Synthesis of 4,6-Dideoxyfuranoses through the Regioselective and Diastereoselective Oxyfunctionalization of a Dimethylphenylsilyl-Substituted Chiral Homoallylic Alcohol

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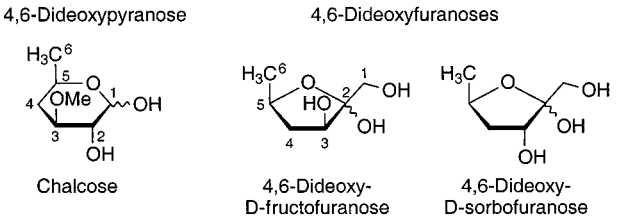
The 4,6-dideoxyfuranoses **10a** and **10b** have been synthesized by starting from the readily available *E*-5-dimethylphenylsilyl-2-hexene-4-ol (**1**) and employing successively three versatile oxyfunctionalization methods, namely photooxygenation, metal-catalyzed epoxidation, and oxidative desilylation. Photooxygenation of the hydroxy vinylsilane **1** and subsequent triphenylphosphine reduction of the hydroperoxides **3** afford the *like*-**4a** and *unlike*-**4b** diols, which have been converted separately to the tetrahydrofurans (2*S**,3*R**,5*R**)-**7a** and (2*S**,3*R**,5*S**)-**7b** by a combination of diastereoselective epoxidation and regioselective intramolecular epoxide-ring opening. In the epoxidation reaction, catalyzed by Ti(O*i*Pr)$_4$ or VO(acac)$_2$, only one diastereomer (dr >95:5) of the epoxide **5** is obtained. Further intramolecular opening of the epoxide ring in *erythro*-**5** occurs regioselectively at the C-α position and diastereoselectively under inversion of the configuration of the silyl-substituted stereogenic center to generate only one diastereomer of the tetrasubstituted tetrahydrofurans **7**. Oxidative desilylation of the latter gave the hitherto unknown 4,6-dideoxyfuranoses **10a** and **10b**. The use of the optically active *E*-5-dimethylphenylsilyl-2-hexene-4-ol (**1**) as starting material, which is readily available through lipase-catalyzed kinetic resolution, leads to the D- and L-4,6-dideoxysorbofuranoses **10a** and D- and L-4,6-dideoxyfructofuranoses **10b** in up to 98% enantiomeric excess.

Introduction

While monodeoxy sugars are present in a wide variety of natural products[1−3] relatively little is known about dideoxy sugars, in particular, the 4,6-dideoxyhexoses. Such dideoxy sugars, e.g., the 4,6-dideoxyhexose chalcose (see structures), are found as structural units in bioactive



compounds.[4] The biosynthetic pathway of 4,6-dideoxypyranoses has been studied,[4] and even a few derivatives have been synthesized by chemical methods.[5,6] In contrast, 4,6-dideoxyfuranoses (see structures) are unknown to date in nature, nor have derivatives been synthesized.

In past years, we have intensively studied the selective oxyfunctionalization of chiral allylic alcohols to the corresponding epoxy diols by photooxygenation[7,8] and direct titanium-catalyzed epoxidation.[9] Alternatively, the intermediary allylic hydroperoxides of the photooxygenation were reduced by triphenylphosphine and subsequently the resulting alkene diols were epoxidized under Ti(O*i*Pr)$_4$ catalysis with *β*-hydroxy hydroperoxides as oxygen donors.[10] Here we report that by employing this methodology, the hitherto unknown 4,6-dideoxyfuranoses **10** may be prepared stereoselectively from the dimethylphenylsilyl-substituted chiral homoallylic alcohol **1** (Scheme 1). Most gratifying, also the optically active 4,6-dideoxysorbofuranose **10a** and 4,6-dideoxyfructofuranose **10b** derivatives have been now made available for the first time by starting from the enantiomerically enriched hydroxy vinylsilane **1**.

Results

The silyl-substituted homoallylic alcohol **1** was synthesized by hydrosilylation, analogous to the method of Oshima et al. (Scheme 2).[11] The active silylating reagent,

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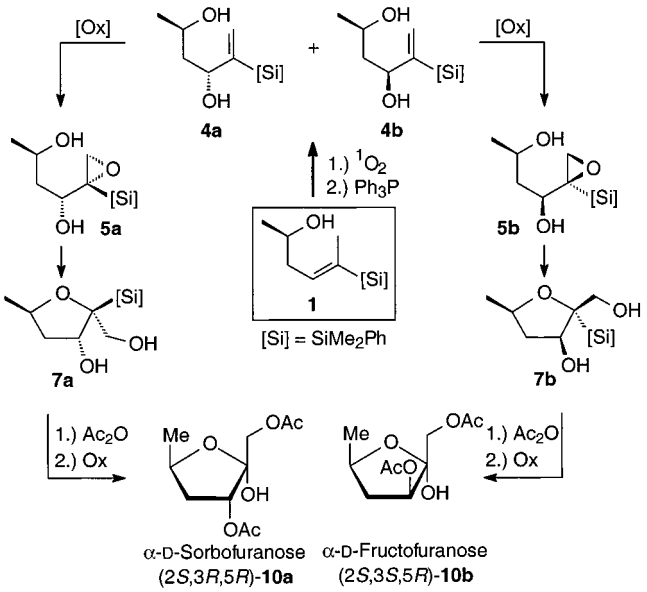
Scheme 1. Synthetic Route to the 4,6-Dideoxyfuranoses 10



$(PhMe_2Si)_3ZnLi$, attacks the triple bond from the less crowded side *cis*-selectively to give the *E*-configured 5-dimethylphenylsilyl-4-hexen-2-ol (**1**) in high regioselectivity and in a 66% yield of isolated material. Only 8% of the regioisomeric *E*-4-dimethylphenylsilyl-4-hexen-2-ol was formed.

Photooxygenation of the homoallylic alcohol **1** with tetraphenylporphyrin (TPP) as sensitizer (Scheme 2) gave the diastereomeric hydroperoxy alcohols **2** in high yield (90%). The silyl group at the double bond in the homoallylic alcohol **1** directs the H abstraction regioselectively to the *gem* allylic position in the singlet-oxygen ene reaction (*gem* effect).[7,12] Only traces (<5%) of the regioisomeric hydroperoxide **2′** were produced, which immediately decomposed to the enone **3** and dimethylphenylsilanol. The diastereomeric hydroperoxy alcohols **2a** (*like*) and **2b** (*unlike*) were obtained as a 50:50 mixture, the lack of diastereoselectivity in this photooxygenation is due to the absence of 1,3-allylic strain.[9b,13]

The diastereomers **2a** and **2b** could not be separated by silica gel chromatography; nevertheless, after reduction by triphenylphosphine to the diastereomeric diols **4a** (*like*) and **4b** *(unlike*), these were isolated individually by silica gel chromatography in a total yield of 91% (Scheme 2). For convenience, the photooxygenation of the homoallylic alcohol **1** and reduction of the hydroperoxide product **2** may be conducted in an one-pot process to afford the diol **4** in 90% overall yield; one tedious purification step is thereby obviated.

Various oxidants were tested for the epoxidation of the diols **4a** and **4b**. Besides the expected epoxides **5**, some enone **6** and also the tetrahydrofuran **7** and tetrahydropyran **8** products (intramolecular nucleophilic attack on the epoxide ring) were obtained (Scheme 3). The product composition depended on the oxidant and the reaction conditions; the results are summarized in Table 1.

The oxidation of the *like*-diol **4a** and the *unlike*-diol **4b** with 2,3-dimethyl-3-hydroperoxy-2-butanol (this oxygen source instead of *tert*-butyl hydroperoxide was necessary to sustain the titanium catalytic cycle[10]) under titanium catalysis gave the tetrahydrofurans **7** as major products, but no epoxides **5** nor tetrahydropyrans **8** were obtained (Table 1, entries 1 and 6). Evidently, the *erythro*-**5** epoxide was immediately converted to the tetrahydrofuran **7** during the reaction. The direct epoxidation of the hydroperoxides **2**, catalyzed by $Ti(OiPr)_4$, is not desirable because much (ca. 30%) reduction to the diols **4** is observed.

The vanadium-catalyzed oxidation[14] of the *like*-diol **4a** with *tert*-butyl hydroperoxide gave essentially exclusively the tetrahydrofuran **7a** in 78% yield of isolated material (entry 2), and only traces of the enone **6**. In contrast, under the same reaction conditions, the oxidation of the *unlike*-diol **4b** led to the (α*R**,1*R**,3*S**)-**5b** epoxide as major product (entry 7), which was isolated in 42% yield when neutral conditions were carefully maintained. Also a significant (30%) amount of tetrahydrofuran **7b** was formed. The latter was obtained as the exclusive product, when the vanadium-catalyzed reaction was conducted at 45 °C for 10 h (entry 8). Thereby, the tetrahydrofuran **7b** was isolated in 82% yield after silica gel chromatography.

The oxidation of the diols **4a** and **4b** with methyltrioxorhenium (MTO) and UHP (urea/hydrogen peroxide adduct) led to the tetrahydrofuran **7** and tetrahydropyran **8** products in a ratio of 65:35, together with small (4−6%) amounts of enone **6** (entries 3 and 9). NMR monitoring of the oxidation showed that initially a mixture of the diastereomeric epoxides was observed (65:35 in favor of the *erythro*-**5** epoxide), which was slowly converted to a mixture of tetrahydrofuran **7** and tetrahydropyran **8**.

The oxidation of the *like*-diol **4a** with *m*CPBA[15] (entry 4) gave the tetrahydrofuran **7a** as major product (69%) and minor amounts (23%) of tetrahydropyran **8a**, as well as a small quantity of a mixture of the diastereomeric epoxides **5a** (8%). NMR monitoring of the reaction progress showed only a moderate diastereoselectivity (ca. 80:20) for the *erythro*-**5a** and *threo*-**5a** epoxides. In contrast, the oxidation of the *unlike*-diol **4b** by *m*CPBA gave a mixture of the epoxides *erythro*-**5b** and *threo*-**5b** as major products (71%) in a *erythro*/*threo* ratio of 96:4 (entry 10). At the beginning of the reaction, a diastereomeric ratio of 81:19 was determined by NMR spectroscopy for the epoxides **5b**. Also, significant amounts of the tetrahydrofuran **7b** (16%) and tetrahydropyran **8b** (13%) were isolated, as well as traces of the enone **6**.

Ethane carboperoxoic acid, which was used to provide mild and nonacidic oxidation conditions (after oxygen transfer the resulting carbonic acid decomposes into the neutral CO_2 and ethanol),[16] epoxidized the diols **4** in low diastereoselectivity (dr ca. 60:40, entries 5 and 11). In the oxidation of the *like*-diol **4a**, 52% of the diastereomeric epoxides **5a** and a total of 48% of the tetrahydrofuran **7a** (40%) and tetrahydropyran **8a** (8%) were obtained (entry 5). Moreover, a small amount of the enone **6** (2%) was detected. After two weeks at room temperature (20 °C), the crude reaction mixture had transformed quantitatively to the cyclic products **7a** and **8a** in a ratio

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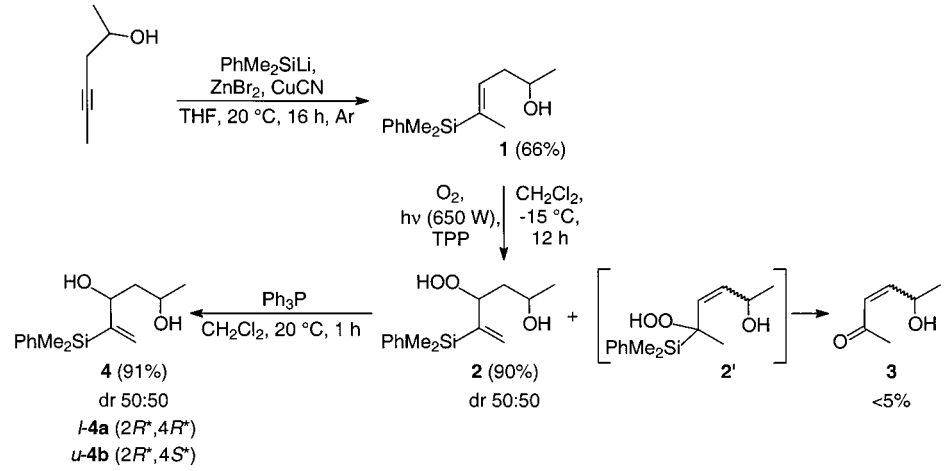
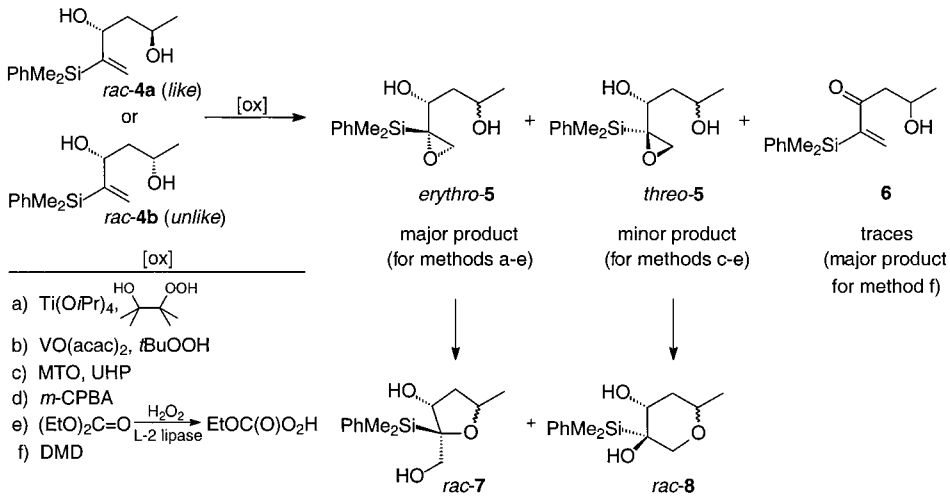
Scheme 2. Synthesis of the Diastereomeric Diols *l*-4a and *u*-4b



Scheme 3. Epoxidation of the Diols 4 by Various Oxidants



of 62:38. However, the oxidation of the *unlike*-diol **4b** by ethane carboperoxoic acid gave exclusively the diastereomeric epoxides **5b** (dr 64:36, entry 11). These were transformed into a mixture (64:36) of the tetrahydrofuran **7b** and the tetrahydropyran **8b** on standing of the crude product mixture at room temperature (20 °C) for two weeks.

With dimethyldioxirane (DMD) as oxidant, allylic oxidation to the enone **6** (54%) was observed instead of epoxidation (<15%). This is not surprising, since DMD is sensitive to steric effects, as previously observed for similar vinylsilanes.[17]

For the Fleming oxidation (oxidative desilylation)[18] of the dimethylphenylsilyl to the hydroxy group by treatment with Br_2−AcOOH under retention of the configuration, the alcohol functionalities in the tetrahydrofurans **7** were protected by acetylation. Under standard conditions,[19] the diacetates **9** were synthesized in 80−90% yield (Scheme 4). The oxidation by KBr−AcOOH gave both anomers of the 4,6-dideoxyfuranoses **10a** (α:β = 55:45, 57% yield) and **10b** (α:β = 70:30, 62% yield). The amount of α anomer may be enriched by crystallization (e.g., for 6-deoxysorbose, α:β = 95:5).[20]

A number of suitable methods for the preparation of trisubstituted tetrahydrofurans have been reported, which include intramolecular nucleophilic attack of hydroxy groups on epoxides[21] and electrophilic[22] as well as radical[23] cyclizations. Protodesilylation of our tetrasubstituted tetrahydrofurans **7** would provide a convenient and efficient entry to trisubstituted tetrahydrofurans. Unfortunately, when the desilylation of the tetrasubstituted tetrahydrofuran **7** with CsF was tried, only Peterson-type elimination products were obtained instead of the expected trisubstituted derivative. Also the conditions of the homo-Brook rearrangement[24] [KO*t*Bu in DMSO/H_2O (10:1)] led to base-catalyzed elimination of dimethylphenylsilanol (cf. Supporting Information). Thus, this potentially attractive synthetic methodology was abandoned.

The nearly enantiomerically pure 4,6-dideoxy sugars **10** were obtained from the optically active hydroxy vinylsilane **1**. For this purpose, the racemic material was submitted to the enzyme-catalyzed kinetic resolution by acetylation.[25] The BSL lipase (*Burkholderia sp.*, CHIRA-

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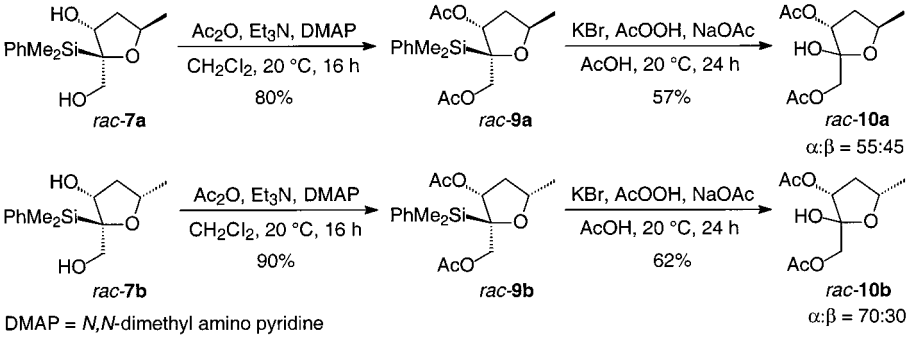
Table 1. Epoxidation of the Dihydroxy Vinylsilanes 4

						product ratio [%][b]		
entry	4	oxidant[c]	time[h]	convn[a] [%]	mb[a] [%]	epoxide **5**[d]	furan **7**	pyran **8**
1	*l*-**4a**	Ti(O*i*Pr)$_4$, ROOH[f]	48	81	60	e	>95	-
2	*l*-**4a**	VO(acac)$_2$, *t*BuOOH	27	94	79	*e*	>95	-
3	*l*-**4a**	MTO/UHP	36	61	47	*g*	66	34
4	*l*-**4a**	*m*CPBA	24	>95	65	8 (80:20)	69	23
5	*l*-**4a**	EtOC(O)O$_2$H	60	>95	>95	52 (55:45)[h]	40	08
6	*u*-**4b**	Ti(O*i*Pr)$_4$, ROOH[f]	20	>95	40	*e*	>95	-
7	*u*-**4b**	VO(acac)$_2$, *t*BuOOH	12	93	60	70 (>95:05)	30	-
8	*u*-**4b**	VO(acac)$_2$, *t*BuOOH[i]	10	>95	82	*e*	>95	-
9	*u*-**4b**	MTO/UHP	36	71	43	*j*	64	36
10	*u*-**4b**	*m*CPBA	24	>95	79	71 (96:04)[k]	16	13
11	*u*-**4b**	EtOC(O)O$_2$H	40	75	89	>95 (64:36)[l]	-	-

[a] Conversion and mass balance (mb) were determined by NMR spectroscopy after silica gel chromatography. [b]Product ratios after silica gel chromatography, determined by NMR spectroscopy (error ±5% of the stated values), except entries 5 and 11, which were analyzed as crude reaction mixtures. [c]Oxidations were conducted in $CHCl_3$ or CH_2Cl_2 at 20 °C, except entries 5 and 11, for which diethyl carbonate was used as solvent at 40 °C. [d]The e*rythro*:*threo* ratio is given in parentheses. [e]On monitoring the reaction mixture by ^{1}H NMR spectroscopy, the intermediary *erythro*-**5** epoxide (dr >95:5) was observed, which was totally converted to the tetrahydrofuran **7** at the end of the reaction. [f]2,3-Dimethyl-3-hydroperoxy-2-butanol was used as oxygen donor. [g]On monitoring the reaction mixture by ^{1}H NMR spectroscopy, the intermediary epoxides *erythro*-**5a**:*threo*-**5a** (dr = 65:35) were observed. [h]After two weeks at 20 °C, the crude reaction mixture had transformed quantitatively to **7a** and **8a** (62:38). [i]The reaction mixture was heated to 45 °C. [j]On monitoring the reaction mixture by ^{1}H NMR spectroscopy, the intermediary epoxides *erythro*-**5b**:*threo*-**5b** (dr = 64:36) were observed. [k]The dr value of the epoxide **5b** (*erythro*:*threo*) was 81:19 at the beginning, but changed as the reaction progressed. [l]After two weeks at 20 °C, the crude reaction mixture had transformed quantitatively to **7b** and **8b** (64:36).

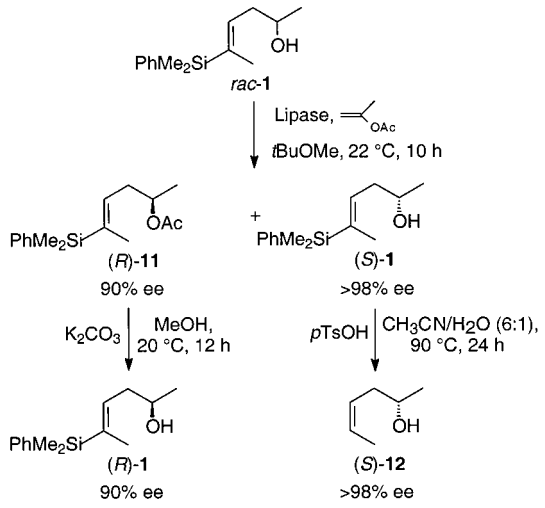
Scheme 4. Acetylation of the Tetrahydrofurans 7 and Oxidative Desilylation of the Resulting Acetates 9 to the 4,6-Dideoxyfuranoses 10



ZYME L-1, Boehringer Mannheim) was chosen for the reactions at the semipreparative scale (4.5 mmol), in which at 52% conversion the nearly enantiomerically pure derivatives (*S*)-**1** (>98% ee) and (*R*)-**11** (90% ee) were obtained (Scheme 5). The mixture of the alcohol (*S*)-**1** and the acetate (*R*)-**11** was readily separated quantitatively by silica gel chromatography.

The *S* configuration of the hydroxy vinylsilane (+)-**1** was determined by chemical correlation. Thus, desilylation of (+)-**1** with toluenesulfonic acid in acetonitrile/water (6:1) gave the known homoallylic alcohol (*S*)-**12** (Scheme 5, 60% yield).[19] The configuration in this enantioselection is in accordance with the established empirical rule proposed by Kazlauskas et al.[26] for the lipase-catalyzed kinetic resolution of secondary alcohols. To obtain the (*R*)-**1** alcohol, the acetate (*R*)-**11** was hydrolyzed quantitatively by K_2CO_3 in methanol (90% ee, Scheme 5). As reference samples for the chiral HPLC analysis, it was necessary to prepare the racemic acetate

Scheme 5. Lipase-Catalyzed Kinetic Resolution of the Hydroxy Vinylsilane 1, Its Desilylation to the Homoallylic Alcohol 12, and the Hydrolysis of the Acetate (*R*)-11 to the Hydroxy Vinylsilane (*R*)-1



11 by acetylation of the alcohol **1** with acetic anhydride under basic conditions (92% yield).[19]

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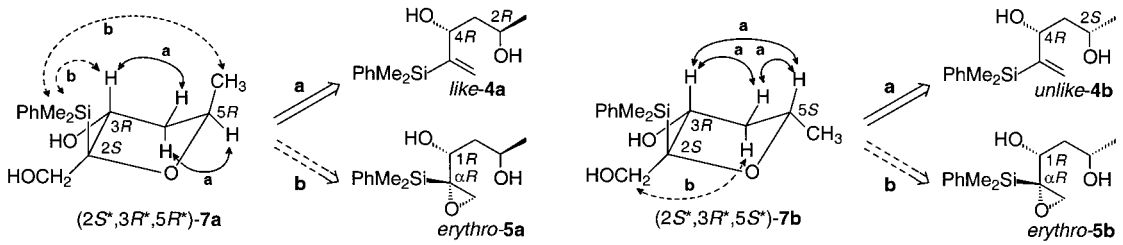
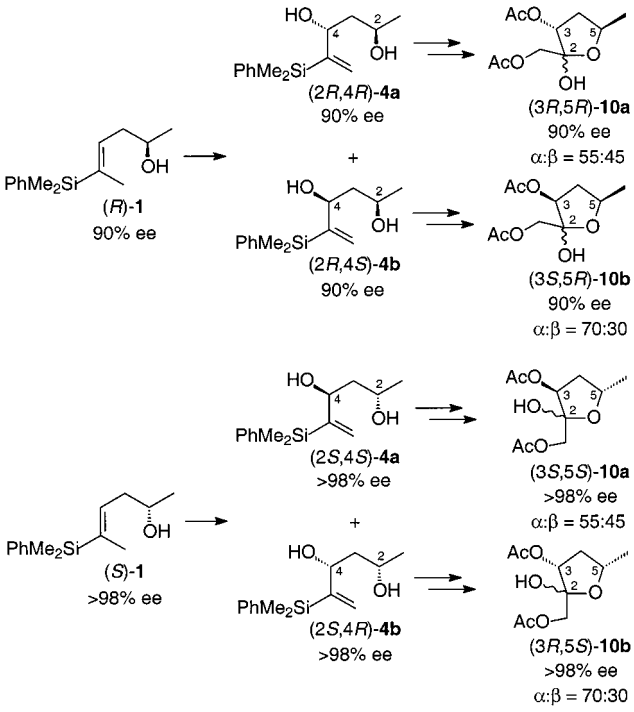


Figure 1. Determination of the relative configuration for the tetrahydrofurans **7** by NOESY experiments.

Scheme 6. Synthesis of the Optically Active 4,6-Dideoxysorbofuranoses 10a and 4,6-Dideoxyfructofuranoses 10b from the Enantiomerically Enriched Hydroxy Vinylsilanes (*R*)-1 and (*S*)-1



Both enantiomers of the hydroxy vinylsilane **1** were submitted to diastereoselective oxyfunctionalization by photooxygenation and subsequent reduction of the hydroperoxides **2** by Ph_3P to afford the diastereomeric diols **4**. The latter were epoxidized by *tert*-butyl hydroperoxide under $VO(acac)_2$ catalysis. The intermediary epoxides **5** were transformed to the tetrahydrofurans **7** by intramolecular attack of the C-3 hydroxy group. After oxidative desilylation[18] of the diacetates **9** (Scheme 6), the D- and L-4,6-dideoxysorbofuranose **10a** and D- and L-4,6-dideoxyfructofuranose **10b** were obtained as anomeric mixtures in 90 to >98% ee, which match the ee values of the starting hydroxy vinylsilanes (*R*)-**1** and (*S*)-**1**.

The relative configurations of the tetrahydrofurans **7** and the tetrahydropyrans **8** were determined by NOESY experiments, those of the diols **4** and the epoxides *erythro*-**5** and *threo*-**5** by chemical correlation. The relative configuration of the tetrahydrofuran **7a** was found to be (2*S**,3*R**,5*R**), as shown in Figure 1 (left). The NOE effects coded by the solid arrows **a** suggest a *trans* arrangement of the C-3 hydroxy (3*R**) group and the C-5 methyl (5*R**) group, from which a *like* configuration may be gathered for the two hydroxy substituents in the diol (2*R**,4*R**)-**4a**. The NOE effects coded by the dashed arrows **b** indicate a trans arrangement between the silyl group at C-2 and the neighboring C-3 hydroxy group. Thus, the silyl-substituted C-2 carbon atom possesses the 2*S** configuration. Since the intramolecular epoxide-ring opening (S_N2 process) of **5a** to the tetrahydrofuran **7a** occurs with inversion of the configuration at the silyl-substituted α epoxide reaction center, the latter stereogenic carbon atom must have the α*R** relative configuration. From these data we infer the (α*R**,1*R**,3*R**) configuration for the *erythro*-**5a** epoxide. In the same way (Figure 1, right), from the NOE effects of the tetrahydrofuran (2*S**,3*R**,5*S**)-**7b**, an *unlike* configuration for the diol (2*S**,4*R**)-**4b** and a (α*R**,1*R**,3*S**) configuration for the *erythro*-**5b** epoxide may be concluded.

The relative configuration of the tetrahydropyran **8a** was found to be (2*R**,4*R**,5*S**), as shown in Figure 2 (left). By proceeding as in the case of the tetrahydrofuran **7a**, from the NOE effects coded by the solid arrows **a**, a *like* configuration may be assigned for the two stereogenic centers of the diol (2*R**,4*R**)-**4a**. The NOE effects coded by the dashed arrows **b** indicate a *cis* arrangement of the silyl group at C-5 and the neighboring C-4 hydroxy group and a 5*S** configuration for the silyl-substituted C-5 carbon atom. The corresponding *threo*-**5a** epoxide possesses an α*S* configuration, because the α-carbon stereogenic center is not changed during this epoxide-opening reaction (*β* attack). In the same way, from the NOE effects of the tetrahydropyran (2*S**,4*R**,5*S**)-**8b** an *unlike* configuration for the diol (2*S**,4*R**)-**4b** and a (α*S**,1*R**,3*S**) configuration for the *threo*-**5b** epoxide may be concluded (Figure 2, right).

Discussion

The best results for the synthesis of the tetrahydrofurans **7** were obtained by the metal-catalyzed (V, Ti) epoxidation of the diols **4**. Thus, the diols **4** were converted by $Ti(OiPr)_4$/ROOH or $VO(acac)_2$/*t*BuOOH to the epoxides *erythro*-**5** in excellent diastereoselectivity (dr >95:5), but which cyclized in situ to the tetrahydrofurans **7** in up to 82% yield (Scheme 3). The epoxidation of the diols **4** by MTO/UHP or peracids was found to be poorly diastereoselective (*erythro*-**5**: *threo*-**5** = 60:40 to 80:20). The *erythro*-**5** epoxides were converted to the tetrahydrofurans **7**, whereas the tetrahydropyrans **8** cyclization products were obtained from the *threo*-**5** epoxides.

The diastereoselectivity in the metal-catalyzed [$Ti(OiPr)_4$, $VO(acac)_2$] epoxidation of the diols **4** with hydroperoxides as oxygen source was shown to be excellent (*erythro*-**5**:*threo*-**5** > 95:5). The nearly exclusive *erythro* diastereoselectivity may be explained by metal-alcoholate binding between the allylic hydroxy group and the metal center, which requires a dihedral angle θ of ~50−70° for effective oxygen-atom transfer (Figure 3).[9b] Thus, the *erythro* transition geometry is favored due to diminution

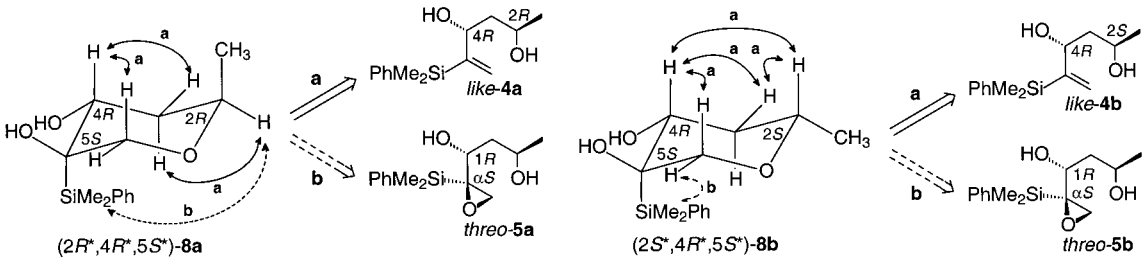


Figure 2. Determination of the relative configuration for the tetrahydropyrans **8** by NOESY experiments.

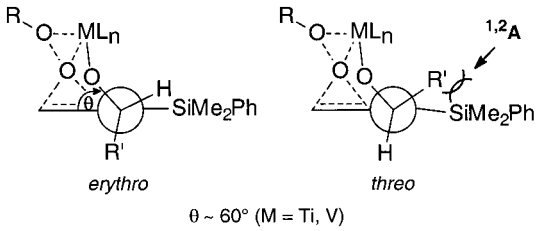


Figure 3. Postulated transition structures for the epoxidation by hydroperoxides under titanium or vanadium catalysis.

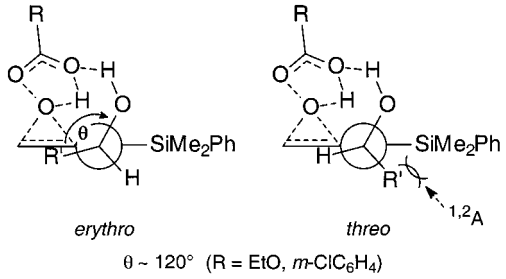


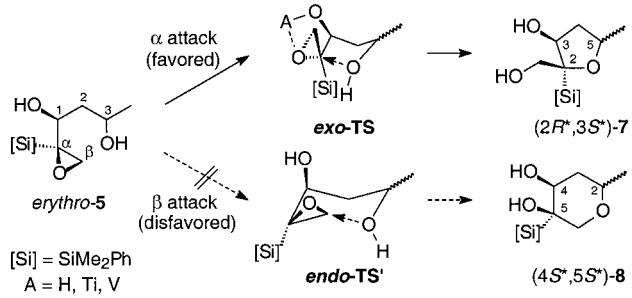
Figure 4. Postulated transition structures for the epoxidation by peracids.

of 1,2-allylic (^{1,2}A) strain. The bulky silyl group, which was introduced in the homoallylic alcohol **1** to generate good regioselectivity in the photooxygenation reaction,[27] is also responsible for this perfect diastereoselection between the *erythro* and *threo* transition states on account of ^{1,2}A strain. For the unsilylated diol, the diastereoselectivity should drop due to less steric repulsion, as it is known for the direct Ti(O*i*Pr)$_4$-catalyzed epoxidation of structurally related hydroperoxy homoallylic alcohols.[28]

In comparison to the vanadium- or titanium-catalyzed epoxidations, the diastereoselectivity of the reactions with MTO/UHP[29] and peracids[15] was lower. Hydrogen bonding between the allylic alcohol and the oxidant requires a dihedral angle θ of ~120° in the transition state and, therefore, ^{1,2}A strain is less important (Figure 4). However, in this geometry the 1,3-allylic strain (^{1,3}A) plays a decisive role for the control of diastereoselectivity.[29,30] Due to the lack of ^{1,3}A strain in the diols **4** (no cis substituent), only a moderate diastereoselectivity was expected in this epoxidation reaction, as observed.

The relative configuration of the two hydroxy groups (*like* and *unlike* diastereomers) in the diols **4** had no influence on the diastereoselectivity of the epoxidation. The only difference was the higher persistence of the isolable (α*R**,1*R**,3*S**)-**5b** from the *unlike*-diol **4b**, whereas the (α*R**,1*R**,3*R**)-**5a** epoxide from the *like*-**4a** was converted to the tetrahydrofuran product **7a** through in-situ ring closure.

Scheme 7. Regioselectivity in the Intramolecular Epoxide-Ring-Opening Reaction of the *Erythro*-5 Epoxide to the Furan *rac*-7



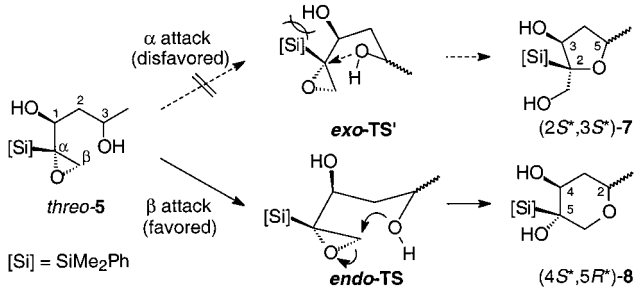
For the nucleophilic ring opening of the *erythro*-**5** and *threo*-**5** epoxides, attack at the α or β positions of the epoxide ring is possible (Scheme 7). The *erythro*-**5** epoxide is converted to the tetrahydrofuran **7**, whereas the *threo*-**5** epoxide is transformed to the tetrahydropyran **8**. A cross reaction (*erythro* **5** to **8** or *threo* **5** to **7**) may be precluded as the ratio of *erythro*-**5**: *threo*-**5** is the same as the **7**:**8** ratio (Table 1, entry 11 and foodnote l).

The intramolecular nucleophilic attack in the *erythro*-**5** epoxide occurs regioselectively (>95:5) at the α position to afford the tetrahydrofuran product **7** (Scheme 7). This S_N2 attack of the C-3 hydroxy group leads to only one diastereomer of the tetrahydrofuran **7** (dr >95:5**)**, with inversion of the configuration at the α position (Table 1, entries 1, 2, 6, and 8). The preference for the α attack is based on the more favorable five-membered-ring transition state ***exo*-TS**, which is stabilized either by hydrogen bonding or metal-alcoholate ligation between the C-1 hydroxy group and the epoxide oxygen (Scheme 7). Additionally, the stereoelectronic effect of the silyl substituent weakens the C_α−O bond,[31] and therefore tetrahydrofuran formation is favored. The ***endo*-TS′** transition state, which would lead to the tetrahydropyran product **8**, is disfavored, because the silyl group would take an axial position in the six-membered pyran ring. Thus, no tetrahydropyran **8** is formed from the *erythro*-**5** epoxide.

The relative configuration (*like* or *unlike*) of the two hydroxy groups at the C-1 and C-3 positions of the *erythro*-**5a** and *erythro*-**5b** epoxides had no influence on the ring-opening pathway (α versus β attack; Table 1,

(27) Adam, W.; Richter, M. J. *J. Org. Chem.* **1994**, *59*, 3341−3346.
(28) Adam, W. Nestler, B. *J. Am. Chem. Soc.* **1993**, *115*, 7226−7231.
(29) Adam, W.; Mitchell, C. M.; Saha-Möller, C. R. *J. Org. Chem.* **1999**, *64*, 3699−3707.
(30) Adam, W.; Corma, A.; Reddy, T. I.; Renz, M. *J. Org. Chem.* **1997**, *62*, 3631−3637.
(31) (a) Fristad, W. E.; Bailey, T. R.; Paquette, L. A.; Gleiter, R.; Böhm, M. C. *J. Am. Chem. Soc.* **1979**, *101*, 4420−4423. (b) Adam, W.; Prein, M.; Richter, M. J. *Tetrahedron* **1996**, *52*, 1231−1234.

Scheme 8. Regioselectivity in the Intramolecular Epoxide-Ring-Opening Reaction of the *threo*-5 Epoxide to the Pyran *rac*-8



entries 1 vs 6 and 2 vs 8). This is not surprising in view of the small energy difference (1−4 kJ/mol) between the pseudoaxial and pseudoequatorial substituents in the transition state of the five-membered-ring, oxygen-containing, saturated heterocycles.[32] Consequently, both *erythro*-epoxides (α*R**,1*R**,3*R**)-**5a** and (α*R**,1*R**,3*S**)-**5b** were converted exclusively to the respective tetrahydrofurans (2*S**,3*R**,5*R**)-**7a** and (2*S**,3*R**,5*S**)-**7b**.

The *threo*-**5** epoxide was converted exclusively to the tetrahydropyran **8** by attack of the C-3 hydroxy group at the β position of the epoxide ring (Scheme 8; Table 1, entries 3−5 and 9−11).

Formation of the tetrahydrofuran **7** is unfavorable because of the steric repulsion between the bulky silyl group and the C-1 hydroxy group in the five-membered-ring transition state ***exo*-TS′**. Therefore, the six-membered-ring transition state ***endo*-TS**, for which steric repulsion is minimized, is preferred and only the tetrahydropyran product **8** is formed. Again, the intramolecular ring closure of the *threo*-**5** epoxides to the tetrahydropyran products **8** is independent of the relative configuration of the two hydroxy groups (Table 1, entries 3 vs 9, 4 vs 10, and 5 vs 11).

The best results for the preparation of the tetrahydrofurans **7** were obtained with the oxidants Ti(O*i*Pr)$_4$/ROOH or VO(acac)$_2$/*t*BuOOH, because no tetrahydropyrans **8** were formed (Table 1, entries 1, 2, 6, and 7). Since both the epoxidation (*erythro* selective) as well as the nucleophilic ring closure (*exo* selective) occur diastereoselectively (dr > 95:5), the diols **4a** and **4b** were converted to only one of the possible diastereomers of the tetrahydrofuran **7**, namely the corresponding (2*S**,3*R**,5*R**)-**7** and (2*S**,3*R**,5*S**)-**7**. Epoxidation with VO(acac)$_2$/*t*BuOOH is more convenient because only 1 mol % of the cheap VO(acac)$_2$ catalyst is necessary, while for the Ti(O*i*Pr)$_4$-catalyzed oxidation the tridentate hydroperoxide, namely 2,3-dimethyl-3-hydroperoxy-2-butanol, is not commercially available and needs to be prepared.[10]

(32) Hartung, J.; Gallou, F. *J. Org. Chem.* **1995**, *60*, 6706−6716.

It should be emphasized that the silyl-substituted tetrahydrofurans **7**, accessible through the above-mentioned diastereoselective route, are promising precursors for dideoxy sugars; moreover, the conversion of the dimethylphenylsilyl substituent of the tetrahydrofurans **7** to a hydroxy group provides 4,6-dideoxyhexoses. In this way, the oxidative desilylation of the dimethylphenylsilyl group in the diacetate derivatives **9** of the tetrahydrofuranes **7** with KBr−AcOOH (Fleming oxidation)[18] afforded the 4,6-dideoxyfuranoses **10** in up to 62% yield (Scheme 4). This transformation offers the opportunity to prepare the hitherto unknown optically active 4,6-dideoxyfuranoses **10** by starting form the enantiomerically enriched hydroxy vinylsilanes (*R*)-**1** (90% ee) and (S)-**1** (>98% ee). Thus, through this newly developed methodology, that is, the sequence regioselective photooxygenation, triphenylphosphine reduction, diastereoselective epoxidation with VO(acac)$_2$/*t*BuOOH, and oxidative desilylation, the optically active D- and L-4,6-dideoxysorbofuranoses **10a** and D- and L-4,6-dideoxyfructofuranoses **10b** have been prepared for the first time in nearly enantiomerically pure form (Scheme 6).

Conclusion

The hydroxy vinylsilane, *E*-5-dimethylphenylsilyl-2-hexen-4-ol (**1**), has been selectively transformed to the hitherto unknown 4,6-dideoxyfuranoses **10a** and **10b** by employing successively three versatile oxyfunctionalization methods, namely photooxygenation, metal-catalyzed epoxidation, and oxidative desilylation. The application of this strategy to the enantiomerically enriched hydroxy vinylsilane **1** has made available for the first time the optically active (up to >98% ee) 4,6-dideoxysorbofuranose **10a** and 4,6-dideoxyfructofuranose **10b**. The availability of these unusual sugar derivatives through our novel synthetic methodology opens the opportunity to assess their potential biologically activity.

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Supporting Information Available: Reported are the synthetic details of the epoxidations, the characteristic spectral data of the epoxidation products **5**−**8**, and the synthesis and characterization of the starting materials **1**, **2**, and **4**, as well as of the diacetates **9** and 4,6-dideoxyfuranoses **10**. This material is available free of charge in the Internet under http://pubs.acs.org.

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