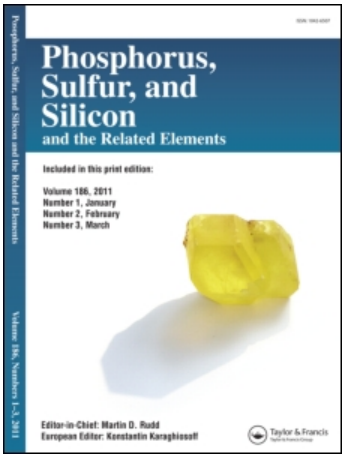

Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

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To cite this Article Mladenova, Margarita , Biserkova, Mariana and Kurtev, Bogdan(1989) 'STEREOCHEMISTRY OF THE ADDITION OF α-METALLATED *N,N*-DIALKYLSULFONAMIDES TO ALDEHYDES', Phosphorus, Sulfur, and Silicon and the Related Elements, 44: 3, 155 — 165
To link to this Article: DOI: 10.1080/10426508908040605
URL: http://dx.doi.org/10.1080/10426508908040605

Phosphorus, Sulfur, and Silicon, 1989, Vol. 44, pp. 155–165
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STEREOCHEMISTRY OF THE ADDITION OF α-METALLATED *N,N*-DIALKYLSULFONAMIDES TO ALDEHYDES

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(Received October 18, 1988)

The stereochemistry of aldol reactions of $R^1CH(M)SO_2N(R)_2$ and aldehydes (R^2CHO) is studied under a wide variety of reaction conditions. Effects of temperature, solvent, counterion and the effect of nature and effective volume of substituents R^1 and R^2 are investigated. These factors do not influence markedly the stereoselectivity of the reaction, which ranges from zero to moderate. A plausible transition state structure for the formation of β-hydroxysulfonamides is discussed.

Key words: *N,N*-dialkylamides of 1-alkyl(aryl)-2-alkyl(aryl)-2-hydroxyethanesulfonic acid; α-metallated *N,N*-dialkylsulfonamides; aldol reaction; stereochemistry; configuration; transition state.

INTRODUCTION

Aldol reactions are among the most versatile tools in the formation of new C—C bonds. At the same time these reactions offer broad possibilities for introduction of various functional groups in 1,3-relationship with the hydroxyl functionality. For this reason we witness an impressive progress and permanent interest in further developments of these reactions.

In connection with our own continuing interest in this area, our attention has been attracted by the stereochemical aspects of sulfonamide carbanion additions to carbonyl compounds.

Amides of sulfonic acids have already been applied as CH-acids in additions to carbonyl compounds.[1-7] Most of the publications deal with the morpholide of α-chloromethanesulfonic acid.[2-5] To our knowledge, no systematic studies on the stereochemistry of the reaction have been carried out up to now. In this respect a study of the asymmetric induction in the addition of chiral amides of α-chloromethanesulfonic acid to aldehydes and ketones to form chlorohydrins and oxiranes deserves special notice.[7]

We report here our studies on the addition of carbanions of *N,N*-dialkylsulfonamides to aldehydes and the influence of different reaction factors on the product stereochemistry.

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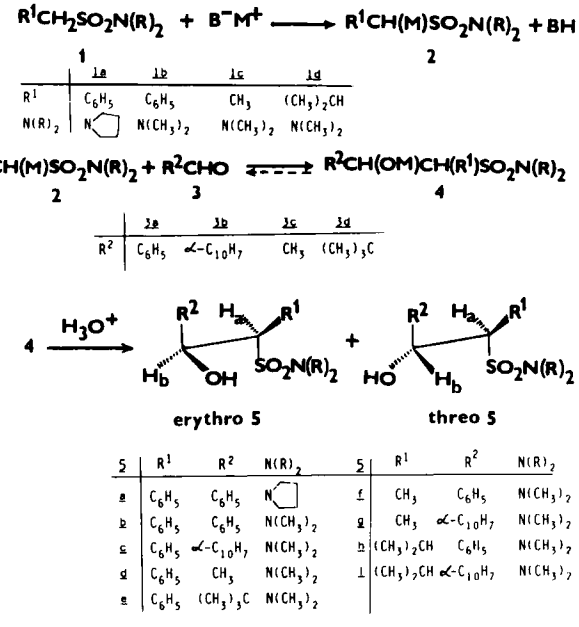
RESULTS AND DISCUSSION

We studied the interaction of metal (mostly lithium) derivatives of *N,N*-dialkylamides ($N(R)_2{=}N(CH_3)_2$ with the exception of **1a** where $N(R)_2{=}N$⬠) of phenylmethanesulfonic, ethanesulfonic and 2-methylpropanesulfonic acids with aldehydes—two aromatic (benzaldehyde **3a** and α-naphthaldehyde **3b**) and two aliphatic ones (acetaldehyde **3c** and pivalaldehyde **3d**) of different nature and steric requirements (Scheme 1). The reaction proceeds smoothly and in high yields to give, after hydrolysis of the salts **4**, diastereoisomeric mixtures of the corresponding β-hydroxysulfonamides **5**.



SCHEME 1

All diastereoisomers are obtained analytically and stereochemically pure by fractional recrystallization or a combination of preparative thin-layer chromatography and recrystallization. Their structures are confirmed by microanalytical and spectroscopic data.

Chemical ionization mass spectra show $(M+H)^+$ peaks and characteristic fragmentations. At the CI–MS conditions, an interesting rearrangement occurs by loss of H_2O and SO_2, yielding the corresponding substituted enamines. The nature of the substituent R^1 influences strongly the intensity of the peaks attributed to $[R^2CH{=}C(R^1)\overset{H}{N}(R)_2]^+$.

The TLC behaviour of studied diastereoisomers on silica gel (with the exception of **5d** for which no suitable conditions for chromatographic separation were found) is characterized by the retention the retention order R_f(erythro) > R_f(threo).

IR spectra (1% chloroform solution) show bands for associated O–H in the region 3500–3580 cm^{-1}, intense bands in the 1315–1328 cm^{-1} and 1136–

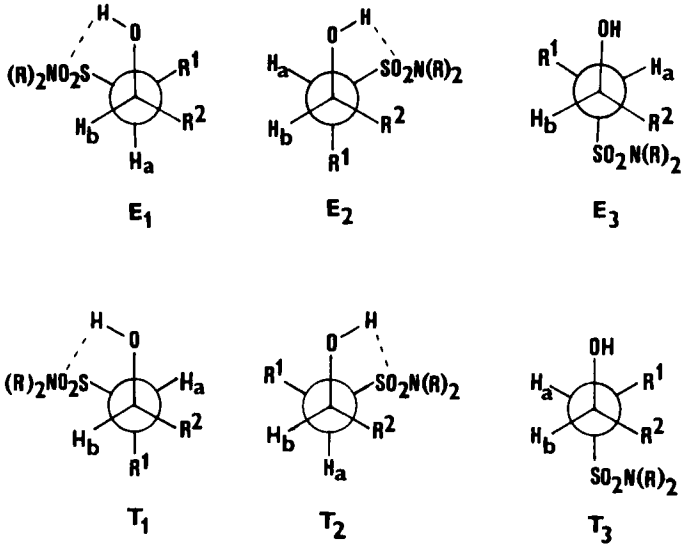


FIGURE 1 Possible staggered conformations of erythro (E) and threo (T) β-hydroxysulfonamides **5**.

1142 cm^{-1} intervals for symmetric and asymmetric SO_2– stretching vibrations and less intense bands in the region 960–1014 cm^{-1} for the S–N-stretching vibrations, characteristic for sulfonamides.[8]

The relative configurations and energetically favoured conformations are determined on the basis of ^{1}H-NMR[9] and IR spectral data and analysis of the possible staggered conformations (Figure 1).

The $J_{H_aH_b}$ coupling constants of vicinal methine protons are shown in Table I. Large differences are observed in the values of these constants for the two diastereoisomers—in the range from 0.9 to 2.6 Hz for the one and from 6.7 to 9.6 Hz (the latter are below 8.9 Hz only for **5h** and **5i**) for the other isomer. Thus, a single strongly populated conformation is indicated for each diastereoisomer.

TABLE I

Configurations and coupling constants (^{1}H-NMR, $CDCl_3$, J in Hz) of compounds **5**

Compound 5	Erythro, $J_{H_aH_b}$	Threo, $J_{H_aH_b}$
5a	2.4	9.6
5b	2.4	9.6
5c	1.6	9.4
5d	2.6	9.0
5e	1.3*	8.9*
5f	1.4	9.1
5g	0.9	9.0
5h	1.9	6.7
5i	1.3	7.2

* C_6D_6 is used as solvent in this case because of the equal chemical shifts for H_a and H_b observed for the erythro isomer in $CDCl_3$.

The IR spectra of dilute (3×10^{-3} mol/l) CCl_4 solutions of five pairs of diastereoisomers in the region 3400–3700 cm^{-1} (Figure 2) show in all cases a strong predominance of intramolecular associated over free O–H bands. Thus, conformations in agreement with observed IR and ^{1}H-NMR spectra are the E_1 and E_2 (Figure 1) for erythro isomer. The favoured erythro conformation should possess small $J_{H_aH_b}$ and synclinal methine protons. Sterical reasons give a slight preference to E_1. For the threo isomer conformation T_1, with high $J_{H_aH_b}$, antiperiplanar methine protons, is favoured.[12] The increase of the effective size of R^1 in threo isomers gives rise to enhanced absorption of the free O–H in the IR. This indicates enhanced population of the conformer T_3, in agreement with the lower $J_{H_aH_b}$ in **5h** and **5i**, although the T_1 conformer is still favoured. Both erythro and threo compounds prefer conformations with synclinal hydroxy- and sulfonamide groups, disregarding the size of R^1 and R^2.[13]

A series of preliminary experiments was carried out with the lithiated pyrrolidide of phenylmethanesulfonic acid **1a** and benzaldehyde. The two problems to solve in these experiments are i) the optimum conditions to follow the stereochemical course of the reaction under kinetic control, and ii) the possibility to direct product stereochemistry changing kinetic to thermodynamic control. Under constant conditions (THF, concentration 0.4 mol/l, −20°C, 3 min.) of strict kinetic control and identical product stereochemistry the reaction yield is higher with metallating agent lithium diisopropylamide (LDA) than with *n*-butyllithium. The former is more ionic (N-Li vs. C-Li) and, therefore, metallates **1a** better to produce higher yield of **5a**. To confirm this suggestion, we add 20% HMPT to obtain quantitative yield also with *n*-BuLi. The rest of experiments thereafter was carried out with LDA, unless specially noted otherwise.

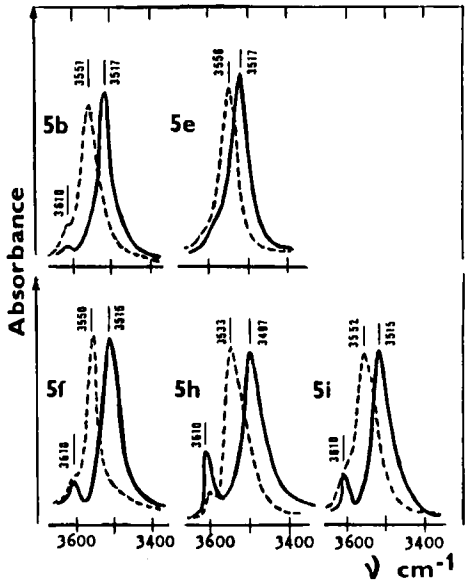


FIGURE 2 IR spectra of dilute solutions (CCl_4, 3×10^{-3} mol/l, KBr, $d = 5$ mm) of erythro **5** (dashed line) and threo **5** (full line).

Under kinetic control, the reaction is moderately stereoselective (36:65) in favour of the threo isomer. If interference of thermodynamic control is possible, e.g. at higher temperature, more polar solvent or longer reaction time, the product ratio approaches the thermodynamically controlled value erythro:threo = 40:60.

The relatively low kinetic stereoselectivity of the reaction as well as the similar thermodynamic stability of aldolates **4a** preclude the use of changes of reaction control as a means to direct it to the predominant production of any stereoisomer. Attempts were made to change the ratio erythro:threo = 40:60 (under thermodynamic control in homogeneous medium) by addition of dry pentane to reduce the solubility of aldolates **4a** and, presumably, introduce conditions for the so called "second order" asymmetric transformation redirecting the equilibrium to the less soluble diastereoisomer. We observe some enhancement of the yield of threo isomer, which is however insufficient to allow for controllable stereoselectivity.

Stereochemical studies of reaction mechanisms stress the problem of reaction control as the principal one. Being aware of the reversibility of aldol reactions, increased by lower basicity of nucleophile (i.e., where $R^1 = C_6H_5$, in the case of our reaction, the erythro–threo equilibrium should be reached more rapidly compared to $R^1 = CH_3$ or $(CH_3)_2CH$), larger substituent size, larger electropositivity of counter-ion, larger solvent polarity, reaction time and temperature and lower concentrations, we selected specific reaction conditions in each case to ensure kinetic control. A general example of experiment to prove kinetic control can be given with the addition of lithiated **1b** to **3a** in THF at −30°C to give **5b**. Pure erythro-**5b** (the minor isomer at kinetic and thermodynamic conditions) is metallated at −30°C by equimolar amount of LDA in THF. The solution has to be diluted twice to preserve homogeneity. After a 10 min. stirring, the mixture is hydrolyzed and worked up as usual to regenerate quantitatively the unchanged erythro **5b**.

Experiments with **1a** and **3a** show that, under kinetic control, reaction temperature and solvent do not influence product stereochemistry. The diastereoisomeric ratio erythro:threo = 35:65 remains constant within the precision of the NMR determination. Similarly, the reaction of lithiated **1b** and acetaldehyde is insensitive to changes of temperature and solvent. The diastereoisomeric ratio erythro:threo = 52:48 is constant at −90°, −60° and −30°C. The observed reversal of stereochemistry at 20°C, erythro:threo = 40:60, is shown to be the result of thermodynamic control, as indicated by the reaction reversibility. Reaction temperature and solvent, however, do change the product stereochemistry under kinetic control in the cases of $R^1 = CH_3$ instead of $R^1 = C_6H_5$. As shown in Table II, the amount of erythro isomer increases in more polar medium (entries 1–3) and at lower reaction temperature (entries 2, 4–6).

Table III summarizes the experiments showing the role of counterions on the reaction of **1b** and **1c** with benzaldehyde in THF. Inspection of entries 1, 2, 4 and 5 shows that Mg-reagents (metallating agent: *i*-PrMgCl) give lower yields than Li-reagents without changing the ratio of diastereoisomers. Sodium reagents (metallating agent: naphthalene-sodium) slightly change the erythro:threo ratio for $R^1 = CH_3$, but significantly favour the threo isomer for $R^1 = C_6H_5$.

TABLE II

Addition of $CH_3CH(Li)SO_2N(CH_3)_2$ to benzaldehyde (concentration 0.4 mol/l)

Entry	Reaction conditions Solvent	Tempera-ture, °C	time (min)	Yield %	Erythro:threo
1	ether	−20	10	80	50:50
2	THF	−20	10	83	56:44
3	THF + 20%HMPT	−20	7	97	66:34
4	THF	−90	60	62	75:25
5	THF	−30	10	78	60:40
6	THF	+65	2	83	59:41

Further variations involve substituents R^1 and R^2 at prochiral carbon atoms to be connected by the newly formed bond. Table IV summarizes the effects of these changes on kinetic stereochemistry. For constant R^2, e.g. $R^2 = C_6H_5$, entries 1, 3 and 7, the erythro:threo ratio is inverted from 60:40 for $R^1 = CH_3$ through 48:52 for $R^1 = (CH_3)_2CH$ to 34:66 for $R^1 = C_6H_5$. Larger R^2, e.g. α-$C_{10}H_7$, preserve this trend: the erythro:threo ratio in cases 2, 4, 8 is reduced from 50:50 for $R^1 = CH_3$ to 28:72 for $R^1 = C_6H_5$. The comparison of odd- with even-numbered entries shows that larger R^2 in all cases favour threo product.

Substituent effects on product stereochemistry in aldol reactions and their rationalizations by various transition state models have been studied in a number of works, see e.g. References 15–17. The results of Table IV can be explained satisfactorily by the assumption of a transition state similar to the one suggested by Dubois *et al.*[17]

The structure of lithiated sulfonamides **2** is unknown, but α-metallated sulfones are the subject of a number of works and the origins of the stabilization of configuration of chiral carbanions by the adjacent SO_2 fragment are still being discussed. Carbanions of this type are currently considered planar or almost planar with the p-orbital of the anion staggered between the sulfonyl oxygens. This statement emerges from stereochemical,[18] spectroscopic[19] and acidity[20] studies. Carbanion stabilization is considered the result of d − p π-conjugation. However, a recent theoretical study of Bors and Streitwieser[21] has been interpreted in terms of electrostatic carbanion stabilization instead of d − p π-conjugation. The "naked", planar methanesulfonylmethyl anion has been

TABLE III

Addition of $R^1CH(M)SO_2N(CH_3)_2$ to benzaldehyde in THF, conc. 0.4 mol/l

Entry	R^1	M	Reaction conditions Tempera-ture, °C	time (min)	Yield %	Erythro:threo
1	CH_3	Mg	−20	30	67	58:42
2	CH_3	Li	−20	10	83	56:44
3	CH_3	Na	−30	3	52	60:40
4	C_6H_5	Mg	−20	10	62	35:65
5	C_6H_5	Li	−20	3	77	34:66
6	C_6H_5	Na	−90	3	40	25:75

TABLE IV

Addition of $R^1CH(Li)SO_2N(CH_3)_2$ to R^2CHO in THF at −30°C, conc. 0.4 mol/l

Entry	R^1	R^2	time (min)	Yield %	Erythro : threo
1	CH_3	C_6H_5	10	88	60:40
2	CH_3	α-$C_{10}H_7$	10	78	50:50
3	$(CH_3)_2CH$	C_6H_5	10	74	48:52
4	$(CH_3)_2CH$	α-$C_{10}H_7$	5	73	35:65
5	C_6H_5	CH_3	10	82	52:48
6	C_6H_5	$(CH_3)_3C$	3	72	45:55
7	C_6H_5	C_6H_5	5	83	34:66
8	C_6H_5	α-$C_{10}H_7$	3	86	28:72

found most stable in a conformation with the p-electron pair staggered between the two sulfonyl oxygens. The lithium derivative, however, has been calculated to prefer pyramidal structure with Li^+ associated with the α-carbon and only one sulfonyl oxygen.

On the basis of these data and the transition state model of Dubois *et al.*[17] we suggest a transition state for the studied reaction as given in Figure 3. With $R^1 = CH_3$, the steric interaction $R^1 \leftrightarrow R^2$ is small enough to allow gauche-conformation around the newly forming C—C bond to give erythro product with slight preference. Bulkier R^1, e.g. $(CH_3)_2CH$, with stronger $R^1 \leftrightarrow R^2$ repulsion,

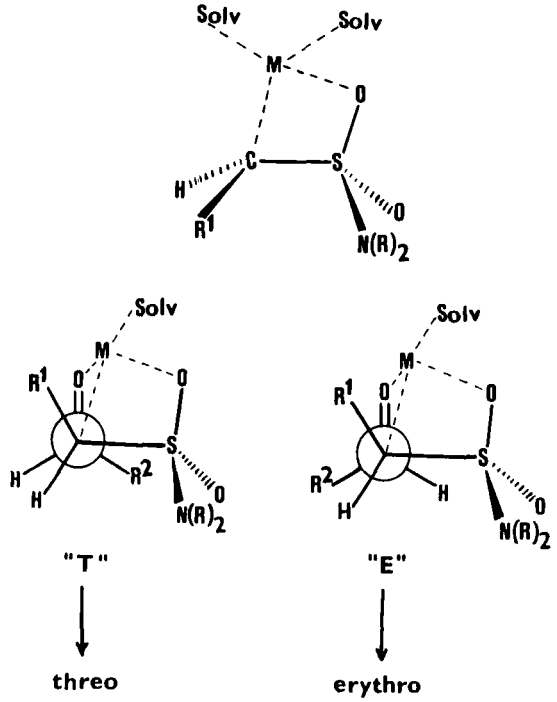


FIGURE 3 Hypothetic structures of reagents **2** and of transition states leading to erythro **5** and threo **5**.

give preference to antiperiplanar conformation around the newly forming C–C bond and to route "T" producing the threo product. Similar considerations hold for the change of R^2, e.g. benzaldehyde with α-naphthaldehyde or acetaldehyde with pivalaldehyde. In both cases the steric interaction $R^1 \leftrightarrow R^2$ should give preference to route "T", i.e. bulkier R^2 favour threo products. Most important for the product stereochemistry in the case of uniformly substituted reactants, e.g. R^1 = alkyl and R^2 = aryl, is the steric requirement of both R^1 and R^2. Entries 1 and 4 (Table IV) indicate a change of erythro:threo ratio from 60:40 to 35:65.

Interpretations as used by Dubois *et al.*[17] in terms of reduced or enhanced steric effects due to conformational changes about the newly forming C—C bond are applicable to counterion and solvent effects as well. For example, with $R^1 = CH_3$, the electron donor CH_3 reduce the effective charge on Li, hence the stability of cationic bridge. This gives rise to a larger angle between the interacting C=O and C—S bonds and slight preference to route "E". For $R^1 = C_6H_5$, in turn, Li bears more positive charge and route "T" becomes the favoured one. Similarly, the replacement of Li for Na (entries 5 and 6, Table III) favours the threo product. Addition of HMPT (entries 2, 3; Table II) and stronger solvatation of Li reduces the stability of the cationic bridge and, hence, favour the erythro product.

The low sensitivity of product stereochemistry with respect to the studied factors and the lower stereoselectivity with respect to other aldol reactions proceeding via similar transition states[22] can be attributed to weaker steric interactions in the transition state of the studied reaction. These are the result of favourable orientation of the $N(R)_2$ group, longer C—S than C=C bond of enolates and pyramidal structure of the carbanion. All these factors reduce the steric interactions of R^1 and R^2 as compared to the planar enolates in other aldol reactions.

EXPERIMENTAL

All reactions were carried out under dry argon. Tetrahydrofuran and ether were freshly distilled over $LiAlH_4$ prior to use. HMPT was distilled over CaH_2 and stored over molecular sieves. The aldehydes were distilled prior to use. The sulfonamides **1a–c** were prepared according to Reference 23; **1d** was prepared by alkylation of the lithium derivative of dimethylamide of methanesulfonic acid with iso-propylbromide in THF/HMPT solution at room temperature.

The ^{1}H-NMR spectra were recorded on a Bruker WM spectrometer at 250 MHz with TMS as internal standard (see Table V); IR spectra were measured on a Bruker IFS 113 V Fourier spectrometer; Mass spectra were obtained on a JEOL IMS D-300 spectrometer in CI conditions with isobutane as reactant gas (10^{-5} Torr, chamber temperature 150°C). Qualitative TLC investigations were carried out on silica gel 60 F_{254} (aluminium sheets "Merck"). Preparative TLC was run on BDH silica gel (13% $CaSO_4$); eluent ether/heptane 2:1 for **5a–e** and 1:1 with two fold elution for **5f–i**.

Synthesis of N,N-dialkylamides of 1-alkyl(aryl)-2-alkyl (aryl)-2-hydroxyethanesulfonic acids **5**. General procedure:

(a) Preparation of metallic reagents **2**.

M = Li: 3 mmol sulfonamide **1**, dissolved in appropriate solvent, was added dropwise at −20°C to 3.3 mmol LDA, prepared from 3.3 mmol *n*-BuLi (1.6 N in hexane, Merck-Schuchardt) and 3.3 mmol diisopropylamine. The mixture was stirred for 1 hr at −20°C.

M = Mg: To 3.3 mmol titrated (by 1 N sec-BuOH in abs. xylene, indicator 1,10-phenanthroline[24]) solution of i-PrMgCl in THF was added dropwise 3 mmol of **1** and the mixture was stirred 1 hr at ambient temperature for **1b**, and at 35–40°C for **1c**.

TABLE V

Constants and ^{1}H-NMR data of compounds **5**

Compound	m.p.(°C)[a] ($CHCl_3$/ heptane)	Molecular formula[b]	^{1}H-NMR ($CDCl_3$, TMS), δ(ppm), J(Hz)
5a, threo	130–131	$C_{18}H_{21}NO_3S$[c]	1.65 (m, 4H); 2.83 (m, 2H); 3.22 (m, 2H); 4.43 (d, 1H$_a$, J = 9.6); 4.48 (d, 1H, J = 1.2); 5.54 (dd, 1H$_b$, J = 9.6 and 1.2); 7.10–7.26 (m, 10H).
5a, erythro	165–166	(331.4)	1.61 (m, 4H); 2.93 (m, 2H); 3.19 (m, 2H); 3.58 (d, 1H, J = 1.9); 4.29 (d, 1H$_a$, J = 2.4); 5.82 (dd, 1H$_b$, J = 2.4 and 1.9); 7.08–7.41 (m, 10H).
5b, threo	109–111	$C_{16}H_{19}NO_3S$[c]	2.56 (s, 6H); 4.35 (s, 1H); 4.39 (d, 1H$_a$, J = 9.6); 5.52 (d, 1H$_b$, J = 9.6); 7.10–7.26 (m, 10H).
5b, erythro	148–149	(305.4)	2.55 (s, 6H); 3.49 (d, 1H, J = 2.1); 4.25 (d, 1H$_a$, J = 2.4); 5.82 (dd, 1H$_b$, J = 2.4 and 2.1); 7.08–7.41 (m, 10H).
5c, threo	102–103	$C_{20}H_{21}NO_3S$	2.58 (s, 6H); 4.36 (d, 1H, J = 1.7); 4.92 (d, 1H$_a$, J = 9.4); 6.25 (dd, 1H$_b$, J = 9.4 and 1.7); 7.02–7.04 (m, 5H); 7.17–7.73 (m, 6H); 8.44 (d, 1H).
5c, erythro	179–180	(355.4)	2.56 (s, 6H); 3.63 (brs, 1H); 4.48 (d, 1H$_a$, J = 1.6); 6.68 (d, 1H$_b$, J = 1.6); 7.11–7.22 (m, 5H); 7.22–8.15 (m, 7H).
5d, threo	105–106	$C_{11}H_{17}NO_3S$	1.01 (d, 3H, J = 6.2); 2.55 (s, 6H); 3.99 (brs, 1H); 4.08 (d, 1H$_a$, J = 9.0); 4.64 (m, 1H$_b$); 7.38 (s, 5H).
5d, erythro	120–122	(243.3)	1.18 (d, 3H, J = 6.4); 2.55 (s, 6H); 3.02 (d, 1H, J = 1.9); 4.05 (d, 1H$_a$, J = 2.6); 4.80 (m, 1H$_b$); 7.32–7.64 (m, 5H).
5e, threo	95–97	$C_{14}H_{23}NO_3S$	[d]0.79 (s, 9H); 2.48 (s, 6H); 3.74 (d, 1H, J = 4); 4.18 (dd, 1H$_b$, J = 9.1 and 4); 4.32 (d, 1H$_a$, J = 9.1); 7.34–7.56 (m, 5H).
5e, erythro	108.5–109	(285.4)	[d]0.80 (s, 9H); 2.56 (s, 6H); 3.27 (s, 1H); 4.34 (s, 2H); 7.30–7.80 (m, 5H).
5f, threo	92–93	$C_{11}H_{17}NO_3S$	0.96 (d, 3H, J = 7.2); 2.98 (s, 6H); 3.31 (dq, 1H$_a$, J = 9.1 and 7.2); 4.20 (d, 1H, J = 1.3); 4.91 (dd, 1H$_b$, J = 9.1 and 1.3); 7.32–7.38 (m, 5H).
5f, erythro	oil	(243.2)	1.21 (d, 3H, J = 7.2); 3.0 (s, 6H); 3.24 (s, 1H); 3.26 (dq, 1H$_a$, J = 7.2 and 1.4); 5.49 (d, 1H$_b$, J = 1.4); 7.26–7.38 (m, 5H).
5g, threo	128–129.5	$C_{15}H_{19}NO_3S$	0.88 (d, 3H, J = 7.1); 3.0 (s, 6H); 3.7 (dq, 1H$_a$, J = 7.1 and 9.0); 4.23 (d, 1H$_b$, J = 9.0); 7.5–7.9 (m, 6H); 8.3 (d, 1H).
5g, erythro	97–99	(293.4)	1.19 (d, 3H, J = 7.0); 3.07 (s, 6H); 3.33 (d, 1H, J = 1.6); 3.55 (dq, 1H$_a$, J = 7.0 and 0.9); 6.32 (brs, 1H$_b$); 7.40–8.03 (m, 7H).
5h, threo	70–71	$C_{13}H_{21}NO_3S$	0.99 (d, 3H, J = 7.1); 1.19 (d, 3H, J = 7.0); 2.20 (m, 1H); 2.68 (s, 6H); 3.34 (dd, 1H$_a$, J = 6.7 and 2.4); 3.38 (d, 1H, J = 5); 5.13 (dd, 1H$_b$, J = 6.7 and 5); 7.26–7.39 (m, 5H).

Constants and ^{1}H-NMR data of compounds **5**

Compound	m.p.(°C)[a] ($CHCl_3$/ heptane)	Molecular formula[b]	^{1}H-NMR ($CDCl_3$, TMS), δ(ppm), J(Hz)
5h, erythro	77–79	(271.4)	1.05 (d, 3H, $J = 7.2$); 1.23 (d, 3H, $J = 7.2$); 2.20 (m, 1H); 2.99 (s, 6H); 3.18 (d, $1H_a$, $J = 1.9$); 3.64 (d, 1H, $J = 1.85$); 5.37 ("t", $1H_b$, $J = 1.9$); 7.26–7.40 (m, 5H).
5i, threo	106–108	$C_{17}H_{23}NO_3S$	1.03 (d, 3H, $J = 7.0$); 1.18 (d, 3H, $J = 7.1$); 2.13 (m, 1H); 2.58 (s, 6H); 3.78 (dd, $1H_a$, $J = 7.2$ and 2.4); 3.93 (d, 1H, $J = 5.8$); 5.78 (dd, $1H_b$, $J = 7.2$ and 5.8); 7.45–7.96 (m, 6H); 8.15 (d, 1H).
5i, erythro	80–82	(321.4)	0.92 (d, 3H, $J = 7.0$); 1.27 (d, 3H, $J = 7.0$); 2.24 (m, 1H); 3.06 (s, 6H); 3.36 (dd, $1H_a$, $J = 1.45$ and 1.3); 3.80 (d, 1H, $J = 1.4$); 6.18 (brs, $1H_b$); 7.45–7.98 (m, 7H).

[a] M.p.s (uncorrected) are taken on a Böetius hot-stage microscope.
[b] Elemental analyses and $(M + H)^+$ peaks in the CI–MS are in good agreement with the theoretical values.
[c] According to ref.[1], the β-hydroxysulfonamides **5a** and **5b** are synthesized, but no data are available on their physical characteristics and configurations.
[d] In C_6D_6: **5e**, threo: 0.81 (s, 9H); 1.99 (s, 6H); 4.16 (d, $1H_a$, $J = 8.9$); 4.31 (dd, $1H_b$, $J = 8.9$ and 3.0); 4.51 (d, 1H, $J = 3.0$); 7.15 (s, 5H). **5e**, erythro: 0.79 (s, 9H); 2.06 (s, 6H); 3.51 (d, 1H, $J = 3.0$); 4.25 (d, $1H_a$, $J = 1.3$); 4.56 (dd, $1H_b$, $J = 1.3$ and 3.0); 6.95–7.15 (m, 5H).

M = Na: To 3.3 mmol naphthalene-sodium in THF[25] was added dropwise at −20°C 3 mmol **1** dissolved in THF. The mixture was stirred 30 min. at −20°C for $R^1 = C_6H_5$ or 1 hr at ambient temperature for $R^1 = CH_3$.

(b) Addition of **2** to **3**.

The total amount of solvent used for the preparation of **2** and the addition of aldehyde was adjusted to a reaction concentration of 0.4 mol/1-3 mmol of aldehyde, dissolved in the necessary amount of solvent, is added dropwise to the solution of **2**. After stirring for predetermined time at the chosen temperature (see Tables II, III and IV) the reaction mixture was acidified with 1:1 HCl, saturated with NaCl and extracted by 20 ml of ether or ethylacetate. The water phase was extracted additionally by 4 × 20 ml of the same solvent. The combined organic extract was washed to neutral reaction with saturated solution of NaCl and dried over $MgSO_4$. The solvent was evaporated in vacuo and the crude product dissolved in $CHCl_3$ to a calibrated volume. Aliquots of these solutions were subjected to NMR determination of the erythro : threo ratio and total yield. The yield was determined independently by preparative TLC (Tables II–IV). Pure diastereoisomers were separated by recrystallization or preparative TLC. Analytical data are given in Table V.

ACKNOWLEDGEMENT

We thank Miss M. Peykova for technical assistance.

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13. This observation, as well as the relatively moderate values of $\Delta\nu_{OH}$, 54 to 75 cm^{-1} for the erythro, and 93 to 113 cm^{-1} for the threo isomers, indicates that this conformation is favoured by the polar interaction of the hydroxyl oxygen and the positively charged sulfur of the sulfonyl group[11] rather than by hydrogen bonding. The same conformations are favoured also in β-hydroxysulfonamides[4,6] and β-hydroxysulfones.[10]
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