Headline Articles

Regio- and Stereoselective Synthesis of 1,5-Dienes Using Allylic Barium Reagents

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The highly α,α' selective and stereocontrolled homocoupling reaction of allylic halides was achieved using barium reagent. The double-bond geometry of the starting allylic chloride was completely retained. The α,α' cross-coupling products were also prepared stereospecifically and regioselectively by this method.

Homo- and cross-coupling of allylic halides are among the most basic carbon–carbon bond forming reactions in organic synthesis.$^{1)}$ Subsequent to early studies on the use of nickel carbonyl in this coupling process by Corey and Hamanaka,$^{2)}$ many groups have made important contributions to the steady improvement in this methodology.$^{3-5)}$ Nonetheless, each of the published approaches suffers from some drawbacks and limitations. Described herein is a new method which is believed to be superior to earlier procedures, especially for stereospecificities and regioselectivities. The highly α,α' selective and stereocontrolled homo- and cross-coupling reactions of allylic halides were first achieved using barium reagent (Scheme 1).$^{6)}$

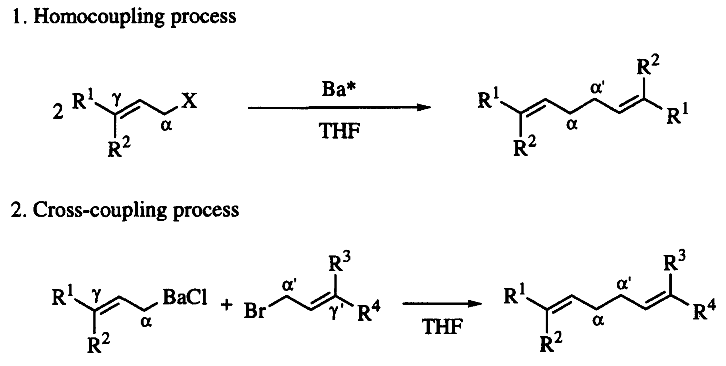
Results and Discussion

We have examined various kinds of metals for homocoupling of geranyl bromide (**1**, Table 1) at low temperature. Alkali metal naphthalenide (2 molar amounts) or reactive alkaline-earth metal (1 molar amount) in THF was exposed to **1** (1.4 molar amount) at −95 or −78 °C.$^{7)}$ Among these metals, reactive barium was found to be unique for α,α' selective homocoupling reaction ($\alpha,\alpha'/\alpha,\gamma'$=97/3, 47% yield, Entry 7). Furthermore, the geometric purity of the α,α' product (**2**/**3**=96/1) indicates that geometric isomerization (trans to cis) of the allylic barium can be suppressed during the coupling conditions.

In an attempt to improve this homocoupling reaction using reactive barium, an extensive study was made of the effect of leaving groups on regioselectivity and reactivity. Some results of the reaction of (E)-2-decen-1-ol derivatives are listed in Table 2. The chloride was shown to be the leaving group of choice in the remarkable α,α' homocoupling reaction (Entry 1). It should be noted that a high α,α' selectivity was obtained using the allylic diphenylphosphate, which provided a γ-allylated product in the cross-coupling reaction with an allylic Grignard reagent (Entry 4).$^{8)}$

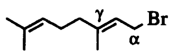
Table 3 summarizes the results obtained for reactions of a variety of allylic halides with reactive barium in THF at −78 °C. Several characteristic features of the reaction have been noted: (1) Reaction of (E)-γ-mono- or disubstituted allyl halide resulted in >90% α,α' selectivities, with the exception of (E)-cinnamyl chloride, which showed an entirely different result and afforded the α,γ' product selectively (Entry 4). Reaction of (Z)-2-decenyl chloride and bromide resulted in unacceptable regioselectivities (Entries 2 and 3).$^{9)}$ (2) Higher yields were obtained for the homocoupling reaction of allylic chlorides than the corresponding allylic bromides, which were less reactive with reactive barium. In contrast, allylic bromides showed superior α,α' selectivities to those of allylic chlorides (Entries 2, 3, 5, and 6). (3) The double-bond geometry of the starting allylic halide was completely retained in each case. (4) (E,E)-Farnesyl chloride was stereospecifically converted to squalene in 64% yield (Entry 8).

We have extended the scope of the reductive coupling method to include the synthesis of unsymmetrical dienes; thus, α,α' cross-coupling products can be prepared regio- and stereoselectively by this method (Table 4). To obtain high α,α' selectivities and yields in the cross-coupling reaction, it is most desirable to

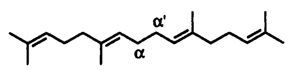


Scheme 1.

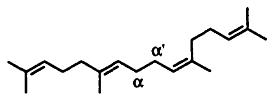
Table 1. Effect of Metals on the Regio- and Stereoselectivities of Homocoupling Reaction of Geranyl Bromide (**1**)[a)]



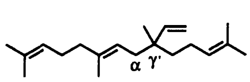
1



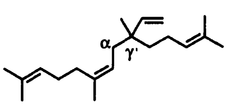
2, α(*E*),α'(*E*)



3, α(*E*),α'(*Z*)



4, α(*E*),γ'



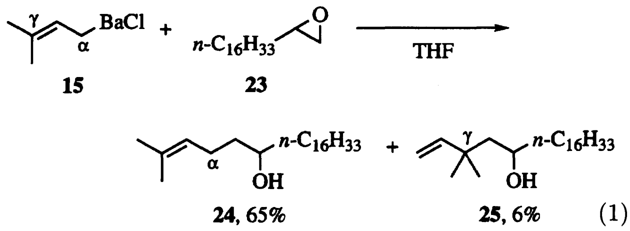
5, α(*Z*),γ'

Entry	M*	Temp/°C	Combined yield/%[b)]	Ratio (α,α'/α,γ')[c)]	Ratio of isomers **2**—**5**[c)] **2**	**3**	**4**	**5**
1	Li-Np[d)]	−95	62	69/31	67	2	31	0
2	Na-Np[d)]	−95	86	61/39	60	1	39	0
3	K-Np[d)]	−95	99	78/22	76	2	22	0
4	Cs-Np[d)]	−95	27	65/35	65	0	35	0
5	Mg	−95	61	63/37	60	3	34	3
6	Ca	−78	58	62/38	58	4	38	0
7	Ba	−78	47	97/3	96	1	3	0
8	Cr	−40	85	74/26	68	6	26	0
9	Mn	−40	60	74/26	62	12	26	0

a) The reaction was carried out using alkali metal naphthalenide (2 molar amounts) or reactive metal (1 molar amount) and geranyl bromide (**1**, 1.4 molar amount) in THF for 1 h. b) Isolated yield. c) Determined by GLC analysis. d) Np=Naphthalene.

couple allylic bromides with allylic barium reagents derived from allylic chlorides. For example, treatment of (*E*)-2-decenylbarium reagent **11** with (*E*)-2-decenyl bromide and (*Z*)-2-decenyl bromide afforded (*E*,*E*)-diene **12** and (*E*,*Z*)-diene **13** in high yields (Entries 1 and 2). However, (*Z*)-2-decenylbarium reagent **14** showed a relatively low α,α' selectivity[9)] and reactivity in the reaction with (*E*)-2-decenyl bromide (Entry 3). Benzyl ether of (2*E*,6*E*)-farnesol **17** and (2*E*,6*E*,10*E*)-geranylgeraniol **19** were obtained selectively by treatment of the primary allylic bromide **16**[10)] with prenylbarium reagent **15** and geranylbarium reagent **18**, respectively, in THF at −78 °C (Entries 4 and 5). The cross-coupling reaction of **16** with nerylbarium reagent **20** produced the (10*Z*)-isomer **21** (Entry 6). Functionalized allylic barium reagent **22** was also readily prepared. When allowed to react with geranyl bromide and neryl bromide, it provided benzyl geranylgeranyl ether **19** and **21** (Entries 7 and 8).

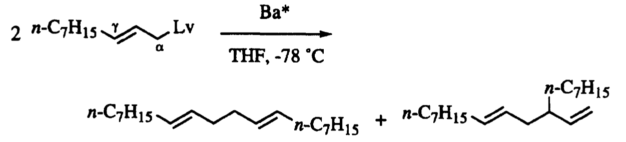
The utility of allylic barium reagents for nucleophilic substitution reaction was further demonstrated by reactions with epoxide.[12)] Treatment of 1,2-epoxyoctadecane (**23**) with prenylbarium reagent **15** in THF at 20 °C afforded a 91 : 9 mixture of α-product **24** and γ-product **25** in 71% combined yield (Eq. 1). The extraordinary α-selectivity and stereospecificity of the allyl–allyl coupling reaction using barium reagent provided an unprecedented route to 1,5-dienes; such reactions are broadly applicable in organic synthesis.



15 **23**

24, 65% **25**, 6% (1)

Table 2. Effect of Leaving Groups on the Regioselectivity of Homocoupling Reaction of (*E*)-2-Decen-1-ol Derivatives[a)]



Entry	Lv	Combined yield/%[b)]	Ratio $(\alpha,\alpha'/\alpha,\gamma')$[c)]
1	Cl	86	95/5
2	Br	68	92/8
3	I	57	77/23
4	OPO(OPh)$_2$	58	95/5
5	OMs	33	92/8

a) The reaction was carried out using reactive barium (1 molar amount) and (*E*)-2-decen-1-ol derivative (1.4 molar amount) in THF at −78 °C for 1 h. b) Isolated yield. c) Determined by GLC analysis. Stereoisomers of the α,α' and α,γ' products were not obtained in each entry.

Experimental

General. Analytical TLC was done on E. Merck precoated (0.25 mm) silica gel 60 F_{254} plates. Column chromatography was conducted using silica gel 60 (E. Merck 9385, 230—400 mesh). Infrared (IR) spectra were recorded on a Shimadzu FTIR-8100 spectrometer. ^{1}H NMR spectra were measured on a Varian Gemini-200 (200 MHz) or Gemini-300 (300 MHz) spectrometer. ^{13}C NMR spectra were measured on a Varian Gemini-300 (75 MHz) spectrometer. Chemical shifts of ^{1}H NMR spectra were reported relative to tetramethylsilane (δ=0) or chloroform (δ=7.26). Chemical shifts of ^{13}C NMR spectra were reported relative to $CDCl_3$ (δ=77.0). Splitting patterns are indicated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. Analytical gas–liquid phase chromatography (GLC) was performed on a Shimadzu GC-8A instrument equipped with a flame ionization detector and a capillary column of PEG-HT (0.25×25000 mm), using nitrogen as carrier gas. Microanalyses were done at the Faculty of Agriculture, Nagoya University.

All experiments were carried out in a Schlenk tube under an atmosphere of standard grade argon gas (oxygen <10 ppm). Dry THF was used as purchased from Aldrich (anhydrous, 99.9%). Anhydrous BaI_2 was prepared by drying $BaI_2 \cdot 2H_2O$ (extra pure reagent, Nacalai Tesque) at 150 °C for 2 h under reduced pressure (<10 Torr, 1 Torr=133.322 Pa). Products of Aldrich, Fluka, Kishida Chemical, and Wako Pure Chemical could be used with equal efficiency. Lithium (wire, 99.9%) was purchased from Aldrich. The wire was cut into 2—3 mg pieces, which were rinsed with dry hexane before use. Biphenyl (guaranteed reagent) was used as purchased from Nacalai Tesque. Stereochemically pure (>99%) allylic chlorides were prepared by treatment of the corresponding allylic alcohols with a mixture of *N*-chlorosuccinimide and dimethyl sulfide in CH_2Cl_2.[13)] Stereochemically pure (>99%) allylic bromides were prepared by treatment of the corresponding allylic alcohols with PBr_3 in ether (0 °C). 1,2-Epoxyoctadecane (**23**) was synthesized from 1-octadecene by epoxidation with MCPBA in CH_2Cl_2. Other chemicals were used as purchased.

Typical Procedure for Homocoupling Reaction of Allylic Halides (Table 3, Entry 8). An oven-dried, 20-ml Schlenk tube, equipped with a Teflon®-coated magnetic stirring bar, was flushed with argon. Freshly cut lithium (17 mg, 2.4 mmol) and biphenyl (365 mg, 2.4 mmol) were placed into the apparatus and covered with dry THF (5 ml); then the mixture was stirred for 2 h at 20—25 °C (lithium was completely consumed). Anhydrous BaI_2 (458 mg, 1.2 mmol) was placed into a separate oven-dried, 50-ml Schlenk tube equipped with a Teflon®-coated magnetic stirring bar under argon atmosphere; this was covered with dry THF (3 ml), and the contents were stirred for 5 min at room temperature. To the suspension of BaI_2 in THF was added at room temperature a solution of the lithium biphenylide in THF through a stainless steel cannula under an argon stream. The reaction mixture was stirred for 30 min at room temperature. A solution of (*E*,*E*)-farnesyl chloride (378 mg, 1.6 mmol) in THF (1.5 ml) was slowly added to the resulting dark brown suspension of reactive barium (1.2 mmol) in THF at −78 °C. The reaction mixture was stirred for 1 h at this temperature. 1 M HCl (10 ml, M=mol dm^{-3}) was added to the mixture at −78 °C and the aqueous layer was extracted with ether (10 ml). The combined organic extracts were washed with dilute sodium thiosulfate solution (20 ml), dried over anhydrous $MgSO_4$, and concentrated in vacuo after filtration. The crude product was purified by flash-column chromatography on silica gel (hexane as the eluant) to afford a mixture of squalene and its regioisomer (220 mg, 68% combined yield) as a colorless oil: the $\alpha,\alpha'/\alpha,\gamma'$ and $\alpha(E),\alpha'(E)/\alpha(E),\alpha'(Z)$ ratios were determined to be 94/6 and >99/1, respectively, by GLC analysis.

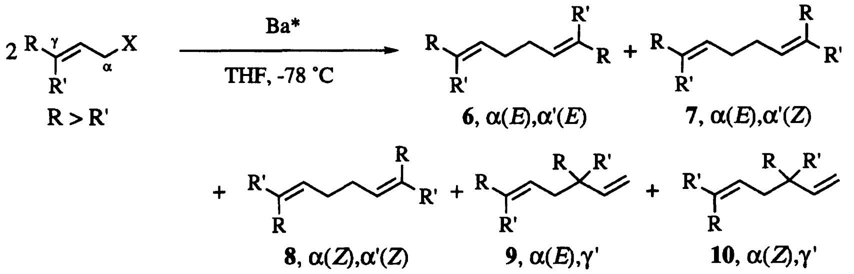
(6*E*,10*E*,14*E*,18*E*)-2,6,10,15,19,23-Hexamethyl-2,6,10,14,18,22-tetracosahexaene (Squalene): TLC R_f 0.50 (hexane); IR ($CHCl_3$) 2973, 2925, 1523, 1449, 930 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ=1.60 (s, 18H, 6CH_3), 1.68 (s, 6H, 2CH_3), 1.89—2.16 (m, 20H, 10CH_2), 5.03—5.21 (m, 6H, 6 vinyls). Found: C, 87.70; H, 12.54%. Calcd for $C_{30}H_{50}$: C, 87.73; H, 12.27%.

(8*E*,12*E*)-8,12-Icosadiene (Table 3, Entry 1 and Table 4, Entry 1): TLC R_f 0.69 (hexane); IR ($CHCl_3$) 2957, 2929, 2855, 1684, 1522, 1508, 1457, 968 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ=0.88 (t, 6H, J=6.3 Hz, 2CH_3), 1.12—1.44 (m, 20H, 10CH_2), 1.87—2.09 (m, 8H, 4CH_2), 5.31—5.44 (m, 4H, 4 vinyls). Found: C, 86.22; H, 14.03%. Calcd for $C_{20}H_{38}$: C, 86.25; H, 13.75%.

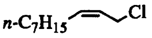
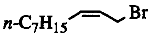
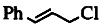
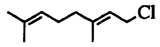
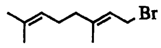
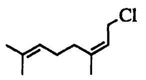
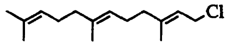
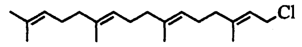
(8*Z*,12*Z*)-8,12-Icosadiene (Table 3, Entries 2 and 3): TLC R_f 0.69 (hexane); ^{1}H NMR (200 MHz, $CDCl_3$) δ= 0.88 (t, 6H, J=6.4 Hz, 2CH_3), 1.11—1.42 (m, 20H, 10CH_2), 1.90—2.12 (m, 8H, 4CH_2), 5.31—5.41 (m, 4H, 4 vinyls). Found: C, 86.22; H, 14.19%. Calcd for $C_{20}H_{38}$: C, 86.25; H, 13.75%.

(1*E*)-1,4-Diphenyl-1,5-hexadiene (Table 3, Entry 4): TLC R_f 0.18 (hexane); IR ($CHCl_3$) 3080, 3065, 2928, 2849, 1637, 1600, 1559, 1497, 967, 922 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ=2.64 (t, 2H, J=7.2 Hz, CH_2), 3.44 (q, 1H, J=7.4 Hz, CH), 5.07 (dd, 1H, J=1.4, 15.4 Hz, vinyl), 5.08 (dd, 1H, J=0.8, 11.2 Hz, vinyl), 5.93—6.19 (m, 2H, 2 vinyls), 6.40 (d, 1H, J=15.8 Hz, vinyl), 7.09—7.38 (m, 10H, aromatic). Found: C, 92.21; H, 7.68%. Calcd for $C_{18}H_{18}$: C, 92.26; H, 7.74%.

Table 3. Regio- and Stereoselective Homocoupling Reaction of Various Allylic Halides Using Reactive Barium[a]

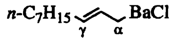
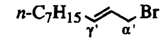
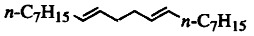
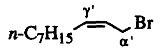
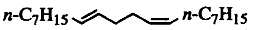
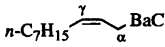
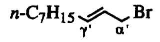
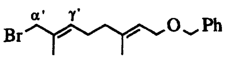
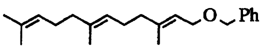
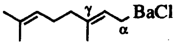
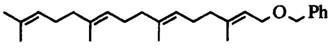
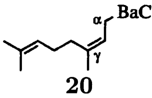
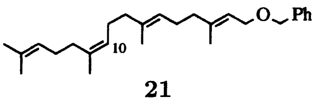
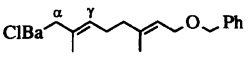
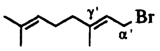
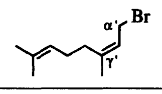


6, α(*E*),α'(*E*) **7**, α(*E*),α'(*Z*) **8**, α(*Z*),α'(*Z*) **9**, α(*E*),γ' **10**, α(*Z*),γ'

Entry	Allylic halide	Combined yield/%[b]	Ratio $(\alpha,\alpha'/\alpha,\gamma')$[c]	Ratio of isomers **6**—**10**[c] **6**	**7**	**8**	**9**	**10**
1		86	95/5	95	0	0	5	0
2		88	51/49	0	0	51	0	49
3		50	77/23	0	0	77	0	23
4		86	24/76	24	0	0	76	0
5		70	91/9	89	2	0	9	0
6		47	97/3	96	1	0	3	0
7		44	92/8	0	2	90	0	8
8		68	94/6	94	0	0	6	0
9		64	93/7	92	1	0	7	0

a) The reaction was carried out using reactive barium (1 molar amount) and allylic halide (1.4 molar amount) in THF at −78 °C for 1 h. b) Isolated yield. c) Determined by GLC analysis.

Table 4. Regio- and Stereoselective Cross-coupling Reaction of Various Allylic Bromides with Allylic Barium Reagents[a]

Entry	Allylic barium reagent	Allylic bromide	Major product	Combined yield/%[b]	Ratio $(\alpha,\alpha'/\alpha,\gamma')$[c]	Stereochemical purity/%[c]
1	 **11**		 **12**	87	96/4	>99
2	**11**		 **13**	91	96/4	>99
3	 **14**		**13**	54	61/39	>99
4[d]	 **15**	 **16**	 **17**	75	76/24	>99
5[d]	 **18**	**16**	 **19**	95	88/12	97
6[d]	 **20**	**16**	 **21**	49	76/24	97
7[e]	 **22**		**19**	83	94/6	95
8[e]	**22**		**21**	63	96/4	>99

a) Unless otherwise specified, the reaction was carried out using allylic barium reagent (1.4 molar amount) and allylic bromide (1 molar amount) in THF at −78 °C for 30 min. b) Isolated yield. c) Determined by GLC analysis. d) Allylic barium reagent (1.8 molar amount) was used. e) Allylic barium reagent (1.1 molar amount) was used.

(6*E*,10*E*)-2,6,11,15-Tetramethyl-2,6,10,14-hexadecatetraene (Table 3, Entries 5 and 6): TLC R_f 0.56 (hexane); IR ($CHCl_3$) 2969, 2928, 1522, 1449, 930 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ=1.61 (s, 12H, $4CH_3$), 1.69 (s, 6H, $2CH_3$), 1.92—2.14 (m, 12H, $6CH_2$), 5.03—5.21 (m, 4H, 4 vinyls). Found: C, 87.39; H, 12.64%. Calcd for $C_{20}H_{34}$: C, 87.52; H, 12.48%.

(6*Z*,10*Z*)-2,6,11,15-Tetramethyl-2,6,10,14-hexadecatetraene (Table 3, Entry 7): TLC R_f 0.56 (hexane); IR (neat) 2979, 2930, 2876, 1541, 1509, 1483, 1456, 1383, 1111 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ=1.61 (s, 6H, $2CH_3$), 1.69 (s, 12H, $4CH_3$), 1.93—2.07 (m, 12H, $6CH_2$), 5.04—5.18 (m, 4H, 4 vinyls). Found: C, 87.60; H, 12.80%. Calcd for $C_{20}H_{34}$: C, 87.52; H, 12.48%.

(6*E*,10*E*,14*E*,18*E*,22*E*,26*E*)-2,6,10,14,19,23,27,31-Octamethyl-2,6,10,14,18,22,26,30-dotriacontaoctaene (Table 3, Entry 9): TLC R_f 0.46 (hexane); IR (neat) 2967, 2924, 2855, 1669, 1449, 1383, 1150, 1107, 984, 911, 837 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ=1.60 (s, 24H, $8CH_3$), 1.68 (s, 6H, $2CH_3$), 1.87—2.14 (m, 28H, $14CH_2$), 5.02—5.18 (m, 8H, 8 vinyls). Found: C, 87.78; H, 12.34%. Calcd for $C_{40}H_{66}$: C, 87.84; H, 12.16%.

Typical Procedure for Cross-Coupling Reaction of Allylic Bromides with Allylic Barium Reagents (Table 4, Entry 8). To the suspension of reactive barium (1.1 mmol) in THF (10 ml) was slowly added a solution of (2*E*,6*E*)-8-(benzyloxy)-1-chloro-2,6-dimethyl-2,6-octadiene (270 mg, 0.97 mmol) in THF (2 ml) at −78 °C. After being stirred for 20 min, the mixture was treated with a solution of neryl bromide (190 mg, 0.88 mmol) in THF (1.5 ml) at −78 °C and stirred for 1 h at this temperature. 1 M HCl (10 ml) was added to the mixture at −78 °C and the aqueous layer was extracted with ether (10 ml). The combined organic extracts were washed with 1 M sodium thiosulfate solution (20 ml), dried over anhydrous $MgSO_4$, and concentrated in vacuo after filtration. The crude product was purified by flash-column chromatography on silica gel (0:1 to 1:50 ether/hexane as the eluant) to afford a mixture of (2*E*,6*E*,10*Z*)-1-(benzyloxy)-3,7,11,15-tetramethyl-2,6,10,14-hexadecatetraene (**21**) and its regio- and stereoisomers (210 mg, 63% combined yield) as a colorless oil: the $\alpha,\alpha'/\alpha,\gamma'$ and $\alpha(E),\alpha'(Z)/\alpha(Z),\alpha'(Z)$ ratios were determined to be 96/4 and >99/1, respectively, by GLC analysis.

(2*E*,6*E*,10*Z*)-1-(Benzyloxy)-3,7,11,15-tetramethyl-2,6,10,14-hexadecatetraene (21): TLC R_f 0.61 (1:5 ether/hexane); IR (neat) 2965, 2924, 2855, 1669, 1498, 1453, 1377, 1363, 1202, 1111, 1091, 1071, 1028 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ=1.61 (s, 6H, $2CH_3$), 1.65 (s, 3H, CH_3), 1.68 (s, 6H, $2CH_3$), 1.91—2.20 (m, 12H, $6CH_2$), 4.03 (d, 2H, J=6.8 Hz, CH_2), 4.51 (s, 2H, CH_2), 5.12 (m, 3H, 3 vinyls), 5.41 (dt, 1H, J=1.2, 6.8 Hz, vinyl), 7.22—7.38 (m, 5H, aromatic). Found: C, 85.20; H, 10.78%. Calcd for $C_{27}H_{40}O$: C, 85.20; H, 10.59%.

(8*E*,12*Z*)-8,12-Icosadiene (13, Table 4, Entry 2): TLC R_f 0.65 (hexane); IR (neat) 2959, 2930, 2857, 1653, 1648, 1541, 1509, 1466, 1379, 1111, 970 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ=0.88 (t, 6H, J=6.4 Hz, $2CH_3$), 1.15—1.44 (m, 20H, $10CH_2$), 1.91—2.15 (m, 8H, $4CH_2$), 5.30—5.43 (m, 4H, 4 vinyls).

(2*E*,6*E*)-1-(Benzyloxy)-3,7,11-trimethyl-2,6,10-dodecatriene (17, Table 4, Entry 4): TLC R_f 0.60 (1:5 ether/hexane); IR (neat) 2967, 2923, 2855, 1669, 1497, 1455, 1380, 1363, 1201, 1110, 1090, 1069, 1028 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ=1.60 (s, 6H, $2CH_3$), 1.65 (s, 3H, CH_3), 1.67 (s, 3H, CH_3), 1.90—2.21 (m, 8H, $4CH_2$), 4.03 (d, 2H, J=7.0 Hz, CH_2), 4.50 (s, 2H, CH_2), 5.10 (m, 2H, 2 vinyls), 5.41 (dt, 1H, J=1.2, 6.8 Hz, vinyl), 7.24—7.40 (m, 5H, aromatic). Found: C, 84.57; H, 10.49%. Calcd for $C_{22}H_{32}O$: C, 84.56; H, 10.32%.

(2*E*,6*E*,10*E*)-1-(Benzyloxy)-3,7,11,15-tetramethyl-2,6,10,14-hexadecatetraene (19, Table 4, Entries 5 and 7): TLC R_f 0.61 (1:5 ether/hexane); IR (neat) 2967, 2924, 2855, 1670, 1497, 1453, 1383, 1362, 1201, 1110, 1090, 1069, 1028 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$ δ=1.60 (s, 9H, $3CH_3$), 1.65 (s, 3H, CH_3), 1.68 (s, 3H, CH_3), 1.90—2.21 (m, 12H $6CH_2$), 4.03 (d, 2H, J=6.6 Hz, CH_2), 4.50 (s, 2H, CH_2), 5.10 (m, 3H, 3 vinyls), 5.41(dt, 1H, J=1.2, 6.8 Hz, vinyl), 7.25—7.39 (m, 5H, aromatic). Found: C, 85.21; H, 10.80%. Calcd for $C_{27}H_{40}O$: C, 85.20; H, 10.59%.

Procedure for Reaction of Prenylbarium Chloride (15) with 1,2-Epoxyoctadecane (23, Eq. 1). A solution of prenyl chloride (107 mg, 1.0 mmol) in THF (2 ml) was slowly added to the suspension of reactive barium (1.0 mmol) in THF (10 ml) at −78 °C. After being stirred for 20 min, the mixture was treated with a solution of 1,2-epoxyoctadecane (**23**, 135 mg, 0.50 mmol) in THF (1 ml) at −78 °C and again stirred for 12 h at 20 °C. A saturated NH_4Cl aqueous solution (10 ml) was added to the mixture and the aqueous layer was extracted with ether (10 ml). The combined organic extracts were washed with 1 M sodium thiosulfate solution (20 ml), dried over anhydrous $MgSO_4$, and concentrated in vacuo after filtration. The crude product was purified by flash-column chromatography on silica gel (1:20 to 1:5 ether/hexane as the eluant) to afford 2-methyl-2-docosen-6-ol (**24**, α-adduct, 110 mg, 65% yield) and 3,3-dimethyl-1-henicosen-5-ol (**25**, γ-adduct, 11 mg, 6% yield).

2-Methyl-2-docosen-6-ol (24): TLC R_f 0.36 (1:5 ethyl acetate/hexane); IR (neat) 3347, 3250, 2959, 2917, 2849, 1472, 1464, 1375, 1354, 1109, 1082, 909, 735 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ=0.88 (t, 3H, J=6.2 Hz, CH_3), 1.15—1.59 (m, 33H, $16CH_2$ and OH), 1.63 (s, 3H, CH_3), 1.69 (s, 3H, CH_3), 2.09 (m, 2H, CH_2), 3.60 (m, 1H, CH), 5.14 (t, 1H, J=6.5 Hz, vinyl); ^{13}C NMR (75 MHz, $CDCl_3$) δ=14.1, 17.7, 22.7, 24.4, 25.7, 29.4, 29.7 (11C), 31.9, 37.4, 37.5, 71.8, 124.2, 132.0. Found: C, 81.51; H, 13.85%. Calcd for $C_{23}H_{46}O$: C, 81.60; H, 13.70%.

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