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Efficient asymmetric synthesis of α-alkylated benzylic methyl sulfonates

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Abstract—The first highly efficient auxiliary-controlled synthesis of various α-substituted sulfonic acid derivatives is described. Alkyl or aryl halides were reacted with lithiated benzylic sulfonic esters bearing 1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose as a removable enantiopure alcohol auxiliary to give the alkylated products in excellent diastereomeric excesses. The racemization-free cleavage conditions provided highly enantioenriched sulfonic acid derivatives (ee≥98%).

1. Introduction

Enantiopure α-substituted sulfonic acids as well as their various derivatives are important building blocks and precursors of biologically interesting compounds. A number of these compounds has been isolated, synthesized, and tested for their biological activity. 6-Gingesulfonic acid **1**, for example, which has been isolated from *Zingiberis rhizoma*, shows potent anti-ulcer activity.[1] The natural products echinosulfonic acid A, B, and C (**2**, R=Et, Me, H, respectively) have been isolated from the southern Australian marine sponge *Echinodictyum* and have antibacterial activity.[2] The semisynthetic penicillin **3**, namely α-sulfobenzylpenicillin, has been reported to show potent antibacterial activity against *Pseudomonas aeruginosa*.[3,4] Cefsulodin, a representative compound of the semisynthetic cephalosporins, exhibits in vivo antipseudomonal activity.[5] Moreover, the synthetic α-phosphono sulfonates **4** are potent squalene synthase inhibitors (Fig. 1).[6,7]

In general, enantiopure α-substituted sulfonic acids are obtained from the corresponding racemates by resolution

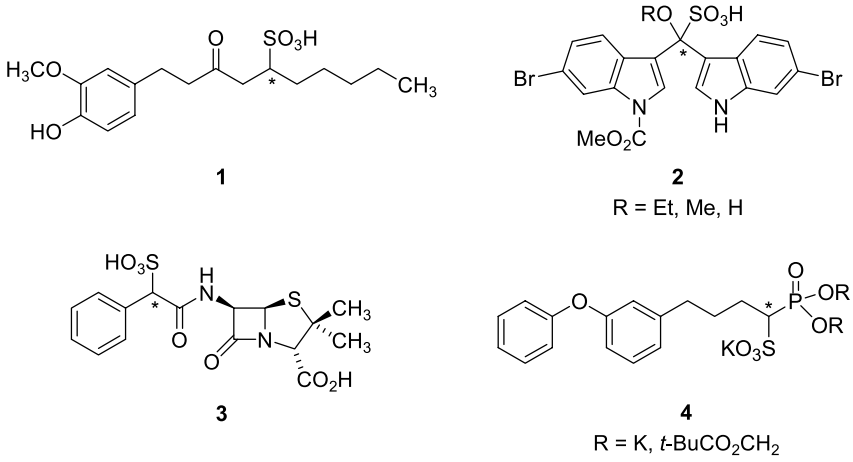

Figure 1. Biologically active α-substituted sulfonic acid derivatives.

Keywords: Asymmetric synthesis; Alkylation; Sulfonates; Sugar auxiliary.
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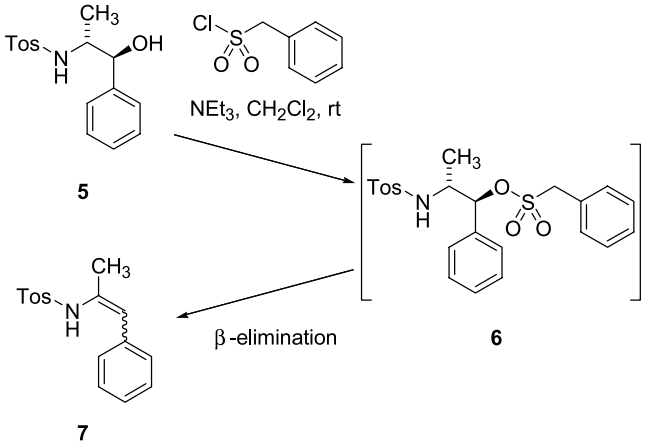
techniques with chiral amines.[8] To the best of our knowledge, only two stereoselective methods for the asymmetric synthesis of α-substituted sulfonic acids have been reported so far. Enantiopure (*R*)-1-phenylethanol, obtained by catalytic asymmetric reduction of methyl phenyl ketone, could be transformed into (*S*)-(−)-1-phenylethane sulfonic acid [(−)-PES] in a two step sequence.[9] In the synthesis of the squalene synthase inhibitor **4**, asymmetric α-alkylation of an α-phosphono sulfonate bearing the chirality information within the phosphono moiety was employed.[10]

In contrast, no efficient method has been reported for asymmetric α-alkylations of metalated sulfonic acid esters derived from enantiopure alcohols as auxiliaries.[11] As a potential drawback we considered β-elimination or substitution reactions during metalation of the sulfonates. However, by choosing a suitable auxiliary system these obstacles should be overcome. In preceding communications,[12–16] we have described the asymmetric synthesis of several α-substituted sulfonic acid derivatives by reacting electrophiles with metalated sulfonic esters which possess a chiral alcohol as auxiliary. Herein, we present in detail the development of this methodology.

2. Results and discussion

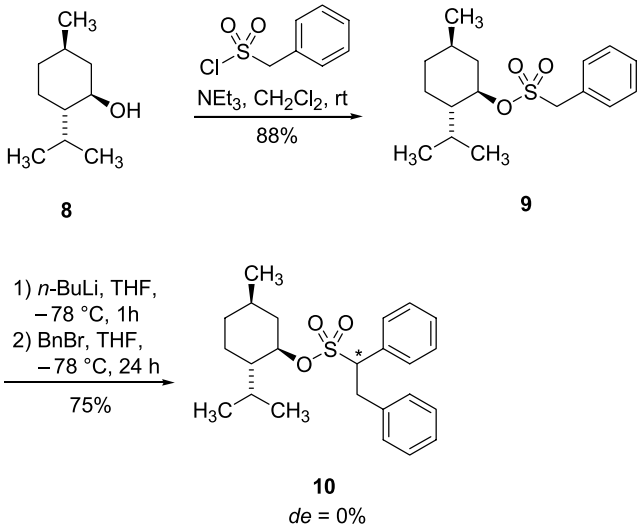
The aim of our project was to develop a practical methodology for an auxiliary controlled asymmetric synthesis of α-alkylated sulfonic acids. The initial concept was to use chiral amines as auxiliaries in order to perform alkylations of the corresponding sulfonamides. Due to the stability of the sulfur–nitrogen-bond, acidic hydrolysis of the sulfonamides did not give the desired sulfonic acids but instead enantioenriched sulfonamides.[17,18] To circumvent this dilemma we had to find a suitable alcohol as chiral auxiliary to provide sulfonic acid esters which are more readily cleaved and would be stable during α-lithiation to be trapped in a stereocontrolled fashion with electrophiles.

The first alcohol we tested was the tosylated norephedrine derivative **5**.[19] Unfortunately, the reaction did not proceed to the desired benzyl sulfonate **6** due to decomposition of the intermediate ester by β-elimination to form the *N*-tosyl enamine **7** (Scheme 1).



Scheme 1. Attempted synthesis of the sulfonate **6** from the norephedrine derivative **5**.

This led us to employ a cyclic auxiliary alcohol where β-elimination is less favourable. Thus, menthol **8** could be easily converted into the corresponding sulfonate **9** in 88% yield under standard conditions. In addition, the deprotonation with *n*-butyllithium and subsequent alkylation with benzyl bromide to form the sulfonate **10** worked well but without any diastereoselectivity (Scheme 2).

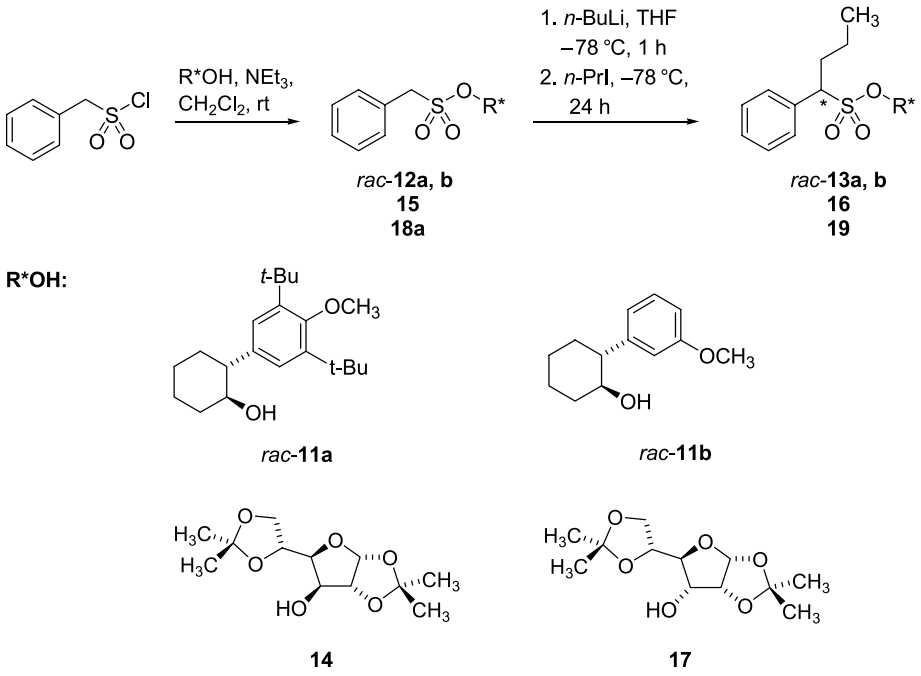


Scheme 2. Menthol as the chiral auxiliary.

The synthetically encouraging results with menthol led us to a screening of different cyclic alcohols (Scheme 3, Table 1). First, two racemic auxiliary alcohols *rac*-**11a**, **b** were synthesized according to a literature procedure[20] by reaction of different aryl Grignard reagents with cyclohexene oxide. These were converted into the corresponding benzyl sulfonates *rac*-**12a**, **b**, lithiated with *n*-butyllithium and trapped with *n*-propyl iodide at −78 °C to afford the alkylated esters **13a**, **b** (entries 1 and 2). Remarkably, the sterically less demanding methoxyphenyl side chain in *rac*-**12b** resulted in a similar diastereomeric excess as the alkylation of the sterically hindered sulfonate *rac*-**12a**.

Thus, we envisioned the methoxy group as a chelating moiety in the lithiated system supporting the asymmetric induction. This led us to use oxygen-rich alcohols like diacetone-D-glucose **14**. The corresponding sulfonate **15** was lithiated and alkylated with *n*-propyl iodide in the presence of hexamethylphosphoric acid triamide (HMPA) to give the alkylated sulfonate **16**. This sugar-auxiliary provided similar inductions as compared to the reactions with the esters *rac*-**12a**, **b** (de=59%, entry 3).

Although the induction was the same, we continued our investigations on the sugar system as a potential auxiliary group. We assumed that inversion of the hydroxy group would provide a species where the reaction center is exposed to better coordination by the rigid dioxolane moiety. We, therefore, inverted the hydroxy group by a simple epimerization procedure to get the new auxiliary.[21] Allowing this 1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose



Scheme 3. Screening of different alcohols *rac*-**11a**, *rac*-**11b**, **14**, **17**.

Table 1. Screening of different alcohols *rac*-**11a**, *rac*-**11b**, **14**, **17**

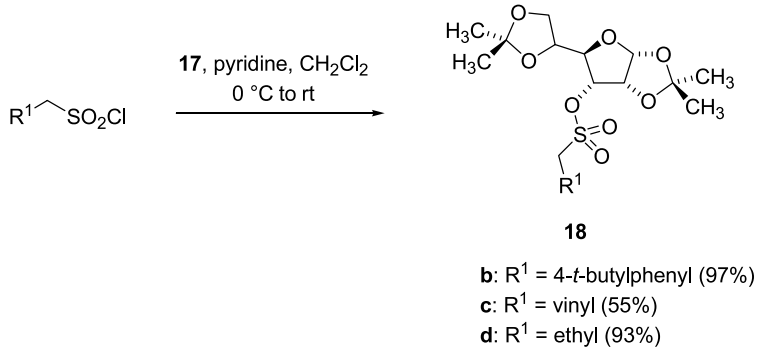
Entry	Alcohol	Substrate/yield (%)	Product/yield (%)	de (%)[a]
1	*rac*-**11a**	*rac*-**12a**/78	*rac*-**13a**/55	60
2	*rac*-**11b**	*rac*-**12b**/62	*rac*-**13b**/71	59
3	**14**	**15**/81	**16**[b]/73	59
4	**17**	**18a**/91	**19**[b]/69	78

[a] Determined by ^{13}C NMR.
[b] The reaction was performed in the presence of HMPA.

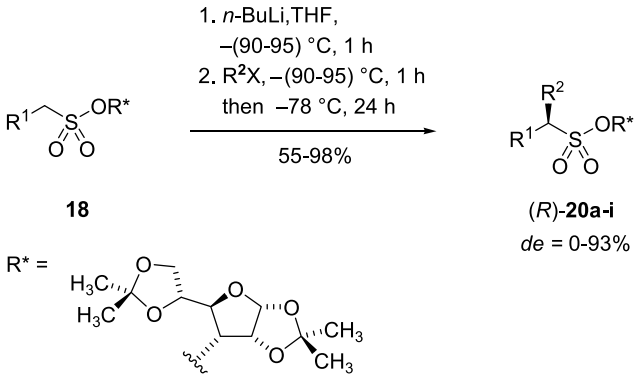
(**17**) to react with benzylsulfonyl chloride provided the epimeric sulfonate **18a**. Following the already known procedure, sulfonate **18a** could be easily alkylated with *n*-propyl iodide under BuLi/HMPA-conditions to afford the alkylated product **19** with an improved diastereomeric excess of de=78% (entry 4).

The co-solvent HMPA, which was essential for the alkylation, could be avoided by using electrophiles that have a higher reactivity than *n*-propyl iodide. Gratifyingly, when using methyl iodide as an electrophile the methylated product (*R*)-**20a** was obtained in high yield and a diastereomeric excess of de=91%. To further explore the scope of the reaction different sulfonates **18b–d** were prepared by treatment of the allofuranose derivative **17** with sulfonyl chlorides, which were commercially available or could be easily obtained from the corresponding sodium sulfonates (Scheme 4).[22–24]

The enantiopure sulfonates **18a**,**b** were lithiated with 1 equiv of *n*-butyllithium in THF at −(90–95) °C and then reacted with different reactive electrophiles at −(90–95) °C for 1 h and at −78 °C for 24 h. After work up and purification, the α-substituted sulfonates **20a–g** were obtained in excellent yields (90–98%) and high diastereoselectivities (Scheme 5, Table 2). In all cases, the



Scheme 4. Different sulfonates possessing 1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose moiety.



Scheme 5. α-Alkylation of the sulfonates **18**.

diastereomerically pure sulfonates could be obtained by recrystallization from 2-propanol (de≥98%).

In order to explore further the scope of the reaction a series of experiments with different sulfonate residues were conducted. Whereas benzylic carbanions lead to very high asymmetric inductions, the allylic lithiosulfonate gave **20 h** with only a de-value of 50% and aliphatic group showed virtually no diastereoselectivity of product **20i**. Thus, at present the methodology seems to be limited to benzylic type of sulfonates.

The configuration of the newly formed stereogenic centre was determined to be *R* by single crystal Röntgen structure analysis in the case of product (*R*)-**20f**.[12] Since we can postulate a uniform reaction mechanism, all described α-alkylated sulfonates should possess the same configuration.

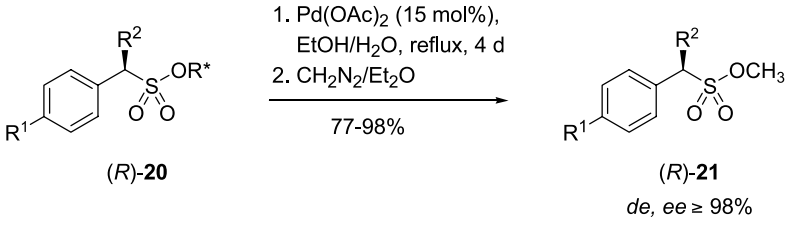
Finally, various procedures were screened for an efficient racemization-free cleavage of the auxiliary, which turned out to be more difficult than expected. Several procedures under basic conditions were unsuccessful. The analysis of the recovered starting material showed a decrease of diastereomeric excess. In addition, the cleavage was attempted by refluxing the sulfonate in aqueous ethanol in order to eliminate the sulfonic acid by nucleophilic substitution or to reach a transesterification or saponification with removal of the sugar alcohol auxiliary. Unfortunately, the protocol was unsuccesfull and obviously the high steric demand blocked the planned cleavage processes.

We assumed that a preceding mild acetonide deprotection would decrease the steric strain and thus allow substitution with a protic solvent, such as water or ethanol, to provide the desired sulfonic acid. Furthermore, this could give rise to an intramolecular substitution reaction with one of the hydroxy groups formed to give a stable bicyclic system. Thus, a mild cleavage method for the removal of the acetal protection

Table 2. α-Alkylation of the sulfonates **18a–d** affording the sulfonates (*R*)-**20a–i**

(*R*)-**20**	R^1	R^2	Yield (%)	de (%)[a,b]
(*R*)-**20a**	Phenyl	Methyl	95	91 (≥98)
(*R*)-**20b**	Phenyl	Allyl	93	90 (≥98)
(*R*)-**20c**	Phenyl	Benzyl	94	89 (≥98)
(*R*)-**20d**	Phenyl	4-Bromophenyl	90	90 (≥98)
(*R*)-**20e**	Phenyl	(2-Naphthyl)methyl	96	91 (≥98)
(*R*)-**20f**	4-*t*-Butylphenyl	Benzyl	95	91 (≥98)
(*R*)-**20g**	4-*t*-Butylphenyl	(2-Naphthyl)methyl	98	93 (≥98)
(*R*)-**20h**	Vinyl	Methyl	55	50
(*R*)-**20i**	Ethyl	Methyl	87	0

[a] In brackets after recrystallization from 2-propanol.
[b] Determined by ^{13}C NMR.



Scheme 6. Removal of the auxiliary to give the α-alkylated methyl sulfonates (*R*)-**21**.

Table 3. Removal of the sugar auxiliary to give the α-alkylated methyl sulfonates (*R*)-**21**

(*R*)-**21**	R^1	R^2	Yield (%)	ee [%][a]	$[\alpha]_D^{rt}$[b]
(*R*)-**21a**	H	Methyl	98	≥98	+25.6
(*R*)-**21b**	H	Allyl	90	≥98	−6.3
(*R*)-**21c**	H	Benzyl	94	≥98	−77.4
(*R*)-**21d**	H	4-Bromophenyl	77	≥98	−93.4
(*R*)-**21e**	H	(2-Naphthyl)methyl	96	≥98	−89.5
(*R*)-**21f**	*t*-Bu	Benzyl	90	≥98	−92.8
(*R*)-**21g**	*t*-Bu	(2-Naphthyl)methyl	87	≥98	−108.2

[a] Determined by HPLC using a chiral stationary phase.
[b] All optical rotations were measured in Uvasol grade $CHCl_3$ with concentrations of 1.0 at rt.

groups based on a protocol reported by Lipshutz et al.[25] was utilized by refluxing the sulfonates **20** in an EtOH/H_2O solution containing a catalytic amount of $Pd(OAc)_2$. To isolate the final products in a more accessible form, the intermediate sulfonic acids were directly converted with diazomethane to the corresponding methyl sulfonates (*R*)-**21** in very good yields and as pure stereoisomers (Scheme 6, Table 3).

In order to provide evidence for the assumptions made concerning the mechanism of the sulfonate cleavage we investigated more closely the by-products of the reaction. The TLC of the reaction mixture indicated besides the desired sulfonic acids two less polar products, which were anticipated to be residues of the sugar moiety. Thus, the reaction was repeated on larger scale in order to isolate and analyse these interesting fragments. The products were identified as intramolecularly cyclized derivatives **22a** and **22b** with yields of 25 and 37%, respectively. A single crystal Röntgen-structure analysis was carried out with compound **22b** proving the structure unambiguously as shown in Figure 2. On the other hand, compound **22a** is a viscous oil, whose structure could be determined as the corresponding α-anomer by NOE-measurements.

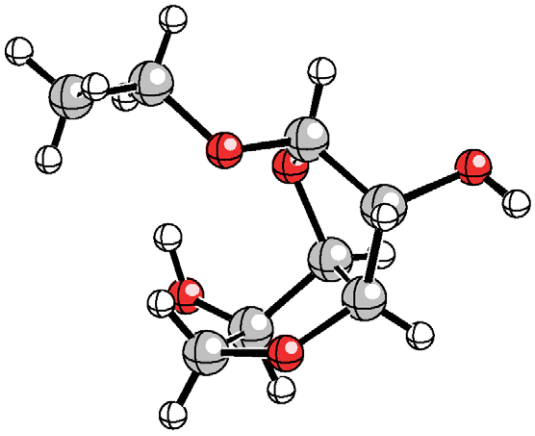
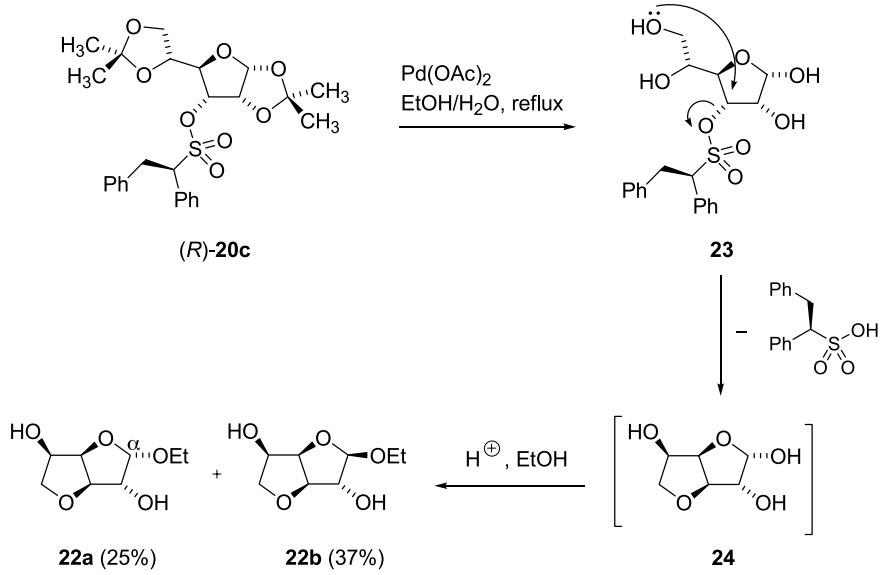


Figure 2. Röntgen crystal structure of compound **22b**.

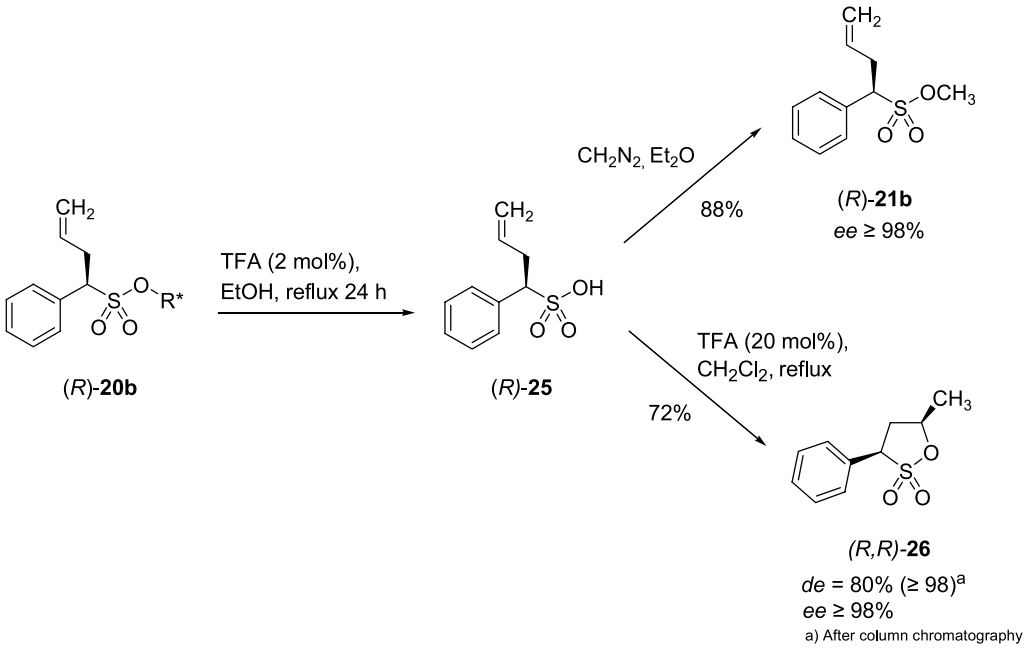
Based on the Röntgen-structure of the residual sugar fragment, the following cleavage mechanism can be proposed as depicted in Scheme 7. First, the acetal groups are cleaved to provide the tetraol **23**. This sets the stage for an intramolecular substitution reaction to afford the desired enantioenriched sulfonic acid derivatives and the intermediate **24**. The bicyclic compound **24** reacts further in the acidic media with the solvent (ethanol) to give the glycosides **22** roughly as a 1:1 mixture of the anomers **22a** and **22b** as witnessed via NMR spectroscopy.

Thus, the removal of the auxiliary depends on the deprotection of the sugar moiety, which allows the intramolecular nucleophilic substitution of the sulfonyl-moiety to provide the desired α-alkylated sulfonic acids without racemization. As the deprotection of the acetals is sufficient for the sulfonic acid formation, the cleavage should also be possible by using trifluoroacetic acid (TFA). This seemed to be more convenient than to use the expensive $Pd(OAc)_2$. The allyl substituted sulfonate (*R*)-**20b** was cleaved with TFA (2 mol%) in ethanol. By trapping the resulting sulfonic acid (*R*)-**25** with diazomethane, the sulfonate (*R*)-**21b** could be obtained with excellent enantiomeric excess. Furthermore, it was found that the intermediate allylic sulfonic acid (*R*)-**25** can also be cyclized to afford enantiopure sultones.[14,15] Refluxing in dichloromethane in the presence of 20% TFA provided the enantioenriched sultone (*R*,*R*)-**26** in good yield and excellent enantiomeric excess with satisfactory diastereoselectivity (Scheme 8).

Moreover, we have expanded this methodology to provide a great variety of different sulfonic acid derivatives as illustrated in Scheme 9. The asymmetric Michael addition of the sulfonate **18a** with nitroalkenes leads to either the



Scheme 7. Proposed reaction sequence of the cleavage reaction.



Scheme 8. TFA cleavage of the sulfonate **20b** to give either the methyl sulfonate (*R*)-**21b** or the γ-sultone (*R*,*R*)-**26**.

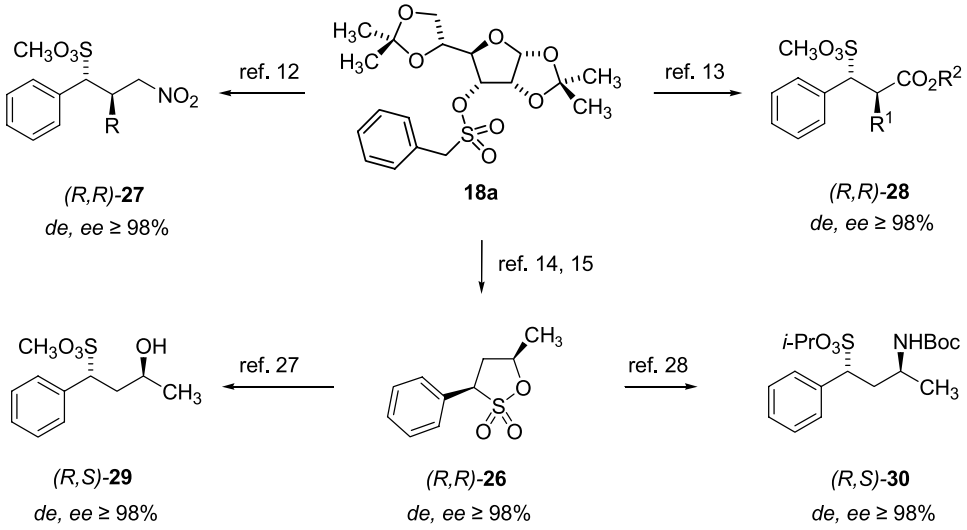
γ-nitro sulfonates (*R*,*R*)-**27** or β-alkoxycarbonyl sulfonates (*R*,*R*)-**28** depending on the conditions used for the cleavage of the chiral auxiliary.[12,13] Further functional groups could be easily introduced by performing diastereoselective ring opening reactions on α,γ-substituted γ-sultones to give enantiopure α,γ-substituted γ-alkoxy,[26] γ-hydroxy[27] (*R*,*S*)-**29** and γ-amino sulfonates (*R*,*S*)-**30**.[28]

In summary, the proper choice of a sugar auxiliary led to the breakthrough in the first asymmetric synthesis of α-substituted sulfonic acid esters. High asymmetric inductions were obtained with the inexpensive and readily available 1,2:5,6-di-*O*-isopropyliden-α-D-allofuranose as auxiliary group which can be cleaved off racemization-free under mild conditions.

3. Experimental

3.1. General

Starting materials and reagents were purchased from commercial suppliers without further purification. Asymmetric alkylations were carried out under Ar in dry solvents. Solvents were dried and purified by conventional methods prior to use. THF was freshly distilled from sodium-lead alloy under Ar. *n*-Butyllithium (1.6 M in hexane) was purchased from Merck, Darmstadt. Preparative column chromatography: Merck silica gel 60, particle size 0.040–0.063 mm (230–240 mesh, flash). Analytical TLC: silica gel 60 F_{254} plates from Merck, Darmstadt. Optical rotation values were measured on a Perkin–Elmer P241 polarimeter.



Scheme 9. Asymmetric synthesis of enantioenriched sulfonic acid derivatives.

Microanalyses were obtained with a Vario EL element analyzer. Mass spectra were acquired on a Finnigan SSQ7000 (EI 70 eV) spectrometer. High-resolution mass spectra were recorded on a Finnigan MAT95 spectrometer. IR spectra were taken on a Perkin–Elmer FT-IR 1760. ^{1}H and ^{13}C spectra were recorded on Varian Gemini 300 or Inova 400 spectrometers with tetramethylsilane as internal standard. δ of the minor diastereomers are indicated in brackets. Melting points were determined on a Tottoli melting point apparatus and are uncorrected.

3.1.1. *rac-trans*-2-(3,5-Di-*tert*-butyl-4-methoxyphenyl)-cyclohexanol (*rac*-11a). To magnesium (1.7 g, 69.0 mmol) in THF (50 mL) was added a solution of 5-bromo-3,5-di-*tert*-butyl-4-methoxybenzene (21.2 g, 71.0 mmol) in THF (50 mL) over 1 h. The resulting mixture was stirred for 0.5 h and then CuI (1.3 g, 7.0 mmol) was added and the mixture was cooled to −30 °C. Cyclohexene oxide (4.6 g, 47.6 mmol) was then added dropwise. After the addition was complete, the mixture was stirred for 3 h and then quenched by pouring into cold saturated NH_4Cl (30 mL). The mixture was partitioned between CH_2Cl_2 and the aqueous layer further 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 6:1) to give *rac*-**11a** (12.0 g, 80%) as a colorless solid; mp = 101 °C. IR (KBr): 3381, 2953, 2920, 2852, 1597, 1449, 1415, 1393, 1361, 1305, 1262, 1224, 1118, 1065, 1015, 993, 857 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.20–2.20 (m, 8H), 1.43 (s, 18H), 2.35 (m, 1H), 3.59 (m, 1H), 3.69 (s, 3H), 7.09 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.0, 26.1, 32.1, 34.1, 35.7, 35.8, 53.0, 63.9, 74.4, 125.6, 136.3, 143.4, 157.9. MS (EI, 70 eV): *m/z* (%) 318 (100) [M^+], 303 (85) [$M^+ - CH_3$], 247 (8), 187 (15), 57 (40). HRMS: *m/z* calcd for $C_{21}H_{34}O_2$ (M^+) 318.2559; found 318.2557.

3.1.2. *rac-trans*-2-(3-Methoxyphenyl)-cyclohexanol (*rac*-11b). To magnesium (1.7 g, 69.0 mmol) in THF (30 mL) was added a solution of 3-bromo anisole (13.3 g, 71.0 mmol) in THF (30 mL) over 1 h. The resulting mixture was stirred for 0.5 h and then CuI (1.3 g, 7.0 mmol) was added and the mixture was cooled to −30 °C. Cyclohexene oxide (4.6 g, 47.6 mmol) was then added dropwise. After the addition was complete, the mixture was stirred for 3 h and then quenched by pouring into cold saturated NH_4Cl (30 mL). The mixture was partitioned between CH_2Cl_2 and the aqueous layer further 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 4:1) to afford *rac*-**11b** (6.9 g, 71%) as a colorless oil. IR (film): 3419, 2929, 2856, 1602, 1584, 1487, 1464, 1449, 1345, 1323, 1285, 1260, 1228, 1200, 1157, 1122, 1049, 854, 780, 700 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.30–2.10 (m, 8H), 2.39 (m, 1H), 3.62 (m, 1H), 3.78 (s, 3H), 6.70–7.30 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.0, 26.0, 33.2, 34.3, 53.2, 55.1, 74.2, 111.8, 113.5, 120.0, 129.5, 144.8, 159.6. MS (EI, 70 eV): *m/z* (%) 206 (74) [M^+], 178 (12) [$M^+ - C_2H_4$], 135 (43), 122 (100), 91 (19) [$C_7H_7^+$]. HRMS: *m/z* calcd for $C_{13}H_{18}O_2$ (M^+) 206.1307; found 206.1308.

3.2. General procedure for the synthesis of the substrate sulfonates (GP 1)

A solution of the alcohol (1.0 equiv) and NEt_3 or pyridine (3.0 equiv) in CH_2Cl_2 (10 mL/mmol) was cooled to 0 °C. After adding the sulfonyl chloride (1.1 equiv), the solution was stirred at rt for 24 h. The mixture was then washed with brine and the aqueous layer 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).

3.2.1. Compound 9. According to GP 1 (−)-menthol (**8**) (0.8 g, 5.0 mmol) was reacted with 1.1 g phenyl-methanesulfonyl chloride (5.5 mmol) in the presence of 1.5 g triethyl amine (15.0 mmol) to give **9** (1.4 g, 88%) as a colorless solid; mp = 72 °C; $[\alpha]_D^{29} = +53.4$ ($c = 1.0$, $CHCl_3$). IR (KBr): 2961, 2943, 2866, 1499, 1456, 1350, 1330, 1275, 1203, 1171, 1160, 1142, 942, 919, 891, 826, 701, 615 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.70 (d, $J = 7.1$ Hz, 3H), 0.86 (d, $J = 4.9$ Hz, 3H), 0.88 (d, $J = 4.9$ Hz, 3H), 0.90–2.00 (m, 9H), 4.32 (s, 2H), 4.53 (dt, $J = 4.7$, 11.0 Hz, 1H), 7.3–7.50 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 15.4, 20.8, 21.8, 23.0, 25.5, 31.6, 33.7, 42.0, 47.5, 57.8, 83.2, 128.7, 128.8, 130.8, 134.5. MS (EI, 70 eV): *m/z* (%) 310 (2) [M^+], 138 (100) [$M^+ - C_7H_7SO_2OH$], 97 (12), 95 (22), 91 (73), 83 (57). Anal. Calcd for $C_{17}H_{26}O_3S$ (310.45): C, 65.77; H, 8.44, found: C, 65.82; H, 8.64.

3.2.2. Compound *rac*-12a. According to GP 1 the alcohol *rac*-**11a** (0.8 g, 2.5 mmol) was reacted with phenyl-methanesulfonyl chloride (0.52 g, 2.8 mmol) in the presence of triethyl amine (0.8 g, 7.5 mmol) to give *rac*-**12a** (0.9 g, 78%) as a colorless solid; mp = 147 °C. IR (KBr): 2952, 2863, 1600, 1455, 1414, 1359, 1332, 1267, 1226, 1171, 1145, 1016, 953, 916, 900, 886, 829, 813, 769, 699, 620, 540 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.30–2.30 (m, 8H), 1.43 (s, 18H), 2.71 (m, 1H), 3.13 (d, $J = 13.7$ Hz, 1H), 3.26 (d, $J = 13.7$ Hz, 1H), 3.49 (s, 3H), 4.73 (m, 1H), 7.00–7.30 (m, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 24.8, 25.3, 32.1, 33.6, 34.5, 35.8, 49.8, 56.0, 64.2, 87.3, 125.9, 128.5, 130.2, 127.6, 136.3, 143.7, 158.4. MS (EI, 70 eV): *m/z* (%) 472 (10) [M^+], 300 (100) [$M^+ - C_7H_7SO_3H$], 217 (2), 285 (26), 243 (17), 91 (12) [$C_7H_7^+$]. Anal. Calcd for $C_{28}H_{40}O_4S$ (472.68): C, 71.15; H, 8.53, found: C, 71.01; H, 8.42.

3.2.3. Compound *rac*-12b. According to GP 1 the alcohol *rac*-**11b** (5.7 g, 36.0 mmol) was reacted with phenyl-methanesulfonyl chloride (7.5 g, 39.6 mmol) in the presence of triethyl amine (10.0 g, 100.0 mmol) to give *rac*-**12b** (8.0 g, 62%) as a colorless solid; mp = 150 °C. IR (KBr): 2952, 2863, 1600, 1455, 1414, 1359, 1332, 1267, 1226, 1171, 1145, 1016, 953, 916, 900, 886, 829, 813, 769, 699, 620, 540 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.20–2.35 (m, 8H), 2.73 (m, 1H), 3.39 (d, $J = 13.7$ Hz, 1H), 3.55 (d, $J = 13.7$ Hz, 1H), 3.81 (s, 3H), 4.79 (m, 1H), 6.78–7.35 (m, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.2, 25.7, 34.3, 34.8, 50.5, 55.6, 56.9, 86.7, 112.7, 114.1, 120.4, 128.8, 129.9, 130.7, 128.1, 144.5, 160.1. MS (EI, 70 eV): *m/z* (%) 360 (16) [M^+], 188 (100) [$M^+ - C_7H_7SO_2OH$], 217 (2),

159 (9), 134 (14), 91 (12) [$C_7H_7^+$]. HRMS: *m/z* calcd for $C_{20}H_{24}O_4S$ (M^+) 360.1395, found 360.1399.

3.2.4. Compound 15. According to GP 1 the alcohol **14** (2.0 g, 8.0 mmol) was reacted with phenyl-methanesulfonyl chloride (1.8 g, 8.8 mmol) in the presence of triethyl amine (2.4 g, 24.0 mmol) to give **15** (2.7 g, 81%) as a colorless oil; $[\alpha]_D^{27} = -42.2$ ($c=1.0$; $CHCl_3$). IR ($CHCl_3$): 2979, 1496, 1456, 1368, 1317, 1265, 1225, 1167, 1162, 1123, 1084, 1043, 1010, 873, 854, 829, 699, 644, 622, 562 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.26 (s, 3H), 1.35 (s, 3H), 1.46 (s, 3H), 1.49 (s, 3H), 4.01 (dd, $J=4.4$, 8.8 Hz, 1H), 4.12 (dd, $J=5.8$, 8.8 Hz, 1H), 4.16 (dd, $J=3.0$, 8.5 Hz, 1H), 4.23 (ddd, $J=8.5$, 6.0, 4.4 Hz), 4.40 (d, $J=14.0$ Hz, 1H), 4.49 (d, $J=14.0$ Hz, 1H), 4.56 (d, $J=3.6$ Hz, 1H), 5.04 (d, $J=3.0$ Hz, 1H), 5.84 (d, $J=3.6$ Hz), 7.30–7.50 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.2, 26.1, 26.5, 26.9, 57.2, 67.2, 71.9, 79.7, 82.4, 83.3, 104.9, 109.5, 112.4, 128.8, 129.0, 130.6, 127.2. MS (EI, 70 eV): *m/z* (%) 414 (9) [M^+], 399 (100) [M^+-CH_3], 385 (11), 113 (23), 91 (44) [$C_7H_7^+$]. Anal. Calcd for $C_{19}H_{26}O_8S$ (414.47): C, 55.06; H, 6.32, found: C, 55.11; H, 6.35.

3.2.5. Compound 18a. According to GP 1 the alcohol **17** (2.6 g, 10.0 mmol) was reacted with phenyl-methanesulfonyl chloride (2.0 g, 11.0 mmol) in the presence of triethyl amine (3.0 g, 30.0 mmol) to give **18a** (3.8 g, 91%) as a colorless solid; mp = 130 °C; $[\alpha]_D^{27} = +59.1$ ($c=1.0$; $CHCl_3$). IR (KBr): 2982, 1496, 1458, 1368, 1317, 1266, 1222, 1177, 1162, 1123, 1084, 1043, 1016, 873, 854, 829, 700, 646, 619, 559 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.36 (s, 3H), 1.37 (s, 3H), 1.46 (s, 3H), 1.60 (s, 3H, 3.84 (dd, $J=6.3$, 8.5 Hz, 1H), 4.01 (dd, $J=6.9$, 8.5 Hz, 1H), 4.15 (dd, $J=4.1$, 8.5 Hz, 1H), 4.26 (ddd, $J=6.6$, 6.3, 4.1 Hz, 1H), 4.44 (d, $J=14.0$ Hz, 1H), 4.53 (d, $J=14.0$ Hz, 1H), 4.56 (dd, $J=4.1$, 4.6 Hz, 1H), 4.76 (dd, $J=4.7$, 8.5 Hz, 1H), 5.77 (d, $J=3.9$ Hz), 7.37–7.50 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.1, 26.18, 3.7, 26.7, 57.6, 65.2, 74.6, 76.8, 77.0, 77.8, 103.6, 110.0, 113.6, 128.9, 129.2, 130.9, 127.41. MS (EI, 70 eV): *m/z* (%) 399 (36) [M^+-CH_3], 113 (47), 101 (60), 91 (100) [$C_7H_7^+$]. Anal. Calcd for $C_{19}H_{26}O_8S$ (414.47): C, 55.06; H, 6.32, found: C, 54.81; H, 6.47.

3.2.6. Compound 18b. According to GP 1 the alcohol **17** (0.5 g, 2.0 mmol) was reacted with (4-*tert*-butylphenyl)-methanesulfonyl chloride (0.6 g, 2.2 mmol) in the presence of pyridine (0.4 g, 6.0 mmol) to give **18b** (0.9 g, 97%) as a colorless solid; mp = 97 °C; $[\alpha]_D^{28} = +49.5$ ($c=1.0$; $CHCl_3$). IR (KBr): 2980, 2881, 1515, 1497, 1373, 1316, 1265, 1241, 1213, 1179, 1121, 1078, 1042, 1016, 975, 873, 839, 609, 585, 545, 527 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.32 (s, 9H), 1.36 (s, 3H), 1.40 (s, 3H), 1.46 (s, 3H), 1.60 (s, 3H), 3.85 (dd, $J=6.3$, 8.5 Hz, 1H), 4.01 (dd, $J=6.9$, 8.5 Hz, 1H), 4.16 (dd, $J=4.1$, 8.5 Hz, 1H), 4.28 (m, 1H), 4.41 (d, $J=14.0$ Hz, 1H), 4.51 (d, $J=14.0$ Hz, 1H), 4.62 (dd, $J=3.9$, 4.7 Hz, 1H), 4.77 (dd, $J=4.7$, 8.5 Hz, 1H), 5.77 (d, $J=3.8$ Hz, 1H), 7.30–7.40 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.2, 26.2, 26.7, 26.7, 31.2, 34.7, 57.3, 65.3, 74.7, 76.9, 77.1, 77.9, 103.8, 110.1, 113.7, 125.9, 130.5, 124.3, 152.3. MS (EI, 70 eV): *m/z* (%) 470 (1) [M^+], 455 (40) [M^+-CH_3], 147 (100) [$C_{11}H_{15}^+$], 113 (35), 101 (48). Anal. Calcd for $C_{23}H_{34}O_8S$ (470.58): C, 58.71; H, 7.28, found: C, 58.71; H, 7.18.

3.2.7. Compound 18c. According to GP 1 the alcohol **17** (0.5 g, 2.0 mmol) was reacted with prop-2-ene-1-sulfonyl chloride (0.3 g, 2.2 mmol) in the presence of pyridine (0.5 g, 6.0 mmol) to give **18c** (0.8 g, 55%) as a colorless solid; mp = 64 °C; $[\alpha]_D^{25} = +75.15$ ($c=1.0$; $CHCl_3$). IR (KBr): 2979, 2933, 1384, 1372, 1344, 1216, 1261, 1217, 1171, 1118, 1082, 1051, 1017, 999, 942, 928, 910, 882, 861, 849, 835, 792, 647, 612, 574, 547 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.37 (s, 6H), 1.49 (s, 3H), 1.58 (s, 3H), 3.93 (dd, $J=6.0$, 8.8 Hz, 1H), 3.96 (m, 2H), 4.09 (dd, $J=4.1$, 8.2 Hz, 1H), 4.33 (m, 1H), 4.76–4.85 (m, 2H), 5.82 (d, $J=3.6$ Hz, 1H), 5.47–5.54 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.0, 26.2, 26.7, 26.7, 55.9, 65.4, 74.6, 76.9, 77.0, 77.9, 103.8, 110.0, 113.6, 123.9, 124.7. MS (EI, 70 eV): *m/z* (%) 349 (100) [M^+-CH_3], 167 (11), 127 (16), 113 (57), 101 (71). Anal. Calcd for $C_{15}H_{24}O_8S$ (364.41): C, 49.44; H, 6.64, found: C, 49.45; H, 49.45.

3.2.8. Compound 18d. According to GP 1 the alcohol **17** (2.0 g, 8.0 mmol) was reacted with propane-1-sulfonyl chloride (1.2 g, 8.8 mmol) in the presence of pyridine (1.8 g, 24.0 mmol) to give **18d** (2.7 g, 93%) as a colorless oil; $[\alpha]_D^{27} = +81.0$ ($c=1.0$; $CHCl_3$). IR ($CHCl_3$): 2986, 2938, 2885, 1458, 1372, 1257, 1218, 1168, 1121, 1045, 1021, 932, 873, 839, 522 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.09 (t, $J=7.4$ Hz, 3H), 1.37 (s, 3H), 1.48 (s, 3H), 1.58 (s, 3H), 1.96 (m, 2H), 3.20 (m, 2H), 3.93 (dd, $J=6.0$, 8.5 Hz, 1H), 4.09 (dd, $J=6.9$, 8.5 Hz, 1H), 4.15 (dd, $J=4.1$, 7.7 Hz, 1H), 4.33 (m, 1H), 4.80 (m, 2H), 5.82 (d, $J=3.6$ Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 12.8, 17.1, 25.1, 26.2, 26.6, 26.7, 53.3, 65.5, 74.7, 76.3, 77.3, 77.9, 103.8, 110.0, 113.5. MS (EI, 70 eV): *m/z* (%) 351 (57) [M^+-CH_3], 127 (17), 113 (75), 101 (100). Anal. Calcd for $C_{15}H_{26}O_8S$ (366.43): C, 49.17; H, 7.15, found: C, 49.07; H, 7.08.

3.3. General procedure for the α-alkylation of chiral sulfonates (GP 2)

The enantiopure sulfonate (1.0 mmol) was dissolved in dry THF (20 mL) and the solution cooled to −(90–95) °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) was added dropwise. The mixture was stirred for 1 h at −(90–95) °C, then at −78 °C. After 24 h the reaction was quenched by adding pH 7 buffer (2 mL). The mixture was partitioned between CH_2Cl_2 and the aqueous layer further 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).

3.3.1. Compound 10. According to GP 2 the sulfonate **9** (310 mg, 1.0 mmol) was reacted with benzylbromide (190 mg, 1.1 mmol) to give **10** (300 mg, 75%) as a colorless solid; de = 75% (^{13}C NMR); mp = 122 °C. IR (KBr): 2960, 2936, 2870, 1496, 1454, 1353, 1326, 1165, 1073, 940, 913, 870, 845, 823, 696, 643, 632, 596, 566, 552, 478 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 0.87–2.10 (m, 17H), 3.40 (m, 1H), 3.77 (dd, $J=3.6$, 13.7 Hz, 1H), 4.35 (m, 1H), 4.52 (m, 1H), 6.98–7.40 (m, 10H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 15.5 [15.3], 20.9, 21.8 [20.8, 21.8], 23.0 [22.8], 25.6 [25.2], 31.6, 33.7, 36.5 [36.4], 41.3 [42.3], 47.6 [47.5], 69.7 [69.3],

83.5 [82.6], 126.6, 128.2, 128.3, 128.6, 128.8, 129.7, 132.0, 136.5. MS (EI, 70 eV): *m/z* (%) 181 (100) [CH(Ph)CH_2-Ph^+], 138 (2) [$M^+ - C_{14}H_{13}SO_2OH$]). Anal. Calcd for $C_{24}H_{32}O_3S$ (400.575): C, 71.96; H, 8.05, found: C, 71.79; H, 7.91.

3.3.2. Compound 13a. According to GP 2 the sulfonate *rac*-**12a** (470 mg, 1.0 mmol) was reacted with *n*-propyl iodide (180 mg, 1.1 mmol) to give **13a** (280 mg, 55%) as a colorless solid; de=60% (^{13}C NMR); mp=72 °C. IR (KBr): 2960, 2869, 1601, 1496, 1455, 1415, 1394, 1359, 1337, 1264, 1223, 1168, 1117, 1070, 1053, 1013, 960, 922, 899, 870, 829, 806, 698, 634 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.71 [0.66] (t, J=7.4 Hz, 3H), 1.20–2.40 (m, 12H), 1.47 [1.46] (s, 18H), 2.60 [2.68] (m, 1H), 3.61 [3.55] (dd, J=3.9, 11.3 Hz, 1H), 3.69 (s, 3H), 4.97 [4.89] (m, 1H), 7.140–7.30 (m, 7H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.4, 19.6 [19.5], 24.7, 25.4, 31.0 [31.2], 32.2, 34.0 [34.4], 35.2 [35.7], 35.8, 49.9 [50.0], 64.1 [64.0], 67.4 [67.6], 83.7 [84.7], 125.3, 128.3, 128.4, 129.4 [129.5], 132.3 [132.1], 136.4 [136.5], 143.2 [143.3], 157.9 [158.0]; MS (EI, 70 eV): *m/z* (%) 514 (13) [M^+], 300 (100) [$M^+ - C_{10}H_{13}SO_2OH$], 217 (2), 285 (16), 91 (20) [$C_7H_7^+$]. HRMS: *m/z* calcd for $C_{31}H_{46}O_4S$ (M^+) 514.3117, found 514.3114.

3.3.3. Compound 13b. According to GP 2 the sulfonate *rac*-**12b** (310 mg, 1.0 mmol) was reacted with *n*-propyl iodide (180 mg, 1.1 mmol) to give **13b** (250 mg, 71%) as a colorless solid; de=59% (^{13}C NMR); mp=74 °C. IR (KBr): 2936, 2866, 1607, 1585, 1493, 1454, 1344, 1290, 1265, 1214, 1168, 1101, 1048, 998, 939, 905, 884, 863, 828, 803, 785, 698, 577 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.71 [0.70] (t, J=7.2 Hz, 3H), 1.20–2.50 (m, 12H), 2.74 [2.63] (m, 1H), 3.39 (dd, J=7.4, 1H), 3.81 [3.82] (s, 3H), 4.86 [4.84] (m, 1H), 6.70–7.35 (m, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.53 [13.19], 19.63 [19.60], 24.74 [24.66], 25.31 [25.34], 31.56 [31.25], 34.41 [34.35], 34.58 [34.50], 55.01 [55.08], 50.28 [50.08], 67.73 [67.51], 85.73 [84.32], 112.05 [112.09], 113.51 [113.44], 119.70 [119.76], 128.23, 128.34 [128.40], 129.21 [129.27], 129.50 [129.33], 132.06 [132.25], 144.46 [144.12], 159.60 [159.55]. MS (EI, 70 eV): *m/z* (%): 402 (8) [M^+], 188 (100) [$M^+ - C_{10}H_{13}SO_2OH$], 133 (18), 121 (23), 91 (76) [$C_7H_7^+$]. Anal. Calcd for $C_{23}H_{30}O_4S$ (402.55): C, 68.63; H, 7.51, found: C, 68.67; H, 7.40.

3.3.4. Compound 16. According to GP 2 the sulfonate **15** (410 mg, 1.0 mmol) was reacted with *n*-propyl iodide (180 mg, 1.1 mmol) in the presence of 1.1 equiv of HMPA (0.19 mL, 1.1 mmol) to give **16** (330 mg, 73%) as a colorless solid; de=59% (^{13}C NMR); mp=93 °C. IR (KBr): 2981, 2960, 2937, 2876, 1456, 1373, 1255, 1210, 1169, 1076, 1047, 1026, 979, 955, 897, 882, 858, 843, 752, 698, 620, 615, 566 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.91 [0.90] (t, J=7.4 Hz, 3H), 1.19 [1.28] (s, 3H), 1.38 [1.35] (s, 3H), 1.44 [1.45] (s, 3H), 1.49 [1.48] (s, 3H), 1.25 [1.22] (m, 2H), 2.17 [2.23] (m, 1H), 2.38 [2.32] (m, 1H), 33.90–4.20 (m, 5H), 4.27 [4.30] (dd, J=3.9, 11.5 Hz, 1H), 4.96 [4.97] (d, J=2.3 Hz, 1H), 5.62 [5.88] (d, J=3.6 Hz, 1H), 7.38–7.50 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.4 [13.6], 19.9 [19.8], 25.2, 25.9, 26.5 [26.6], 26.9, 31.6, 67.0 [67.1], 68.2 [67.8], 71.9 [72.0], 79.8, 81.9 [82.1], 82.6 [83.4], 104.7, 109.4, 112.1 [112.3], 128.7, 129.0, 129.4, 132.3 [131.5]. MS (EI, 70 eV): *m/z* (%) 441 (12) [$M^+ - CH_3$], 133 (100) [$C_{10}H_{13}^+$], 113 (66), 101 (40), 91 (96) [C_7H_7]. Anal. Calcd for $C_{22}H_{32}O_8S$ (456.55): C, 57.88; H, 7.06, found: C, 57.74; H, 7.20.

3.3.5. Compound 19. According to GP 2 the sulfonate **18a** (410 mg, 1.0 mmol) was reacted with *n*-propyl iodide (180 mg, 1.1 mmol) in the presence of 1.1 equiv of HMPA (0.19 mL, 1.1 mmol) to give **19** (310 mg, 69%) as a colorless solid; de=78% (^{13}C NMR); mp=124 °C. IR (KBr): 2976, 2955, 2934, 2890, 1638, 1498, 1471, 1457, 1372, 1353, 1312, 1296, 1259, 1233, 1216, 1173, 1116, 1053, 1041, 1018, 999, 932, 880, 867, 837, 804, 734, 697, 659, 630 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.91 (t, J=7.4 Hz, 3H), 1.33 (s, 3H), 1.38 [1.36] (s, 3H), 1.48 [1.43] (s, 3H), 1.56 (s, 3H), 1.25 (m, 2H), 2.20 (m, 1H), 2.41 (m, 1H), 3.89 [3.6] (dd, J=6.6. 8.5 Hz, 1H), 4.04 (dd, J=6.6. 8.5 Hz, 1H), 4.14 (dd, J=3.8, 8.5 Hz, 1H), 4.22 (dd, J=4.1, 4.7 Hz, 1H), 4.33 (m, 2H), 4.66 [4.69] (dd, J=4.7, 8.5 Hz, 1H), 5.71 [5.8] (d, J=3.6 Hz, 1H), 7.36–7.55 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.4 [13.5], 19.8, 25.3, 26.2 [26.3], 26.6, 26.7, 31.9 [31.5], 65.2 [64.9], 68.2 [67.8], 74.6, 76.8, 77.0, 77.5, 103.7 [103.8], 110.1, 113.5, 128.8, 129.1, 129.9 [129.7], 131.9. MS (EI, 70 eV): *m/z* (%) 441 (10) [$M^+ - CH_3$], 133 (97) [$C_{10}H_{13}^+$], 113 (43), 101 (48), 91 (100) [$C_7H_7^+$]. Anal. Calcd for $C_{22}H_{32}O_8S$ (456.55): C, 57.88; H, 7.06, found: C, 58.08; H, 7.07.

3.3.6. (*R*)-1-Phenyl-ethanesulfonate (*R*)-20a. According to GP 2 the sulfonate **18a** (410 mg, 1.0 mmol) was reacted with methyl iodide (200 mg, 1.5 mmol) to give (*R*)-**20a** (410 mg, 95%) as a colorless solid; de=91% (^{13}C NMR); de≥98 (after recrystallization from 2-propanol); mp=103.4 °C; $[\alpha]_D^{25} = +91.3$ (c=1.0, $CHCl_3$). IR (KBr): 2980, 2934, 2908, 1496, 1456, 1383, 1366, 1351, 1314, 1267, 1237, 1216, 1173, 1117, 1096, 1078, 1048, 1015, 1000, 931, 890, 873, 831, 695, 628, 614, 563, 506 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.33 (s, 3H), 1.37 (s, 3H), 1.46 (s, 3H), 1.56 (s, 3H), 1.87 (d, J=7.2 Hz, 3H), 3.86 (dd, J=6.6, 8.5 Hz, 1H), 4.01 (dd, J=6.6, 8.5 Hz, 1H), 4.14 (dd, J=4.1, 8.5 Hz, 1H), 4.27 (ddd, J=3.9, 4.1, 6.6 Hz, 1H), 4.35 (dd, J=3.8, 4.7 Hz, 1H), 4.49 (q, J=7.2 Hz, 1H), 4.64 (dd, J=4.7, 8.5 Hz, 1H), 5.72 (d, J=3.9 Hz, 1H), 7.30–7.40 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 16.2, 25.1, 25.2, 26.2, 26.6, 63.1, 65.2, 74.6, 76.8, 77.5, 77.8, 103.6, 109.9, 113.3, 128.5, 129.0, 128.2, 129.2, 130.7, 133.2. MS (EI, 70 eV): *m/z* (%) 413 (62) [$M^+ - CH_3$], 113 (29), 105 (100) [$(CH_3)(C_6H_5)CH^+$], 101 (33). Anal. Calcd for $C_{20}H_{28}O_8S$ (428.50): C, 56.06; H, 6.59, found: C, 55.92; H, 6.76.

3.3.7. (*R*)-1-Phenyl-but-3-ene-1-sulfonate (*R*)-20b. According to GP 2 the sulfonate **18a** (410 mg, 1.0 mmol) was reacted with allyl bromide (180 mg, 1.5 mmol) to give (*R*)-**20b** (420 mg, 93%) as a colorless solid; de=90% (^{13}C NMR); de≥98 (after recryst. from 2-propanol); mp=149.2 °C; $[\alpha]_D^{24} = +77.0$ (c=1.0, $CHCl_3$). IR (KBr): 2978, 2934, 1497, 1457, 1370, 1355, 1313, 1255, 1220, 1172, 1115, 1054, 1038, 1015, 1001, 933, 880, 864, 840, 810, 698, 627, 571, 503 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.33 (s, 3H), 1.37 (s, 3H), 1.47 (s, 3H), 1.56 (s, 3H), 2.98 (m, 1H), 3.21 (m, 1H), 3.89 (dd, J=6.6, 8.5 Hz, 1H), 4.04 (dd, J=6.9, 8.5 Hz, 1H), 4.14 (dd, J=3.9, 8.5 Hz, 1H), 4.26–4.32 (m, 2H), 4.37 (dd, J=4.1, 11.3 Hz, 1H), 4.68 (dd, J=4.7,

8.8 Hz, 1H), 5.01 (d, J=9.9 Hz, 1H), 5.08 (d, J=17.0 Hz, 1H), 5.54 (m, 1H), 5.72 (d, J=3.9 Hz, 1H), 7.30–7.50 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.2, 26.2, 26.6, 26.6, 34.3, 65.2, 67.8, 74.6, 76.8, 77.19, 103.6, 110.0, 113.4, 118.5, 128.6, 129.1, 129.8, 131.1, 132.4. MS (EI, 70 eV): m/z (%) 439 (78) [M^+-CH_3], 131 (100) [$(C_3H_5)(C_6H_5)CH^+$], 113 (30), 101 (32). Anal. Calcd for $C_{22}H_{30}O_8S$ (454.53): C, 58.13; H, 6.65, found: C, 57.78; H, 6.61.

3.3.8. (*R*)-1,2-Diphenyl-ethanesulfonate (*R*)-20c. According to GP 2 the sulfonate **18a** (410 mg, 1.0 mmol) was reacted with benzyl bromide (260 mg, 1.5 mmol) to give (*R*)-**20c** (470 mg, 94%) as a colorless solid; de=89% (^{13}C NMR); de≥98 (after recryst. from 2-propanol); mp=143 °C; $[\alpha]_D^{24}=+34.4$ (c=1.1, $CHCl_3$). IR (KBr): 2979, 2932, 1498, 1456, 1369, 1315, 1259, 1246, 1218, 1167, 1118, 1049, 1015, 998, 876, 857, 824, 697 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.35 (s, 3H), 1.38 (s, 3H), 1.48 (s, 3H), 1.58 (s, 3H), 3.41 (dd, J=11.5, 13.7 Hz, 1H), 3.81 (dd, J=3.6, 13.7 Hz, 1H), 3.92 (dd, J=6.6, 8.5 Hz, 1H), 4.06 (dd, J=6.9, 8.5 Hz, 1H), 4.16 (dd, J=3.9, 8.8 Hz, 1H), 4.30–4.37 (m, 2H), 4.57 (dd, J=3.6, 11.5 Hz, 1H), 4.77 (dd, J=4.7, 8.8 Hz, 1H), 5.74 (d, J=3.6 Hz, 1H), 6.9–7.5 (m, 10H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 25.2, 26.2, 26.6, 26.7, 36.5, 65.2, 69.8, 74.5, 76.7, 77.2, 77.4, 103.6, 110.0, 113.5, 128.2, 128.5, 128.7, 128.8, 129.0, 129.8, 131.0, 136.1. MS (EI, 70 eV): m/z (%) 489 (48, M^+-CH_3), 245 (2), 181 (100) [$(C_7H_7)(C_6H_5)CH^+$], 113 (25), 101 (30). Anal. Calcd for $C_{26}H_{32}O_8S$ (504.59): C, 61.89; H, 6.39, found: C, 61.60; H, 6.33.

3.3.9. (*R*)-2-(4-Bromophenyl)-1-phenyl-ethanesulfonate (*R*)-20d. According to GP 2 the sulfonate **18a** (410 mg, 1.0 mmol) was reacted with 1-bromo-4-bromomethyl-benzene (380 mg, 1.5 mmol) to give the (*R*)-**20d** (520 mg, 90%) as a colorless solid; de=90% (^{13}C NMR); de≥98 (after recryst. from 2-propanol); mp=143 °C; $[\alpha]_D^{25}=+17.8$ (c=0.8, $CHCl_3$). IR (KBr): 2985, 2939, 2900, 1491, 1457, 1372, 1312, 1260, 1217, 1177, 1164, 1115, 1073, 1053, 1040, 1015, 929, 876, 835, 810, 698, 642, 569, 528, 514 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.35 (s, 3H), 1.37 (s, 3H), 1.47 (s, 3H), 1.57 (s, 3H), 3.36 (dd, J=11.5, 13.7 Hz, 1H), 3.78 (dd, J=3.6, 13.7 Hz, 1H), 3.90 (dd, J=6.6, 8.8 Hz, 1H), 4.05 (dd, J=6.6, 8.8 Hz, 1H), 4.15 (dd, J=4.1, 8.8 Hz, 1H), 4.30–4.40 (m, 2H), 4.50 (dd, J=3.6, 11.5 Hz, 1H), 4.76 (dd, J=4.7, 8.8 Hz, 1H), 5.74 (d, J=3.6 Hz, 1H), 6.90–7.40 (m, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 25.2, 26.2, 26.7, 26.7, 36.0, 65.2, 69.5, 74.5, 76.6, 76.9, 77.4, 103.6, 110.1, 113.5, 120.7, 130.7, 135.1, 128.6, 129.2, 129.7, 130.5, 131.3. MS (EI, 70 eV): m/z (%) 569 (77) [$M^+(Br^{81})-CH_3$], 567 (65) [$M^+(Br^{79})-CH_3$], 261 (89) [$(Br^{81}C_7H_6)(C_6H_5)CH^+$], 259 (100) [$(Br^{79}C_7H_6)(C_6H_5)CH^+$], 180 (73), 165 (14), 113 (69), 101 (9). Anal. Calcd for $C_{26}H_{31}O_8SBr$ (583.50): C, 53.52; H, 5.35, found: C, 53.64; H, 5.38.

3.3.10. (*R*)-2-Naphtalen-2-yl-1-phenyl-ethanesulfonate (*R*)-20e. According to GP 2 the sulfonate **18a** (410 mg, 1.0 mmol) was reacted with 2-bromomethyl-naphthalene (330 mg, 1.5 mmol) to give (*R*)-**20e** (530 mg, 96%) as a colorless solid; de=91% (^{13}C NMR); de≥98 (after recryst. from 2-propanol); mp=136 °C; $[\alpha]_D^{26}=+17.3$ (c=1.0, $CHCl_3$). IR (KBr): 2987, 2937, 2899, 2185, 1637, 1602, 1457, 1373, 1218, 1168, 1121, 1019, 930, 872, 843, 822, 752, 699, 570 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.36 (s, 3H), 1.37 (s, 3H), 1.48 (s, 3H), 1.59 (s, 3H), 3.57 (dd, J=11.5, 13.7 Hz, 1H), 3.89 (dd, J=6.6, 8.5 Hz, 1H), 3.97–4.05 (m, 2H), 4.16 (dd, J=3.8, 8.8 Hz, 1H), 4.32 (ddd, J=3.8, 6.6, 6.6 Hz, 1H), 4.68 (dd, J=3.6, 4.7 Hz, 1H), 4.68 (dd, J=3.6, 11.5 Hz, 1H), 4.73 (dd, J=4.7, 8.5 Hz, 1H), 5.74 (d, J=3.6 Hz, 1H), 7.10–7.90 (m, 12H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 25.2, 26.2, 26.7, 26.7, 36.7, 65.1, 69.7, 74.5, 76.9, 77.2, 77.4, 103.6, 110.0, 113.5, 125.6, 126.0, 126.8, 127.3, 127.4, 127.7, 127.9, 131.0, 132.0, 133.1, 133.6. MS (EI, 70 eV): m/z (%) 554 (14) [M^+], 539 (23) [M^+-CH_3], 312 (21), 231 (100) [$(C_{11}H_9)(C_6H_5)CH^+$], 215 (8), 153 (35), 141 (39), 101 (17). Anal. Calcd for $C_{30}H_{34}O_8S$ (554.65): C, 64.96; H, 6.18, found: C, 64.83; H, 6.34.

3.3.11. (*R*)-1-(4-*tert*-Butylphenyl)-2-phenyl-ethanesulfonate (*R*)-20f. According to GP 2 the sulfonate **18b** (470 mg, 1.0 mmol) was reacted with benzyl bromide (260 mg, 1.5 mmol) to give (*R*)-**20f** (530 mg, 95%) as a colorless solid; de=91% (^{13}C NMR); de≥98 (after recryst. from 2-propanol); mp=143 °C; $[\alpha]_D^{26}=+22.6$ (c=1.0, $CHCl_3$). IR (KBr): 2903, 1606, 1455, 1370, 1313, 1246, 1215, 1177, 1165, 1117, 1083, 1057, 1043, 1019, 877, 859, 834, 745, 699, 672, 615, 576, 557, 521 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.28 (s, 9H), 1.34 (s, 3H), 1.37 (s, 3H), 1.47 (s, 3H), 1.57 (s, 3H), 3.41 (dd, J=11.3, 14.0 Hz, 1H), 3.81 (dd, J=3.6, 14.0 Hz, 1H), 3.90 (dd, J=6.6, 8.5 Hz, 1H), 4.04 (dd, J=6.6, 8.5 Hz, 1H), 4.14 (dd, J=3.9, 8.8 Hz, 1H), 4.27 (dd, J=3.8, 4.7 Hz, 1H), 4.32 (ddd, J=3.9, 6.6, 6.6 Hz, 1H), 4.55 (dd, J=3.6, 11.3 Hz, 1H), 4.73 (dd, J=4.7, 8.8 Hz, 1H), 5.72 (d, J=3.9 Hz, 1H), 6.90–7.40 (m, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 25.3, 26.2, 26.7, 26.7, 31.2, 34.6, 36.4, 65.1, 69.4, 74.6), 76.7, 77.4, 77.6, 103.5, 110.0, 113.4, 125.5, 126.6, 128.2, 128.8, 129.4, 127.8, 136.4, 152.1. MS (EI, 70 eV): m/z (%) 545 (15) [M^+-CH_3], 237 (100), 113 (4), 101 (7), 91 (20) [$C_7H_7^+$]. Anal. Calcd for $C_{30}H_{40}O_8S$ (560.70): C, 64.26; H, 7.19, found: C, 64.29; H, 7.20.

3.3.12. (*R*)-1-(4-*tert*-Butylphenyl)-2-naphtalen-2-yl-ethanesulfonate (*R*)-20g. According to GP 2 the sulfonate **18b** (470 mg, 1.0 mmol) was reacted with 2-bromomethyl-naphthalene (330 mg, 1.5 mmol) to give (*R*)-**20g** (600 mg, 98%) as a colorless solid; de=93% (^{13}C NMR); de≥98 (after recryst. from 2-propanol); mp=139 °C; $[\alpha]_D^{26}=+3.8$ (c=1.0., $CHCl_3$). IR (KBr): 2978, 2903, 1602, 1510, 1454, 1370, 1318, 1258, 1217, 1166, 1122, 1018, 933, 893, 878, 839, 819, 795, 746, 625, 607 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 11.26 (s, 9H), 1.36 (s, 3H), 1.37 (s, 3H), 1.48 (s, 3H), 1.59 (s, 3H), 3.57 (dd, J=11.3, 14.0 Hz, 2H), 3.88 (dd, J=6.6, 8.5 Hz, 1H), 3.95–4.03 (m, 2H), 4.15 (dd, J=3.6, 8.5 Hz, 1H), 4.29–4.36 (m, 2H), 4.67 (dd, J=3.6, 11.3 Hz, 1H), 4.76 (dd, J=4.7, 8.5 Hz, 1H), 5.73 (d, J=3.9 Hz, 1H), 7.10–7.80 (m, 12H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 25.3, 26.2, 26.7, 26.7, 31.2, 34.6, 36.6, 65.1, 69.3, 74.5, 76.7, 77.2, 77.2, 77.4, 103.6, 110.0, 113.5, 125.5, 125.9, 126.8, 127.3, 127.4, 127.7, 127.8, 127.8, 129.4, 132.0, 133.1, 133.8, 152.1. MS (EI, 70 eV): m/z (%) 595 (4) [M^+-CH_3], 287 (100), 141 (16) [$C_{11}H_9^+$], 101 (7). Anal. Calcd for $C_{34}H_{42}O_8S$ (610.76): C, 66.86; H, 6.93, found: C, 67.12; H, 6.86.

3.3.13. Compound 20h. According to GP 2 the sulfonate **18c** (360 mg, 1.0 mmol) was reacted with methyl iodide (200 mg, 1.5 mmol) to give **20h** (210 mg, 55%) as a colorless oil; de = 50% (^{13}C NMR). IR (film): 2987, 2939, 2900, 1640, 1457, 1373, 1360, 1217, 1167, 1121, 1020, 934, 873, 832, 751, 657 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.38 (s, 3H), 1.49 (s, 3H), 1.60 (s, 3H), 1.62 (s, 3H), 1.62 [1.61] (d, J = 6.9 Hz, 3H), 3.80–4.35 (m, 4H), 4.77–4.83 (m, 2H), 5.47–5.54 (m, 2H), 5.82 (d, J = 3.6 Hz, 1H), 6.00 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.3 [14.4], 25.1, 26.2, 26.6, 26.7, 55.9, 65.4 [65.5], 74.65, 76.6, 76.9, 77.9 [77.8], 103.7 [103.7], 110.0, 113.5, 121.9 [121.7], 130.0 [130.3]. MS (EI, 70 eV): *m/z* (%) 363 (100) [$M^+ - CH_3$], 167 (7), 127 (14), 113 (49), 101 (70). Anal. Calcd for $C_{16}H_{26}O_8S$ (378.44): C, 50.78; H, 6.92, found: C, 50.41; H, 7.12.

3.3.14. Compound 20i. According to GP 2 the sulfonate **18d** (370 mg, 1.0 mmol) was reacted with methyl iodide (200 mg, 1.5 mmol) to give **20i** (330 mg, 87%) as a colorless oil; de = 0% (^{13}C NMR). IR (film): 2987, 2940, 2884, 1458, 1373, 1218, 1175, 1121, 1021, 931, 872, 829, 793, 757, 599, 524 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.05 [1.06] (t, J = 7.4 Hz, 3H), 1.37 (s, 3H), 1.45 (s, 3H), 1.48 (s, 3H), 1.57 (s, 3H), 1.46 (d, J = 7.4 Hz, 3H), 1.65 [2.17] (m, 2H), 3.19 (m, 1H), 3.92 (dd, J = 6.9, 8.5 Hz, 1H), 4.09 (dd, J = 6.9, 8.5 Hz, 1H), 4.14–4.19 (m, 1H), 4.32 (m, 1H), 4.78 (m, 2H), 5.82 (d, J = 3.0 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 10.9 [11.0], 13.3 [13.4], 23.4 [23.5], 25.2, 26.2, 26.7, 26.7, 58.9 [59.0], 65.4 [65.5], 74.7 [74.8], 76.1, 78.0, 78.0, 103.8, 110.0, 113.4. MS (EI, 70 eV): *m/z* (%) 363 (100) [$M^+ - CH_3$], 167 (7), 127 (14), 113 (49), 101 (70). Anal. Calcd for $C_{16}H_{28}O_8S$ (380.45): C, 50.51; H, 7.42, found: C, 50.36; H, 7.67.

3.4. General procedure for the removal of the chiral auxiliary to form the α-alkylated methyl sulfonates (*R*)-21a–g (GP 3)

The sulfonate (*R*)-**20** (0.6 mmol) was dissolved in an EtOH/H_2O-solution (19:1 mL). To the solution was added $Pd(OAc)_2$ (15 mol%, 20 mg) and the mixture was refluxed for 4 d (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, 1:6) to afford the methyl sulfonate (*R*)-**21**.

3.4.1. Methyl (*R*)-1-phenylethane sulfonate (*R*)-21a. The sulfonate (*R*)-**20a** (260 mg, 0.6 mmol) was reacted according to GP 3 to give (*R*)-**21a** (120 mg, 98%) as a colorless oil; ee ≥ 98% (HPLC, Daicel OJ); $[\alpha]_D^{26} = +25.6$ (c = 1.0; $CHCl_3$). IR ($CHCl_3$): 2992, 2960, 1496, 1455, 1353, 1304, 1168, 1056, 1030, 991, 802, 781, 767, 699, 624, 566 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.84 (d, J = 7.1 Hz, 3H), 3.66 (s, 3H), 4.40 (q, J = 7.1 Hz, 1H), 7.37–7.47 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 15.9, 56.7, 61.8, 128.6, 128.9, 128.9, 133.5. MS (EI, 70 eV): *m/z* (%) 200 (5) [M^+], 105 (100) [$M^+ - SO_3CH_3$), 103 (8), 79 (9). HRMS: *m/z* calcd for $C_9H_{12}O_3S$ (M^+) 200.0507, found 200.0507.

3.4.2. Methyl (*R*)-1-phenyl-3-butene sulfonate (*R*)-21b. The sulfonate (*R*)-**20b** (270 mg, 0.6 mmol) was reacted according to GP 3 to give (*R*)-**21b** (130 mg, 90%) as a colorless solid; mp = 58 °C; ee ≥ 98% (HPLC, (*S*,*S*)-Whelk-O1); $[\alpha]_D^{28} = -6.3$ (c = 1.0; $CHCl_3$). IR (KBr): 2959, 2944, 2922, 1643, 1456, 1350, 1320, 1228, 1163, 993, 939, 835, 767, 734, 700, 654 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.95 (m, 1H), 3.13 (m, 1H), 3.64 (s, 3H), 4.26 (dd, J = 4.7, 11.0 Hz, 1H), 5.02 (d, J = 10.2 Hz, 1H), 5.10 (d, J = 17.0 Hz, 1H), 5.57 (m, 1H), 7.36–7.44 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 34.0, 56.8, 66.7, 118.6, 128.7, 129.0, 129.5, 132.3, 132.7. MS (EI, 70 eV): *m/z* (%) 181 (100) [$M^+ - SO_3CH_3$], 103 (5), 91 (28) [$C_7H_7^+$]. Anal. Calcd for $C_{11}H_{14}O_3S$ (226.29): C, 58.39; H, 6.24, found: C, 58.30; H, 6.32.

3.4.3. Methyl (*R*)-1,2-diphenylethane sulfonate (*R*)-21c. The sulfonate (*R*)-**20c** (300 mg, 0.6 mmol) was reacted according to GP 3 to give (*R*)-**21c** (160 mg, 94%) as a colorless solid; mp = 67 °C; ee ≥ 98% (HPLC, Daicel OD); $[\alpha]_D^{27} = -77.4$ (c = 1.0; $CHCl_3$). IR (KBr): 3032, 2964, 2935, 1497, 1454, 1347, 1329, 1158, 984, 848, 818, 767, 755, 724, 697, 628, 582, 556 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.41 (dd, J = 11.0, 13.7 Hz, 1H), 3.63 (s, 3H), 3.73 (dd, J = 3.6, 13.7 Hz, 1H), 4.44 (dd, J = 3.6, 11.0 Hz, 1H), 6.98–7.37 (m, 10H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 36.3, 56.9, 68.6, 126.9, 128.5, 128.8, 129.0, 129.2, 129.7, 131.7, 136.4. MS (EI, 70 eV): *m/z* (%) 276 (3) [M^+], 181 (100) [$M^+ - SO_3CH_3$], 166 (18), 115 (1), 103 (14), 91 (19) [$C_7H_7^+$]. Anal. Calcd for $C_{15}H_{16}O_3S$ (276.35): C, 65.19; H, 5.84, found: C, 65.00; H, 5.83.

3.4.4. Methyl (*R*)-2-(4-bromophenyl)-1-phenylethane sulfonate (*R*)-21d. The sulfonate (*R*)-**20d** (350 mg, 0.6 mmol) was reacted according to GP 3 to give (*R*)-**21d** (160 mg, 77%) as a colorless solid; mp = 82 °C; ee ≥ 98% (HPLC, (*S*,*S*)-Whelk-O1); $[\alpha]_D^{32} = -93.4$ (c = 1.0; $CHCl_3$). IR (KBr): 3037, 2967, 1490, 1454, 1439, 1489, 1455, 1439, 1347, 1164, 1075, 1048, 1017, 981, 921, 856, 820, 809, 775, 731, 701, 638, 608, 569, 545, 509, 482, 462 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.37 (dd, J = 11.3, 14.0 Hz, 1H), 3.63 (s, 3H), 3.68 (dd, J = 3.9, 14.0 Hz, 1H), 4.38 (dd, J = 3.9, 11.3 Hz, 1H), 6.87 (d, J = 8.5 Hz, 2H), 7.29 (d, J = 8.2 Hz, 2H), 7.33–7.36 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 35.7, 56.9, 68.6, 128.7, 129.1, 129.4, 130.5, 131.4, 120.7, 131.2, 135.1 (Aryl-C). MS (EI, 70 eV): *m/z* (%) 356 (10) [$M^+(Br^{81})$], 354 (11) [$M^+(Br^{79})$], 261 (47) [$M^+(Br^{81}) - SO_3CH_3$)], 259 (73) [$M^+(Br^{79}) - SO_3CH_3$], 180 (100), 169 (4), 89 (36). Anal. Calcd for $C_{15}H_{15}O_3SBr$ (355.25): C, 50.72; H, 4.26, found: C, 50.40; H, 4.51.

3.4.5. Methyl (*R*)-2-naphtalen-2-yl-1-phenylethane sulfonate (*R*)-21e. The sulfonate (*R*)-**20e** (330 mg, 0.6 mmol) was reacted according to GP 3 to give (*R*)-**21e** (190 mg, 96%) as a colorless solid; mp = 67 °C, ee ≥ 98% (HPLC, Daicel OD); $[\alpha]_D^{31} = -89.5$ (c = 1.0; $CHCl_3$). IR (KBr): 3056, 2959, 1602, 1455, 1356, 1327, 1180, 1167, 1081, 990, 863, 821, 784, 767, 696, 610, 577, 483 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.58 (dd, J = 11.3, 14.0 Hz, 1H), 3.65 (s, 3H), 3.90 (dd, J = 3.8, 14.0 Hz, 1H), 4.38 (dd, J = 3.9, 11.3 Hz, 1H), 7.20–7.80 (m, 12H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 36.5, 56.8, 68.5, 125.6, 125.9, 126.7, 127.4, 127.4, 127.7, 128.0, 128.6, 129.0, 129.5, 131.5, 132.0, 133.1, 133.7. MS (EI, 70 eV): *m/z* (%) 326 (27) [M^+], 230

(40), 215 (18), 153 (58), 141 (42) [$C_{11}H_9^+$], 172 (9) [$C_{10}H_7^+$], 115 (31). Anal. Calcd for $C_{19}H_{18}O_3S$ (326.41): C, 69.91; H, 5.56, found: C, 69.75; H, 5.77.

3.4.6. Methyl (*R*)-1-(4-*tert*-butylphenyl)-2-phenylethane sulfonate (*R*)-21f. The sulfonate (*R*)-**20f** (340 mg, 0.6 mmol) was reacted according to GP 3 to give (*R*)-**21f** (180 mg, 90%) as a colorless oil; ee≥98% (HPLC, Daicel AD); $[\alpha]_D^{26}=-92.8$ ($c=1.0$; $CHCl_3$). IR (film) 3031, 3005, 2961, 2906, 2870, 1604, 1512, 1497, 1456, 1416, 1357, 1166, 989, 861, 829, 794, 756, 727, 699, 673, 611, 576 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.29 (s, 9H), 3.41 (dd, $J=$ 10.7, 14.0 Hz, 1H), 3.62 (s, 3H), 3.71 (dd, $J=4.1$, 14.0 Hz, 1H), 4.42 (dd, $J=4.1$, 10.7 Hz, 1H), 7.00–7.40 (m, 12H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 30.9, 34.7, 36.5, 56.8, 68.5, 125.6, 125.9, 126.7, 127.4, 127.4, 127.7, 128.0, 128.6, 129.0, 129.5, 131.5, 132.1, 133.1, 133.7. MS (EI, 70 eV): *m/z* (%) 332 (2) [M^+], 237 (2) [$M^+-SO_3CH_3$], 172 (9) [$C_{10}H_7^+$], 115 (2), 91 (22) [$C_7H_7^+$], 57 (74). HRMS: *m/z* calcd for $C_{19}H_{24}O_3S$ (M^+) 332.1446, found 332.1446.

3.4.7. Methyl (*R*)-1-(4-*tert*-butylphenyl)-2-naphtalen-2-yl-ethane sulfonate (*R*)-21g. The sulfonate (*R*)-**20g** (340 mg, 0.6 mmol) was reacted according to GP 3 to give (*R*)-**21g** (200 mg, 87%) as a colorless solid; mp= 94 °C; ee≥98% (HPLC, Daicel AD); $[\alpha]_D^{28}=-108.2$ ($c=$ 1.0; $CHCl_3$). IR (KBr) 2962, 1599, 1560, 1508, 1351, 1162, 994, 960, 859, 827, 809, 777, 765, 749, 673, 623, 603, 518, 484, 474 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.27 (s, 9H), 3.58 (dd, $J=11.0$, 14.0 Hz, 1H), 3.63 (s, 3H), 3.88 (dd, $J=3.9$, 14.0 Hz, 1H), 4.53 (dd, $J=3.9$, 10.7 Hz, 1H), 7.10–8.00 (m, 11H). ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=31.2$, 34.6, 36.5, 56.8, 68.1, 125.8, 126.0, 126.1, 127.0, 127.6, 127.6, 127.9, 128.1, 129.4, 128.5, 132.3, 133.3, 134.1, 152.3. MS (EI, 70 eV): *m/z* (%) 382 (39) [M^+], 287 (100) [$M^+-SO_3CH_3$], 231 (12), 153 (16), 141 (22) [$C_{11}H_9^+$], 122 (26), 57 (88). Anal. Calcd for $C_{23}H_{26}O_3S$ (382.52): C, 72.22; H, 6.85, found: C, 71.84; H, 6.71.

3.5. Investigations on the cleavage mechanism

The sulfonate (*R*)-**20c** (1.7 g, 4.0 mmol) was dissolved in an EtOH/H_2O solution (80:5 mL). To the solution was added $Pd(OAc)_2$ (15 mol%, 150 mg) and the mixture was refluxed for 4 d (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 compounds **22a** and **22b** were isolated by flash column chromatography (SiO_2, CH_2Cl_2/MeOH, 30:1).

3.5.1. Compound 22a. 25% yield (190 mg); colorless oil; $[\alpha]_D^{25}=+137.8$ ($c=1.15$; $CHCl_3$). IR ($CHCl_3$): 3414, 2975, 2898, 1725, 1642, 1445, 1404, 1376, 1355, 1111, 1085, 1054, 1006, 976, 947, 889, 839, 756, 700, 667, 648, 592 cm^{-1}. ^1H NMR (400 MHz, C_5D_5N): δ 1.09 (t, $J=$ 7.1 Hz, 3H), 3.49 (dq, $J=7.1$, 9.6 Hz, 1H), 3.81 (dt, $J=7.1$, 9.6 Hz, 1H), 3.86 (dd, $J=8.2$, 8.5 Hz, 1H), 4.05 (dd, $J=6.1$, 8.5 Hz, 1H), 4.38 (m, 1H), 4.53 (t, $J=3.9$ Hz, 1H), 4.76 (dd, $J=5.4$, 5.5 Hz, 1H), 4.86 (dd, $J=3.6$, 5.5 Hz, 1H), 5.29 (d, $J=4.1$ Hz, 1H). ^{13}C NMR (100 MHz, C_5D_5N): $\delta=15.5$, 64.0, 71.4, 72.3, 78.6, 79.9, 88.8, 105.0. MS (EI, 70 eV): *m/z* (%)=192 (9) [M^++2], 191 (100) [M^++1], 173 (10) [$(M^++1)-H_2O$], 145 (61, [$(M^++1)-C_2H_5O$], 130 (4), 103 (2), 85 (4), 73 (1). Anal. Calcd for $C_8H_{14}O_5$ (190.20): C, 50.52; H, 7.42, found: C, 50.50; H, 7.31.

3.5.2. Compound 22b. 37% yield (280 mg); colorless solid; mp=79 °C; $[\alpha]_D^{24}=-46.3$ ($c=1.0$; $CHCl_3$). IR (KBr): 3414, 2975, 2899, 1725, 1640, 1445, 1404, 1376, 1360, 1111, 1085, 1054, 1001, 972, 947, 889, 839, 756, 700, 660, 648, 590 cm^{-1}. ^1H NMR (400 MHz, C_5D_5N): δ 1.10 (t, $J=$ 7.1 Hz, 3H), 3.47 (dq, $J=7.1$, 9.3 Hz, 1H), 4.02 (dq, $J=7.1$, 9.3 Hz, 1H), 4.08 (t, $J=7.1$ Hz, 1H), 4.17 (t, $J=8.5$ Hz, 1H), 4.47 (m, 1H), 4.66 (s, 1H), 4.81 (d, $J=4.7$ Hz), 5.04 (dd, $J=4.7$, 5.0 Hz, 1H), 5.50 (s, 1H). ^{13}C NMR (100 MHz, C_5D_5N): $\delta=15.3$, 63.79, 71.8, 72.9, 81.4, 84.6, 88.7, 111.5. MS (EI, 70 eV): *m/z* (%)=192 (9) [M^++2], 191 (100) [M^++1], 173 (12) [$(M^++1)-H_2O$], 145 (61, [$(M^++1)-C_2H_5O$], 130 (4), 103 (2), 85 (6), 73 (2). Anal. Calcd for $C_8H_{14}O_5$ (190.20): C, 50.52; H, 7.42, found: C, 50.49; H, 7.35.

Röntgen crystal structure determination of **22b**. Single crystals were obtained by recrystallization from a *n*-heptane/CH_2Cl_2 mixture (10:1). A single crystal (colorless, transparent parallelepiped with dimensions $0.18\times0.35\times0.70$ mm^3) was measured on a SIEMENS SMART diffractometer at a temperature of about −130 °C. The substance ($C_8H_{14}O_5$ $M_r=190.19$) crystallized in the orthorhombic space group $P2_12_12_1$, $a=5.3014$ (6) Å, $b=7.0086$ (11) Å, $c=24.599$ (3) Å, $V=914.0$ (2) $Å^3$, $Z=4$, $\rho_{calcd}=1.382$ g/cm^3. Repeatedly measured reflections remained stable. A numerical absorption correction using six indexed crystal faces gave a transmission factor between 0.943 and 0.980. Equivalent reflections were averaged. Friedel opposites were not averaged. $R(I)_{int}=0.025$. The structure was determined by direct methods using program SHELXS. The H atoms were taken from a difference Fourier synthesis and were refined with isotropic thermal parameters. The structure was refined on F^2 values using program SHELXL-97. The final difference density was between −0.17 and +0.31 $e/Å^{-3}$. Crystallographic data (excluding structure factors) have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-248428. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: +44 1223 336 033; e-mail: deposit@ccdc.cam.ac.uk).

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References and notes

1. Yoshikawa, M.; Yamaguchi, S.; Kunimi, K.; Matsuda, H.; Kuno, Y.; Yamahara, J.; Murakami, N. *Chem. Pharm. Bull.* **1994**, *42*, 1226–1230.
2. Ovenden, S. P. B.; Capon, R. J. *J. Nat. Prod.* **1999**, *62*, 1246–1249.
3. Morimoto, S.; Nomura, H.; Ishiguro, T.; Fugono, T.; Maeda, K. *J. Med. Chem.* **1972**, *15*, 1105–1108.
4. Morimoto, S.; Nomura, H.; Fugono, T.; Azuma, T.; Minami, I.; Hori, M.; Masuda, T. *J. Med. Chem.* **1972**, *15*, 1108–1111.
5. Minami, I.; Akimoto, H.; Kondo, M.; Nomura, H. *Chem. Pharm. Bull.* **1983**, *42*, 482–489.
6. Magnin, D. R.; Biller, S. A.; Chen, Y.; Dickson, J. K.; Fryszman, O. M.; Lawrence, R. M.; Logan, J. V. H.; Sieber-McMaster, E. S.; Sulsky, R. B.; Traeger, S. C.; Hsieh, D. C.; Lan, S.; Rinehart, J. K.; Harrity, T. W.; Jolibois, K. G.; Kunselmann, L. K.; Rich, L. C.; Slusarchyk, D. A.; Ciosek, C. P., Jr. *J. Med. Chem.* **1996**, *39*, 657–660.
7. Dickson, J. K.; Biller, S. A.; Magnin, D. R.; Petrillo, E. W., Jr.; Hillyer, J. W.; Hsieh, D. C.; Lan, S.; Rinehart, J. K.; Gregg, R. E.; Harrity, T. W.; Jolibois, K. G.; Kalinoski, S. S.; Kunselmann, L. K.; Mookhtiar, K. A.; Ciosek, C. P., Jr. *J. Med. Chem.* **1996**, *39*, 661–664.
8. Evans, E. B.; Mabbott, E. E.; Turner, E. E. *J. Chem. Soc.* **1927**, 1159–1168.
9. Corey, E. J.; Cimprich, K. A. *Tetrahedron Lett.* **1992**, *33*, 4099–4102.
10. Lawrence, R. M.; Biller, S. A.; Dickson, J. K.; Logan, J. V. H.; Mignin, D. R.; Sulsky, R. B.; DiMarco, J. D.; Gougoutas, J. Z.; Beyer, B. D.; Taylor, S. C.; Lan, S.; Ciosek, C. P.; Harrity, T. W.; Jolibois, K. G.; Kunselman, L. K.; Slusarchyk, D. A. *J. Am. Chem. Soc.* **1996**, *118*, 11668–11669.
11. Nkunya, M. H. H.; Zwanenburg, B. *Recl. Trav. Chim. Pays-Bas* **1983**, *102*, 461–465.
12. Enders, D.; Vignola, N.; Berner, O. M.; Bats, J. W. *Angew. Chem.* **2002**, *114*, 116–119. Enders, D.; Vignola, N.; Berner, O. M.; Bats, J. W. *Angew. Chem. Int. Ed.* **2002**, *41*, 109–111.
13. Enders, D.; Berner, O. M.; Vignola, N.; Bats, J. W. *Chem. Commun.* **2001**, 2498–2499.
14. Enders, D.; Berner, O. M.; Vignola, N.; Harnying, W. *Synthesis* **2002**, 1945–1952.
15. Enders, D.; Vignola, N.; Harnying, W. *Synlett* **2002**, 1727–1729.
16. Enders, D.; Harnying, W.; Vignola, N. *Eur. J. Org. Chem.* **2003**, 3939–3947.
17. Enders, D.; Thomas, C. R.; Raabe, G.; Runsink, J. *Helv. Chim. Acta* **1998**, *81*, 1329–1336.
18. Enders, D.; Thomas, C. R.; Vignola, N.; Raabe, G. *Helv. Chim. Acta* **2002**, *85*, 3657–3677.
19. Bernardi, A.; Cardani, S.; Pilati, T.; Poli, G.; Scolastico, C.; Villa, R. *J. Org. Chem.* **1988**, *53*, 1600–1607.
20. Whitesell, J. K.; R, M.; Lawrence, R. M.; Huang-Hsing, C. *J. Org. Chem.* **1986**, *51*, 4779–4784.
21. Sowa, W.; Thomas, G. H. S. *Can. J. Chem.* **1966**, *44*, 836–837.
22. Otto, S.; Engberts, J. B. F. N.; Kwak, J. C. T. *J. Am. Chem. Soc.* **1998**, *120*, 9517–9525.
23. Abdellaoui, H.; Depreux, P.; Lesieur, D.; Pfeiffer, B.; Bontempelli, P. *Synth. Commun.* **1995**, *25*, 1303–1311.
24. Brundish, D.; Bull, A.; Donovan, V.; Fullerton, J. D.; Garman, S. M.; Hayler, J. F.; Janus, D.; Kane, P. D.; McDonell, M.; Smith, G. P.; Wakeford, R.; Walker, C. V.; Howarth, G.; Hoyle, W.; Allen, M. C.; Ambler, J.; Butler, K.; Talbot, M. D. *J. Med. Chem.* **1999**, *42*, 4584–4603.
25. Lipshutz, B. H.; Pollart, D.; Monforte, J.; Kotsuki, H. *Tetrahedron Lett.* **1985**, *26*, 705–708.
26. Enders, D.; Harnying, W. *Arkivoc* **2004**, *2*, 181–188.
27. Enders, D.; Harnying, W.; Raabe, G. *Synthesis* **2004**, 590–594.
28. Enders, D.; Harnying, W. in press *Synthesis* **2004**, 2910–2918.