gradients with a strength of 56 G cm^{-1}. All spectra were acquired with a 5 mm TBI probehead. For the DOSY experiments the BPPLED[3, 15] pulse sequence or a modification of the INEPT–DOSY sequence were used.[8] The pulse-field gradients (g) were incremented in 32 steps from 2% up to 95% of the maximum gradient strength in a linear ramp. Gradient lengths δ between 1.5 and 2.0 ms, diffusion times Δ between 90 and 200 ms, and an eddy current delay (T_e) of 5 ms were employed. After Fourier transformation and baseline correction, the diffusion dimension was processed by using the Bruker xwinnmr package (version 3.0) and the diffusion values were read directly from the spectra.

For the experiment with a mixture of **4** and **6**, a solution of **4** (0.013 mmol) and **6** (0.041 mmol) in [D_8]THF (400 μL) was prepared. For the monitoring of the reaction of **1** with $^{13}CO_2$, **1** (0.050 mmol) and [D_8]THF (350 μL) were placed in a pressure-stable NMR tube (Wilmad 522-PP), degassed, and then frozen. $^{13}CO_2$ (0.060 mmol) was condensed in vacuo on top of the frozen mixture. The tube was sealed and transferred into the precooled magnet.

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[12] Signal-to-noise ratio in the ^{13}C INEPT spectrum: 20:1.

[13] The signal at $\delta = 114.6$ arises from the overlapping Cp signals of the complexes **3** and **4**, which due to their almost identical molecular weight cannot be resolved in the diffusion dimension. However, the assignment of the Cp signal of **3** is clear since the CH_2 signal can be used as a reference for the self-diffusion coefficient.

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The First Highly Efficient Asymmetric Synthesis of α-Substituted Methyl Sulfonates**

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Dedicated to Professor Dieter Hoppe on the occasion of his 60th birthday

A number of α-substituted sulfonic acids with interesting pharmacological properties is known, and numerous compounds of this class have been isolated, synthesized, and tested for their biological activity. For instance, 6-gingesulfonic acid, which shows anti-ulcer activity, was isolated from *Zingiberis Rhizoma*.[1] Several α-substituted sulfonic acids, which are known as semisynthetic β-lactam antibiotics, have been examined with regard to their antibacterial activity.[2] Cefsulodin, a representative compound of the semisynthetic cephalosporins, shows potent in vivo antipseudomonal activity against *Pseudomonas aeruginosa*.[3] Other compounds such as α-phosphonosulfonic acid derivatives are known as potent squalene synthase inhibitors.[4]

Enantiopure α-substituted sulfonic acids are also employed in synthesis as strongly acidic resolving agents, especially for free neutral amino acids. For example, (*S*)-(−)-1-phenylethanesulfonic acid ((−)-PES) was found to be an efficient resolving agent for the optical resolution of DL-leucine.[5] The related (+)-2-(2,3,4-trichlorophenyl)ethanesulfonic acid ((+)-TCPES) has been used as resolving agent for antifungal sulfoximines.[6]

Considering their synthesis, enantiopure α-substituted sulfonic acids are commonly obtained from the corresponding racemates by resolution techniques with chiral amines.[7] To the best of our knowledge, only two stereoselective methods are known for the synthesis of optically active α-substituted sulfonic acids. Corey et al. reported the conversion of enantiopure (*R*)-1-phenylethanol to ((−)-PES) in a multistep procedure.[8] For the synthesis of a squalene synthase inhibitor, the asymmetric α-alkylation of an α-phosphonosulfonate bearing the chirality information within the phosphono moiety was employed. To date this is the only known auxiliary-controlled method for the asymmetric synthesis of α-substituted sulfonates.[9]

In contrast, no method is known to perform asymmetric α-alkylations of metalated sulfonic esters prepared from enantiopure alcohols as auxiliaries. A serious problem during metalation of sulfonic esters could be β-elimination under these basic conditions.

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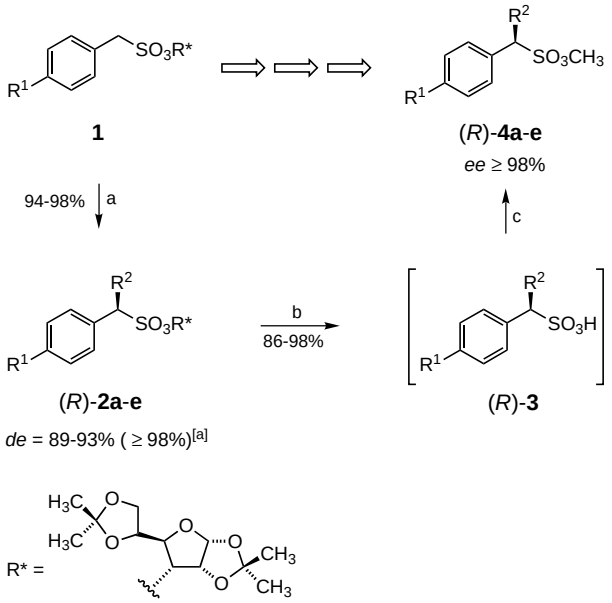
We report here the first asymmetric α-alkylations of lithiated sulfonic esters bearing a removable enantiopure alcohol auxiliary. As chiral auxiliary 1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose was used, which was synthesized on a 30 g scale from inexpensive 1,2:5,6-di-*O*-isopropylidene-α-D-glucose according to an improved and simple epimerization procedure in 70% yield.[10] This sugar has also been used as a chiral auxiliary in the alkylation of ester enolates,[11] but only moderate diastereoselectivities were observed.

We obtained the sulfonates **1** by reaction of the allofuranose derivative with benzylic sulfonyl chlorides, which are commercially available or can be easily prepared from the corresponding sodium sulfonates[12] starting from the benzylic bromides.[13] As shown in Scheme 1, the enantiopure sulfonates **1** were metalated with one equivalent of *n*-butyllithium



Scheme 1. Asymmetric synthesis of α-alkylated methyl sulfonates. a) 1. *n*BuLi (1.0 equiv), THF, $-(90-95)\,^{\circ}C$, 1 h; 2. R^2X (1.5 equiv), $-(90-95)\,^{\circ}C$, 1 h, $-78\,^{\circ}C$, 24 h; b) $Pd(OAc)_2$ (15 mol%), $EtOH/H_2O$, reflux, 4 d; c) CH_2N_2 (ethereal solution). [a] After recrystallization from 2-propanol.

in tetrahydrofuran at $-(90-95)\,^{\circ}C$. At low temperatures any side reactions are minimized, such as the attack of *n*-butyllithium on the sulfonate moiety or a β-elimination of the lithium alcoholate of the sugar auxiliary. The lithiated sulfonic esters are allowed to react with the electrophiles at $-(90-95)\,^{\circ}C$ for one hour and then at $-78\,^{\circ}C$ for 24 h. Work-up and purification gave the α-substituted sulfonates **2** in excellent yields (94–98%) and high diastereomeric excesses of *de* = 89–93% (Table 1). Virtually diastereomerically pure sulfonates could be obtained by recrystallization from 2-propanol (*de* $\geq$ 98%).

The configuration of the newly formed stereogenic center was determined to be *R* through single-crystal X-ray structure analysis in the case of product **2d** (Figure 1).[14] Since we can postulate a uniform reaction mechanism, all the described examples should possess the same configuration.

Table 1. Asymmetric α-alkylation of sulfonates **1** to afford sulfonates **2**.

2	R^1	R^2	Yield [%]	*de* [%][a,b]	$[\alpha]_D$[c]
a	H	methyl	95	91 ($\geq$98)	+91.3
b	H	allyl	93	90 ($\geq$98)	+77.0
c	H	benzyl	94	89 ($\geq$98)	+34.4
d	*t*Bu	benzyl	95	91 ($\geq$98)	+22.6
e	*t*Bu	(2-naphtyl)methyl	98	93 ($\geq$98)	+3.8

[a] Values in parentheses after recrystallization from 2-propanol. [b] Determined by ^{13}C NMR spectroscopy. [c] All optical rotations were measured in Uvasol grade $CHCl_3$ with concentrations of 1.0 at room temperature.

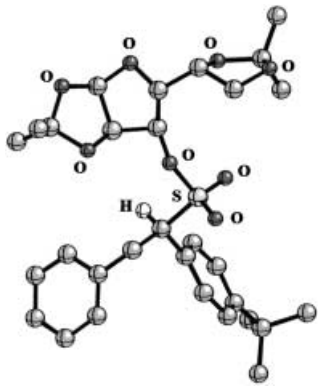


Figure 1. X-ray crystal structure of **2d**.[14]

Finally, many procedures were screened for an efficient racemization-free cleavage of the auxiliary. The best results were achieved by refluxing the sulfonates **2** in an $EtOH/H_2O$ solution containing 15 mol% $Pd(OAc)_2$ for four days.[15] To isolate the final products in a more accessible form, the sulfonic acids **3** were directly converted with diazomethane to the corresponding title methyl sulfonates (*R*)-**4**,[16] which were obtained in very good yields and as pure stereoisomers (Scheme 1, Table 2).

To explain the high diastereofacial selectivity of the electrophilic substitutions in the α-position to the sulfonate function, the solution structure and aggregation of the lithiated chiral sulfonates remains to be determined.

In conclusion, the novel protocol provides an efficient and first practical route to optically active α-substituted methyl sulfonates. The asymmetric α-alkylation and the removal of the auxiliary proceed in good overall yields and lead to the final products in excellent enantiomeric excesses. The highly enantioenriched title compounds are valuable substrates for

Table 2. Removal of the chiral auxiliary to form the title methyl sulfonates **4**.

(*R*)-**4**	R^1	R^2	Yield [%]	*ee* [%][a]	$[\alpha]_D$[b]
a	H	methyl	98	$\geq$98	+25.6
b	H	allyl	90	$\geq$98	−6.3
c	H	benzyl	94	$\geq$98	−77.4
d	*t*Bu	benzyl	88	$\geq$98	−92.8
e	*t*Bu	(2-naphtyl)methyl	86	$\geq$98	−108.2

[a] Determined by HPLC using a chiral stationary phase ((*R*)-**4a**: Daicel OJ, *n*-heptane/2-propanol 85/15; (*R*)-**4b**: Whelk O1, *n*-heptane/2-propanol 95/5; (*R*)-**4c**–**e**: Daicel OD 2, *n*-heptane/2-propanol 95/5). [b] All optical rotations were measured in Uvasol grade $CHCl_3$ with concentrations of 1.0 at room temperature.

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further synthetic transformations, which are currently being investigated in our laboratory.

Experimental Section

Typical procedure for the α-alkylation: The enantiopure sulfonate **1** (1 mmol) was dissolved in dry THF (20 mL) and the solution cooled to $-(90-95)\,^{\circ}C$. After 30 min *n*BuLi (1.0 equiv) was added dropwise. The solution was stirred for an additional hour after which the electrophile (1.5 equiv in 5 mL THF) was added dropwise. The mixture was stirred for 1 h at $-(90-95)\,^{\circ}C$, then at $-78\,^{\circ}C$. After 24 h the reaction was quenched by adding pH 7 buffer (2 mL). The mixture was partitioned between H_2O and CH_2Cl_2 and washed with brine. The aqueous layer was then extracted three times with CH_2Cl_2. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (SiO_2, pentane/diethyl ether).

Typical procedure for the removal of the chiral auxiliary: The sulfonate **2** (0.6 mmol) was dissolved in an EtOH/H_2O solution (19 mL/1 mL). $Pd(OAc)_2$ (15 mol%) was added to the solution and the mixture was refluxed for four days (TLC control). The palladium residues were removed by filtration and washed twice with EtOH. The filtrate was treated with an ethereal solution of diazomethane until the yellow color persisted. The solvent was evaporated under reduced pressure and the crude product purified by flash column chromatography (SiO_2, pentane/diethyl ether).

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[14] Crystal data for **2d**: single crystals were obtained by recrystallization from ethyl acetate. The substance ($C_{30}H_{40}O_8S$, $M_r = 560.68$) crystallized in the monoclinic space group $P2_1$, $a = 17.624(2)$, $b = 18.704(2)$, $c = 26.905(5)$ Å, $\beta = 92.436(14)^{\circ}$, $V = 8861(2)$ Å^3, $Z = 12$, $\rho_{calcd} = 1.216\ g\,cm^{-3}$, $F(000) = 3600$, $T = 173(2)$ K. Data collection: A single crystal (colorless transparent block with dimensions $0.12 \times 0.2 \times 1.3$ mm) was measured on a SIEMENS SMART diffractometer at a temperature of about $-100\,^{\circ}C$. Repeatedly measured reflections remained stable. An empirical absorption correction was made by using the program SADABS. The correction factor ranged from 0.950 to 1.000. Equivalent reflections were averaged. Friedel opposites were not averaged. $R(I)_{int} = 0.092$. The structure was solved by direct methods using the program SHELXS. The H atoms were placed at calculated positions and were treated as riding atoms. The structure was refined on F^2 values using the program SHELXL-97. Max./min. resiual electron denisty $-0.25/+0.25\ e\,Å^{-3}$. The absolute configuration of the structure was confirmed by the value of the Flack *x* parameter ($x = -0.04(3)$). Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-168530. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

[15] As the sugar auxiliary is rather cheap, it is acceptable at the present stage that the auxiliary cannot be recycled under these conditions.

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Protonated Sulfuric Acid: Preparation of Trihydroxyoxosulfonium Hexafluoroantimonate $H_3SO_4^+SbF_6^-$**

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Dedicated to Professor Karl Otto Christe on the occasion of his 65th birthday

One of the strongest acids is 100% sulfuric acid and this marks per definition the border to the superacids. Among the ions that are formed by the autoprotolysis of sulfuric acid according to Equation (1), only the structure of the hydrogensulfate ion in solid salts and that of sulfuric acid itself is known.[1, 2]

$$2\,H_2SO_4 \longrightarrow H_3SO_4^+ + HSO_4^- \qquad (1)$$

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