experiments: IR 3386, 3080, 2917, 1637, 1438, 1075 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.73 (ddt, J = 17.1, 10.0, 6.8 Hz, 1H), 5.09 (dq, J = 17.1, 1.5 Hz, 1H), 5.07 (dq, J = 10.0, 1.5 Hz, 1H), 4.36 (s, 2H), 3.00 (d, J = 6.5 Hz, 2H), 1.94 (br s, 1H), 1.82 (s, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 135.9, 133.4, 122.0, 116.8, 64.7, 43.3, 18.5; HRMS calcd for $C_7H_{11}BrO$ (M^+) 189.9993, found 189.9998.

2-Iodo-3-methylhexa-2-(*Z*),5-dien-1-ol (36). A 2 mmol portion of **15** was allylindated and quenched as described for **35**, using 4 mmol NIS (2 equiv). Silica gel chromatography (hexanes/ethyl acetate = 4:1), followed by HPLC, afforded 193 mg (0.81 mmol, 41%) of the iodinated allylindation product **36** as a colorless oil in >99% purity (GC−MS analysis). Assignment of the *Z* stereochemistry was done by NOE experiments: IR 3355, 3077, 2920, 1637, 1434, 993 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.72 (ddt, J = 16.9, 10.3, 6.5 Hz, 1H), 5.12 (dq, J = 17.1, 1.5 Hz, 1H), 5.09 (dq, J = 10.0, 1.5 Hz, 1H), 4.35 (s, 2H), 3.02 (d, J = 6.5 Hz, 2H), 1.88 (s, 4H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 141.4, 133.3, 116.9, 103.6, 67.8, 49.1, 18.1; HRMS calcd for $C_7H_{11}IO$ (M^+) 237.9853, found 237.9862.

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Supporting Information Available: Experimental and analytical data for **3a**,**b**, **10**, **18a**, **19b**, **20**, **21a**,**b**, **27a**,**b**, **29**, **30a**,**b** and for monohalogenated **9**. ^1H and ^{13}C NMR spectra for the following representative products: **3c**, **4**, **6a**−**c**, **7c**, **8**, **9**, **11**, **19a**, **22**−**26**, **30a**, **31a**−**c**, **32a**−**d**, **34d**, and **36**. This material is available free of charge via the Internet at http://pubs.acs.org

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