JOC Article

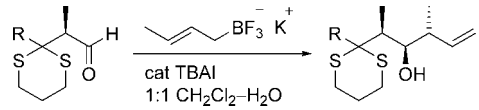
Diastereoselective Synthesis of Useful Building Blocks by Crotylation of β-Branched α-Methylaldehydes with Potassium Crotyltrifluoroborates

Kyosuke Tanaka, Yukiko Fujimori, Yoko Saikawa,* and Masaya Nakata*

Department of Applied Chemistry, Faculty of Science and Technology, Keio University, 3-14-1 Hiyoshi, Kohoku-ku, Yokohama 223-8522, Japan

saikawa@applc.keio.ac.jp; msynktxa@applc.keio.ac.jp

Received May 22, 2008

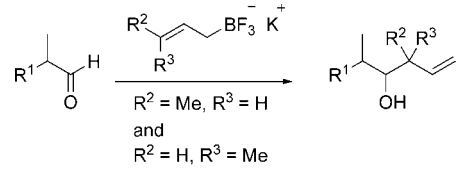


The diastereoselective construction of stereotriads having consecutive methyl, hydroxy, and methyl substituents was realized by the substrate-controlled crotylation of β-branched α-methylaldehydes with potassium crotyltrifluoroborates. Especially, crotylation of 2-(1,3-dithian-2-yl)propanal with potassium (*E*)-crotyltrifluoroborate afforded, in good yield and with excellent diastereoselectivity, a useful building block that has different and potential functional groups on both ends.

Introduction

Stereotriads characterized by their consecutive methyl, hydroxy, and methyl substituents are important building blocks for the synthesis of natural products such as macrolides and polyethers. Aldol reactions between enolates derived from ethyl ketones and α-methylaldehydes are a conventional method for constructing such stereotriads. The reactions of crotylmetal reagents with α-methylaldehydes are an important alternative to aldol reactions and have been successfully used for the same purpose.[1] Recently, Batey et al. reported a new class of crotylboron compounds, potassium crotyltrifluoroborates, and their addition to aldehydes.[2] Potassium organotrifluoroborates have become versatile organometallic reagents for carbon−carbon bond formation because of their air and moisture stable properties and thereby easy handling.[3,4] Among them, potassium alkenyl- and aryltrifluoroborates are widely employed for coupling reactions such as the Suzuki−Miyaura coupling.[4,5] On the other hand, there have been few reports concerning allylation and crotylation of aldehydes by allyl- and crotyltrifluoroborates.[2] Encouraged by Batey's diastereoselective crotylation of α- and β-silyloxy-substituted aldehydes,[2b,d] we anticipated that crotylation of α-methylaldehydes with potassium crotyltrifluoroborates would be a good method for the diastereoselective synthesis of the aforementioned stereotriads (Scheme 1).[6] We now report that 2-(1,3-dithian-2-yl)propanal is an excellent substrate and both ends of the resulting coupling product are available for further elaboration.

SCHEME 1. Addition of Potassium Crotyltrifluoroborates to α-Methylaldehydes



(1) For reviews, see: (a) Roush, W. R. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Heathcock, C. H. Eds.; Pergamon: Oxford, UK, 1991; Vol. 2, pp 1−53. (b) Yamamoto, Y.; Asao, N. *Chem. Rev.* **1993**, *93*, 2207–2293. (c) Kennedy, J. W. J.; Hall, D. G. *Angew. Chem., Int. Ed.* **2003**, *42*, 4732–4739. (d) Denmark, S. E.; Fu, J. *Chem. Rev.* **2003**, *103*, 2763–2793. (e) Hall, D. G. *Synlett* **2007**, 1644–1655.

(2) (a) Batey, R. A.; Thadani, A. N.; Smil, D. V. *Tetrahedron Lett.* **1999**, *40*, 4289–4292. (b) Batey, R. A.; Thadani, A. N.; Smil, D. V.; Lough, A. J. *Synthesis* **2000**, 990–998. (c) Thadani, A. N.; Batey, R. A. *Org. Lett.* **2002**, *4*, 3827–3830. (d) Thadani, A. N.; Batey, R. A. *Tetrahedron Lett.* **2003**, *44*, 8051–8055.

(3) (a) Chambers, R. D.; Clark, H. C.; Willis, C. J. *J. Am. Chem. Soc.* **1960**, *82*, 5298–5301. (b) Vedejs, E.; Chapman, R. W.; Fields, S. C.; Lin, S.; Schrimpf, M. R. *J. Org. Chem.* **1995**, *60*, 3020–3027.

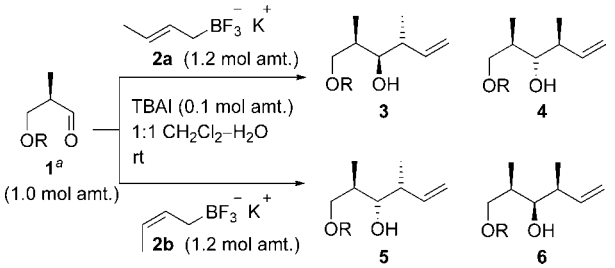
(4) For recent reviews on organotrifluoroborates, see: (a) Darses, S.; Genet, J.-P. *Eur. J. Org. Chem.* **2003**, 4313–4327. (b) Molander, G. A.; Figueroa, R. *Aldrichim. Acta* **2005**, *38*, 49–56. (c) Molander, G. A.; Ellis, N. *Acc. Chem. Res.* **2007**, *40*, 275–286. (d) Stefani, H. A.; Cella, R.; Vieira, A. S. *Tetrahedron* **2007**, *63*, 3623–3658. (e) Darses, S.; Genet, J.-P. *Chem. Rev.* **2008**, *108*, 288–325.

(5) (a) Darses, S.; Genet, J.-P. *Tetrahedron Lett.* **1997**, *38*, 4393–4396. (b) Batey, R. A.; Quach, T. D. *Tetrahedron Lett.* **2001**, *42*, 9099–9103. (c) Molander, G. A.; Biolatto, B. *J. Org. Chem.* **2003**, *68*, 4302–4314, and references cited therein.

(6) Synthesis of a stereotriad having the identical vinyl ends, using the coupling of vinyloxiranes and potassium crotyltrifluoroborates, has been reported. See: Lautens, M., Ouellet, S. G., Raeppel, S. *Angew. Chem., Int. Ed.* **2000**, *39*, 4079−4082.

10.1021/jo801106b CCC: $40.75
Published on Web 07/16/2008

TABLE 1. Crotylation of β-Alkoxy-α-methylaldehydes 1 with Potassium Crotyltrifluoroborates 2



entry	substrate[a] (R)	borate	time (h)	% yield[b] (ratio)[c]
1	**1a** (PMB)	**2a**	1	87 (**3a**:**4a** = 2:1)
2	**1b** (TBS)	**2a**	1	77 (**3b**:**4b** = 2:1)
3	**1c** (Tr)	**2a**	1	95 (**3c**:**4c** = 2.5:1)
4	**1d** (TBDPS)	**2a**	0.5	98 (**3d**:**4d** = 3:1)
5	**1a** (PMB)	**2b**	1	99[d] (**5a**:**6a** = 1.5:1)
6	**1b** (TBS)	**2b**	1	69[d] (**5b**:**6b** = 2:1)
7	**1c** (Tr)	**2b**	1	97[d] (**5c**:**6c** = 1.5:1)
8	**1d** (TBDPS)	**2b**	0.5	91[d] (**5d**:**6d** = 2:1)

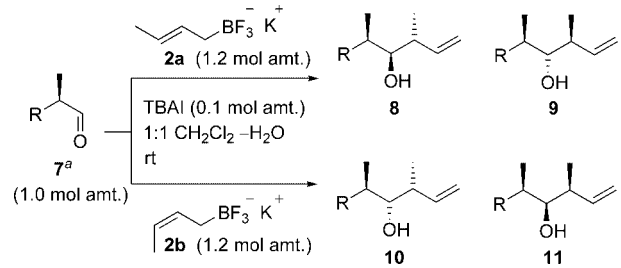
[a] Aldehydes **1** were racemates. [b] Combined yield of the barely separable adducts after silica gel column chromatography. [c] The ratio was determined by ^{1}H NMR analysis of the adducts. [d] Trace amounts of **3** and **4** also present in the adducts.

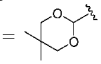
Results and Discussion

We first examined the crotylation of the racemic β-alkoxy-α-methylaldehydes (**1**, R = PMB, TBS, Tr, and TBDPS)[7] with potassium (*E*)-crotyltrifluoroborate (**2a**) under Batey's conditions[2c,d] using a 0.1 molar amount of tetrabutylammonium iodide (TBAI) as a catalyst in 1:1 $CH_2Cl_2-H_2O$ at rt. The results are shown in Table 1. For each reaction, the yield was satisfactory; however, the diastereoselectivity was modest (entries 1−4).[8] We next examined the crotylation of **1** with potassium (*Z*)-crotyltrifluoroborate (**2b**) (entries 5−8). The yield was also satisfactory, but the diastereoselectivity was worse than that in the *E*-case.

These results implied that, at least in the *E*-case, the bulkiness at the aldehyde β-position somewhat affects the diastereoselectivity. Therefore, we next chose β-branched α-methylaldehydes as the substrates (Table 2).[9] The result of the crotylation of 2-(1,3-dioxan-2-yl)propanal **7a**[9a] with **2a** (entry 1) was what we had expected: **8a**:**9a** = 11:1.[10] In 1982, Kishi et al. reported that the $CrCl_2$-mediated crotylation of **7a** afforded **8a** and **9a** with the same selectivity as our case.[11] Gratifingly, we found that the crotylation of 2-(1,3-dithian-2-yl)propanal (**7b**)[9b] with **2a** gave **8b** in high yield with excellent selectivity (**8b**:**9b** = 24:1, entry 2).[10] Furthermore, we attempted crotylation of

TABLE 2. Crotylation of β-Branched α-Methylaldehydes 7 with Potassium Crotyltrifluoroborates 2



entry	substrate[a]	borate	time (h)	% yield[b] (ratio)[c]
1	**7a** R = 	**2a**	7	85 (**8a**:**9a** = 11:1)
2	**7b** R = 	**2a**	4	97 (**8b**:**9b** = 24:1)
3	**7c**[d] R = 	**2a**	4	95 (**8c** only)
4	**7c'**[d]	**2a**	4	98 (**8c'** only)
5	**7a**	**2b**	7	79[e] (**10a**:**11a** =1.1:1)
6	**7b**	**2b**	4	93[e] (**10b**:**11b** = 2:1)
7	**7c**[d]	**2b**	4	96[e] (**10c**:**11c** = 8:1)
8	**7c'**[d]	**2b**	4	98[e] (**10c'**:**11c'** = 10:1)

[a] Aldehydes **7** were racemates. [b] Combined yield of the barely separable adducts after silica gel column chromatography. [c] The ratio was determined by ^{1}H NMR analysis of the adducts. [d] **7c** and **7c′** are diastereomers. [e] Trace amounts of **8** and **9** also present in the adducts.

aldehydes **7c**[9c] and its diastereomer **7c′**[9c] with **2a** and obtained **8c** and **8c′**[10] as a single isomer, respectively (entries 3 and 4). In contrast to the favorable *E*-case, crotylation of **7a** and **7b** with **2b** gave the adducts with miserable diastereoselectivity (**10a**:**11a** = 1.1:1 and **10b**:**11b** = 2:1, entries 5 and 6). Only the crotylation of **7c** and **7c′** with **2b** displayed higher levels of diastereoselectivity (**10c**:**11c** = 8:1 and **10c′**:**11c′** = 10:1 depending on the diastereomers used, entries 7 and 8).

Addition of potassium crotyltrifluoroborates to aldehydes is believed to involve the six-membered transition states.[2d] Our first results (Table 1) obtained for the crotylation of β-alkoxy-α-methylaldehydes **1** with **2** were consistent with those of the previous report with pinacol crotylboronates.[8a] We consider the mechanistic origin of the observed diastereoselectivity for the

(7) Aldehydes **1** were prepared from 2-methyl-1,3-propanediol in two steps. For **1b** see: (a) Kiyooka, S.; Shahid, K. A.; Goto, F.; Okazaki, M.; Shuto, Y. *J. Org. Chem.* **2003**, *68*, 7967–7978. For **1d** see: (b) Kiyooka, S. *Tetrahedron: Asymmetry* **2003, 14**, 2897–2910. **1a** and **1c** were similarly prepared.

(8) Stereochemical assignments of **3b**−**6b**, **3c**, and **3d**−**6d** were based on ^{1}H NMR comparisons with the reported data. For **3b**-**6b** and **3d**-**6d** see: (a) Roush, W. R.; Palkowitz, A. D.; Ando, K. *J. Am. Chem. Soc.* **1990, 112**, 6348–6359. For **3c** see: (b) Morita, A.; Kuwahara, S. *Tetrahedron Lett.* **2007**, *48*, 3163–3166. Stereochemical assignments of **3a**−**6a** and **4c**−**6c** were based on the similarities of their ^{1}H NMR spectra with **3d**−**6d** and mechanistic considerations.

(9) **7a** was prepared from methacrolein and 2,2-dimethyl-1,3-propanediol according to the reported procedure. See: (a) Kelly, T. R.; Fu, Y.; Xie, R. L. *Tetrahedron Lett.* **1999**, *40*, 1857–1860. For (−)-**7b** see: (b) Smith, A. B., III; Adams, C. M.; Barbosa, S. A. L.; Degnan, A. P. *Proc. Nat. Acc. Sci.* **2004**, *101*, 12042–12047. Racemate **7b** was prepared from **1d** according to the same procedure. (c) For preparation of **7c** and **7c′**, see the Supporting Information.

(10) Structure determination of the adducts, see the Supporting Information.

(11) Lewis, M. D.; Kishi, Y. *Tetrahedron Lett.* **1982**, *23*, 2343–2346.

(12) The β-substituent effects on the aldehyde π-facial selectivity are suggested in the previous reports, see: (a) Hoffmann, R. W.; Weidmann, U. *Chem. Ber.* **1985**, *118*, 3966–3979. (b) Hoffmann, R. W.; Brinkmann, H.; Frenking, G. *Chem. Ber.* **1990**, *123*, 2387–2394. (c) Evans, D. A.; Dart, M. J.; Duffy, J. L.; Yang, M. G. *J. Am. Chem. Soc.* **1996**, *118*, 4322–4343. See also: (d) Still, W. C.; Schneider, J. A. *Tetrahedron Lett.* **1980**, *21*, 1035–1038.

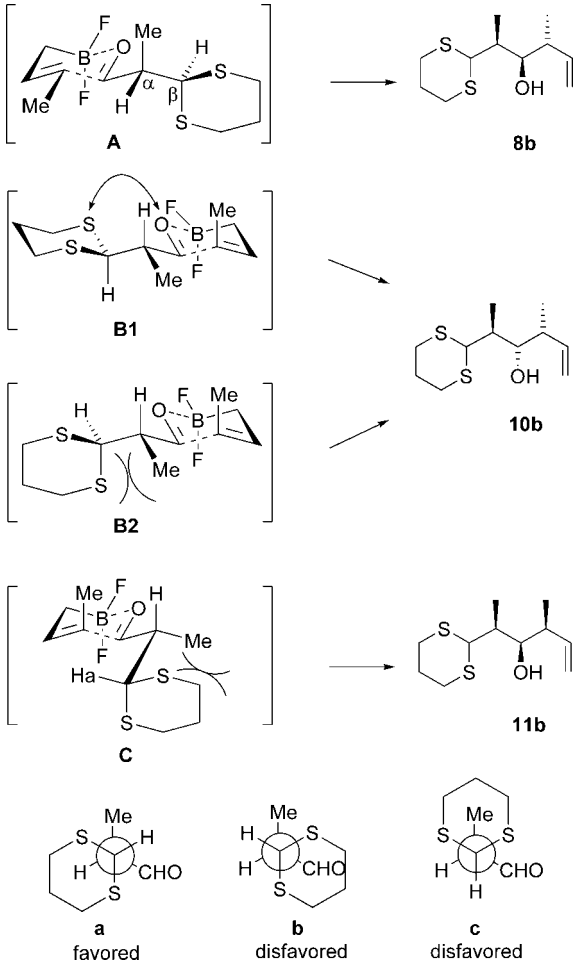
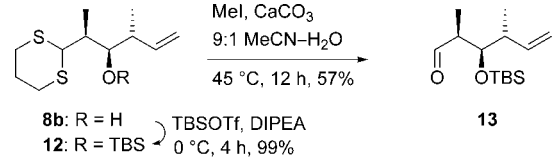


FIGURE 1. Plausible transition state geometries of crotylation of **7b** with **2**.

crotylation of aldehyde **7b** as a representative, based on the previously reported hypotheses concerning crotylation[8a,12a,b] and aldol reactions.[12c,13] It is reasonable to presume that avoidance of a serious gauche−gauche pentane interaction is a dominant rule.[12a,b,13] Despite the favorable transition states (Figure 1, **A** and **B**), which satisfy this assumption, the resulting diastereoselectivities are quite different in the *E*- and *Z*-cases. In general, in spite of the anti-Felkin transition state (i.e., **B** in Figure 1), excellent diastereoselectivity is often observed when aldehydes have a sufficiently large α-substituent in addition to the α-methyl group.[13] Therefore, to account for the difference in our case, the conformation of the β-position must be considered.[11] Among three aldehyde conformations (Figure 1, **a**−**c**), conformation **a** is the most favorable based on sterics. For the crotylation of the *E*-case, the transition structure **A** is ideal including the β-substituent effects (corresponding to **a**). For the crotylation of the *Z*-case, the favored conformation at the β-position produces a severe electronic repulsion between the lone pairs of the sulfur and oxygen atoms (**B1**), which was previously recognized as a destabilizing dipolar interaction.[12c] Another transition structure **B2** without such an electronic repulsion suffers from the disfavored conformation at the β-position (corresponding to **c**). Transition structure **C**, which avoids placing the sulfur atom in the Ha position,[12b] also suffers from

(13) Roush, W. R. *J. Org. Chem.* **1991**, *56*, 4151–4157, and references cited therein.

SCHEME 2. Removal of Dithioacetal in 12



the disfavored conformation at the β-position (corresponding to **c**). The competition of these steric and electronic repulsions can explain the less pronounced diastereoselectivity for the crotylation of the *Z*-case. Similarly, the observation on the crotylation of **7a** can be rationalized by considering these β-substituent effects. The origin of the different level of diastereoselectivity between **7a** and **7b** is probably due to the size of the β-substituent (dioxane vs dithiane). In the case of the fully β-substituted aldehydes **7c** and **7c′**, the steric effect of the conformation at the β-position would be canceled, and the bulkiness at the α-position must be responsible for improvement of diastereoselectivity.[13]

The usefulness of thus-obtained **8b** as a building block for natural product syntheses was next demonstrated. Prior to this, we confirmed the utility of **8b** as a chiral building block. Thus, an attempt was made to crotylate the chiral aldehyde (−)-**7b**,[9b] which was prepared from commercially available methyl (*S*)-3-hydroxy-2-methylpropionate (Roche ester) in six steps[9b] or prepared by oxidation of the corresponding alcohol derived from Roche ester in three steps.[14] The crotylation of (−)-**7b** with **2a** afforded the optically pure **8b** without racemization. The following demonstrations were thus carried out by using the racemic **8b** (Schemes 2–4). After silylation of **8b** with TBSOTf and *N*,*N*-diisopropylethylamine (DIPEA) in CH_2Cl_2, the resulting TBS ether **12** was subjected to dedithioacetalization conditions (Scheme 2). Although both the starting material **12** and the product **13** were found to be unstable under several deprotection conditions (e.g., MeI,[15] $PhI(CO_2CF_3)_2$,[16] NBS,[17] and DMP[18]), we found that MeI[15] and NBS[17] were the reagents of choice, giving the desired aldehyde **13**[19] in 57% and 54% yields, respectively.

An alternative sequence suggests the possibility of using **8b** for conversion from the opposite side (Scheme 3). Oxidative cleavage of the terminal alkene by ozonolysis[20] afforded aldehyde **14** whose dithiane portion was also oxidized to the mono-oxide (7:3 mixture of diastereomers). Even when ozonolysis of **12** was carried out for 1 h, no overoxidized products were obtained. The resulting dithiane mono-oxide was stable for further conversion. Aldehyde **14** was reduced to the alcohol, which was protected as the TBDPS ether. Dedithioacetalization

(14) (a) Ide, M.; Nakata, M. *Bull. Chem. Soc. Jpn.* **1999**, *72*, 2491–2499. (b) Ide, M.; Yasuda, M.; Nakata, M. *Synlett* **1998**, 936–938.

(15) (a) Jin, M.; Taylor, R. E. *Org. Lett.* **2005**, *7*, 1303–1305. (b) Fetizon, M.; Jurion, M. *J. Chem. Soc., Chem. Commun.* **1972**, 382–383. (c) Colombo, L.; Gennari, C.; Scolastico, C.; Beretta, M. G. *J. Chem. Soc., Perkin Trans. 1* **1978**, 1036–1041.

(16) Stork, G.; Zhao, K. *Tetrahedron Lett.* **1989**, *30*, 287–290.

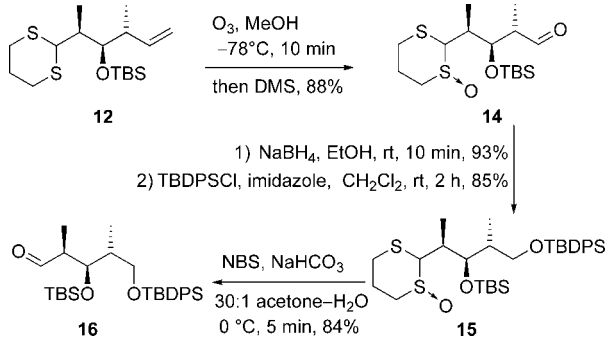
(17) (a) Corey, E. J.; Erickson, B. W. *J. Org. Chem.* **1971**, *36*, 3553–3560. (b) Shmidt, U.; Meyer, R.; Leitenberger, V.; Griesser, H.; Lieberknecht, A. *Synthesis* **1992**, 1025–1030.

(18) Langille, N. F.; Dakin, L. A.; Panek, J. S. *Org. Lett.* **2003**, *5*, 575–578.

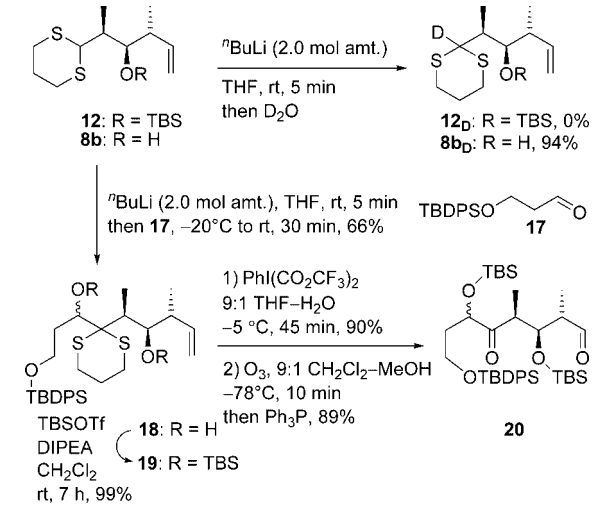
(19) Mínguez, J. M.; Kim, S.-Y.; Giuliano, K. A.; Balachadran, R.; Madiraju, C.; Day, B. W.; Curran, D. P. *Bioorg. Med. Chem.* **2003**, *11*, 3335–3357. The reported ^{1}H NMR spectral datum was not identical with **13** for some unknown reason. Aldehyde **13** was then reduced ($NaBH_4$, MeOH) and the resulting alcohol was identified on the basis of the spectral data reported in the same paper. See the Supporting Information.

(20) Anaya, J.; Gero, S. D.; Grande, M.; Hernando, J. I. M.; Laso, N. M. *Bioorg. Med. Chem.* **1999**, *7*, 837–850.

SCHEME 3. Oxidative Cleavage of 12 and Subsequent Conversion



SCHEME 4. Lithiation and Addition Reaction of 8b



of the resulting **15** was performed with NBS[17a,21] in the presence of $NaHCO_3$ to give aldehyde **16**[22] in good yield (Scheme 3).

A special characteristic of the 1,3-dithianes is the utility of their carbanions in coupling reactions for natural product syntheses.[23] Smith et al. suggested that δ-alkenyldithianes resist lithiation due to through-space donation of electrons from the olefin π orbital to the C−S σ^* orbital.[24] Similar to Smith's results, lithiation of **12** with BuLi gave no **12D** after deuteration (Scheme 4). In contrast, it was found that the nonprotected **8b** was readily lithiated to give **8bD** after the addition of D_2O. The above anion was successfully coupled with aldehyde **17**[25] to give a 2:1 mixture of **18** in 66% yield. After silylation of **18**, the resulting **19** was subjected to dedithioacetalization, using $PhI(CO_2CF_3)_2$[16] followed by ozonolysis to give aldehyde **20** in good yield.

Conclusions

In summary, the crotylation of 2-dithianylaldehydes **7b**, **7c**, and **7c′** with air- and moisture-stable potassium (*E*)-crotyltrifluoroborate was readily realized in good yield and with excellent diastereoselectivity. In addition, the usefulness of the coupling product **8b** as a building block aiming at a further elaboration was demonstrated. The results presented in this article would broaden the synthetic usefulness of organotrifluoroborate chemistry. Application of **8b** for natural product syntheses is now underway in our laboratories.

Experimental Section

General Procedure for Crotylation of Aldehydes with Potassium Crotyltrifluoroborates. To a stirred solution of aldehyde (1.0 equiv) in 1:1 $CH_2Cl_2-H_2O$ (0.17 M) were added at rt tetra-*n*-butylammonium iodide (0.10 molar amount) and potassium crotyltrifluoroborate (1.2 equiv). After the reaction time indicated in Tables 1 and 2, saturated aqueous $NaHCO_3$ was added and the mixture was extracted with $CHCl_3$. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel to afford a mixture of diastereomers of homoallylalcohols as a colorless syrup.

Homoallylalcohol 8a[11] from 7a and 2a. R_f 0.49 (toluene/EtOAc = 10:1); ^{1}H NMR (300 MHz, $CDCl_3$, TMS = 0.00) δ 0.72 (s, 3H), 0.95 (d, J = 6.6 Hz, 3H), 0.99 (d, J = 6.6 Hz, 3H), 1.19 (s, 3H), 1.92 (ddq, J = 7.8, 3.8, 1.8 Hz, 1H), 2.28 (m, 1H), 2.82 (d, J = 1.5 Hz, 1H), 3.42 (d, J = 10.0 Hz, 1H), 3.45 (d, J = 10.0 Hz, 1H), 3.64 (d, J = 10.0 Hz, 2H), 3.74 (br d, J = 9.3 Hz, 1H), 4.48 (d, J = 3.9 Hz, 1H), 5.06 (ddd, J = 9.9, 2.0, 0.8 Hz, 1H), 5.10 (br d, J = 17.6 Hz, 1H), 5.86 (ddd, J = 17.6, 9.9, 7.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, $CDCl_3$ = 77.00) δ 7.1, 16.6, 21.7, 22.9, 30.2, 38.7, 41.3, 73.8, 77.1, 77.3, 105.0, 114.6, 142.2; IR (neat, cm^{-1}) 3520, 3080, 2958, 2850, 1640, 1465, 1397, 1310, 1238, 1208, 1160, 1108, 1040, 1018, 995, 963, 922, 790, 758; LRMS (EI) *m*/*z* (M^+) 228.1; HRMS (EI) *m*/*z* (M^+) calcd for $C_{13}H_{24}O_3$ 228.1726, found 228.1747.

Homoallylalcohol 8b from 7b and 2a. R_f 0.46 (toluene/EtOAc = 10:1); ^{1}H NMR (300 MHz, $CDCl_3$, TMS = 0.00) δ 0.98 (d, J = 6.6 Hz, 3H), 1.12 (d, J = 6.8 Hz, 3H), 1.79−1.94 (m, 1H), 1.89 (d, J = 3.6 Hz, 1H), 2.01 (m, 1H), 2.08−2.19 (m, 1H), 2.32 (m, 1H), 2.81−2.98 (m, 4H), 3.71 (ddd, J = 8.2, 3.6, 3.6 Hz, 1H), 4.20 (d, J = 7.8 Hz, 1H), 5.13 (dd, J = 10.0, 1.8, 1H), 5.14 (ddd, J = 17.4, 1.8, 1.2, 1H), 5.78 (ddd, J = 17.4, 10.0, 8.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, $CDCl_3$ = 77.00) δ 10.5, 16.5, 26.1, 30.6, 30.8, 39.7, 41.9, 52.8, 74.1, 116.3, 141.1; IR (neat, cm^{-1}) 3470, 3078, 2970, 2930, 2900, 1640, 1458, 1420, 1380, 1320, 1278, 1250, 1190, 1092, 1001, 980, 915, 760; LRMS (EI) *m*/*z* (M^+) 232.1; HRMS (EI) *m*/*z* (M^+) calcd for $C_{11}H_{20}OS_2$ 232.0956, found 232.0949. (−)-**8b**: $[\alpha]^{29.5}_D$ −11 (*c* 0.35, $CHCl_3$)

Homoallylalcohol 8c from 7c and 2a. R_f 0.51 (toluene/EtOAc = 10:1); ^{1}H NMR (300 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.95 (d, J = 7.0 Hz, 3H), 1.07 (s, 9H), 1.24 (d, J = 7.0 Hz, 3H), 1.71−1.91 (m, 2H), 1.96−2.09 (m, 2H), 2.05 (s, 3H), 2.20 (d, J = 2.8 Hz, 1H), 2.27 (m, 1H), 2.45−2.64 (m, 3H), 3.04−3.28 (m, 2H), 3.63 (ddd, J = 10.2, 10.2, 4.8 Hz, 1H), 3.71 (ddd, J = 10.2, 6.8, 3.4 Hz, 1H), 4.13 (dd, J = 9.0, 2.8 Hz, 1H), 5.05 (dd, J = 9.8, 1.6 Hz, 1H), 5.09 (br d, J = 17.2 Hz, 1H), 5.86 (ddd, J = 17.2, 9.8, 8.0 Hz, 1H), 5.93 (d, J = 9.8 Hz, 1H), 7.35−7.47 (m, 6H), 7.66−7.72 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$ $CDCl_3$ = 77.00) δ 9.1, 16.9, 19.1, 21.1, 24.2, 26.2, 26.7, 26.8, 33.3, 41.3, 41.8, 60.6, 60.9, 72.0, 74.8, 114.4, 127.6, 129.6, 129.6, 133.4, 133.6, 135.5, 135.7, 142.2, 170.1; IR (neat, cm^{-1}) 3562, 3073, 2960, 2930, 2860, 1743, 1640, 1590, 1472, 1462, 1428, 1372, 1280, 1232, 1112, 1018, 963, 910, 822, 768, 700; LRMS (EI) *m*/*z* (M^+) 586.2; HRMS (EI) *m*/*z* (M^+) calcd for $C_{32}H_{46}O_4SiS_2$ 586.2607, found 586.2604.

(21) Page, P. C. B.; McKenzie, M. J.; Buckle, D. R. *J. Chem. Soc., Perkin Trans. 1* **1995**, 2673–2676.

(22) Zampella, A.; Sepe, V.; D'Orsi, R.; Bifulco, G.; Bassarello, C.; D'Auria, M. V. *Tetrahedron: Asymmetry* **2003**, *14*, 1787–1798.

(23) (a) Nakata, M. In *Science of Synthesis*, Otera, J. Ed.; Thieme: Stuttgart, Germany, 2007; Vol. 30, pp 351−434. (b) Smith, A. B., III; Adams, C. M. *Acc. Chem. Res.* **2004**, *37*, 366–377.

(24) (a) Smith, A. B., III; Friestad, G. K.; Barbosa, J.; Bertounesque, E.; Hull, K. G.; Iwashima, M.; Qiu, Y.; Salvatore, B. A.; Spoors, P. G.; Duan, J. J.-W. *J. Am. Chem. Soc.* **1999**, *121*, 10468–10477. (b) Fürstner, A.; Fenster, M. D. B.; Fasching, B.; Godbout, C.; Radkowski, K. *Angew. Chem., Int. Ed.* **2006**, *45*, 5510–5515.

(25) Holmes, A. B.; Hughes, A. B.; Smith, A. L. *J. Chem. Soc., Perkin Trans. 1* **1993**, 633–643.

Homoallylalcohol 8c′ from 7c′ and 2a. R_f 0.51 (toluene/EtOAc = 10:1); ^{1}H NMR (300 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 1.00 (d, J = 6.4 Hz, 3H), 1.06 (s, 9H), 1.10 (d, J = 7.2 Hz, 3H), 1.70−1.87 (m, 2H), 1.98−2.11 (m, 2H), 2.04 (s, 3H), 2.25 (m, 1H), 2.47−2.67 (m, 3H), 2.63 (d, J = 2.8 Hz, 1H), 3.05−3.25 (m, 2H), 3.61 (ddd, J = 10.0, 10.0, 4.4 Hz, 1H), 3.72 (ddd, J = 10.0, 6.4, 3.8 Hz, 1H), 4.31 (dd, J = 8.2, 2.8 Hz, 1H), 5.05 (br dd, J = 10.0 Hz, 1H), 5.08 (br d, J = 17.0 Hz, 1H), 5.83 (d, J = 10.2 Hz, 1H), 5.90 (ddd, J = 17.0, 10.0, 8.0 Hz, 1H), 7.34−7.47 (m, 6H), 7.66−7.72 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$, $CDCl_3$ = 77.00) δ 8.9, 17.3, 19.1, 21.1, 24.5, 26.4, 26.5, 26.8, 33.0, 41.7, 42.7, 60.3, 60.8, 71.0, 74.2, 114.5, 127.6, 129.6, 129.6, 133.4, 133.6, 135.5, 135.7, 141.9, 170.2; IR (neat, cm^{-1}) 3540, 3072, 2960, 2930, 2860, 1740, 1640, 1590, 1473, 1462, 1428, 1390, 1372, 1280, 1238, 1110, 1020, 968, 910, 821, 758, 700; LRMS (EI) m/z (M^+) 586.2; HRMS (EI) m/z (M^+) calcd for $C_{32}H_{46}O_4SiS_2$ 586.2607, found 586.2632.

Homoallylalcohols 10a and 11a from 7a and 2b. R_f 0.52 (toluene/EtOAc = 10:1); ^{1}H NMR (300 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.72 (s, 6H), 0.96, 0.98, 1.02, and 1.12 (each d, J = 7.0, 7.2, 7.0, and 6.8 Hz, each 3H), 1.19 (s, 6H), 1.86−1.98 (m, 2H), 2.22−2.40 (m, 2H), 3.10 and 3.22 (each br, each 1H), 3.43 (m, 4H), 3.53−3.62 and 3.75 (m and br d, J = 11.0 Hz, each 1H), 3.62 (br d, J = 11.0 Hz, 2H), 4.46 and 4.58 (each d, J = 3.0 and 3.4 Hz, each 1H), 4.95 and 5.45 (each dd, J = 10.0, 2.0 and 10.0, 1.2 Hz, each 1H), 5.04 and 5.06 (each br d, J = 16.0 and 18.0 Hz, each 1H), 5.60 and 5.90 (each ddd, J = 16.0, 10.0, 9.0 and 18.0, 10.0, 7.0 Hz, each 1H); ^{13}C NMR (75 MHz, $CDCl_3$, $CDCl_3$ = 77.00) δ 6.7, 11.4, 12.4, 17.7, 21.7, 21.7, 22.9, 22.9, 30.3, 30.3, 38.9, 39.7, 40.2, 41.9, 74.1, 75.5, 77.1, 77.2, 77.3, 77.3, 104.2, 105.6, 114.1, 114.6, 141.1, 142.3; IR (neat, cm^{-1}) 3520, 3080, 2959, 2850, 1640, 1465, 1392, 1365, 1310, 1261, 1236, 1219, 1165, 1110, 1040, 1020, 995, 965, 910, 810, 790; LRMS (EI) m/z (M^+) 228.1; HRMS (EI) m/z (M^+) calcd for $C_{13}H_{24}O_3$ 228.1726, found 228.1723.

Homoallylalcohols 10b and 11b from 7b and 2b. The NMR chemical shifts of each **10b** and **11b** were determined by using the spectra of a mixture of **10b** and **11b**. **10b**: R_f 0.46 (toluene/EtOAc = 10:1); ^{1}H NMR (300 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.98 (d, J = 7.0 Hz, 3H), 1.07 (d, J = 7.0 Hz, 3H), 1.76−1.96 (m, 2H), 1.96−2.19 (m, 2H), 2.43 (m, 1H), 2.80−2.94 (m, 4H), 3.63 (dd, J = 8.0, 3.0 Hz, 1H), 4.66 (d, J = 2.4 Hz, 1H), 5.13 (br d, J = 17.4 Hz, 1H), 5.15 (br d, J = 11.2 Hz, 1H), 5.91 (ddd, J = 17.4, 11.2, 6.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, $CDCl_3$ = 77.00) δ 10.5, 12.8, 26.4, 30.7, 31.5, 38.9, 41.4, 52.3, 74.2, 115.2, 141.8. **11b**: R_f 0.46 (toluene/EtOAc = 10:1); ^{1}H NMR (300 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 1.09 (d, J = 7.0 Hz, 6H),1.76−1.96 (m, 2H), 1.96−2.19 (m, 2H), 2.34 (m, 1H), 2.80−3.08 (m, 4H), 3.74 (dd, J = 8.2, 2.9 Hz, 1H), 4.14 (d, J = 6.2 Hz, 1H), 5.01 (dd, J = 10.4, 1.5 Hz, 1H), 5.07 (br d, J = 16.4 Hz, 1H), 5.63 (ddd, J = 16.4, 10.4, 8.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, $CDCl_3$ = 77.00) δ 10.1, 17.0, 26.1, 30.6, 31.0, 40.3, 41.8, 53.6, 75.6, 115.1, 140.7. Mixture of **10b** and **11b**: IR (neat, cm^{-1}) 3470, 3078, 2970, 2938, 2898, 2830, 1640, 1458, 1420, 1381, 1318, 1278, 1242, 1190, 1110, 1090, 1000, 978, 913, 876, 858, 816, 760; LRMS (EI) m/z (M^+) 232.1; HRMS (EI) m/z (M^+) calcd for $C_{11}H_{20}OS_2$ 232.0956, found 232.0961.

Homoallylalcohol 10c from 7c and 2b. R_f 0.51 (toluene/EtOAc = 10:1); ^{1}H NMR (300 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 1.07 (s, 9H), 1.10 (d, J = 6.0 Hz, 3H), 1.22 (d, J = 6.2 Hz, 3H), 1.72−1.88 (m, 2H), 1.96−2.07 (m, 2H), 2.06 (s, 3H), 2.25 (d, J = 2.6 Hz, 1H), 2.19−2.34 (m, 1H), 2.45−2.60 (m, 3H), 3.04−3.28 (m 2H), 3.63 (ddd, J = 10.0, 10.0, 4.8 Hz, 1H), 3.71 (ddd, J = 10.0, 7.0, 4.0 Hz, 1H), 4.11 (dd, J = 10.4, 2.6 Hz, 1H), 4.98 (dd, J = 10.2, 1.8 Hz, 1H), 5.07 (dd, J = 17.4, 1.8 Hz, 1H), 5.56 (ddd, J = 17.4, 10.2, 10.2 Hz, 1H), 5.92 (d, J = 9.0 Hz, 1H), 7.34−7.47 (m, 6H), 7.65−7.73 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$, $CDCl_3$ = 77.00) δ 8.7, 18.2, 19.1, 21.1, 24.3, 26.1, 26.6, 26.8, 33.3, 41.5, 42.3, 60.7, 60.9, 72.1, 75.3, 115.1, 127.6, 129.6, 129.6, 133.4, 133.6, 135.5, 135.7, 140.8, 170.1; IR (neat, cm^{-1}) 3560, 3078, 2960, 2930, 2860, 1743, 1640, 1590, 1472, 1460, 1427, 1373, 1280, 1233, 1111, 1019, 979, 963, 912, 823, 759, 740, 702; LRMS (EI) m/z (M^+) 586.2; HRMS (EI) m/z (M^+) calcd for $C_{32}H_{46}O_4SiS_2$ 586.2607, found 586.2600.

Homoallylalcohol 10c′ from 7c′ and 2b. R_f 0.51 (toluene/EtOAc = 10:1); ^{1}H NMR (300 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 1.05 (s, 9H), 1.05 (d, J = 7.0 Hz, 3H), 1.12 (d, J = 6.8 Hz, 3H), 1.60−1.88 (m, 2H), 2.03 (s, 3H), 2.04−2.17 (m, 2H), 2.26 (m, 1H), 2.45−2.64 (m, 3H), 2.78 (d, J = 2.6 Hz, 1H), 3.03−3.24 (m, 2H), 3.57 (ddd, J = 10.0, 10.0, 4.8 Hz, 1H), 3.67 (ddd, J = 10.0, 6.4, 4.0 Hz, 1H), 4.28 (dd, J = 9.6, 2.8 Hz, 1H), 4.98 (dd, J = 9.6, 2.4 Hz, 1H), 5.02 (dd, J = 16.6, 2.4 Hz, 1H), 5.62 (ddd, J = 16.6, 9.6, 9.0 Hz, 1H), 5.81 (d, J = 10.0 Hz, 1H), 7.33−7.45 (m, 6H), 7.64−7.71 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$, $CDCl_3$ = 77.00) δ 8.2, 18.2, 19.1, 21.1, 24.6, 26.4, 26.8, 26.8, 32.9, 41.5, 42.7, 60.2, 60.7, 71.1, 74.3, 114.9, 127.6, 129.6, 133.4, 133.6, 135.6, 135.7, 141.6, 170.2; IR (neat, cm^{-1}) 3500, 3073, 3050, 2960, 2930, 2860, 1740, 1640, 1590, 1472, 1460, 1440, 1428, 1390, 1373, 1310, 1280, 1238, 1113, 1085, 1020, 1000, 970, 912, 822, 759, 738, 701; LRMS (EI) m/z (M^+) 586.1; HRMS calcd for $C_{32}H_{46}O_4SiS_2$ 586.2607, found 586.2584.

Conversion of Homoallylalcohol 8b: Dedithioacetalization. Silyl Ether 12. To a stirred solution of **8b** (411 mg, 1.77 mmol) in dry CH_2Cl_2 (17.7 mL) were added at 0 °C *N*-ethyldiisopropylamine (1.30 mL, 7.43 mmol) and *tert*-butyldimethylsilyl trifluoromethanesulfonate (1.06 mL, 4.60 mmol). After 4 h at 0 °C, saturated aqueous NH_4Cl was added and the mixture was extracted with $CHCl_3$. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (25 g, hexane/EtOAc = 50:1) to afford **12** (610 mg, 99%) as a colorless syrup: R_f 0.71 (hexane/EtOAc = 4:1); ^{1}H NMR (300 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.07 (s, 3H), 0.11 (s, 3H), 0.90 (s, 9H), 1.02 (d, J = 7.0 Hz, 3H), 1.07 (d, J = 7.0 Hz, 3H), 1.75−2.02 (m, 2H), 2.02−2.14 (m, 1H), 2.39 (m, 1H), 2.74−2.92 (m, 4H), 3.92 (dd, J = 4.3, 4.1 Hz, 1H), 4.04 (d, J = 6.8 Hz, 1H), 5.02 (dd, J = 9.4, 1.4 Hz, 1H), 5.04 (ddd, J = 17.4, 1.4, 0.8 Hz, 1H), 5.89 (ddd, J = 17.4, 9.4, 7.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, $CDCl_3$ = 77.00) δ −3.8, −3.6, 12.8, 16.2, 18.4, 26.1, 26.1, 30.4, 30.9, 41.0, 43.2, 52.6, 75.3, 114.4, 141.3; IR (neat, cm^{-1}) 3075, 2955, 2930, 2895, 2857, 1639, 1471, 1461, 1421, 1387, 1380, 1360, 1279, 1253, 1188, 1100, 1068, 1041, 1029, 1004, 940, 910, 869, 839, 774, 668; LRMS (EI) m/z (M^+) 346.2; HRMS (EI) m/z (M^+) calcd for $C_{17}H_{34}OSiS_2$ 346.1821, found 346.1824.

Aldehyde 13.[19] To a stirred solution of **12** (8.5 mg, 0.0245 mmol) and $CaCO_3$ (13.0 mg, 0.123 mmol) in MeCN/H_2O = 9:1 (0.35 mL) was added at 0 °C MeI (0.015 mL, 0.245 mmol) and the mixture was heated at 45 °C. After 12 h at 45 °C, the mixture was diluted with hexane (0.50 mL) and then directly subjected to column chromatography on silica gel (0.5 g, hexane/TEA = 20:1) to afford **13** (3.6 mg, 57%) as a colorless syrup: R_f 0.60 (toluene/EtOAc = 10:1); ^{1}H NMR (300 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.03 (s, 3H), 0.08 (s, 3H), 0.89 (s, 9H), 1.04 (d, J = 7.0 Hz, 3H), 1.09 (d, J = 7.0 Hz, 3H), 2.40 (m, 1H), 2.49 (m, 1H), 3.99 (dd, J = 4.0, 4.0 Hz, 1H), 5.02 (br d, J = 16.0 Hz, 1H), 5.04 (br d, J = 10.2 Hz, 1H), 5.78 (ddd, J = 16.0, 10.2, 8.0 Hz, 1H), 9.78 (br s, 1H).

Conversion of 12: Oxidative Cleavage of Olefin. Aldehyde 14. A solution of **12** (50.0 mg, 0.143 mmol) in MeOH (1.43 mL) was cooled to −78 °C and ozone was bubbled through the solution until a blue color was observed. After 10 min at −78 °C, oxygen was bubbled through the solution until no blue color remained. After addition of dimethylsulfide (0.210 mL), the reaction mixture was warmed to rt. After 7 h at rt, saturated aqueous $NaHCO_3$ was added and the mixture was extracted with EtOAc. The residue was purified by column chromatography on silica gel (1 g, EtOAc) to afford **14** (46.2 mg, 88%: a 7:3 mixture of diastereomers) as colorless crystals. The NMR chemical shifts of each isomer were determined by using the spectra of the mixture. Major isomer of **14**: R_f 0.24 (EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.09 (s, 3H), 0.10 (a, 3H), 0.87 (s, 9H), 1.09 (d, J = 6.6 Hz, 3H), 1.17 (d, J = 6.6

Hz, 3H), 2.06−2.70 (m, 6H), 2.74 (m, 1H), 3.44 (m, 1H), 3.45 (d, J = 3.5 Hz, 1H), 4.17 (dd, J = 8.2, 2.6 Hz, 1H), 9.91 (d, J = 1.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, $CDCl_3$ = 77.00) δ −4.4, −4.4, 8.7, 12.6, 18.0, 25.7, 29.4, 29.5, 34.6, 52.7, 54.5, 68.2, 73.7, 202.7. Minor isomer of **14**: R_f 0.24 (EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.08 (s, 3H), 0.12 (s, 3H), 0.87 (s, 9H), 1.12 (d, J = 6.6 Hz, 3H), 1.27 (d, J = 6.6 Hz, 3H), 2.06−2.70 (m, 6H), 2.82 (m, 1H), 3.34 (m, 1H), 3.68 (d, J = 4.0 Hz, 1H), 4.44 (dd, J = 6.6, 3.6 Hz, 1H), 9.82 (d, J = 1.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, $CDCl_3$ = 77.00) δ −4.0, −3.9, 10.5, 13.6, 18.2, 25.9, 28.6, 30.0, 41.2, 52.0, 53.7, 67.3, 73.9, 204.7. Mixture of two isomers of **14**: IR (KBr, cm^{-1}) 3430, 2960, 2934, 2860, 2740, 1719, 1475, 1463, 1428, 1390, 1362, 1258, 1095, 1078, 1038, 960, 940, 909, 839, 779, 670; LRMS (EI) m/z (M^+) 364.2; HRMS (EI) m/z (M^+) calcd for $C_{16}H_{32}O_3SiS_2$ 364.1562, found 364.1578.

Silyl Ether 15. To a stirred solution of **14** (46.2 mg, 0.126 mmol) in EtOH (1.26 mL) was added at 0 °C $NaBH_4$ (4.99 mg, 0.126 mmol). After 10 min at rt, saturated aqueous NH_4Cl was added and the mixture was extracted with EtOAc. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (10 g, $CHCl_3$/MeOH = 4:1) to afford alcohol (42.8 mg, 93%: a 7:3 mixture of diastereomers) as a colorless syrup. This alcohol (147 mg, 0.419 mmol) was dissolved in dry CH_2Cl_2 (17.7 mL) and to this solution were added at 0 °C imidazole (57.1 mg, 0.838 mmol) and *tert*-butyldiphenylsilyl chloride (0.164 mL, 0.629 mmol). After 2 h at rt, water was added and the mixture was extracted with $CHCl_3$. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (15 g, hexane/EtOAc = 1:1) to afford **15** (210 mg, 85%; a 7:3 mixture of diastereomers) as colorless solids. For analytical samples, the isomers were partially separated by column chromatography (hexane/EtOAc = 1:1) to give colorless crystals. Major isomer of **15**: R_f 0.54 (hexane/EtOAc = 1:1); ^{1}H NMR (300 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.03 (s, 3H), 0.10 (s, 3H), 0.85 (s, 9H), 0.89 (d, J = 7.0 Hz, 3H), 1.01 (d, J = 7.0 Hz, 3H), 1.09 (s, 9H), 2.04−2.54 (m, 6H), 2.90 (m, 1H), 3.40 (br ddd, J = 13.0, 4.0, 4.0 Hz, 1H), 3.54 (dd, J = 11.0, 7.2 Hz, 1H), 3.75 (d, J = 2.6 Hz, 1H), 3.84 (dd, J = 11.0, 8.2 Hz, 1H), 4.12 (dd, J = 5.8, 2.4 Hz, 1H), 7.34−7.46 (m, 6H), 7.64−7.73 (m, 4H); ^{13}C NMR (300 MHz, $CDCl_3$, $CDCl_3$ = 77.00) δ −4.2, −4.0, 11.8, 11.9, 18.2, 19.3, 26.0, 27.0, 29.6, 31.7, 41.9, 54.1, 65.7, 71.3, 73.2, 127.7, 127.7, 129.6, 129.6, 133.6, 133.8, 135.6; IR (neat, cm^{-1}) 3070, 3050, 2959, 2930, 2858, 1590, 1472, 1464, 1428, 1390, 1360, 1258, 1219, 1185, 1160, 1110, 1080, 1066, 1040, 1008, 940, 870, 840, 778, 758, 700, 692, 662; LRMS (EI) m/z (M^+) 604.3; HRMS (EI) m/z (M^+) calcd for $C_{32}H_{52}O_3Si_2S_2$ 604.2897, found 604.2876. Minor isomer of **15**: R_f 0.39 (hexane/EtOAc = 1:1); ^{1}H NMR (300 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ −0.02 (s, 3H), 0.09 (s, 3H), 0.84 (s, 9H), 0.88 (d, J = 6.6 Hz, 3H), 1.07 (s, 9H), 1.20 (d, J = 6.6 Hz, 3H), 1.96−2.24 (m, 2H), 2.35−2.71 (m, 5H), 3.31 (m, 1H), 3.45 (dd, J = 10.6, 7.0 Hz, 1H), 3.67 (d, J = 5.0 Hz, 1H), 3.82 (dd, J = 10.6, 6.6 Hz, 1H), 4.21 (dd, J = 4.2, 4.2 Hz, 1H), 7.33−7.46 (m, 6H), 7.66−7.73 (m, 4H); ^{13}C NMR (300 MHz, $CDCl_3$, $CDCl_3$ = 77.00) δ −3.8, −3.7, 13.5, 13.7, 18.4, 19.2, 26.1, 26.9, 27.9, 29.4, 37.3, 41.2, 53.1, 65.7, 69.97, 73.1, 127.6, 129.5, 129.5, 133.9, 135.6, 135.7; IR (neat, cm^{-1}) 3078, 3050, 2958, 2932, 2858, 1717, 1590, 1472, 1462, 1428, 1390, 1360, 1252, 1219, 1188, 1110, 1080, 1038, 1008, 940, 910, 858, 838, 768, 759, 704, 690, 663, 617; LRMS (EI) m/z (M^+) 604.3; HRMS (EI) m/z (M^+) calcd for $C_{32}H_{52}O_3Si_2S_2$ 604.2897, found 604.2889.

Aldehyde 16.[22] To a stirred solution of **15** (58.8 mg, 0.0972 mmol) in 30:1 acetone−H_2O (1.95 mL) was added at 0 °C *N*-bromosuccinimide (103.8 mg, 0.583 mmol). After 5 min at 0 °C, saturated aqueous $NaHCO_3$ was added and the mixture was extracted with EtOAc. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (10 g, hexane/EtOAc = 4:1) to afford **16** (40.8 mg, 84%) as colorless crystals: R_f 0.69 (hexane/EtOAc = 4:1); ^{1}H NMR (300 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ −0.07 (s, 3H), −0.04 (s, 3H), 0.79 (s, 9H), 0.92 (d, J = 7.0 Hz, 3H), 1.08 (s, 9H), 1.09 (d, J = 7.0 Hz, 3H), 1.98 (m, 1H), 2.49 (m, 1H), 3.50 (dd, J = 10.0, 7.0 Hz, 1H), 3.70 (dd, J = 10.0, 6.2 Hz, 1H), 4.26 (dd, J = 6.2, 3.2 Hz, 1H), 7.34−7.48 (m, 6H), 7.62−7.70 (m, 4H), 9.67 (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, $CDCl_3$ = 77.00) δ −4.4, −4.3, 8.1, 13.4, 18.1, 19.2, 25.8, 26.9, 40.9, 49.7, 65.9, 71.8, 127.6, 129.6, 129.7, 133.6, 135.6, 135.6, 205.0; IR (neat, cm^{-1}) 3078, 3050, 2958, 2930, 2890, 2860, 2710, 1728, 1590, 1474, 1462, 1428, 1390, 1361, 1300, 1258, 1219, 1189, 1113, 1088, 1030, 1009, 959, 940, 912, 839, 778, 760, 720, 700, 670; LRMS (EI) m/z (M^+) 498.2; HRMS (EI) m/z (M^+) calcd for $C_{29}H_{46}O_3Si_2$ 498.2986, found 498.3010.

Conversion of 8b: Coupling Reaction with Aldehyde 17. Diols 18 and 18′. To a stirred solution of **8b** (18.5 mg, 0.0796 mmol) in dry THF (0.90 mL) was added at rt 1.65 M *n*-BuLi in hexane (0.0965 mL, 0.159 mmol). After 5 min at −20 °C, a solution of 3-(*tert*-butyldiphenylsiloxy)propanal[25] (**17**, 49.7 mg, 0.159 mmol) in dry THF (0.20 mL) was added and the mixture was warmed to rt. After 30 min at rt, saturated aqueous NH_4Cl was added and the mixture was extracted with EtOAc. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (10 g, hexane/EtOAc = 4:1) to afford **18** and **18′** (20.8 mg, 66%: a 1:2 mixture of diastereomers) as a colorless syrup. The analytical data of each isolated **18** and **18′** derived from the different route are shown below (for details of the different route, see the Supporting Information). **18**: colorless crystals: R_f 0.37 (hexane/EtOAc = 4:1); ^{1}H NMR (300 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 1.04 (s, 9H), 1.07 (d, J = 6.6 Hz, 3H), 1.21 (d, J = 7.2 Hz, 3H), 1.83−2.05 (m, 2H), 2.11 (m, 1H), 2.25−2.40 (m, 2H), 2.48 (m, 1H), 2.66−2.85 (m, 4H), 3.83−4.00 (m, 2H), 4.22 (br d, J = 10.4 Hz, 1H), 4.25 (br d, J = 10.0 Hz, 1H), 5.10 (dd, J = 10.0, 1.6 Hz, 1H), 5.14 (dd, J = 17.6, 1.6 Hz, 1H), 5.87 (ddd, J = 17.6, 10.0, 8.2 Hz, 1H), 7.35−7.48 (m, 6H), 7.64−7.72 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$, $CDCl_3$ = 77.00) δ 8.2, 17.6, 19.0, 24.8, 25.2, 26.2, 26.8, 34.2, 40.7, 43.2, 63.2, 63.2, 72.6, 73.0, 115.3, 127.7, 129.7, 133.0, 133.1, 135.5, 135.5, 142.2; IR (neat, cm^{-1}) 3380, 3073, 2960, 2930, 2860, 1640, 1590, 1473, 1460, 1427, 1390, 1313, 1278, 1112, 999, 910, 822, 738, 700; LRMS (EI) m/z (M^+) 544.1; HRMS (EI) m/z (M^+) calcd for $C_{30}H_{44}O_3SiS_2$ 544.2501, found 544.2508. **18′**: colorless crystals: R_f 0.37 (hexane/EtOAc = 4:1); ^{1}H NMR (300 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 1.01 (d, J = 6.2 Hz, 3H), 1.06 (s, 9H), 1.22 (d, J = 7.0 Hz, 3H), 1.83−2.03 (m, 3H), 2.30 (m, 1H), 2.36−2.49 (m, 2H), 2.64 (ddd, J = 14.4, 6.2, 4.6 Hz, 1H), 2.69−2.84 (m, 2H), 2.88 (ddd, J = 14.4, 6.2, 4.2 Hz, 1H), 3.28 (br, 1H), 3.81−3.97 (m, 3H), 4.09 (d, J = 8.8 Hz, 1H), 4.33 (d, J = 10.4 Hz, 1H), 5.11 (dd, J = 10.0, 2.0 Hz, 1H), 5.13 (ddd, J = 17.6, 2.0, 0.8 Hz, 1H), 5.83 (ddd, J = 17.6, 10.0, 8.2 Hz, 1H), 7.34−7.46 (m, 6H), 7.64−7.72 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$, $CDCl_3$ = 77.00) δ 9.8, 17.2, 19.2, 24.7, 25.8, 25.8, 26.8, 34.7, 42.0, 42.6, 61.8, 62.2, 72.2, 72.5, 115.5, 127.6, 129.6, 133.5, 133.6, 135.5, 142.1; IR (KBr, cm^{-1}) 3410, 3078, 2960, 2930, 2860, 1640, 1590, 1473, 1462, 1427, 1390, 1278, 1219, 1112, 990, 910, 822, 758, 738, 703; LRMS (EI) m/z (M^+) 544.2; HRMS (EI) m/z (M^+) calcd for $C_{30}H_{44}O_3SiS_2$ 544.2501, found 544.2517.

Silyl Ethers 19 and 19′. To a stirred solution of a mixture of **18** and **18′** (8.3 mg, 0.0152 mmol) in dry CH_2Cl_2 (0.152 mL) were added at rt *N*-ethyldiisopropylamine (0.0223 mL, 0.128 mmol) and *tert*-butyldimethylsilyl trifluoromethanesulfonate (0.0182 mL, 0.0790 mmol). After 7 h at rt, saturated aqueous NH_4Cl was added and the mixture was extracted with $CHCl_3$. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (3 g, hexane/EtOAc = 50:1) to afford **19** and **19′** (11.6 mg, 99%: a 1:2 mixture of diastereomers) as a colorless syrup. The NMR chemical shifts of each **19** and **19′** were determined by using the spectra of a mixture of **19** and **19′**. **19**: R_f 0.95 (hexane/EtOAc =

4:1); ^{1}H NMR (270 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.00 (s, 3H), 0.15 (s, 3H), 0.16 (s, 3H), 0.22 (s, 3H), 0.80 (s, 9H), 0.91 (m, 3H), 0.92 (s, 9H), 1.02 (d, J = 7.0 Hz, 3H), 1.06 (s, 9H), 1.72−1.88 (m, 2H), 1.94 (m, 1H), 2.11 (m, 1H), 2.26−2.44 (m, 2H), 2.59 (m, 1H), 2.78 (m, 1H), 2.89−3.10 (m, 2H), 3.73 (dd, J = 9.2, 4.2 Hz, 1H), 3.78 (dd, J = 9.2, 5.0 Hz, 1H), 4.53 (dd, J = 2.2, 2.2 Hz, 1H), 4.61 (br d, J = 8.4 Hz, 1H), 4.98 (br d, J = 17.0 Hz, 1H), 4.99 (br d, J = 8.4 Hz, 1H), 5.94 (ddd, J = 17.0, 8.4, 7.0 Hz, 1H), 7.33−7.46 (m, 6H), 7.61−7.72 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$, $CDCl_3$ = 77.00) δ −4.6, −3.9, −2.9, −2.9, 11.8, 15.4, 18.1, 18.3, 18,6, 19.1, 25.7, 26.3, 26.9, 27.4, 39.5, 41.9, 47.1, 62.1, 63.5, 74.3, 114.5, 127.6, 127.6, 129.6, 129.7, 133.7, 133.8, 135.6, 140.5. **19′**: R_f 0.95 (hexane/EtOAc = 4:1); ^{1}H NMR (270 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.04 (s, 3H), 0.14 (s, 3H), 0.15 (s, 3H), 0.21 (s, 3H), 0.83 (s, 9H), 0.91 (s, 9H), 0.97 (d, J = 7.2 Hz, 3H), 1.03 (d, J = 7.2 Hz, 3H), 1.06 (s, 9H), 1.66 (m, 1H), 1.80 (m, 1H), 1.93−2.08 (m, 2H), 2.29−2.63 (m, 4H), 2.76 (m, 1H), 2.95 (m, 1H), 3.73−3.87 (m, 2H), 4.43 (br d, J = 8.0 Hz, 1H), 4.49 (dd, J = 2.2, 2.2 Hz, 1H), 4.98 (br d, J = 18.0 Hz, 1H), 5.00 (br d, J = 8.4 Hz, 1H), 5.94 (ddd, J = 18.0, 8.4, 7.0 Hz, 1H), 7.33−7.46 (m, 6H), 7.66−7.72 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$, $CDCl_3$ = 77.00) δ −4.1, −4.0, −3.4, −3.4, 12.4, 15.7, 18.7, 18.8, 18.8, 19.2, 25.1, 25.7, 26.2, 26.4, 26.9, 36.9, 42.0, 47.2, 62.0, 63.3, 74.0, 114.4, 127.6, 127.6, 129.5, 129.6, 133.9, 134.0, 135.6, 135.7, 140.7. Mixture of **19** and **19′**: IR (neat, cm^{-1}) 3078, 3050, 2958, 2930, 2894, 2859, 1639, 1590, 1472, 1462, 1428, 1390, 1360, 1278, 1253, 1218, 1186, 1110, 1043, 1003, 959, 940, 914, 882, 838, 777, 760, 740, 701, 690, 664; LRMS (EI) m/z (M^+) 772.3; HRMS (EI) m/z (M^+) calcd for $C_{42}H_{72}O_3Si_3S_2$ 772.4231, found 772.4233.

Aldehydes 20 and 20′. To a stirred solution of a mixture of **19** and **19′** (64.3 mg, 0.0831 mmol) in 9:1 THF−H_2O (0.66 mL) was added at −5 °C $(CF_3CO_2)_2IPh$ (214.4 mg, 0.499 mmol). After 45 min at −5 °C, saturated aqueous $NaHCO_3$ was added and the mixture was extracted with EtOAc. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (10 g, hexane/EtOAc = 4:1) to afford ketone (51.1 mg, 90%: a 1:2 mixture of diasteromers) as a colorless syrup. A portion of this ketone (41.1 mg, 0.0602 mmol) was dissolved in 9:1 CH_2Cl_2−MeOH (6.00 mL) and cooled to −78 °C. Ozone was bubbled through the solution until a blue color was observed. After 10 min at −78 °C, oxygen was bubbled through the solution until no blue color remained. After addition of triphenylphosphine (15.8 mg, 0.0602 mmol), the mixture was warmed to −30 °C. Saturated aqueous $NaHCO_3$ was added and the mixture was extracted with EtOAc. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (1 g, hexane/EtOAc = 3:1) to afford **20** and **20′** (36.5 mg, 89%: a 1:2 mixture of diastereomers) as a colorless syrup. The NMR chemical shifts of each **20** and **20′** were determined by using the spectra of a mixture of **20** and **20′**. **20**: R_f 0.42 (hexane/EtOAc = 10:1); ^{1}H NMR (300 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.04 (s, 3H), 0.07 (s, 3H), 0.08 (s, 3H), 0.13 (s, 3 H), 0.89 (s, 9H), 0.89 (s, 9H), 1.06 (s, 9H), 1.07 (d, J = 7.0 Hz, 3H) 1.14 (d, J = 7.0 Hz, 3H), 1.62−1.81 (m, 1H), 1.88−2.02 (m, 1H), 2.32 (m, 1H), 3.12 (m, 1H), 3.65−3.86 (m, 2H), 4.25 (dd, J = 8.0, 2,4 Hz, 1H), 4.42−4.52 (m, 1H), 7.33−7.48 (m, 6H), 7.63−7.72 (m, 4H), 9.68 (d, J = 2.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, $CDCl_3$ = 77.00) δ −4.9, −4.7, −4.1, −3.9, 11.4, 14.8, 18.1, 19.1, 25.8, 26.0, 26.9, 37.4, 46.2, 51.7, 60.0, 74.1, 74.6, 127.7, 129.6, 133.7, 135.6, 203.5, 214.6. **20′**: R_f 0.42 (hexane/EtOAc = 10:1); ^{1}H NMR (300 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.05 (s, 3H), 0.08 (s, 3H), 0.09 (s, 3H), 0.11 (s, 3 H), 0.88 (s, 9H), 0.89 (s, 9H), 1.06 (s, 9H), 1.09 (d, J = 6.8 Hz, 3H), 1.11 (d, J = 7.0 Hz, 3H), 1.62−1.81 (m, 1H), 1.88−2.02 (m, 1H), 2.32 (m, 1H), 3.19 (m, 1H), 3.65−3.86 (m, 2H), 4.08 (dd, J = 8.0, 2.4 Hz, 1H), 4.42−4.52 (m, 1H), 7.33−7.48 (m, 6H), 7.63−7.72 (m, 4H), 9.69 (d, J = 3.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, $CDCl_3$ = 77.00) δ −4.7, −4.7, −4.1, −3.8, 12.0, 15.1, 18.3, 19.2, 25.8, 25.9, 26.0, 26.9, 36.8, 45.7, 51.1, 60.2, 75.1, 75.8, 127.7, 129.6, 133.7, 135.6, 203.5, 214.3. Mixture of **20** and **20′**: IR (neat, cm^{-1}) 3078, 3052, 2958, 2932, 2890, 2860, 1723, 1590, 1473, 1464, 1428, 1390, 1361, 1258, 1114, 1042, 1005, 940, 839, 779, 740, 701; LRMS (EI) m/z (M^+) 684.2; HRMS (EI) m/z (M^+) calcd for $C_{38}H_{64}O_5Si_3$ 684.4062, found 684.4046.

Supporting Information Available: Characterization data of the adducts **3**−**6**, structure determination of the adducts, and preparation of the substrates **7a**−**c** and **7c′**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO801106B