(*E*)-α-Sulfonamidocrotylboronates as Reagents for the Stereoselective Homoaldol Synthesis[‡]

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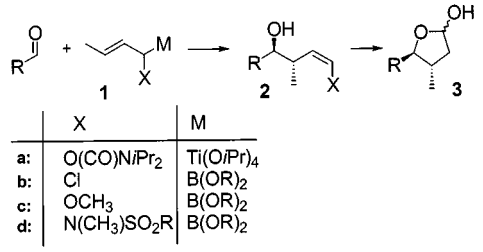
The α-sulfonamidocrotylboronates **9** and **10** have been generated by nucleophilic substitution at the α-chlorocrotylboronates **1b**, in yields of up to 70%. The α-sulfonamidocrotylboronates **9** and **10** react with aldehydes at room temp. and 4 kbar pressure to give the *anti*-homoallylic alcohols **13** and **14** with high simple diastereoselectivity. These latter may be directly converted into the lactol ethers **15** in a one-pot procedure.

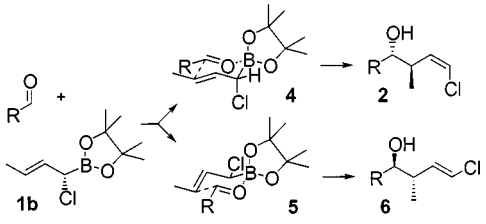
Introduction

The allylmetallation of aldehydes with α-heterosubstituted allylmetal species **1** leads to homoallylic alcohols, with high selectivity towards the *anti* stereoisomer **2**. These homoallylic alcohols are of general synthetic interest, because they may easily be converted into the corresponding lactols **3**. Reagents **1** are therefore considered to be homoaldol equivalents.[2,3]



	X	M
a:	O(CO)N*i*Pr$_2$	Ti(O*i*Pr)$_4$
b:	Cl	B(OR)$_2$
c:	OCH$_3$	B(OR)$_2$
d:	N(CH$_3$)SO$_2$R	B(OR)$_2$

Among the reagents **1**, the titanated allylcarbamates **1** developed by Hoppe[4] are most prominent.[5–9] In particular, the enantioselective generation of homoallylic alcohols has become established[4,9–12] with the enantiomerically pure reagent **1a**. Reagents of this type perform very well when reacting with chiral aldehydes in matched situations.[13] In mismatched situations, the asymmetric induction from the reagent **1** may not always be high enough to exert sufficient reagent control of stereoselectivity.[14] Out of a general interest in reagent control of stereoselectivity in allylboration reactions, we studied the allylboration reactions of the (*E*)-α-chlorocrotylboronates **1b**. These react smoothly with aldehydes to give the homoallylic alcohols **2b**, with high simple diastereoselectivity.[15] The latter compounds may likewise be refunctionalized to lactols and related compounds.[16] Moreover, chiral α-chlorocrotylboronates **1b** react with aldehydes to give the homoallylic alcohols **2b** with > 95% *ee*.[15] In reactions with chiral aldehydes, however, the limits of this reagent have also come to light in mismatched situations.[17,18] We realized that the level of asymmetric induction depends on the energy difference between the two competing transition states **4** and **5**: i.e., on the tendency of the substitutent X to adopt an axial position in the six-membered cyclic reaction transition state **4**.



This preference for transition state **4** over **5** is influenced by the polarity of the C–X bond.[19] This prompted us to study the α-methoxycrotylboronates **1c**, which indeed turned out to be superior reagents,[20] especially when reagent control of diastereoselectivity on reaction with chiral aldehydes (mismatched cases) were concerned.[18] The improvement in going from the α-chlorocrotylboronate **1b** to the α-methoxycrotylboronate **1c** encouraged us to evaluate the potential of α-sulfonamidocrotylboronates **1d** in stereoselective allylmetallation reactions.

Results and Discussion

Synthesis of the Starting Crotylboronates

D. S. Matteson[21] worked out a route to α-amidoallylboronates, involving substitution on α-chloroallylboronates by lithium hexamethyldisilazide, followed by acylation of the resulting silylaminoallylboronate. When applied to the α-chlorocrotylboronate **1b**, this transformation furnished the α-acetamidocrotylboronate **8** in 45% overall yield. Compound **8** showed an ^{11}B NMR signal at δ = 13, already

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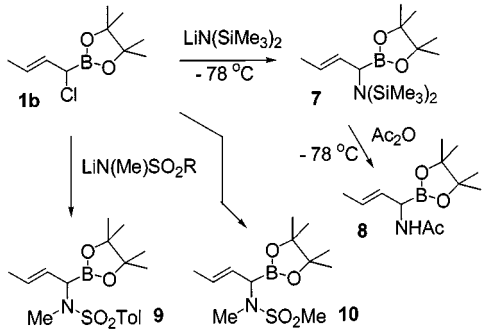
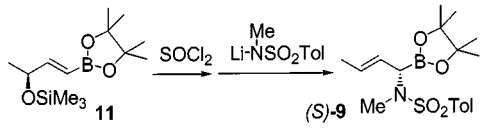
noted by Matteson[21] as characteristic for intramolecular coordination of the boron atom.



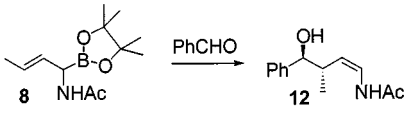
We initially considered the analogous reaction of the silylaminoboronate **7** with sulfonyl chlorides as a route to the reagents **1d**, but found that the desired compounds **9** or **10** can be accessed directly in good yield by treatment of **1b** with the lithium salts of *N*-methyltoluenesulfonamide (71%) or *N*-methylmethanesulfonamide (57%).

Likewise, (*S*)-**9** could be obtained starting from the γ-silyloxyvinylboronate **11**,[22] via (*R*)-**1b**, in a one-pot procedure (65%).



Reaction with Aldehydes

The reactivities of **8**−**10** in the crotylboration of aldehydes were found to be low. In order to achieve reasonable conversion over 3 d at room temperature, it was necessary to apply high pressure (4 kbar). Thus, on treatment of **8** with benzaldehyde under 4 kbar pressure, the homoallylic alcohol **12** was obtained in 82% yield, with a (*Z*)-configured double bond. The relative configuration at the two stereogenic centers was not ascertained in this case, but assumed to be *anti* on the basis of the precedent set in the crotylboration reactions of **1b** and **1c**.[15,20]

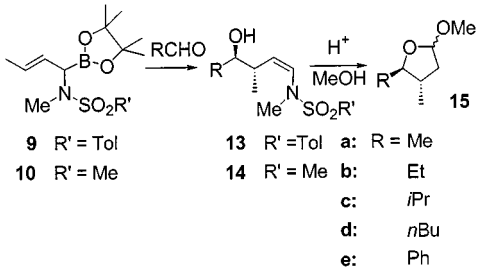


The results obtained on crotylboration of aldehydes with the α-sulfonamidocrotylboronates **9** and **10** are summarized in Table 1.

Table 1. Treatment of α-sulfonamidocrotylboronates **9** and **10** with aldehydes to give γ-sulfonamido homoallylic alcohols **13** and **14**, and γ-lactol ethers **15**

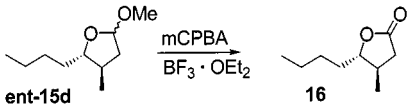
Crotyl-boronate	Aldehyde R =	Products	13, 14 Yield, %	15 Yield, %	15 *trans/cis*
9	Me	**a**	69	65	97 : 3
9	Et	**b**	62	69	97 : 3
9	*i*Pr	**c**	75	70	98 : 2
(*S*)-**9**	*n*Bu	**d**	→	87	98 : 2
9	Ph	**e**	64	70	99 : 1
10	Me	**a**	→	48	96 : 4
10	Et	**b**	→	81	97 : 3
10	*i*Pr	**c**	→	76	96 : 4
10	Ph	**e**	→	56	99 : 1

In all cases, the homoallylic alcohols **13** or **14** were obtained as the (*Z*) isomers ($^3J_{H,H}$ of the olefinic protons 7.5−7.7 Hz). Since the (*E*)/(*Z*) selectivity is linked to the capability of the reagents **1** to effect asymmetric induction on reaction with aldehydes (cf. the transition states **4** and **5**), it turns out that the α-sulfonamidocrotylboronates **9** and **10** are more powerful in this respect than the α-chlorocrotylboronates **1b**. The former apparently measure up to the α-methoxycrotylboronates **1c** in this respect. For this reason, enantiomerically pure α-sulfonamidocrotylboronates **9** and **10** might be interesting candidates for reaction with chiral aldehydes in mismatched situations. Furthermore, the simple diastereoselectivity in the reaction of **9** and **10** with aldehydes was evaluated by GC analysis after conversion of the enamides **13** and **14** into the lactol ethers **15** by treatment with a polymer-supported sulfonic acid (Lewatit S100) in aqueous methanol. It became apparent that simple diastereoselectivities, (e.g., *syn*/*anti*) were in the range of only 96−99%. This detracts from the use of the reagents **9** and **10** in situations in which extreme stereoselectivity is required.



The reaction of **9** or **10** with aldehydes and the conversion of the enamides **13** or **14** to the lactol ethers **15** were frequently carried out without isolation of the enamides. Most of the reactions were carried out under 4 kbar of pressure at room temperature. Treatment of **9** with benzaldehyde for 3 d at reflux in hexane, however, likewise resulted in a 72% yield of **15e**. This represents the easier way to carry out these crotylboration reactions if elevated temperatures are not a concern.

It remained to verify that the addition of the α-sulfonamido-substituted crotylboronates to aldehydes resulted in the homoallylic alcohols **13** and **14**, with the *anti* configuration at the two newly formed stereocenters. To this end we oxidized[23] the lactol ether **ent-15d** to the known (−)-quercus-lactone A (**16**).[24,25] For other syntheses of enantiomerically enriched quercus lactone see ref.[26−46] This confirmed the *anti* configuration of **13d,** a result which should hold for all compounds **13** and **14** obtained.



In this case, we started out from (*S*)-**9**, which was generated from **11** of ≥ 98% *ee*. The (−)-quercus-lactone **16** obtained had the absolute configuration depicted, in line with our expectations for the stereochemical course of the transformation from the vinylboronate **11** to **1b** (retention),[22] to **9** (inversion), and the crotylboration reaction.[47] We noted, however, that the quercus-lactone obtained had an optical purity of only 85%. While we do not know where the partial racemization occurred, we surmise that the substitution step **1b** → **9** is critical. In this step, chloride ions are released; these may racemize unchanged **1b** through an S_N2 process. In fact, partial racemization has been noted on conversion of **1b** into **1c** by substitution with lithium methoxide (ca. 8%).[20]

Experimental Section

General Remarks: All temperatures quoted are uncorrected. − ^{1}H NMR, ^{13}C NMR: Bruker AC-300, AM-400. − Boiling range of petroleum ether: 40−60 °C. − Flash chromatography: Silica gel SI 60, E. Merck AG, Darmstadt, 40−63 μm. − Analytical gas chromatography: Siemens Sichromat 3 with a 30 m × 0.3 mm quartz capillary column with DB5, 0.9 bar He.

1. 2-{(*E*)-1-[Bis(trimethylsilyl)amino]-2-butenyl}-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (7): *n*-Butyllithium in *n*-hexane (1.43 M, 5.60 mL, 8.0 mmol) was added dropwise at −78 °C over 10 min to a solution of 1,1,1,3,3,3-hexamethyldisilazane (1.68 mL, 8.0 mmol) in THF (40 mL). After stirring for 1 h, a solution of (*E*)-α-chlorocrotylboronate **1b**[15] (2.00 g, ca. 8 mmol) in THF (10 mL) was added dropwise over 10 min. After 1 h at −78 °C, the mixture was allowed to come to room temperature. The solvents were removed in vacuum and the residue was taken up in petroleum ether (40 mL). The mixture was filtered and the filtrate was concentrated. The residue was subjected to bulb-to-bulb distillation to give **7** (1.41 g, 52%) as a colorless liquid of b.p. 100−105 °C/0.1 Torr. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.07 (s, 18 H), 1.23 (s, 6 H), 1.24 (s, 6 H), 1.63−1.67 (m, 3 H), 3.24 (br. d, *J* = 2.1 Hz, 1 H), 5.49 (dqd, *J* = 15.2, 7.5 and 2.1 Hz, 1 H), 5.60 (ddq, *J* = 15.2, 3.7 and 1.5 Hz, 1 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 2.5, 17.8, 24.7, 25.2, ca. 47 (br.), 83.5, 122.4, 133.9. − ^{11}B NMR (96 MHz, $CDCl_3$): δ = 20.4. − $C_{16}H_{36}BNO_2Si_2$ requires M^+ = 341.23776, found 341.23599.

2. 2-[(*E*)-1-Acetamido-2-butenyl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (8): *n*-Butyllithium in hexane (1.45 M, 6.90 mL, 10.0 mmol) was added dropwise at −78 °C to a solution of hexamethyldisilazane (1.61 g, 10.0 mmol) in THF (50 mL). After stirring for 1 h, a solution of (*E*)-α-chlorocrotylboronate **1b**[15] (2.50 g, ca. 10 mmol) in THF (5 mL) was added dropwise at −78 °C. After stirring for 1 h, the mixture was allowed to come to room temperature and was recooled to −78 °C. Acetic anhydride (2.84 mL, 30.0 mmol), and then acetic acid (0.57 mL, 10 mmol), were added. The mixture was allowed to come to room temperature and the solvents were removed in vacuum. The residue was partitioned between diethyl ether (50 mL) and water (20 mL). The phases were separated and the aqueous phase was extracted with ether (3 × 20 mL). The combined organic phases were washed with brine (10 mL), dried ($MgSO_4$), and concentrated. Flash chromatography of the residue with ether/methanol (20:1) furnished **8** (1.03 g, 45%) as a colorless, viscous oil. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.10 (s, 6 H), 1.11 (s, 6 H), 1.64 (d, *J* = 4.5 Hz, 3 H), 2.05 (s, 3 H), 3.0 (br. d, *J* = 5.6 Hz, 1 H), 5.32−5.46 (m, 2 H), 9.76 (br. s, 1 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 16.9, 17.6, 24.6, 25.0, ca. 50 (br.), 80.3, 124.6, 129.9, 175.4. − ^{11}B NMR (96 MHz, $CDCl_3$): δ = 13.4. − $C_{11}H_{22}BNO_3$ (239.1): calcd. C 60.28, H 9.27, N 5.86; found C 60.39, H 9.47, N 5.92.

3. 4,4,5,5-Tetramethyl-2-{(*E*)-1-[methyl(tolylsulfonyl)amino]-2-butenyl}-1,3,2-dioxaborolane (9): *n*-Butyllithium in *n*-hexane (1.43 M, 7.70 mL, 11.0 mmol) was added dropwise at −78 °C to a solution of *N*-methyl-*p*-toluenesulfonamide (2.04 g, 11.0 mmol) in THF (40 mL). After stirring for 1 h at −78 °C, a solution of (*E*)-α-chlorocrotylboronate **1b**[15] (ca. 11 mmol) in THF (10 mL) was added dropwise. After another 1 h at −78 °C, the mixture was allowed to come to room temperature. Semisaturated, aqueous NH_4Cl solution (30 mL) and diethyl ether (30 mL) were added. The phases were separated and the aqueous phase was extracted with ether (3 × 30 mL). The combined organic phases were washed with brine (20 mL), dried ($MgSO_4$), and concentrated. Flash chromatography of the residue with petroleum ether/ethyl acetate (4:1) furnished **9** (2.85 g, 71%) as a viscous oil. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.22 (s, 6 H), 1.24 (s, 6 H), 1.63 (d, *J* = 6.2 Hz, 3 H), 2.40 (s, 3 H), 2.63 (s, 3 H), 3.41 (d, *J* = 8.3 Hz, 1 H), 5.37 (ddq, *J* = 15.3, 8.2, and 1.4 Hz, 1 H), 5.54 (dqd, *J* = 15.3, 6.4, and 0.65 Hz, 1 H), 7.27 (d, *J* = 8.2 Hz, 2 H), 7.73 (d, *J* = 8.2 Hz, 2 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 17.8, 21.5, 24.6, 24.7, 33.8, 83.9, 126.6, 127.3, 128.0, 129.2, 129.3, 142.9. − ^{11}B NMR (96 MHz, THF): δ = 30.8. − $C_{18}H_{28}BNO_4S$ (365.3): calcd. C 59.18, H 7.73, N 3.83; found C 59.13, H 7.63, N 3.90.

Compound (*S*)-9: $SOCl_2$ (distilled from linseed oil and quinoline 0.25 mL, 3.5 mmol) and $Co(NO_3)_3(H_2O)_6$ (ca. 5 mg) were added to a solution of (*S*)-4,4,5,5-tetramethyl-2-[(*E*)-3-trimethylsilyloxy-1-butenyl]-1,3,2-dioxaborolane (**11**)[22] (0.81 g, 3.0 mmol) in petroleum ether (30 mL). The mixture was stirred at room temperature and the reaction was monitored by ^{1}H NMR. After 8 h, the solvents were removed in vacuum. The residue was taken up in petroleum ether (50 mL) and concentrated again, giving the crude (*R*)-**1b**. Its enantiomeric purity was determined (by treatment of an aliquot with benzaldehyde, treatment of the resulting homoallylic alcohol with isopropyl isocyanate and GC analysis of the resulting carbamate using a chiral column)[15] to be > 98%. The crude **1b** obtained was converted into **9** (0.71 g, 65%) as described above.

4. 4,4,5,5-Tetramethyl-2-[(*E*)-1-{methyl(methylsulfonyl)amino]-2-butenyl}-1,3,2-dioxaborolane (10): *n*-Butyllithium in hexane (1.47 M, 13.6 mL, 20.0 mmol) was added dropwise at −78 °C to a solution of *N*-methylmethanesulfonamide (2.18 g, 20.0 mmol) in THF (80 mL). After stirring for 1 h, a solution of (*E*)-α-chlorocrotylboronate **1b**[15] (ca. 20 mmol) in THF (20 mL) was added. After

stirring for 1 h at −78 °C, the mixture was allowed to come to room temperature. Semisaturated, aqueous NH_4Cl solution (50 mL) was added and the mixture was extracted with ether (4 × 40 mL). The combined organic phases were washed with brine (30 mL), dried ($MgSO_4$), and concentrated. Rapid flash chromatography with petroleum ether/ethyl acetate (3:1) furnished **10** (3.32 g, 57%) as a yellowish, viscous oil. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.25 (s, 12 H), 1.71 (dt, *J* = 6.4 and 1.0 Hz, 3 H), 2.81 (s, 3 H), 2.86 (s, 3 H), 3.58 (d, *J* = 7.9 Hz, 1 H), 5.49 (ddq, *J* = 15.3, 6.7, and 1.4 Hz, 1 H), 5.66 (dqd, *J* = 15.3, 6.4, and 0.7 Hz, 1 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 17.9, 24.7, 24.8, 33.8, 38.0, 84.1, 126.4, 129.2. − ^{11}B NMR (96 MHz, $CDCl_3$): δ = 30.8. − $C_{12}H_{24}BNO_4S$ (290.2): calcd. C 49.84, H 8.36, N 4.84, found C 49.89, H 8.08, N 4.76.

5. (1*R,2*R**,3*Z*)-4-Acetamido-2-methyl-1-phenyl-3-buten-1-ol (12):** A solution of **8** (0.19 g, 0.83 mmol) and benzaldehyde (96 mg, 0.91 mmol) in diethyl ether (2 mL) was pressurized to 4 kbar for 3 d. Triethanolamine (127 mg, 0.85 mmol) was added and the mixture was stirred for 3 h at room temperature. The mixture was filtered and the filtrate was concentrated. A ^{1}H NMR spectrum of the residue showed the presence of a single diastereomer. Flash chromatography of the residue with ethyl acetate furnished **12** (149 mg, 82%) as a colorless solid of m.p. 133 °C. − ^{1}H NMR (300 MHz, [D_6]acetone): δ = 0.83 (d, *J* = 6.8 Hz, 3 H), 1.89 (s, 3 H), 2.75−2.86 (m, 1 H), 4.29 (d, *J* = 3.9 Hz, 1 H), 4.45 (dd, *J* = 6.6 and 3.9 Hz, 1 H), 4.58 (t, *J* = 9.4 Hz, 1 H), 6.61−6.68 (m, 1 H), 7.21 (tt, *J* = 7.0 and 3.3 Hz, 1 H), 7.27−7.37 (m, 4 H), 8.53 (br. s, 1 H). − ^{13}C NMR (75 MHz, [D_6]acetone): δ = 18.0, 22.8, 39.4, 78.7, 113.5, 122.9. 127.6, 127.8, 128.6, 145.2, 167.8. − $C_{13}H_{17}NO_2$ (219.3): calcd. C 71.21, H 7.81, N 6.39; found C 71.24, H 8.01, N 6.24.

6. (2*S,3*R**,4*Z*)-3-Methyl-5-[methyl(tolylsulfonyl)amino]-4-penten-2-ol (13a):** A solution of **9** (0.73 g, 2.0 mmol) and acetaldehyde (0.13 g, 3.0 mmol) in petroleum ether (5 mL) was pressurized to 4 kbar for 3 d. ^{1}H NMR analysis of the crude product verified that the geometry of the double bond was (*Z*). The crude product was taken up in diethyl ether (10 mL), and triethanolamine (0.30 g, 2.0 mmol) was added. After 3 h at room temperature, saturated, aqueous NH_4Cl solution (5 mL) was added. The phases were separated and the aqueous phase was extracted with ether (3 × 15 mL). The combined organic extracts were washed with brine (10 mL), dried ($MgSO_4$), and concentrated. Flash chromatography of the residue with petroleum ether/ethyl acetate (4:1) furnished **13a** (0.39 g, 69%) as a colorless oil. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.97 (d, *J* = 6.8 Hz, 3 H), 1.20 (d, *J* = 6.2 Hz, 3 H), 2.30 (d, *J* = 5.9 Hz, 1 H), 2.42 (s, 3 H), 2.78 (s, 3 H), 2.88−3.01 (m, 1 H), 3.46−3.59 (m, 1 H), 5.35 (d, *J* = 7.8 Hz, 1 H), 5.42 (dd, *J* = 10.2 and 7.8 Hz, 1 H), 7.30 (d, *J* = 8.3 Hz, 2 H), 7.63 (d, *J* = 8.3 Hz, 2 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 17.1, 21.2, 24.7, 38.0, 39.2, 71.4, 127.2, 127.7, 129.6, 133.2, 136.1, 143.7. − For elemental analysis, a sample of the alcohol was converted into the acetate: $C_{16}H_{23}NO_4S$ (325.4): calcd. C 59.05, H 7.12, N 4.30; found C 59.01, H 7.08, N 4.26.

7. (3*S,4*R**,5*Z*)-4-Methyl-6-[methyl(tolylsulfonyl)amino]-5-hexen-3-ol (13b):** Compound **9** (0.36 g, 1.0 mmol), propanal (70 mg, 1.2 mmol), and triethanolamine (149 mg, 1.0 mmol) were allowed to react as described under 6. to give **13b** (185 mg, 62%) as a colorless oil. − ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.97 (t, *J* = 7.4 Hz, 3 H), 0.99 (d, *J* = 6.8 Hz, 3 H), 1.32−1.44 (m, 1 H), 1.56−1.66 (m, 1 H), 2.18 (d, *J* = 6.2 Hz, 1 H), 2.42 (s, 3 H), 2.78 (s, 3 H), 2.99−3.08 (m, 1 H), 3.27−3.33 (m, 1 H), 5.32 (d, *J* = 7.6 Hz, 1 H), 5.45 (dd, *J* = 10.5 and 7.6 Hz, 1 H), 7.31 (d, *J* = 8.0 Hz, 2 H), 7.62−7.65 (m, 2 H). − ^{13}C NMR (100 MHz, $CDCl_3$): δ = 9.7, 17.4, 21.5, 27.8, 37.1, 38.2, 76.8, 127.0, 127.8, 129.6, 136.7, 143.8, one signal obscured. The material was not characterized further.

8. (3*S,4*R**,5*Z*)-2,4-Dimethyl-6-[methyl(*p*-tolylsulfonyl)amino]-5-hexen-3-ol (13c):** Compound **9** (365 mg, 1.0 mmol), 2-methylpropanal (86 mg, 1.2 mmol), and triethanolamine (149 mg, 1.0 mmol) were allowed to react as described under 6. to give **13c** (233 mg, 75%) as a colorless oil. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.90 (d, *J* = 6.8 Hz, 3 H), 0.96 (d, *J* = 5.5 Hz, 3 H), 0.98 (d, *J* = 6.8 Hz, 3 H), 1.70−1.80 (m, 1 H), 2.34−2.41 (m, 1 H), 2.41 (s, 3 H), 2.76 (s, 3 H), 3.09−3.23 (m, 2 H), 5.23 (d, *J* = 7.7 Hz, 1 H), 5.47 (dd, *J* = 10.2 and 7.7 Hz, 1 H), 7.30 (d, *J* = 8.1 Hz, 2 H), 7.63 (d, *J* = 8.1 Hz, 2 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.2, 17.6, 20.2, 21.5, 30.2, 35.0, 38.2, 80.1, 126.7, 127.9, 129.6, 137.5, 143.8, one signal obscured. The material was not characterized further.

9. (1*R,2*R**,3*Z*)-2-Methyl-4-[methyl(*p*-tolylsulfonyl)amino]-1-phenyl-3-buten-1-ol (13e):** Compound **9** (365 mg, 1.0 mmol), benzaldehyde (127 mg, 1.2 mmol), and triethanolamine (149 mg, 1.0 mmol) were allowed to react as described under 6. Flash chromatography with petroleum ether/ethyl acetate (3:1) furnished **13e** (0.220 g, 64%) as a colorless oil. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.85 (d, *J* = 6.7 Hz, 3 H), 2.42 (s, 3 H), 2.67 (s, 3 H), 3.23 (br. d, *J* = 5.8 Hz, 1 H), 3.28−3.41 (m, 1 H), 4.35 (dd, *J* = 8.4 and 5.8 Hz, 1 H), 5.33 (d, *J* = 7.7 Hz, 1 H), 5.55 (dd, *J* = 10.6 and 7.7 Hz, 1 H), 7.22−7.38 (m, 7 H), 7.64−7.67 (m, 2 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 17.5, 21.5, 38.0, 39.7, 78.8, 126.8, 127.5, 127.8, 128.2, 129.7, 133.2, 136.7, 143.3, 143.9, one signal obscured. − $C_{19}H_{23}NO_3S$ (345.5): calcd. C 66.06, H 6.71, N 4.05; found C 66.32, H 6.36, N 4.01.

10. (4*R,5*S**)-2-Methoxy-4,5-dimethyloxolane (15a):** A solution of **9** (730 mg, 2.0 mmol) and acetaldehyde (132 mg, 3.0 mmol) in petroleum ether (5 mL) was pressurized to 4 kbar for 3 d. The mixture was concentrated, and methanol (10 mL) and water (10 mL) were added. Ion exchange resin (Lewatit S 100, 1.0 g) was added and the mixture was maintained under reflux for 1 d. The mixture was filtered and the solution was saturated with NaCl. The solution was extracted with ether (4 × 30 mL). The combined extracts were washed with brine (10 mL), dried ($MgSO_4$), and concentrated. Distillation of the residue at 60 °C/100 Torr furnished **15a** (1.69 g, 65%) as a 55:45 anomer mixture. The diastereomer ratio was determined as 97:3 by gas chromatography. − The material showed ^{1}H and ^{13}C NMR spectroscopic data identical to those reported earlier.[20] − Likewise, compound **10** (290 mg, 1.0 mmol) and acetaldehyde (66 mg, 1.5 mmol) were allowed to react as described above to furnish **15a** (62 mg, 48%) with a diastereoselectivity of 95.8:4.2.

11. (4*R,5*S**)-5-Ethyl-2-methoxy-4-methyloxolane (15b):** Compound **9** (365 mg, 1.0 mmol), propanal (70 mg, 1.2 mmol), and Lewatit S 100 (1.00 g) were allowed to react as described under 10. to give **15b** (100 mg, 69%) as a 1:1 anomer mixture of b.p. 60 °C/100 Torr. GC analysis showed the diastereoselectivity to be 97.1:2.9. − ^{1}H NMR (300 MHz, $CDCl_3$): anomer 1: δ = 3.34 (s, 3 H), 4.95 (dd, *J* = 5.7 and 2.9 Hz, 1 H); anomer 2: δ = 3.30 (s, 3 H), 4.89 (d, *J* = 4.9 Hz, 1 H). − ^{13}C NMR (75 MHz, $CDCl_3$): anomer 1: δ = 10.4, 17.4, 28.5, 36.2, 41.9, 54.1, 88.3, 104.4; anomer 2: δ = 10.4, 17.4, 26.5, 37.7, 41.4, 54.7, 85.4, 104.6. − $C_8H_{16}O_2$ (144.2): calcd. C 66.63, H 11.18; found C 66.47, H 11.16.

12. (4*R,5*S**)-2-Methoxy-4-methyl-5-(1-methylethyl)oxolane (15c):** Compound **9** (365 mg, 1.0 mmol), 2-methylpropanal (87 mg, 1.2 mmol), and Lewatit S 100 (1.00 g) were allowed to react as described under 10. to give **15c** (2:1 anomer mixture, 110 mg, 70%) of b.p. 80 °C/100 Torr. The diastereoselectivity was determined as

98.2:1.8. − ^{1}H NMR (300 MHz, $CDCl_3$): anomer 1: δ = 0.93 (d, *J* = 6.9 Hz, 3 H), 0.97 (d, *J* = 6.7 Hz, 3 H), 1.03 (d, *J* = 6.5 Hz, 3 H), 1.59 (ddd, *J* = 12.5, 10.9 and 4.9 Hz, 1 H), 1.64−1.82 (m, 1 H), 2.06 (dd, *J* = 12.5 and 7.0 Hz, 1 H), 2.12−2.29 (m, 1 H), 3.25−3.28 (m, 1 H), 3.30 (s, 3 H), 4.87 (d, *J* = 4.9 Hz, 1 H); anomer 2: δ = 0.92 (d, *J* = 6.7 Hz, 3 H), 0.93 (d, *J* = 6.9 Hz, 3 H), 1.07 (d, *J* = 6.8 Hz, 3 H), 1.49 (ddd, *J* = 13.2, 5.5 and 2.0 Hz, 1 H), 1.64−1.82 (m, 1 H), 1.86−1.99 (m, 1 H), 2.12−2.29 (m, 1 H), 3.31 (s, 3 H), 3.38 (dd, *J* = 7.3 and 5.4 Hz, 1 H), 4.94 (dd, *J* = 5.4 and 2.0 Hz, 1 H). − ^{13}C NMR (75 MHz, $CDCl_3$): anomer 1: δ = 18.5, 18.6, 19.5, 33.1, 34.3, 42.4, 54.2, 92.3, 104.2; anomer 2: 18.0, 18.9, 19.6, 31.3, 34.3, 41.4, 54.4, 89.4, 104.6. − $C_9H_{18}O_2$ (158.2): calcd. C 68.31, H 11.47; found C 68.24, H 11.40.

13. (4*R*,5*S*)-2-Methoxy-4-methyl-5-butyloxolane (ent-15d): Compound (*S*)-**9** (548 mg, 1.5 mmol), *n*-pentanal (172 mg, 2.0 mmol), and Lewatit S100 (0.750 g) were allowed to react as described under 10. to give **15d** (1:1 anomer mixture, 241 mg, 87%) of b.p. 80 °C/100 Torr. The diastereomer ratio was determined as 98.2:1.8. − ^{1}H NMR (300 MHz, $CDCl_3$): anomer 1: δ = 0.89 (t, *J* = 6.7 Hz, 3 H), 1.01 (d, *J* = 6.7 Hz, 3 H), 1.30−1.63 (m, 7 H), 1.66−1.78 (m, 1 H), 2.33 (ddd, *J* = 13.3, 9.3, and 5.7 Hz, 1 H), 3.33 (s, 3 H), 3.45−3.53 (m, 1 H), 4.95 (dd, *J* = 5.7 and 2.9 Hz, 1 H); anomer 2: δ = 0.90 (t, *J* = 6.7 Hz, 3 H), 1.01 (d, *J* = 6.2 Hz, 3 H), 1.26−1.64 (m, 7 H), 2.00−2.12 (m, 2 H), 3.30 (s, 3 H), 3.50 (td, *J* = 7.6 and 4.2 Hz, 1 H), 4.89 (d, *J* = 4.9 Hz, 1 H). − ^{13}C NMR (75 MHz, $CDCl_3$): anomer 1: δ = 14.0, 17.2, 22.8, 28.6, 33.5, 38.3, 41.4, 54.8, 84.1, 104.6; anomer 2: δ = 14.0, 17.3, 22.9, 28.6, 35.7, 36.8, 41.9, 54.2, 87.1, 104.4. − $C_{10}H_{20}O_2$ (172.3): calcd.C 69.72, H 11.70; found C 69.70, H 11.89.

14. (4*R,5*R**)-2-Methoxy-4-methyl-5-phenyloxolane (15e):** Compound **9** (365 mg, 1.0 mmol), benzaldehyde (106 mg, 1.0 mmol), and Lewatit S100 (1.00 g) were allowed to react as described under 10. Flash chromatography of the crude product with petroleum ether/ether (20:1) furnished **15e** (55:45 anomer mixture, 135 mg, 70%) as a colorless oil. The diastereoselectivity was determined as 99.1:0.9. − Likewise, treatment of **9** with benzaldehyde in hexane for 3 d under reflux furnished 72% of **15e**, with a diastereoselectivity of 99.0:1.0. − The ^{1}H NMR and ^{13}C NMR spectroscopic data were identical to those reported earlier.[20]

15. (4*R*,5*S*)-5-Butyl-4,5-dihydro-4-methylfuran-2(3*H*)-one (16): *m*-Chloroperbenzoic acid (previously dried in solution with 4-Å molecular sieves, 276 mg, 1.60 mmol) was dissolved in dichloromethane (3 mL). This solution was added to a solution of **15d** (149 mg, 0.80 mmol) in dichloromethane (4 mL) at 0 °C. $BF_3{\cdot}OEt_2$ (0.20 mL, 1.6 mmol) was added dropwise and stirring was continued for 5 h at 0 °C. Saturated, aqueous $NaHCO_3$ solution (5 mL) was added, the phases were separated, and the aqueous phase was extracted with dichloromethane (3 × 10 mL). The combined organic phases were dried ($MgSO_4$) and concentrated. Flash chromatography of the residue with petroleum ether/ether (3:1) furnished **16** (98 mg, 73%) as a colorless oil. − $[\alpha]_D^{24}$ = −66.9 (*c* = 1.20, methanol); cf. ref.[24]: $[\alpha]_D^{15}$ = +79 (*c* = 1.04, methanol). − The ^{1}H NMR and ^{13}C NMR data corresponded to those given in ref.[25]

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[1] R. W. Hoffmann, J. Krüger, D. Brückner, *New. J. Chem.*, *in press.*
[2] D. Hoppe, *Angew. Chem.* **1984**, *96*, 930−946; *Angew. Chem. Int. Ed. Engl.* **1984**, *23*, 932.
[3] D. Hoppe; O. Zschage, in: *Organic Synthesis via Organometallics* (Eds.: K. H. Dötz; R. W. Hoffmann), Vieweg, Braunschweig, **1991**, pp. 267−283.
[4] O. Zschage, D. Hoppe, *Tetrahedron* **1992**, *48*, 5657−5666.
[5] D. Hoppe, T. Krämer, J.-R. Schwark, O. Zschage, *Pure Appl. Chem.* **1990**, *62*, 1999−2006.
[6] D. Hoppe, T. Hense, *Angew. Chem.* **1997**, *109*, 2376−3410; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 2282−2316.
[7] L. Le Menez, V. Fargeas, J. Poisson, J. Ardisson, J.-Y. Lallemand, A. Pancrazi, *Tetrahedron Lett.* **1994**, *35*, 7767−7770.
[8] P. Le Menez, N. Firmo, V. Fargeas, J. Ardisson, A. Pancrazi, *Synlett* **1994**, 995−997.
[9] D. Hoppe, G. Tarara, M. Wilckens, P. G. Jones, D. Schmidt, J. J. Stezowski, *Angew. Chem.* **1987**, *99*, 1079−1081; *Angew. Chem. Int. Ed. Engl.* **1987**, *26*, 1034−1036.
[10] H. Paulsen, D. Hoppe, *Tetrahedron* **1992**, *48*, 5667−5670.
[11] O. Zschage, J.-R. Schwark, T. Krämer, D. Hoppe, *Tetrahedron* **1992**, *48*, 8377−8388.
[12] B. Peschke, J. Lüßmann, M. Dyrbusch, D. Hoppe, *Chem. Ber.* **1992**, *125*, 1421−1430.
[13] R. W. Hoffmann, W. Ladner, *Chem. Ber.* **1983**, *116*, 1631−1642.
[14] D. Hoppe, T. Krämer, C. F. Erdbrügger, E. Egert, *Tetrahedron Lett.* **1989**, *30*, 1233−1236.
[15] R. W. Hoffmann, S. Dresely, J. W. Lanz, *Chem. Ber.* **1988**, *121*, 1501−1507.
[16] R. W. Hoffmann, V. Giesen, M. Fuest, *Liebigs Ann. Chem.* **1993**, 629−639.
[17] R. W. Hoffmann, S. Dresely, B. Hildebrandt, *Chem. Ber.* **1988**, *121*, 2225−2230.
[18] M. W. Andersen, B. Hildebrandt, G. Dahmann, R. W. Hoffmann, *Chem. Ber.* **1991**, *124*, 2127−2139.
[19] R. W. Hoffmann, J. J. Wolff, *Chem. Ber.* **1991**, *124*, 563−569.
[20] R.W. Hoffmann, S. Dresely, *Chem. Ber.* **1989**, *122*, 903−909.
[21] D. J. Matteson, T. J. Michnick, R. D. Willett, C. D. Patterson, *Organometallics* **1989**, *8*, 726−729.
[22] R. W. Hoffmann, S. Dresely, *Synthesis* **1988**, 103−106.
[23] P. A. Grieco, T. Oguri, Y. Yokoyama, *Tetrahedron Lett.* **1978**, 419−420.
[24] N. Masuda, K. Nishimura, *Chem. Lett.* **1981**, 1333−1336.
[25] C. Günther, A. Mosandl, *Liebigs Ann. Chem.* **1986**, 2112−2122.
[26] H. Nishikori, K. Ito, T. Katsuki, *Tetrahedron: Asymmetry* **1998**, *9*, 1165−1170.
[27] S. Tsuboi, J.-I. Sakamoto, H. Yamashita, T. Sakai, M. Utaka, *J. Org. Chem.* **1998**, *63*, 1102−1108.
[28] C. Harcken, R. Brueckner, *Angew. Chem.* **1997**, *109*, 2866−2868; *Angew. Chem. Int. Ed.* **1997**, *36*, 2750−2752.
[29] T. Chevtchouk, J. Ollivier, J. Salaun, *Tetrahedron: Asymmetry* **1997**, *8*, 1011−1014.
[30] K. Ito, M. Yoshitake, T. Katsuki, *Tetrahedron* **1996**, *52*, 3905−3920.
[31] K. Ito, M. Yoshitake, T. Katsuki, *Chem. Lett.* **1995**, 1027−1028.
[32] H. Takahata, Y. Uchida, T. Momose, *J. Org. Chem.* **1995**, *60*, 5628−5633.
[33] Y.-C. Pai, J.-M. Fang, S.-H. Wu, *J. Org. Chem.* **1994**, *59*, 6018−6025.
[34] H. Takahata, Y. Momose, T. Uchida, *Tetrahedron Lett.* **1994**, *35*, 4123−4124.
[35] D. F. Taber, J. B. Houze, *J. Org. Chem.* **1994**, *59*, 4004−4006.
[36] T. Ebata, K. Matsumoto, H. Yoshikoshi, K. Koseki, H. Kawakami, K. Okano, H. Matsuhita, *Heterocycles* **1993**, *36*, 1017−1026.
[37] B. Sarmah, N. C. Barua, *Tetrahedron* **1993**, *49*, 2253−2260.
[38] O. Miyata, T. Shinada, K. Kawakami, K. Taji, I. Ninomiya, T. Naito, T. Date, K. Okamura, *Chem. Pharm. Bull.* **1992**, *40*, 2579−2581.
[39] O. Zschage, D. Hoppe, *Tetrahedron* **1992**, *48*, 5657−5666.
[40] G. V. M. Sharma, S. R. Vepachedu, S. Chandrasekhar, *Synth. Commun.* **1990**, *20*, 3403−3410.
[41] T. Ebata, K. Matsumoto, H. Yoshikoshi, K. Koseki, H. Kawakami, H. Matsushita, *Heterocycles* **1990**, *31*, 1585−1588.

[42] D. Hoppe, O. Zschage, *Angew. Chem.* **1989**, *101*, 67−69; *Angew. Chem. Int. Ed. Engl.* **1989**, *28*, 69−71.
[43] R. M. Ortuno, M. Merce, J. Font, *Tetrahedron* **1987**, *43*, 4497−4506.
[44] J. Salaun, B. Karkour, *Tetrahedron Lett.* **1988**, *29*, 1537−1540.
[45] R. Bloch, L. Gilbert, *J. Org. Chem.* **1987**, *52*, 4603−4605.
[46] J. P. Marino, R. Fernández de la Pradilla, *Tetrahedron Lett.* **1985**, *26*, 5381−5384.
[47] R. W. Hoffmann, *Pure Appl. Chem.* **1988**, *60*, 123−130.
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