Nozaki−Hiyama Reactions on Halogenated Allylchromium Reagents: A New Entry for the Preparation of Quaternary Halogenated Carbons

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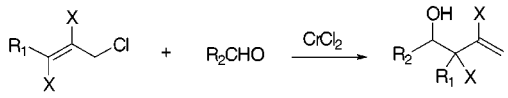
Received September 28, 1999

The addition of organochromium compounds to aldehydes originally described by Nozaki and Hiyama et al. has evolved into a powerful method for the construction of C−C bonds.[1] The nucleophiles are prepared in situ by oxidative insertion of Cr(II) into a wide range of substrates including allyl, propargyl, aryl or alkenyl halides, alkenyl triflates, allyl phosphates, and acrolein acetals.[2] The synthetic interest of this reaction is its chemoselectivity and its exceptional compatibility with a wide range of functional groups in both reaction partners. In addition, later improvements of this reaction by Kishi[3] and Nozaki[4] (catalytic effect of nickel salts) and more recently by Fürstner[5] (Nozaki−Hiyama−Kishi reaction using a catalytic amount of chromium) have greatly increased the value of this reaction, especially in the synthesis of highly functionalized natural products.[6]

As part of our program aimed at the synthesis of halogenated biologically active compounds,[7] we were interested in the possibility of using bis-halogenated allylic chlorides as potential substrates for the Nozaki−Hiyama reaction (Scheme 1). This reaction should provide highly functionalized halohydrins that might be used for the preparation of epoxides or as advanced synthetic intermediates for the total synthesis of halogenated natural compounds.[8] In particular, β,γ,γ-trisubstituted allylic halides possessing a halogen atom on the terminal position should lead to homoallylic alcohols including a quaternary halogenated center.

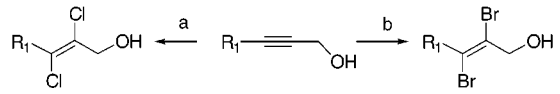
Scheme 1



X= F, Cl, Br
R_1= H, alkyl, $CH_2OTBDMS$; R_2=Ph, $-CH=CH_2$ or $-CH=CHPh$

Scheme 2

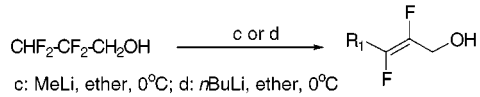
Preparation of *trans*-dibromo and *trans*-dichloroallylic alcohols **1a-d**



a: $NEt_4^+ Cl_3^-$, CH_2Cl_2 ; b: pyridinium tribromide, CH_2Cl_2,0°C

1a R_1=Pr yield: 90%
1b R_1=$CH_2OTBDMS$ yield: 81%
1c R_1=Pr yield: 83%
1d R_1=H yield: 65%

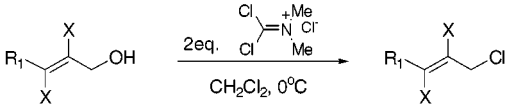
Preparation of *trans*-difluoroallylic alcohols **1e** and **1f**



c: MeLi, ether, 0°C; d: *n*BuLi, ether, 0°C

1e condition c R_1=Me yield: 49%
1f condition d R_1=*n*Bu yield: 54%

Preparation of *trans*-difluoro,dichloro- and dibromo- allylic chlorides **2a-f**



2a X=Cl, R_1=*n*Pr yield: 85%
2b X=Cl, R_1=$CH_2OTBDMS$ yield: 91%
2c X=Br, R_1=*n*Pr yield: 76%
2d X=Br, R_1=H yield: 64%
2e X=F, R_1=Me yield: 64%
2f X=F, R_1=*n*Bu yield: 81%

Results and Discussion

Substrates Synthesis. A series of differently substituted *trans*-difluoro-, *trans*-dichloro-, and *trans*-dibromoallylic chlorides was prepared according to procedures which are described in the literature (Scheme 2). All the substrates were prepared from the corresponding allylic alcohols. The *trans*-dichloroallylic alcohols **1a** and **1b** and the *trans*-dibromoallylic alcohols **1c** and **1d** were obtained stereoselectively from the corresponding propargylic alcohols using tetraethylammonium trichloride[9] and pyridinium tribromide,[10] respectively. The *trans*-difluoroallylic alcohols **1e** and **1f** were prepared in good yields by

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(1) (a) Okude, Y.; Hirano, S.; Hiyama, T.; Nozaki, H. *J. Am. Chem. Soc.* **1977**, 3179. (b) Hiyama, T.; Kimura, K.; Nozaki, H. *Tetrahedron Lett.* **1981**, *22*, 1037−1040. (c) Hiyama, T.; Okude, Y.; Kimura, K.; Nozaki, H. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 561−568. (d) Buse, C. T.; Heathcock, C. H. *Tetrahedron Lett.* **1978**, *19*, 1685−1688. For recent reviews: Fürstner, A. *Chem. Rev.* **1999**, *99*, 991−1045. Wessjohann, L. A.; Scheid, G. *Synthesis* **1999**, *1*, 1−36. Avalos, M.; Babiano, R.; Cintas, P.; Jimenez, J. L.; Palacios, J. C. *Chem. Soc. Rev.* **1999**, *28*, 169−179 and references therein.

(2) For the use of substrates other than halides, see the following. (a) *Alkenyl triflates*: Takai, K.; Tagashira, M.; Kuroda, T.; Utimoto, K.; Nozaki, H. *J. Am. Chem. Soc.* **1986**, *108*, 6048−6050. (b) *Allylic phosphates*: Nowotny, S.; Tucker, C. E.; Jubert, C.; Knochel, P. *J. Org. Chem.* **1995**, *60*, 2762−2772. (c) *Acrolein acetals*: Boeckman, R. K.; Hudack, R. A. *J. Org. Chem.* **1998**, *63*, 3524−3525.

(3) Jin, H.; Uenishi, J.-I.; Christ, W. J.; Kishi, Y. *J. Am. Chem. Soc.* **1986**, *108*, 5644.

(4) Takai, K.; Tagashira, M.; Kuroda, T.; Oshima, K.; Utimoto, K.; Nozaki, H. *J. Am. Chem. Soc.* **1986**, *108*, 6048.

(5) Fürstner, A.; Shi, N. *J. Am. Chem. Soc.* **1996**, *118*, 12349. Fürstner, A.; Shi, N. *J. Am. Chem. Soc.* **1996**, *118*, 2533.

(6) For example: Nicolaou, K. C.; Theodorakis, E. A.; Rutjes, F. P.; Tiebe, J.; Sato, M.; Untersteller, E.; Xiao, X. Y. *J. Am. Chem. Soc.* **1995**, *117*, 1171−1172. MacMillan, D. W. C.; Overman, L. E. *J. Am. Chem. Soc.* **1995**, *117*, 10391−10392.

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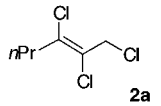
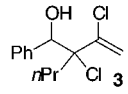
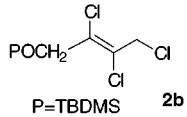
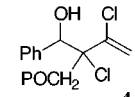
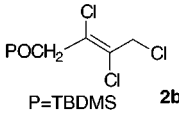
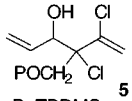
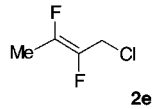
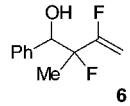
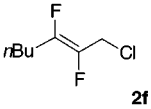
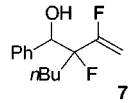
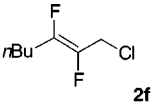
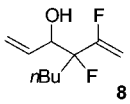
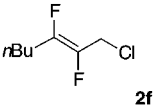
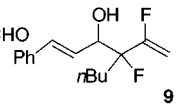
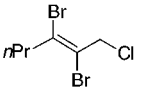
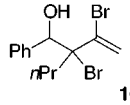
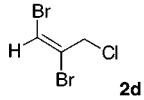
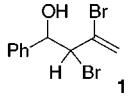
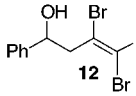
(10) Kodomari, M.; Sakamoto, T.; Yoshitomi, B. *Bull. Chem. Soc. Jpn.* **1959**, *62*, 12, 4053−4054.

10.1021/jo9915269 CCC: $19.00
Published on Web 01/28/2000

Table 1. Nozaki−Hiyama Reactions of Allylic Chlorides 2a−f

Entry	Substrates		Product	Yield[a] (d.r.)
1	 **2a**	PhCHO	 **3**	45%[b] (64:36) 73%[c] (56:44)
2	 P=TBDMS **2b**	PhCHO	 P=TBDMS **4**	18%[b] (69:31) 81%[c] (77:23)
3	 P=TBDMS **2b**	CH_2=CHCHO	 P=TBDMS **5**	87%[c] (63:37)
4	 **2e**	PhCHO	 **6**	89%[c] (56:44)
5	 **2f**	PhCHO	 **7**	70%[c] (55:45)
6	 **2f**	CH_2=CHCHO	 **8**	87%[c] (59:41)
7	 **2f**	PhCH=CHCHO	 **9**	91%[c] (57:43)
8	 **2c**	PhCHO	 **10**	0%[c,d]
9	 **2d**	PhCHO	 **11**	0%[c,d]
			 **12**	81%[b,e]

[a] Isolated yield. [b] Reaction performed in THF. [c] Reaction performed in DMF. [d] Degradation of the reaction mixture. [e] No trace of the expected bromohydrin; 81% of **12** only.

treatment of the commercially available 2,2,3,3-tetrafluoroethanol with methyllithium and *n*-butyllithium, respectively, in ether at 0 °C.[11] The desired *trans*-halogenated allylic chlorides **2a**−**f** were all obtained in satisfactory yields (64−91%) by reaction of the corresponding allylic alcohols with 2 equiv of *N*,*N*-dichlorophosgeniminium chloride at 0 °C in CH_2Cl_2.[12]

Nozaki−Hiyama Reactions. Our results are summarized in Table 1. The reaction of *trans*-1,2,3-trichlorohex-2-ene **2a**, benzaldehyde, and 4 equiv of $CrCl_2$ in tetrahydrofuran at room-temperature proceeded following a "one-pot Barbier type" addition to give the desired product **3** with a chemical yield of 45%. Two diastereomers were formed in a ratio of 64:36 as evaluated by ^{1}H NMR on the crude mixture (entry 1). In aprotic, dipolar *N*,*N*-dimethylformamide, the same reaction proceeded with an improved chemical yield of 73%. Similar observation was previously reported with non halogenated allylic halides by Hiyama and Nozaki et al. and was ascribed to the fact that DMF dissolves the chromium salts to a higher extent and also modulates its reducing ability.[13] It was also observed that in DMF the diastereoselectivity for this reaction was slightly decreased (from 64:36 to 56:44).[14] The improvement of the chemical yield using DMF instead of THF was confirmed with substrate **2b** possessing a protected primary alcohol group (entry 2). Indeed, in DMF, the desired product **4** was formed with a chemical yield of 81% instead of 18% in THF. Surprisingly, the diastereoselectivity was slightly improved from 69:31 to 77:23. Consequently, all the reactions were subsequently performed in DMF. Acrolein was found to be a suitable substrate as the electrophilic partner. Indeed, the reaction of **2b** with acrolein gave the expected chlorohydrin **5** with a chemical yield of 87% and as a mixture of two diastereomers (63:37) (entry 3). All the reactions involving *trans*-chloroallylic chlorides were completed within 8 h.

This method was extended to β,γ,γ-trisubstituted *trans*-difluoroallylic chlorides. The *trans*-difluoroallylic chloride **2e** reacted under standard conditions to give the fluorohydrin **6** as a mixture of two diastereomers (56/44) with a chemical yield of 89% (entry 4). Similar results were obtained for the Nozaki−Hiyama reaction of 2,3-difluoro-1-chlorohept-2-ene **2f** with benzaldehyde, acrolein, or *trans*-cinnamaldehyde. The yields for the corresponding products **7**, **8**, and **9** ranged from 70 to 91% but the diastereoselectivity for all these reactions remained disappointingly low (entries 5, 6, and 7). Interestingly, in contrast to *trans*-dichloroallylic chlorides (entries 1−3), the reactions using the *trans*-difluoroallylic chlorides **2e** and **2f** were faster and were all completed within 4 h.

The treatment of 1-chloro-2,3-dibromohex-2-ene **2c** or 1,2-dibromo-3-chloropropene **2d** with 4 equiv of $CrCl_2$ and 1 equiv of benzaldehyde in DMF did not lead to the formation of the expected bromohydrins **10** and **11**. Only degradation of the reaction mixture was observed (entries 8 and 9). However, under the same conditions, if THF was used instead of DMF, the reaction of 1,2-dibromo-3-chloropropene **2d** provided compound **12** with a chemical yield of 81%. This product results from a linear addition of the intermediate allylchromium on benzaldehyde (entry 9).

Our results showed that all the dihalo-substituted chromium allyls were selectively derived through oxidative insertion to the allylic halogen bond. Insertion into the vinylic halogen bonds did not compete. The reactions proceeded predominantly with allylic transposition except with the *trans*-dibromoallylic chloride **2d**. Interestingly, in contrast with the use of monohalogenated allylic chromium reagents,[15] no side products formed by over-reduction processes were observed in the crude reaction mixtures. In general, poor stereoselectivities were ob-

(11) Nguyen, T.; Wakselman, C. *J. Org. Chem.* **1989**, *54*, 5640−5642.

(12) For review on this reagent: Viehe, H. G.; Janousek, Z. *Angew. Chem., Int. Ed. Engl.* **1973**, *10*, 806−818. Viehe, H. G.; Janousek, Z. Chemistry of dichloromethylen-iminium Salts. *Iminium Salts in Organic Chemistry*; Wiley Interscience, New York, 1976; Part I, p 343.

(13) See ref 1a and Okude, Y.; Hiyama, T.; Nozaki, H. *Tetrahedron Lett.* **1977**, 3829.

(14) Effect of the solvent on the diastereoselectivity: Hiyama, T.; Okude, Y.; Kimura, K.; Nozaki, H. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 561. Hiyama, T.; Kimura, K.; Nozaki, H. *Tetrahedron Lett.* **1981**, *22*, 1087.

(15) Wender, P. A.; Wisniewski-Grissom, J.; Hoffmann, U.; Mah, R. *Tetrahedron Lett.* **1990**, *31*, 6605−6608. Augé, J. *Tetrahedron Lett.* **1998**, *29*, 6107−6107.

served for all the reactions involving *trans*-β,γ,γ-trisubstituted allylic chlorides. These results are in contrast with the observation of Knochel et al. who reported that the Nozaki−Hiyama reactions of other γ,γ-disubstituted allylic chromium reagents are highly stereodivergent.[16]

Conclusions

This paper reports the first examples of the Nozaki−Hiyama reactions on bis-halogenated allylic chlorides including difluorinated derivatives. These latter substrates are of particular interest as the products obtained by the Nozaki−Hiyama reaction are not easily accessible by other means.[17] The high yields of these reactions combined with the ease of preparation of the halogenated allylic chlorides makes this methodology an attractive alternative to the formation of fluorinated and chlorinated quaternary centers. Further work is presently undergoing in our laboratory to apply this methodology for the preparation of natural halogenated compounds.

Experimental Section

$CrCl_2$ (95%) was purchased from Lancaster and used without further purification. All reactions were performed under argon, and anhydrous solvents were dried and distilled before use.

General Procedure for the Allylation of Aldehydes with Halogenated Substrates. To a stirred solution of chromium(II) chloride (4 equiv) in DMF (or THF) was successively added the halogenated allylic chloride (3 equiv) and then the aldehyde (1 equiv). The reaction mixture was stirred at room temperature until total conversion of the aldehyde. The reaction mixture was quenched with water and vigorously stirred for 10 min. The resulting green solution was extracted with three portions of diethyl ether. The combined organic extracts were washed with water and brine, dried over $MgSO_4$, and concentrated in vacuo to give the crude halohydrins as oils. Purification by column on silica gel (hexane/diethyl ether 95/5) afforded analytically pure compounds.

2,3-Dichloro-1-phenyl-2-propylbut-3-en-1-ol 3. Reagents: 106.9 mg (0.57 mmol) of 1,2,3-trichloroprop-2-ene, 19.8 μL (0.19 mmol) of benzaldehyde, 95.9 mg (0.78 mmol) of $CrCl_2$, 4 mL (of THF or DMF); yield in THF: 22.2 mg (45%); yield in DMF: 35.9 mg (73%); R_f = 0.3 (hexane/ether, 95/5); ^{1}H NMR ($CDCl_3$): 0.87 (t, J = 6.6, 3H), 1.39 (m, 3H), 2.00 (m, 1H), 2.51 (d, J = 5.5, 1H), 5.15 (d, J = 5.5, 1H), 5.65 (d, J = 1.8, 1H), 5.95 (d, J = 1.8, 1H), 7.3 (m, 5H); ^{13}C NMR ($CDCl_3$): 13.8, 17.1, 38.8, 76.4, 82.3, 119.0, 127.7, 128.4, 128.6, 137.9, 139.9; IR (neat, cm^{-1}) 3426, 1630, 849, 786. Anal. Calcd for $C_{13}H_{16}OCl_2$ (259.17): C, 60.25; H, 6.22; Cl, 27.36. Found: C, 60.23; H, 6.17; Cl, 27.41; MS (DCI/NH_3) m/z (MNH_4^+) = 277.

2-(*tert*-Butyl-dimethylsilyloxymethyl)-2,3-dichloro-1-phenylbut-3-en-1-ol 4. Reagents: 141.1 mg (0.49 mmol) of 1,2,3-trichloro-4-(*tert*-butyldimethylsilyloxy)but-2-ene, 16.3 μL (0.16 mmol) of benzaldehyde, 80.0 mg (0.65 mmol) of $CrCl_2$, 4 mL (THF or DMF); yield in THF: 8.3 mg (18%); yield in DMF: 37.3 mg (81%); R_f = 0.4 (hexane/ether, 90/10); ^{1}H NMR ($CDCl_3$): 0.06 (s, 6H), 0.92 (s, 9H), 3.08 (d, J = 6.8, 1H), 3.67 (d, J = 10.8,1H), 3.83 (d, J = 10.8, 1H), 5.35 (d, J = 6.8, 1H), 5.61 (d, J = 1.9, 1H), 5.74 (d, J = 1.9, 1H) 7,40 (m, 5H); ^{13}C NMR ($CDCl_3$): −5.6, 18.2, 25.7, 66.5, 75.3, 79.5, 118.8, 127.8, 128.4, 138.3, 146.1; IR (neat, cm^{-1}) 3400, 1623, 847, 784. Anal. Calcd for $C_{17}H_{26}O_2SiCl_2$ (361.39): C, 56.50; H, 7.25; Cl, 19.62. Found: C, 56.52; H, 7.31; Cl, 19.66; MS (DCI/NH_3) m/z (MNH_4^+) = 379.

4-(*tert*-Butyl-dimethylsilyloxymethyl)-4,5-dichlorohexa-1,5-dien-3-ol 5. Reagents: 172.8 mg (0.6 mmol) of 1,2,3-trichloro-4-(*tert*-butyldimethylsilyloxy)but-2-ene, 13.6 μL (0.2 mmol) of acrolein, 100.0 mg (0.81 mmol) of $CrCl_2$, 4 mL of DMF; yield in DMF: 54.2 mg (87%); R_f = 0.35 (hexane/ether, 95/5); ^{1}H NMR ($CDCl_3$): 0.14 (s, 6H), 0.94 (s, 9H), 3.18 (d, J = 9.2, 1H), 4.10 (d, J = 10.7, 1H), 4.20 (d, J = 10.7, 1H), 4.76 (m, 1H), 5.38 (dt, J = 10.6, J = 1.7, 1H), 5.53 (dt, J = 17.1, J = 1.7, 1H), 5.63 (d, J = 1.9, 1H), 5.92 (d, J = 1.9, 1H), 6.12 (ddd, J = 17.1, J = 10.6, J = 4.9, 1H); ^{13}C NMR ($CDCl_3$): −5.6, 18.1, 25.7, 67.5, 74.9, 76.3, 118.0, 118.1, 134.8, 139.3; IR (neat, cm^{-1}) 3392, 1632, 1005, 836, 732. Anal. Calcd for $C_{13}H_{24}OSiCl_2$ (311.33): C, 50.11; H, 7.77; Cl, 22.77. Found: C, 50.16; H, 7.71; Cl, 22.83; MS (DCI/NH_3) m/z (MNH_4^+) = 329.

2-Methyl-2,3-difluoro-1-phenylbut-3-en-1-ol 6. Reagents: 65.8 mg (0.52 mmol) of 1-chloro-2,3-difluorobut-2-ene, 17.3 μL (0.17 mmol) of benzaldehyde, 85.0 mg (0.69 mmol) of $CrCl_2$, 4 mL of DMF; yield in DMF: 30.0 mg (89%); R_f = 0.4 (hexane/ether, 90/10); mixture of diastereomers 56/44: ^{1}H NMR ($CDCl_3$): 1.39 (dd, J = 22.4, J = 1.6, 3H), 1.55 (dd, J = 22.5, J = 1.6, 3H), 2.33 (d, J = 5.0, 1H) 2.44 (dd, J = 4.0, J = 1.9, 1H), 5.10−4.40 (m, 6H), 7.32 (m, 10H); ^{13}C NMR ($CDCl_3$): 18.6 (d, J = 23.2), 19.4 (d, J = 22.5), 75.7 (d, J = 24.7), 75.9 (d, J = 22.5), 92.4 (dd, J = 10.2, J = 5.1), 92.5 (dd, J = 42.8, J = 4.4), 95.8 (dd, J = 178.8, J = 29.8), 96.7 (dd, J = 178.8, J = 30.5), 128.2, 128.3, 128.7, 128.8, 128.9, 129.2, 138.3 (d, J = 3.6), 138.9 (d, J = 1.5), 164.3 (dd, J = 260.1, J = 21.8), 164.6 (dd, J = 260.1, J = 21.1); ^{19}F NMR ($CFCl_3$) (^{1}H decoupled): −162.9 (d, J = 15.2), −161.7 (d, J = 15.6), −110.9 (d, J = 15.6), −110.3 (d, J = 17.1); ^{19}F NMR ($CFCl_3$): −162.9 (m), −161,7 (m), −110.9 (ddd, J = 49.5, J = 15.1, J = 15.1), −110.3 (ddd, J = 50.5, J = 17.4, J = 17.4); IR (neat, cm^{-1}) 3462, 1680, 1383. Anal. Calcd for $C_{11}H_{12}OF_2$ (198.21): C, 66.57; H, 6.10; F, 19.17. Found: C, 66.80; H, 5.99; F, 19.21; MS (DCI/NH_3) m/z (MNH_4^+) = 216.

2-Butyl-2,3-difluoro-1-phenylbut-3-en-2-ol 7. Reagents: 114.6 mg (0.68 mmol) of 1-chloro-2,3-difluorohept-2-ene, 23.4 μL (0.23 mmol) of benzaldehyde, 112.0 mg (0.91 mmol) of $CrCl_2$; 4 mL of DMF; yield in DMF: 38.7 mg (70%); ***more polar diastereomer***: R_f = 0.25 (hexane/ether, 95/5); ^{1}H NMR ($CDCl_3$): 0.84 (t, J = 7.1, 3H), 1.7−1.1 (m, 6H), 2.35 (d, J = 4.9, 1H), 4.79 (ddd, J = 20.7, J = 4.9, J = 1.9, 1H), 4.81 (dt, J = 50.1, J = 3.5, 1H), 4.96 (ddd, J = 18.9, J = 4.9, J = 3.4, 1H), 7.37 (m, 5H); ^{13}C NMR ($CDCl_3$) 13.9, 22.6, 24.9, 31.7 (d, J = 21 Hz), 76.2 (d, J = 21 Hz), 92.9 (dd, J = 15.2, J = 4.4), 98.1 (dd, J = 183.4, J = 32.5), 128.0, 128.2, 128.5, 137.9, 161.7 (dd, J = 258.0, J = 34.6); ^{19}F NMR ($CFCl_3$) ^{1}H decoupled: −177.4 (d, J = 8.3), −111.3 (d, J = 8.3); ^{19}F NMR ($CFCl_3$): −177.4 (m), −111.3 (ddd, J = 49.7, J = 19.3, J = 8.3); IR (neat, cm^{-1}) 3458, 2998, 1674, 1389; Elem Anal. Calcd for $C_{14}H_{18}OF_2$ (240.29): C, 69.97; H, 7.55; F, 15.81. Found: C, 70.02; H, 7.49; F, 15.69. MS (DCI/NH_3) m/z (MNH_4^+) = 258; ***less polar diastereomer***: R_f = 0.3 (hexane/ether, 95/5); ^{1}H NMR ($CDCl_3$): 0.91 (t, J = 6.8, 3H), 1.41 (m, 6H), 2.01 (m, 2H), 2.33 (dd, J = 5.3, J = 1.5, 1H), 4.49 (dt, J = 50.4, J = 3.8, 1H), 4.69 (ddd, J = 19.2, J = 5.3, J = 3.4), 4.81 (ddd, J = 19.2, J = 5.3, J = 2.3, 1H); ^{19}F NMR ($CFCl_3$) ^{1}H decoupled: −174.9 (d, J = 10.7), −108.9 (d, J = 10.7); ^{19}F NMR ($CFCl_3$): −174.9 (m), −108.9 (ddd, J = 50.5, J = 19.2, J = 10.1).

4-Butyl-4,5-difluorohexa-1,5-dien-3-ol 8. Reagents: 128.4 mg (0.76 mmol) of 1-chloro-2,3-difluorohept-2-ene, 17.4 μL (0.26 mmol) of acrolein, 125.0 mg (1.02 mmol) of $CrCl_2$, 4 mL of DMF; yield in DMF: 42.8 mg (87%); mixture of diastereomers 59/41; R_f = 0.5 (hexane/ether, 85/15); ^{1}H NMR ($CDCl_3$): 0.91 (m, 3H), 1.40 (m, 4H), 1.95 (m, 3H), 4.23 (m, 1H), 4.67 (m, 0.5H), 4.85 (m, 1.5), 5.35 (m, 2H), 5.92 (m, 1H); ^{13}C NMR ($CDCl_3$): 14.1, 22.7, 24.8, 31.4 (d, J = 20.2), 32.02 (d, J = 21.7), 75.4 (d, J = 21.6), 75.8 (d, J = 23.1), 92.5 (m), 97.7 (dd, J = 181.9, J = 33.5), 118.5, 119.3, 133.8 (d, J = 4.4), 134.3 (d, J = 4.3), 161.8 (dd J = 255.6, J = 7.2), 161.2 (dd, J = 257.1, J = 7.2); ^{19}F NMR ($CFCl_3$) ^{1}H decoupled: −175.9 (d, J = 9.2), −174.4 (d, J = 9.2), −111.4 (d, J = 9.2), −110.3 (d, J = 9.2); ^{19}F NMR ($CFCl_3$): −175.9 (m), −174.5 (m), −111.4 (ddd, J = 50.5, J = 19.3, J = 8.3), −110.3 (ddd, J = 50.6, J = 19.3, J = 10.1); IR (neat, cm^{-1}) 3256, 2962, 1682, 1386; HRMS calcd for $C_{10}H_{16}OF_2$ (M + H)$^+$ 190.2301, found 190.2305; MS (DCI/NH_3) m/z (MNH_4^+) = 208.

4-Butyl-4,5-difluoro-1-phenylhexa-1,5-dien-3-ol 9. Reagents: 116.3 mg (0.69 mmol) of 1-chloro-2,3-difluorohept-2-ene, 28.0 μL (0.23 mmol) of *trans*-cinnamaldehyde, 110.0 mg (0.89 mmol) of $CrCl_2$, 4 mL of DMF; yield in DMF: 55.5 mg (91%); mixture of diastereomers 57/43; R_f = 0.35 (hexane/ether, 90/10); ^{1}H NMR ($CDCl_3$): 0.91 (m, 3H), 1.20−2.05 (m, 6H), 2.12 (m, 1H),

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4.40 (m, 1H), 4.66 (m, 0.5H), 4.92 (m, 1.5H), 6.26 (m, 1H), 6.71 (m, 1H), 7.35 (m, 5H); ^{13}C NMR ($CDCl_3$): 14.4, 23.1, 23.2, 25.3, 25.4, 32.1 (d, J = 20.5), 32.6 (d, J = 20.1), 75.6 (dd, J = 22.0, J = 1.8), 76.2 (dd, J = 22.5, J = 2.3), 93.1 (m), 98.2 (dd, J = 181.5, J = 32.6), 125.2, 125.3, 125.8, 125.9, 127.1, 128.5, 134.2, 134.9, 136.6, 136.7, 161.1 (J = 258.3, J = 33.5), 162.2 (d, J = 258.3, J = 34); ^{19}F NMR ($CFCl_3$)^{1}H decoupled: −175.9 (d, J = 9.2), −173.8 (d, J = 9.1), −111.4 (d, J = 8.3), −110.3 (d, J = 10.1); ^{19}F NMR ($CFCl_3$): −175.9 (m), −173.8 (m), −111.4 (ddd, J = 49.7, J = 19.3, J = 9.2), −110.3 (ddd, J = 50.5, J = 20.2, J = 10.2); IR (neat, cm^{-1}) 3399, 2933, 1690, 1390; HRMS calcd for $C_{16}H_{20}OF_2$ $(M + H)^+$ 266.3264, found 266.3269; MS (DCI/NH_3) m/z $(M + 1)$ = 266, (MNH_4^+) = 284.

3,4-Dibromo-1-phenylbut-3-en-1-ol 12. Reagents: 176.0 mg (0.75 mmol) of 1-chloro-2,3-dibromoprop-2-ene, 25.4 μL (0.25 mmol) of benzaldehyde, 123.0 mg (1.0 mmol) of $CrCl_2$, 4 mL of DMF; yield in DMF: 61.3 mg (81%); R_f = 0.5 (hexane/ether, 90/10); ^{1}H NMR ($CDCl_3$): 2.01 (d, J = 3.4, 1H), 2.89 (dd, J = 14.3, J = 4.9, 1H), 3.25 (dd, J = 14.3, J = 8.3, 1H), 5.13 (m, 1H), 6.57 (s, 1H), 7.41 (m, 5H); ^{13}C NMR ($CDCl_3$): 46.3, 72.2, 105.4, 122.2, 125.9, 128.1, 128.6, 142.6; IR (neat, cm^{-1}) 3412, 3010, 1620. Anal. Calcd for $C_{10}H_{10}OBr_2$ (305.99): C, 39.25; H, 3.29; Br, 52.22. Found: C, 39.21; H, 3.26; Br, 52.25; MS (DCI/NH_3) m/z $(M + 1)$ = 324.

Acknowledgment. R. Baati is grateful to the Centre National pour la Recherche Scientifique (CNRS) and to the "Institut de Recherche Pierre Fabre" for generous financial support.

Supporting Information Available: Copies of the ^{1}H, ^{13}C, ^{19}F spectra of compounds **3**−**9** and **12**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO9915269