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Chiral β-Amino Sulfoxides. Synthesis, Configurational Assignment and Conformational Analysis Based on X-ray, CD, ^{1}H NMR and Theoretical Calculations

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Abstract: Enantiomerically pure *u* and *l* β-amino sulfoxides have been easily obtained from the respective homochiral α-amino alcohols. The absolute configuration at the created stereogenic centre was assigned by CD spectra and by X-ray analysis. Conformational analysis of the title compounds was carried out using quantum chemical energy-geometry optimization. Thus established conformational behavior explained the strongly configuration dependent NMR spectral patterns observed for the *u* and *l* diastereomers. © 1998 Elsevier Science Ltd. All rights reserved.

Keywords: amino sulfoxides; CD spectra; X–ray structure; conformational analysis

INTRODUCTION

Diastereomerically pure, optically active β-functionalized sulfoxides with two stereogenic centers constitute an interesting class of chiral building blocks for the construction of various important compounds.[1] The respective β-amino derivatives are rather scarcely used because they are usually prepared in a multistep synthesis from the other non racemic sulfoxides.[2] Recently, we have developed a facile method for the preparation of homochiral N-protected β-amino sulfoxides from the readily accessible optically active α-amino alcohols.[3] The efficient thioether oxidation made the title compounds easily available, however, a question arose about the absolute configuration at the created sulfur stereocenter. We observed substantial differences in the ^{1}H NMR spectral patterns for two diastereomers. Similar spectral regularities have already been observed for other diastereomeric β-functionalized sulfoxides with two stereogenic centers.[4-6] The spectral analogy suggested that diastereomers formed in our case as the major ones were *l* (e.g., *S*, S_S) and the minor ones were *u* (e.g., *S*, R_S).[3] This assignment has been confirmed by the tentative results of X-ray structural analysis.[7] The spectral regularities

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already found for the diastereomeric β-substituted sulfoxides have been interpreted in the terms of *n*(substituent)–*d*(sulfur) electron state interactions, stabilizing the respective conformations.[5] However, the same pattern has also been observed for the cases where intramolecular hydrogen bonding played the significant role in stabilization the responsible conformers.[6] In order to clarify the general validity of the ^{1}H NMR spectral pattern rule for assigning diastereomer configuration we undertook more detailed structural analysis of the synthesized compounds.

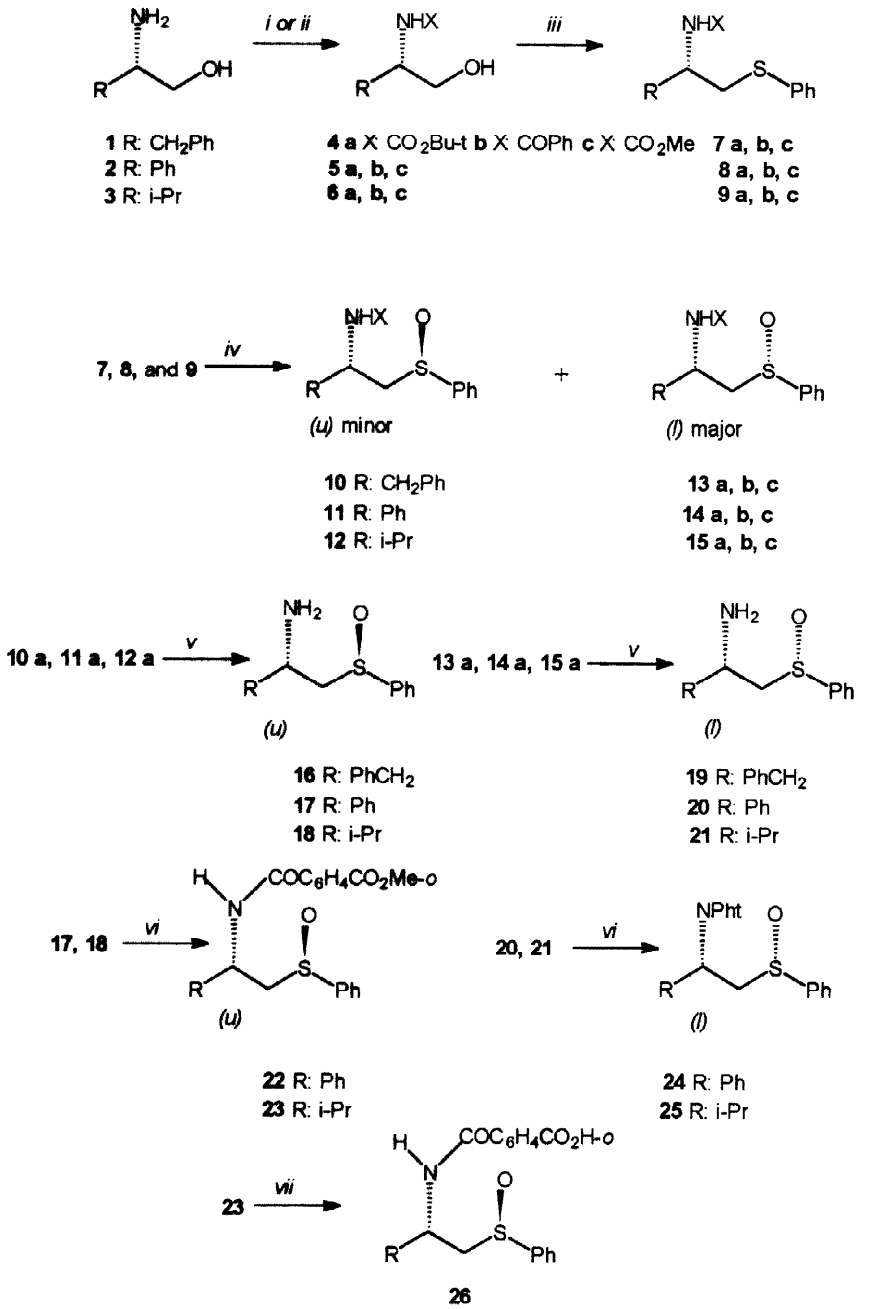
In this paper we report full synthetic procedures for the preparation of β-amino sulfoxides and their configurational assignment based on chiroptical properties and X–ray analysis. We also describe here the results of conformational analysis performed for N-protected and deprotected derivatives using quantum chemical computation. Thus obtained geometry of the dominating conformers were applied for the simulation of ^{1}H NMR spectra and the results were verified by a comparison with the recorded spectra.

RESULTS AND DISCUSSION

Synthesis

The synthetic routes used for the preparation of title compounds are presented in Scheme. For clarity, the transformations of derivatives with one configuration at the carbon atom only are depicted there. Both enantiomers of the easily available α-amino alcohols **1–3** were N-protected as the corresponding carbamates and benzamides **4–6**. We found that the highly selective N-acylation of **1–3** can be achieved by addition of chloroformate or benzoyl chloride to the methanolic solution of amino alcohol in the presence of solid potassium carbonate. Simple filtration and evaporation of solvent left the products suitable for the next reaction. N-Protected α-amino alcohols **4–6** were efficiently converted to the respective phenyl sulfides **7–9** using the Hata reagent[8] (diphenyl disulfide and tributylphosphine) under the modified conditions (sealed ampoule, 76 °C, 72 h). The two-phase oxidation of the sulfides with the buffered sodium hypochlorite, mediated by 2,2,6,6-tetramethylpiperydine-1-oxyl (TEMPO) and potassium bromide at 0 °C led exclusively to the diastereomeric sulfoxides **10–12** (less polar, *u*, minor) and **13–15** (more polar, *l*, major, up to 88 % d.e.).[3] The use of other oxidants (sodium periodate or m-chloroperbenzoic acid) gave both diastereomers in equal amounts. Recrystallisation or chromatography readily separated two diastereomers and their configurational assignment was based on the ^{1}H NMR spectral similarities, chiroptical properties and X–ray analysis (see below). N-*tert*-Butoxycarbonyl derivatives **10a–12a** and **13a–15a** underwent acidolysis[9] to give the corresponding free β-amino sulfoxides **16–18** and **19–21**, respectively, with conservation of configuration at the sulfoxide centre. When we attempted the transformation of free amino derivatives into the corresponding N-phthaloyl compounds[10] unexpectedly the reaction of *l* diastereomers **17** and **18** gave the respective *o*-methoxy-carbonylbenzamides **22** and **23** only. Under the same reaction conditions the diastereomers *u* (**20** and **21**) furnished the desired products **24** and **25** in high yield.

Scheme



i. R'COCl or R''OCOCl / K_2CO_3 in MeOH, r.t.; *ii*. $(Boc)_2O$, MeCN, r.t.; *iii*. $(PhS)_2$, Bu_3P in THF, 76°C; *iv*. NaOCl / KBr /TEMPO, CH_2Cl_2-H_2O, 0°C; *v*. CF_3COOH in CH_2Cl_2, r.t. ; *vi*. o-$MeO_2C(C_6H_4)COCl$, Et_3N, THF, 0°C; *vii*. KOH, MeOH, r.t.

Thus the reaction is diastereospecific, clearly discriminating opposite configurations at the sulfur atom. Saponification of the methyl ester **23** gave the optically pure acid **26**. It is noteworthy that the observed diastereospecific transformation opens a promising way for further synthetic applications.

CONFIGURATIONAL ASSIGNMENT

Chiroptical Properties

Starting from homochiral *R* sulfides derived from D-α-amino acids we obtained major diastereomeric sulfoxides exhibiting positive specific rotation (more polar), along with the minor sulfoxides of negative specific rotation. When *S* sulfides derived from L-α-amino acids were used, major diastereomeric sulfoxides were also more polar, but had negative specific rotation while the minor showed the positive one. It has been known for decades that a correlation exists between the absolute configuration of sulfoxides and their chiroptical properties.[11] It was expressed in terms of the sings and rotational strengths of the appropriate Cotton effects (CE). The phenylsulfinyl group is an inherently chiral chromophore and the sign of CE is determined solely by the chirality of the chromophore. Its primary UV band (usually at 235–255 nm, log ε ca. 3.6) is optically active with CE, $\Delta\varepsilon$ ca. 20. Also a shorter wavelength absorption band (ca. 220 nm, log ε ca. 4.1) demonstrates CE of similar amplitude but opposite sign. For the phenyl-sulfinyl group, a negative CE for the primary band corresponds to the (*S*)-configuration.[11,12] With all this in mind we measured the UV and CD spectra of our diastereomeric sulfoxides. The results are shown in Table 1 and Fig. 1–3.

Table 1. Characteristic features of the absorption bands: UV and CD spectra [a]

Compound	UV absorption properties	Circular dichroism		
	λ_{max} (10^{-3} ε)	λ ($\Delta\varepsilon$)	λ (0)	λ ($\Delta\varepsilon$)
(S,R_S)-**10 a**	216 (13.4), 246 (5.50)	215 (-30.7)	228	244 (21.0)
(R,S_S)-**12 b**	220 (13.7), 246 (8.60)	218 (25.3)	231	246 (-16.0)
(R,S_S)-**12 d**[b]	216 (7.72), 246 (5.36)	215 (28.2)	228	244 (-18.2)
(S,S_S)-**13 a**	216 (13.4), 246 (4.72)	215 (37.9)	230	246 (-18.7)
(R,R_S)-**13 b**	218 (18.2), 248 (7.29)	218 (-26.6)	232	248 (15.0)
(R,R_S)-**14 b**	218 (18.8), 250 (7.89)	218 (-32.5)	232	250 (18.8)
(R,R_S)-**15 b**	220 (15.0), 244 (8.44)	218 (-32.9)	235	251 (16.2)
(S,R_S)-**22**	222 (35.0), 240 (12.1), 288 (1.80)	218 (-28.7)	233	248 (12.5)
(S,R_S)-**23**	194 (37.8), 244 (7.86)	216 (-30.0)	230	247 (15.0)
(S,S_S)-**24**	222 (37.0), 240 (11.4), 298 (1.90)	217 (24.3)	226	247 (-17.4)
(S,S_S)-**25**	218 (96.1), 242 (29.5), 294 (0.50)	216 (34.3)	230	247 (-33.6)

[a] The spectra were recorded in acetonitrile at the concentration range of 10^{-4}-10^{-5}M. [b] Isobutyl carbamate N-protection was used (X: CO_2Bu-i).

In the absence of the other UV chromophore typical electronic and CD spectra were observed (Fig. 1), disregarding the presence of the stereogenic carbon atom. Even in the presence of the additional UV-absorbing group the CD curve for one diastereomeric sulfoxide was almost mirror image of the curve for the other (Fig. 2).

coupling CD spectrum.[13] However, also here CE for both UV-bands of inherently chiral phenylsulfinyl group dominated the CD spectrum. On the other hand, the phthalimido and phenyl chromophores located at the stereogenic carbon masked the presence of phenylsulfinyl function in the UV spectrum (Fig. 3). Two CE observed as shoulders on the main CD curve (208 nm, +14 and 230 nm, −12) may correspond to their absorption, but they are too weak to come from the exciton coupling. Results collected in Table 1 allow for unambiguous assignment of configuration at the created sulfur stereocentres. Thus the major diastereomers formed from sulfides were *l*, i.e., *S*, S_S or *R*, R_S, and the minor were *u*, i.e., *R*, S_S or *S*, R_S.

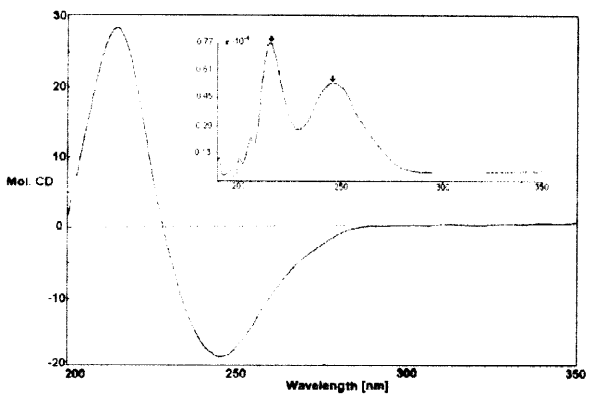


Fig. 1. UV and CD spectra of (R,S_S)–**12d**.

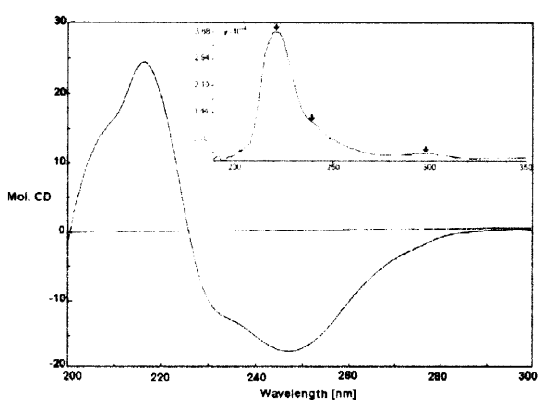


Fig. 3. UV and CD spectra of (S,S_S) –**24**.

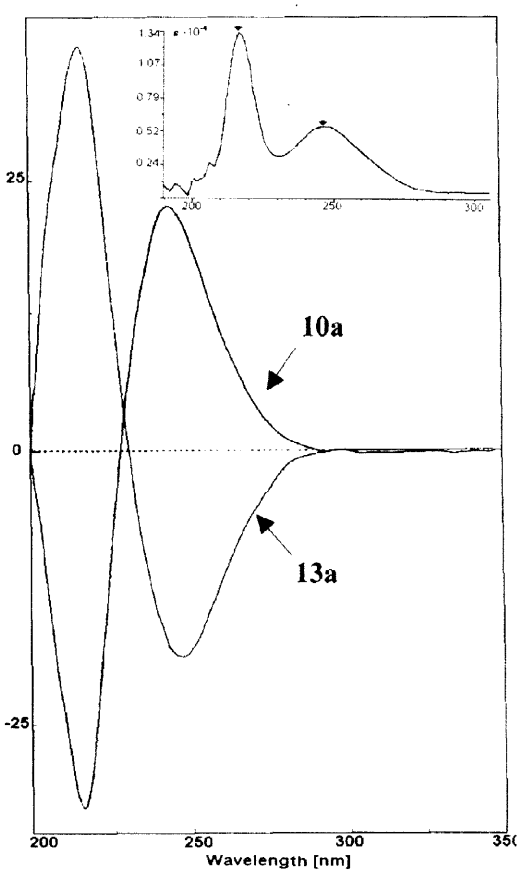


Fig. 2. UV and CD spectra of (S,R_S)–**10a** and (S,S_S)–**13a**.

X-ray structure

Single crystal of (R, S_S)–**12a**, orthorhombic was grown from the n-hexane-toluene mixture by slow solvent evaporation at room temperature. Space group was $P2_12_12_1$ with unit cell parameters: a = 9.067(1); b = 12.622(1); c = 16.134(1) in angstroms. The structure was solved using SHELXS–86 program[14] with R = 0.058, S = 1.097 for 823 reflections.

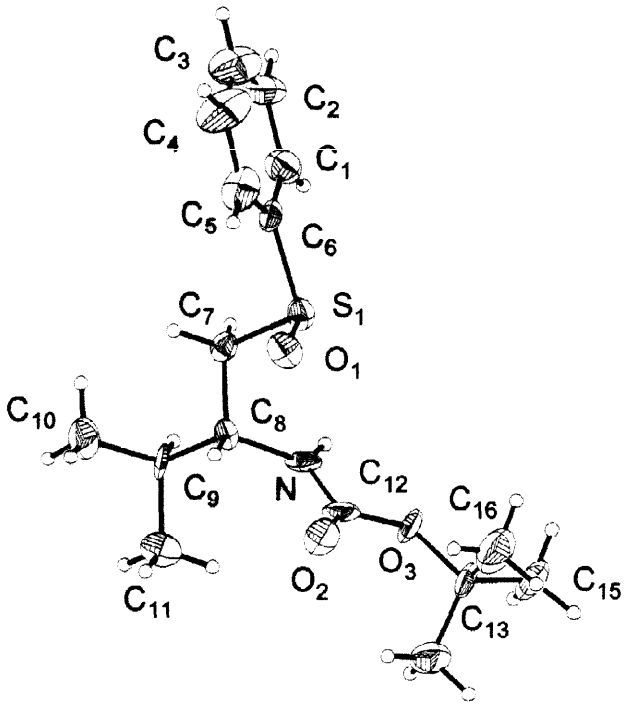


Fig. 4. ORTEP drawing of (R,S_S)–**12a**

Thus obtained molecular structure of **12a** is shown on Fig. 4. The absolute configurations at both stereogenic centers are indeed R, S_S .

CONFORMATIONAL ANALYSIS

Quantum-chemical calculations

Quantum-chemical calculations were performed in order to examine molecular geometry of the possibly most stable conformers for the respective diastereoisomers of all N-Boc protected β-amino sulfoxides. We calculated the ground-state geometry of all molecules using the semi-empirical MNDO method of Dewar et al[15] including the optional molecular mechanics correction for HCON linkages (keyword MMOK). Initially each of the structure was completely optimized (allowing all bond lengths and all bond angles to relax). The resulting molecular geometry obtained in such way was in agreement with that of the X-ray structure.

The intramolecular interatomic distance for N–H···O–S non-bonded atoms obtained from both, X–ray structure and theoretical calculations excluded intramolecular hydrogen bond. Moreover, the IR spectra of N-protected β-amino sulfoxides measured at different concentrations showed in all cases free N-H stretching vibration, thus eliminating any meaningful hydrogen bond interaction.

In the next step, the energy map as a function of two dihedral angles (α = [C–C–S–O] and β = [H–C–C–S]) of the molecules was calculated (e.g., see Fig. 5, 6, and 7). The resulting parameters for the respective most stable conformers are presented in Table 2. The calculations confirmed the possibility of the existence of

one (**10a**, **11a**, **12a**, **18**, and **21**), two (**14a**) or even three (**13a**, **15a**) low energy conformers for β-amino sulfoxides. However, it should also be stressed that the ground state energies of some conformers are similar.

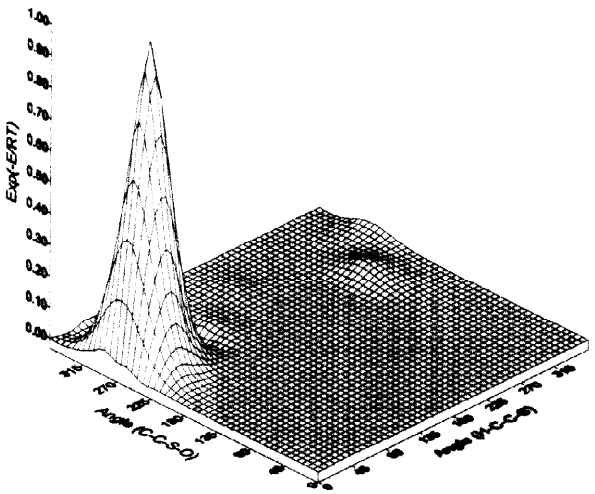


Fig. 5. Three dimensional plot of conformer's population for (R,S_S)-**12a**.

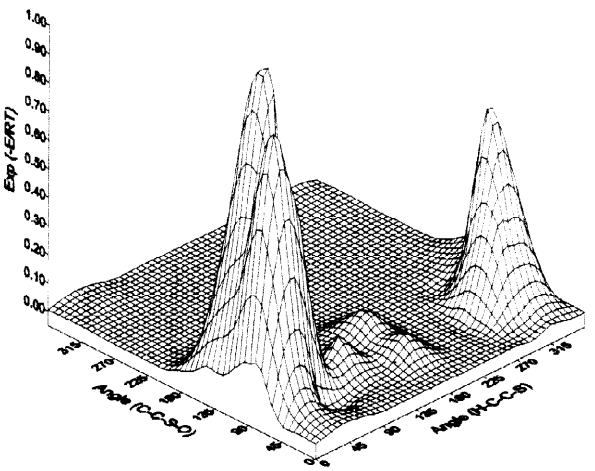


Fig. 6. Three dimensional plot of conformer's population for (R,R_S)-**15a**.

Table 2. The most stable conformers, their heats of formation (ΔH_f in kcal/mol), dipole moments (μ in D) and conformational populations (x_n).

Molecule/ conformation	α (deg)	β (deg)	ΔH_f (kcal/mol)	μ (D)	x_n
10a	270	60	-17.51	3.02	1.00
11a	273	56	-12.97	3.43	1.00
12a	270	45	-50.22	2.79	1.00
18	275	55	28.65	4.97	1.00
21	168	64	29.29	5.54	1.00
13a I	120	60	-16.10	6.58	0.27
13a II	63	303	-16.19	3.40	0.32
13a III	90	173	-16.34	4.92	0.41
				4.88*	
14a I	120	61	-12.08	6.97	0.42
14a II	87	300	-12.27	4.06	0.58
				5.28*	
15a I	120	60	-49.29	6.74	0.68
15a II	90	315	-48.76	4.31	0.28
15a III	120	173	-47.58	4.18	0.04
				5.96*	

*Averaged value

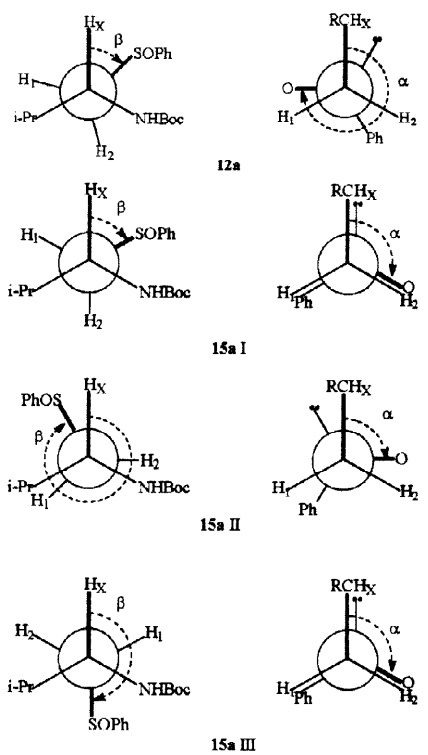


Fig. 7. The Newman projections of the lower energy conformers of **12a** and **15a**.

It is therefore possible that even small modifications of these energies (due to, e.g. solute–solvent interactions) may influence the relative abundance of these conformers, thus contributing to the NMR parameters of the whole molecules. Additionally, the dipole moments calculated theoretically (Table 2) are in agreement with the experimentally observed tendency, i.e. *u* isomers are less polar than the *l* ones.

NMR spectra

As it was already noted, we observed remarkable differences in ^{1}H NMR spectra (300 MHz, DMSO-d_6) for both diastereomers, namely the differences of chemical shifts for the diastereotopic methylene hydrogens PhS*(O)$CH_AH_BC^*H_X$ were ca. two times less for the major *l* isomer than for the minor *u* one. Also, the vicinal coupling constants $^3J_{AX}$ and $^3J_{BX}$ differed for both diastereomers, being respectively 8.3–9.6 Hz and 4.1–5.8 Hz for *l* and 11.0–12.9 Hz and 2.0–3.1 Hz for the *u* isomer (see: Table 3 and Experimental part). These different NMR patterns are parallel with the conformational behavior of both diastereomers. The vicinal coupling constants ^{3}J were calculated from eq. (1), where x_n and ^3J_n denote the population and the "pure" vicinal spin-spin coupling constants of the n-th conformer, respectively.

$$^3J = \Sigma\, x_n\, ^3J_n \qquad (1)$$

The evaluation of the ^3J_n has been carried out by means of the simple empirical Karplus-like equation (2).[16]

$$^3J_n = A\cos^2\phi_n + B\cos\phi_n + C. \qquad (2)$$

We obtained A, B, and C parameters from the least-squares fit (R^2, 0.99; SD, 0.676) of the experimental coupling constants for the compounds, which according to our calculations possess only one conformational minimum (**10a**, **11a**, **12a**, **18**, and **21**). The obtained values (in Hz) A = 7.42; B = –2.38; C = 2.39 are reasonable and agree well with the standard Karplus data.[16] The "pure" (eq. 2) and averaged according to eq.1 vicinal coupling constants are presented in Table 3.

Table 3. The comparison of calculated and experimental values of vicinal coupling constants (in Hz)

Molecule		$^3J_{BX}$	$^3J_{AX}$
10a	calc.	2.9	12.2
	exp.	2.7	11.5
11a	calc.	2.7	12.2
	exp.	3.1	12.5
12a	calc.	2.2	11.7
	exp.	2.0	12.4
13a I	calc.	3.1	12.2
13a II	calc.	12.1	2.6
13a III	calc.	3.6	2.9
	av. calc	6.1	7.5
	exp.	6.9	7.9

Molecule		$^3J_{BX}$	$^3J_{AX}$
14a I	calc.	3.0	12.2
14a II	calc.	12.2	3.0
	av. calc.	8.3	6.9
	exp.	9.0	5.8
15a I	calc.	12.2	3.0
15a II	calc.	2.2	11.7
15a III	calc.	3.8	2.8
	av. calc.	9.1	5.4
	exp.	9.6	4.1
18	calc.	2.6	12.1
	exp.	2.4	10.9
21	calc.	3.1	12.2
	exp.	3.9	8.7

Thus the obtained results confirm general validity of the ^{1}H NMR spectral pattern rule for assigning diastereomer configuration. Clearly, these of *u* configurations appear in one conformation with almost antiperiplanar and synclinal vicinal hydrogen atoms (Fig. 7), so the relatively large and small coupling constants are observed. In the case of *l* diastereomers, as a consequence of their existence in two or three low energy conformers, the averaged positions of both diastereotopic hydrogens diminish the value of large coupling constants and increase the small ones (Fig. 7). The same conclusion about the conformational equilibrium for two diastereomers of *rac*-1-phenyl-2-methylsulfinylethylamine has been drawn reasoning from the protonation effect in the NMR spectra.[5] Also molecular mechanics calculations carried out for the conformers of homochiral β-hydroxy sulfoxides selected on the NMR spectra bases have led to the results similar to ours.[6] Thus, it seems that the ^{1}H NMR spectral pattern rule used for assigning diastereomer configuration[4-6] is observed generally as a result of the conformational preferences of sulfoxide group, disregarding the character of β-substituent.

In summary, homochiral *u* and *l* β-amino sulfoxides are easily prepared from the optically active α-amino alcohols. Conformational analysis for these compounds explains their strongly configuration dependent ^{1}H NMR spectral patterns. The combined NMR and CD spectra measured both for homochiral β-amino sulfoxide give the direct assignment of the absolute configuration at both stereogenic centers. This is also confirmed by the X-ray structure determined for this type of compounds for the first time. We are currently investigating the use of the described β-amino sulfoxides and sulfides as ligands in transition metal catalyzed reactions.

EXPERIMENTAL PART

Melting points were determined using a Boetius hot-stage apparatus and are uncorrected. IR spectra were recorded on a Perkin Elmer 1600 FTIR spectrophotometer. ^{1}H NMR spectra were measured on a Bruker CPX (300 MHz) spectrometer using TMS as an internal standard. Observed rotations at 578 nm were measured using an Optical Activity Ltd. Model AA-5 automatic polarimeter. CD spectra were recorded with a JASCO J 600 instrument. Separations of products by chromatography were performed on silica gel 60 (230-400 mesh) purchased from Merck or florisil from Fluka. Thin layer chromatography analyses were performed using silica gel 60 precoated plates (Merck).

X-ray details:

Colourless crystals of **12a** suitable for X-ray diffraction studies were grown by dissolving the compound in *n*-hexane–toluene mixture, and then by the slow evaporation at room temperature. X-ray diffraction data were collected at room temperature on Nonius CAD-4 computer controlled diffractometer with rotating anode using MoK_α radiation with $\omega/2\Theta$ scan. Unit cell parameters were determining by least square fitting of the setting angles of 25 centered reflections in range $10 \leq 2\Theta \leq 15°$. The intensities of five standard reflections were measured every 120 min. during the data collection. No significant intensity variation for standard reflections was observed. The intensities were measured in range $2 \leq 2\Theta \leq 60°$ and recording domain was limited by $0 \leq h \leq 12$, $0 \leq k \leq 17$, $0 \leq l \leq 9$. A total 1710 reflection were collected of which 823 reflection satisfying $I > 3\sigma(I)$ were taken as observed. The structure was solved by Patterson method using SHELLXS-86 and refined by full-matrix least-square technique using SHELX-76 and SHELXS-86 computer programs. Positions of the hydrogen atoms were found using a difference Fourier map and refined isotropically. Anisotropic thermal parameters were refined for non-hydrogen atoms. Least-square refinement with 192 variable parameters were

carried out by minimizing function $\Sigma\omega\,(|F_o|-|F_c|^2)$, where F_o and F_c were observed and calculated structure factors, $\omega = \sigma^2(F_o) + (aP)^2 + bP$ and $P = [f_{max}$ of F_o^2 or) + $2F_c^2]$. Final residual obtained at convergence is R = 0.58 and goodness of fit S = 1.097. Weight bases on counting statistics were used. The maximum Δ/σ ratio was 0.15. In the final difference map the deepest hole $\Delta\rho_{min} = -0.15$ eÅ^2 and the highest peak $\Delta\rho_{max} = 0.21$ eÅ^{-3}

Protection of the amino group with di-tert-butyl dicarbonate:

Di-tert-butyl dicarbonate (11.0 mmol, 2.42 g) was added in one portion to the solution of 10.0 mmol of aminoalcohol in absolute acetonitrile (20 ml). The solution was stirred at room temperature during 3 hrs. Within the first 2 hrs the evolution of CO_2 was observed. Then the solvent was removed under reduced pressure and the product was purified by recrystallization or by chromatography.

Protection of the amino group with acid chloride or chloroformate:

Benzoyl chloride (or methyl chloroformate) 11.0 mmol (10% excess) was added in one portion to the solution of 10.0 mmol of aminoalcohol and K_2CO_3 (1.5 g) in methanol (50 ml). Reaction mixture was stirred at room temperature overnight. The solid was filtered off and washed with methanol (5 ml). The solvent was evaporated and the residue was dissolved in water (10 ml) and extracted with chloroform (4×10 ml). The chloroform solution was washed with brine and dried over anhydrous Na_2SO_4. After removing the solvent the crude product was purified by recrystallization or chromatography.

4a, yield 99%, m.p. 95.5-96.5 °C (toluene), $[\alpha]_D^{20} = -28.5°$ (1.0, MeOH); lit.[17] m.p. 94-95 °C, $[\alpha]_D^{20} = -28.9°$ (1.0, MeOH);

4b, yield 98%, m.p. 172.5-173.5 °C (toluene), $[\alpha]_D^{20} = 76.5°$ (0.9, MeOH); lit.[18] m.p. 171-172°C, $[\alpha]_D^{20} = 77.3°$ (0.356, EtOH);

4c, yield 99%, m.p. 40-45 °C (toluene/ hexane); lit.[19] m.p. 50.5-52.5 °C;

5a, yield 99%, m.p.137-138 °C (toluene), $[\alpha]_D^{20} = -38.6°$ (1.0, $CHCl_3$); lit.[20] m.p. 135-136 °C, $[\alpha]_D^{20} = -39.0°$ (1%, $CHCl_1$);

5b, yield 98%, m.p. 179-180 °C (toluene), $[\alpha]_D^{20} = 19.2°$ (1.0, MeOH); lit.[21] m.p. 181 °C, lit.[22] $[\alpha]_D^{20} = 19.7°$ (0.15, EtOH);

5c, yield 95%, m.p. 96-97 °C (toluene), ^{1}H NMR ($CDCl_3$): 7.39-7.26 (m, 5H, Ph); 5.42 (br s, 1H, NH); 4.85-4.79 (m, 1H, *CH); 3.92-3.85 (m, 2H, CH_2); 3.68 (s, 3H, Me); 2.13 (br s, 1H, OH); IR (KBr): 3343, 3066, 3031, 2942, 1686, 1537, 1288, 1058, 1025; $[\alpha]_D^{20} = -55.0°$ (0.6, $CHCl_3$);

6a, yield 88%, oil, ^{1}H NMR ($CDCl_3$): 4.66 (br s, 1H, NH); 3.69 (dd, 1H, J_1=10.91, J_2=3.12Hz, CH_AH_B); 3.60 (dd, 1H, J_1=10.91, J_2=6.44Hz, CH_AH_B); 3.45-3.39 (m, 1H, *CH); 2.46 (br s, 1H, OH); 1.89-1.78 (m, 1H, CH); 1.45 (s, 9H, Bu-*t*); 0.94 (dd, 1H, $J_1 = J_2$=6.5Hz, Me_2); IR (CCl_4): 3449, 2966, 2875, 1698, 1501, 1391, 1367, 1248, 1173, 1077, 1047; $[\alpha]_D^{20} = 23.9.6°$ (1.34, $CHCl_3$);

6b, yield 86%, m.p.76- 77 °C (toluene, hexane), lit.[23] m. p. 75-77°C; $[\alpha]_D^{20} = 38.2°$ (1.1, $CHCl_3$);

6c, yield 95%, oil, ^{1}H NMR ($CDCl_3$): 6.67 (s, 1H, NH); 4.44 (dd, 1H, $J_1 = J_2 = 8.64$ Hz, CH_AH_B); 4.10 (dd, 1H, J_1=8.64, J_2=6.33Hz, CH_AH_B); 3.67 (s, 3H, Me); 3.65-3.58 (m, 1H, *CH); 1.78-1.68 (m, 1H, CH); 0.93 (dd, 6H, J_1=18.40, J_2=6.73Hz, Me_2); IR ($CHCl_3$): 3269, 2967, 2877, 1751, 1408, 1242, 1051; $[\alpha]_D^{20} = -16.8°$ (2.42, MeOH);

Preparation of sulfides:

A solution of N-protected aminoalcohol (5.3 mmol), PhSSPh (3.53 g, 15.9 mmol) and Bu_3P (5.2 ml, 21.1 mmol) in dry THF was placed under nitrogen in a reaction ampoule. The sealed ampoule was heated at 76°C for 72 hrs. Thereafter the mixture was diluted with ether and washed with 2M NaOH, brine and dried over anhydrous Na_2SO_4. After evaporation, the crude product was purified by filtration through a pad of silica gel.

7a, yield 87%, m.p. 84.5-85.5°C (toluene), ^{1}H NMR ($CDCl_3$): 7.36-7.16 (m, 10H, Ph); 4.66 (br s, 1H, NH); 4.11-4.00 (m , 1H, *CH); 3.03 (d, 2H, J=5.4Hz, CH_2S); 2.92 (d, 2H, J=6.6Hz, CH_2Ph); 1.39 (s, 9H, Bu-*t*); IR (KBr): 3372, 3058, 2979, 2924, 1693, 1679, 1525, 1173, 1040, 1024; $[\alpha]_D^{20} = -20.0°$ (2.0, CCl_4); lit.[24] m.p. 80-83°C;

7b, yield 70%, m.p. 161-162.5 °C (toluene), ^{1}H NMR ($CDCl_3$): 7.73-7.28 (m, 15H, Ph); 6.73 (d, 1H, J=5.8 Hz, NH); 5.41 (q, 1H, J=6.6 Hz, *CH); 3.51 (AB, 2H, J_1=12.1, J_2=13.6Hz, CH_2S); IR (KBr): 3370, 3287, 3054, 3028, 1634, 1534, 1490, 1291, 1025; $[\alpha]_D^{20} = -55.0°$ (2.0, THF); Anal. calcd. for: $C_{22}H_{21}NOS$ (347.47): C 76.05, H 6.09; found: C 76.12, H 6.01.

7c, yield 84%, m.p. 70-71 °C (toluene), ^{1}H NMR ($CDCl_3$): 7.34- 7.17 (m, 10H, Ph); 4.82-4.74 (m, 1H, NH); 4.11-4.02 (m, 1H, *CH); 3.61 (s, 3H, Me); 3.06-3.04 (m, 2H, CH_2S); 2.94 (d, 2H, J=6.54, CH_2Ph); IR (CCl_4): 3440, 3350, 3064, 3029, 2955, 1728, 1503, 1242, 1040; $[\alpha]_D^{20} = -15.0°$ (2.0, $CHCl_3$); Anal. calcd. for: $C_{17}H_{19}NO_2S$ (301.40): C 67.75, H 6.35; found: C 67.58, H 6.19.

8a, yield 82%, m.p. 64.5-65.5°C (toluene), ^{1}H NMR ($CDCl_3$): 7.40-7.28 (m, 10H, Ph); 5.12 (br s, 1H, NH); 4.90-4.83 (m, 1H, *CH); 3.83 (d, 2H, J=6.4Hz, CH_2S); 1.43 (s, 9H, Bu-*t*); IR (CCl_4): 3383, 3061, 2977, 2931, 1699, 1513, 1248, 1171, 1045, 1024; $[\alpha]_D^{20} = 17.5°$ (2.0, $CHCl_3$); Anal. calcd. for: $C_{19}H_{23}NO_2S$ (329.46): C 69.27, H 7.04; found: C 69.18, H 7.08.

8b, yield 89%, m.p. 96-96.5 °C (toluene), ^{1}H NMR ($CDCl_3$): 7.71-7.18 (m, 15H, Ph); 6.67 (d, 1H, J=6.66Hz, NH); 5.39 (q, 1H, J=6.70Hz, *CH); 3.53 (dd, 1H, J_1=13.68, J_2=6.94Hz, CH_AH_B); 3.45 (dd, 1H, J_1=13.68, J_2=6.11Hz, CH_AH_B); IR (KBr): 3370, 3287, 3054, 3028, 1634, 1534, 1291, 1024; $[\alpha]_D^{20} = -55.0°$ (2.0, $CHCl_3$); Anal. calcd. for: $C_{21}H_{19}NOS$ (333.45): C 75.64, H 5.74; found: C 75.52, H 5.79.

8c, yield 85%, m.p. 73.5-74.5 °C (toluene), ^{1}H NMR ($CDCl_3$): 7.40-7.29 (m, 10H, Ph); 5.30 (d, 1H, J=5.8 Hz, NH); 4.90 (q, 1H, J=6.2Hz, *CH); 3.68 (s, 3H, Me); 3.34 (A_2B, 2H, CH_2S); IR (KBr): 3296, 3029, 2951, 2915, 1720, 1693, 1538, 1247, 1045, 1023; $[\alpha]_D^{20} = -20.5°$ (2.0, $CHCl_3$); Anal. calcd. for: $C_{16}H_{17}NO_2S$ (287.38): C 66.87, H 5.96; found: C 66.90, H 5.95.

9a, yield 70%, m.p. 68-69 °C (toluene), ^{1}H NMR ($CDCl_3$): 7.40-7.18 (m, 5H, Ph); 4.59 (d, 1H, J=8Hz, NH); 3.68 (br s, 1H, *CH); 3.09 (d, 2H, J=5.2Hz, CH_2S); 1.99-1.88 (m, 1H, CH); 1.44 (s, 9H, Bu-*t*); 0.93 (dd, 6H, J_1= J_2=7.1Hz, Me_2); IR (KBr): 3307, 3062, 2976, 2928, 2873, 1677, 1536, 1366, 1174, 1045, 1024; $[\alpha]_D^{20} = -20.0°$ (2.0, CCl_4); Anal. calcd. for: $C_{16}H_{25}NO_2S$ (295.44): C 65.05, H 8.53; found: C 65.09, H 8.50.

9b, yield 94%, m.p. 118,5-119 °C (toluene), ^{1}H NMR ($CDCl_3$): 7.68-7.18 (m, 10H, Ph); 6.18 (d, 1H, J=8.8Hz, NH); 4.29-4.20 (m, 1H, *CH); 3.27 (d, 2H, J=5.5Hz, CH_2S); 2.17-2.05 (m, 1H, CH); 1.05 (dd, 6H, J_1= 6.8 J_2=7.2Hz, Me_2); IR (KBr): 3310, 3058, 2962, 2935, 2869, 1635, 1530, 1346, 1184, 1026; $[\alpha]_D^{20} = -63.5°$ (2.0, $CHCl_3$); Anal. calcd. for: $C_{18}H_{21}NOS$ (299.43): C 72.20, H 7.07; found: C 72.13, H 7.11.

9c, yield 80%, oil, ^{1}H NMR ($CDCl_3$): 7.39-7.19 (m, 5H, Ph); 4.71 (br s, 1H, NH); 3.72-3.68 (m, 1H, *CH); 3.65 (s, 3H, Me); 3.09 (d, 2H, J=5.76Hz, CH_2S); 1.99-1.90 (m, 1H, CH); 0.92 (dd, 6H, J_1=8.68, J_2=6.83Hz, Me_2); IR

(CCl_4): 3447, 3349, 3063, 2964, 2875, 1729, 1506, 1481, 1228, 1092, 1026; $[\alpha]_D^{20} = -12.5°$ (2.0, $CHCl_3$); Anal. calcd. for: $C_{13}H_{19}NO_2S$ (253.36): C 61.63, H 7.56; found: C 61.58, H 7.60.

Oxidation of sulfides:

A 50 ml flask was charged with a solution of the sulfide (1.5 mmol) in CH_2Cl_2 (10 ml), TEMPO (2.25 mg, 0.015 mmol) and saturated aqueous solution of $NaHCO_3$ (8 ml) containing KBr (18 mg, 0.15 mmol). To this cooled (0°C, ice–water bath) and well stirred mixture a solution of NaOCl (0.90 M) in saturated $NaHCO_3$ (2 ml) was added dropwise. The mixture was stirred for 2-5 hrs at 0°C (monitored by TLC) and the layers were separated. The aqueous phase was extracted with CH_2Cl_2 (3×5 ml) and the combined organic phases were washed with water, brine and dried (Na_2SO_4). The diastereomeric products were separated and purified by chromatography on silica gel or recrystallization.

10a (*R,S*), yield 6%, m.p.184.5-186.5 °C (MeOH), ^{1}H NMR ($CDCl_3$): 7.89-7.86 (m, 2H, Ph); 7.57-7.42 (m, 3H, Ph); 7.28-7.13 (m, 5H, Ph); 4.88 (br s, 1H, NH); 4.17-4.08 (m, 1H,*CH); 3.41 (dd, 1H, J_1=14.5, J_2=6.9Hz, CH_AH_B); 3.26 (dd, 1H, J_1=14.5, J_2=4.7Hz, CH_AH_B); 3.05-2.94 (m, 2H, CH_2); 1.38 (s, 9H, Bu-*t*); $[\alpha]_D^{20}$ = -114.5° (1.31, $CHCl_3$); R_f=0.48 (*t*-BuOMe:$CHCl_3$,2.5:2.0); Anal. calcd. for: $C_{20}H_{25}NO_3S$ (359.48): C 66.82, H 7.01; found: C 66.75, H 6.99.

10a (*S,R*), yield 8%, $[\alpha]_D^{20}$ = 115.0° (0.9, $CHCl_3$); R_f=0.49 (*t*-BuOMe:$CHCl_3$,2.5:2.0).

10b (*R,S*), yield 43%, m.p.166-167 °C (toluene/ $CHCl_3$), ^{1}H NMR ($CDCl_3$): 8.17 (br s, 1H, NH); 7.87-7.26 (m, 15H, Ph);4.81-4.75 (m, 1H, *CH); 3.52-3.45 (m, 1H, CH_AH_B); 3.24-3.09 (m, 1H, CH_AH_B); 3.00 (br s, 2H, CH_2Ph); IR ($CHCl_3$): 3360, 3067, 2930, 1660, 1527, 1488, 1306, 1086, 1018; $[\alpha]_D^{20} = -7.22°$ (1.0, $CHCl_3$); Anal. calcd. for: $C_{22}H_{21}NO_2S$ (363.47): C 72.70, H 5.82; found: C 72.58, H 5.84.

10c (*S,R*), yield 30%, m.p. 118-118.5 °C (toluene), ^{1}H NMR (DMSO): 7.58 (s, 5H, Ph); 7.47 (d,1H, J=8.2Hz, NH); 7.28-7.13 (m, 5H, Ph); 4.15-4.10 (m, 1H, *CH); 3.54 (s, 3H, Me); 2.96-2.84 (m, 2H, CH_2S); 2.80-2.72 (m, 2H, CH_2Ph); IR (KBr): 3346, 3054, 3029, 2952, 2910, 1698, 1532, 1261, 1042; $[\alpha]_D^{20}$ = 136.1° (1.47, $CHCl_3$); Anal. calcd. for: $C_{17}H_{19}NO_3S$ (317.40): C 64.33, H 6.03; found: C 64.28, H 6.07.

11a (*S,R*), yield 10%, m.p. 157-159 °C (toluene), ^{1}H NMR ($CDCl_3$): 7.61-7.29 (m, 10H, Ph); 6.27 (br s, 1H, NH); 5.20-5.16 (m, 1H,*CH); 3.17 (d, 2H, J=5.4Hz, CH_2S); 1.43 (s, 9H, Bu-*t*); IR (KBr): 3365, 2973, 2922, 1679, 1509, 1248, 1166, 1035, 1020; $[\alpha]_D^{20}$ = 156.5° (0.66, $CHCl_3$); R_f=0.51 (*t*-BuOMe:$CHCl_3$,2.5:2.0); Anal. calcd. for: $C_{19}H_{23}NO_3S$ (345.46): C 66.06, H 6.71; found: C 65.98, H 6.65.

11b (*R,S*), yield 14%, m.p. 184-185.5 °C (toluene), ^{1}H NMR (DMSO): 9.21 (d, 1H, J=8.1Hz, NH); 7.94-7.70 (m, 4H, Ph); 7.63-7.53 (m, 6H, Ph); 7.42-7.22 (m, 5H, Ph); 5.54-5.47 (m, 1H, *CH); 3.55 (dd, 1H, J_1= J_2=12.5Hz, CH_AH_B); 3.06 (dd, 1H, J_1=13.0, J_2=3.0Hz, CH_AH_B); IR (CCl_4): 3360, 3066, 2928, 1659, 1527, 1488, 1306, 1087, 1018; $[\alpha]_D^{20} = -121.4°$ (0.906, $CHCl_3$); R_f=0.31(*t*-BuOMe:$CHCl_3$,2.5:2.0); Anal. calcd. for: $C_{21}H_{19}NO_2S$ (349.45): C 72.18, H 5.48; found: C 72.12, H 5.40.

11c (*R,S*), yield 2%, m.p.148.5-149.5 °C (toluene), ^{1}H NMR ($CDCl_3$): 7.84-7.20 (m, 10H, Ph); 5.70-5.60 (m, 1H, NH); 5.14-5.08 (m, 1H, *CH); 3.72 (dd, 1H, J_1=14.7, J_2=9.0Hz, CH_AH_B); 3.50 (dd, 1H, J_1=14.7, J_2=4.4Hz, CH_AH_B); IR (KBr): 3317, 3065, 2976, 2946, 1693, 1551, 1271, 1297, 1146, 1029; $[\alpha]_D^{20} = -30.5°$ (2.3, $CHCl_3$); R_f=0.38 (*t*-BuOMe:$CHCl_3$,2.5:2.0); Anal. calcd. for: $C_{16}H_{17}NO_3S$ (303.38): C 63.35, H 5.65; found: C 63.28, H 5.69.

12a (*R,S*), yield 30%, m.p.155-156 °C (toluene), ^{1}H NMR (DMSO): 7.63-7.54 (m., 5H, Ph); 7.04 (d, 1H, J=9.0Hz, NH); 3.84-3.75 (m, 1H, *CH); 2.86 (dd, 1H, J_1=J_2=12.0Hz, CH_AH_B); 2.69 (dd, 1H, J_1=12.8,

J_2=2.0Hz, CH_AH_B); 1.82-1.71 (m, 1H, CH); 1.43 (s, 9H, Bu-*t*); 0.80 (dd, 6H, J_1=6.8, J_2=1.5Hz, Me_2); IR (KBr): 3248, 3056, 3027, 2968, 2930, 1699, 1530, 1249, 1171, 1044, 1015; $[\alpha]_D^{20}$ = −154.9° (1.0, $CHCl_3$); Anal. calcd. for: $C_{16}H_{25}NO_3S$ (311.44): C 61.71, H 8.09; found: C 61.62, H 8.02.

12b (*R,S*), yield 35%, m.p. 165-167°C (toluene), ^{1}H NMR ($CDCl_3$): 7.87-7.42 (m, 11H, Ph, NH); 4.37-4.34 (m, 1H, *CH); 3.16 (dd, 1H, J_1=13.5, J_2=6.0Hz, CH_AH_B); 3.06 (dd, 1H, J_1=13.5, J_2=2.4Hz, CH_AH_B); 2.49-2.38 (m, 1H, CH); 1.11 (dd, 6H, J_1=15.8, J_2=6.6Hz, Me_2); IR (KBr): 3329, 3059, 2955, 2870, 1647, 1532, 1489, 1312, 1018; $[\alpha]_D^{20}$ = −200.0° (1.0, $CHCl_3$); Anal. calcd. for: $C_{18}H_{21}NO_2S$ (315.43): C 68.54, H 6.71; found: C 68.48, H 6.73.

12c (*R,S*), yield 30%, m.p. 100-101.5 °C (toluene/hexane), ^{1}H NMR ($CDCl_3$): 7.59-7.55 (m, 2H, Ph); 7.47-7.42 (m, 3H, Ph); 5.40 (br s, 1H, NH); 3.81-3.79 (m, 1H, *CH); 3.61 (s, 3H, Me); 2.99-2.86 (m, 2H, CH_2S); 2.10-2.08 (m, 1H, CH); 0.92 (d, 6H, J=6.60Hz, Me_2); IR (KBr): 3209, 3044, 2974, 2874, 1717, 1552, 1250, 1043, 1022; $[\alpha]_D^{20}$ = -169.1° (0.98, $CHCl_3$); Anal. calcd. for: $C_{13}H_{19}NO_3S$ (269.36): C 57.97, H 7.11; found: C 57.88, H 7.06.

13a (*R,R*), yield 88%, m.p. 140-141 °C (toluene), ^{1}H NMR ($CDCl_3$): 7.68-7.65 (m, 2H, Ph); 7.55-7.51 (m,3H, Ph); 7.31-7.14 (m,5H, Ph); 4.90 (br s, 1H, NH); 4.17-4.10 (m, 1H, *CH); 3.03 (d, 2H, J=6.1Hz, CH_2); 2.95 (dd, 2H, J_1=13.7, J_2=6.9Hz, CH_2S); 1.38 (s,9H, Bu-*t*); IR (KBr): 3296, 3059, 3027, 3010, 2981, 2929, 1701, 1364, 1175, 1025; $[\alpha]_D^{20}$ = 65.0° (1.0, $CHCl_3$); R_f=0.37 (*t*-BuOMe:$CHCl_3$,2.5:2.0); Anal. calcd. for: $C_{20}H_{25}NO_3S$ (359.48): C 66.82, H 7.01; found: C 66.64, H 6.98.

13a (*S,S*), yield 87%, $[\alpha]_D^{20}$ = − 66.3° (0.98, $CHCl_3$); R_f=0.37 (*t*-BuOMe:$CHCl_3$,2.5:2.0).

13b (*R,R*), yield 49%, m.p.200-202 °C (toluene/ $CHCl_3$), ^{1}H NMR (DMSO): 8.55 (d, 1H, J=8.4Hz, NH); 7.73-7.14 (m, 15H, Ph); 4.50-4.38 (m, 1H, *CH); 3.22 (dd, 1H, J_1=13.1, J_2=8.3Hz, CH_AH_B); 3.10 (dd, 1H, J_1=13.1, J_2=5.3Hz, CH_AH_B); 2.97 (brs, 1H, CH_2Ph); 2.95 (d, 1H, J=2.2Hz, CH_2Ph); IR ($CHCl_3$): 3345, 3066, 2928, 1659, 1527, 1488, 1286, 1086, 1029; $[\alpha]_D^{20}$ = 67.5° (2.0, $CHCl_3$); R_f=0.36 (*t*-BuOMe:$CHCl_3$:hexane, 2.5:1.5:3.0); Anal. calcd. for: $C_{22}H_{21}NO_2S$ (363.47): C 72.70, H 5.82; found: C 72.50, H 5.87.

13c(*S,S*), yield 59%, m.p. 132-132.5 °C (toluene), ^{1}H NMR (DMSO):7.65-7.56 (m., 5H, Ph); 7.38 (d, 1H, J=8.4Hz, NH); 7.27-7.09 (m, 5H, Ph); 3.89 (d, 1H, J=6.2Hz, *CH); 3.44 (s, 3H, Me); 3.93 (m, 4H, CH_2S, CH_2Ph); $[\alpha]_D^{20}$ = −89.7° (2.9, $CHCl_3$); R_f=0.28 (*t*-BuOMe:$CHCl_3$, 2.5:2.0); Anal. calcd. for: $C_{17}H_{19}NO_3S$ (317.40): C 64.33, H 6.03; found: C 64.70, H 6.12.

14a (*S,S*), yield 80%, m.p. 160-162 °C (MeOH), ^{1}H NMR ($CDCl_3$): 7.70-7.49 (m, 5H, Ph); 7.33-7.26 (m, 5H, Ph); 5.48 (br s, 1H, NH); 5.10-5.01 (m,1H,*CH); 3.29 (dd, 1H, J_1=13.3, J_2=9.5Hz, CH_AH_B); 3.08 (dd, 1H, J_1=13.3, J_2=4.8Hz, CH_AH_B); 1.42 (s, 9H, Bu-*t*); IR (KBr): 3365, 2973, 2922, 1679, 1509, 1248, 1166, 1035, 1020; $[\alpha]_D^{20}$ = −65.0° (1.0, $CHCl_3$); R_f=0.41 (*t*-BuOMe:$CHCl_3$,2.5:2.0); Anal. calcd. for: $C_{19}H_{23}NO_3S$ (345.46): C 66.06, H 6.71; found: C 66.29, H 6.56.

14b (*R,R*), yield 78%, m.p.163.5-164.5 °C (MeOH), ^{1}H NMR (DMSO): 9.0 (d, 1H, J=8.4Hz, NH); 7.77-7.35 (m, 15H, Ph); 5.45-5.37 (m, 1H, *CH); 3.56 (dd, 1H, J_1=13.0, J_2=9.0Hz, CH_AH_B); 3.33 (dd, 1H, J_1=13.0, J_2=5.8Hz, CH_AH_B); IR ($CHCl_3$): 3345, 3066, 2929, 1659, 1527, 1488, 1286, 1086, 1029; $[\alpha]_D^{20}$ = 88.4° (3.28, $CHCl_3$); R_f=0.23 (*t*- BuOMe:$CHCl_3$,2.5:2.0); Anal. calcd. for: $C_{21}H_{19}NO_2S$ (349.45): C 72.18, H 5.48; found: C 72.10, H 5.46.

14c (*R,R*), yield 92%, m.p.163-164 °C (toluene), ^{1}H NMR ($CDCl_3$): 7.50-7.26 (m 10H, Ph); 5.72 (br s, 1H, NH); 5.17-5.08 (m, 1H, *CH); 3.65 (s, 3H, Me); 3.30 (dd, 1H, J_1=13.4, J_2=9.7Hz, CH_AH_B); 3.10 (dd, 1H,

J_1=13.4, J_2=5.3Hz, CH_AH_B); IR (KBr): 3307, 3054, 2947, 2909, 1725, 1541, 1261, 1019; $[\alpha]_D^{20}$ = 43.2° (3.36, $CHCl_3$); R_f=0.23 (*t*- BuOMe:$CHCl_3$,2.5:2.0); Anal. calcd. for: $C_{16}H_{17}NO_3S$ (303.38): C 63.35, H 5.65; found: C 63.20, H 5.70.

15a (*R,R*), yield 68%, m.p.104-105 °C (toluene), ^{1}H NMR ($CDCl_3$): 7.77-7.51 (m, 5H, Ph); 4.85 (br s, 1H, NH); 3.69 (br s, 1H, *CH); 3.02 (t, 1H, J=13Hz, CH_AH_B); 2.99 (br s, 1H, CH_AH_B); 1.88-1.81 (m, 1H, CH); 1.46 (s, 9H, Bu-*t*); 0.85 (dd, 6H, J_1=8.4, J_2=6.9Hz, Me_2); IR (KBr): 3291, 3057, 2970, 2933, 1689, 1673, 1542, 1366, 1278, 1169, 1045; $[\alpha]_D^{20}$ = 12.36° (1.0, $CHCl_3$); R_f=0.27 (*t*- BuOMe:$CHCl_3$:hexane,2.5:1.5:1.5); Anal. calcd. for: $C_{16}H_{25}NO_3S$ (311.44): C 61.71, H 8.09; found: C 61.66, H 8.11.

15b (*R,R*), yield 62%, m.p.127-129 °C (toluene), ^{1}H NMR ($CDCl_3$): 7.83-7.38 (m, 10H, Ph); 6.90 (d, 1H, J=8.1Hz, NH); 4.38-4.28 (m, 1H, *CH); 3.18 (dd, 1H, J_1=13.45, J_2=9.9Hz, CH_AH_B); 3.08 (dd, 1H, J_1=13.45, J_2=4.39Hz, CH_AH_B); 2.13-2.02 (m, 1H, CH); 0.92 (dd, 6H, J_1=6.9, J_2=0.8Hz, Me_2); IR (KBr): 3301, 3059, 2955, 2868, 1630, 1531, 1032; $[\alpha]_D^{20}$ = 41.0° (1.22, $CHCl_3$); R_f=0.14 (*t*- BuOMe:$CHCl_3$,2.5:2.0); Anal. calcd. for: $C_{18}H_{21}NO_2S$ (315.43): C 68.54, H 6.71; found: C 68.35, H 6.72.

15c (*R,R*), yield 60%, m.p. 70-71 °C (toluene/hexane), ^{1}H NMR ($CDCl_3$): 7.74-7.71 (m, 2H, Ph); 7.58-7.50 (m, 3H, Ph); 5.01 (d, 1H, J=7.74Hz, NH); 3.85-3.75 (m, 1H, *CH); 3.68 (s, 3H, Me); 3.02 (dd, 1H, J_1=13.39, J_2=9.0Hz, CH_AH_B); 2.95 (dd, 1H, J_1=13.39, J_2=4.71Hz, CH_AH_B); 1.94-1.88 (m, 1H, CH); 0.87 (dd, 6H, J_1=8.82, J_2=6.87Hz, Me_2); IR (KBr): 3298, 3075, 2966, 2944, 2879, 1713, 1689, 1555, 1266, 1046, 1028; $[\alpha]_D^{20}$ = 72.8° (1.02, $CHCl_3$); Anal. calcd. for: $C_{13}H_{19}NO_3S$ (269.36): C 57.97, H 7.11; found: C 57.86, H 7.31.

Removing the Boc-protection:

The protected aminosulfoxide 1 mmol was added to the equimolar mixture of CF_3COOH (100 mmol, 7.64 ml) and CH_2Cl_2 (100 mmol, 6.64 ml). The solution was stirred at room temperature during about 45 min. The reaction was monitored by TLC. After that time the solvent was evaporated under the reduced pressure from the cold bath. 2Ml of 3M NaOH was added to the residue and the mixture was extracted with chloroform (4×5 ml). The organic layers were collected, washed with brine and dried over anhydrous Na_2SO_4.

16 (*R,S*), yield 98%, oil, ^{1}H NMR ($CDCl_3$): 7.61-7.58 (m, 2H, Ph); 7.53-7.49 (m, 3H, Ph); 7.30-7.12 (m, 5H, Ph); 3.66 (m, 1H,*CH); 2.89 (dd, 1H, J_1=13.3, J_2=2.6Hz, CH_2); 2.82 (dd, 1H, J_1=13.3, J_2=5.5Hz, CH_2); 2.71 (dd, 1H, J_1=13.2, J_2=10.0Hz, CH_AH_B); 2.65 (dd, 1H, J_1=13.2, J_2=8.2Hz, CH_AH_B); 1.63 (s, 2H, NH_2); IR (CCl_4): 3380, 3066, 2972, 2885, 1612, 1447, 1085, 1030; $[\alpha]_D^{20}$ = –225.0° (0.2, $CHCl_3$); R_f=0.39 (*t*-BuOMe:$CHCl_3$: MeOH, 1.5:1:1); Anal. calcd. for: $C_{15}H_{17}NOS$ (259.37): C 69.46, H 6.61; found: C 69.40, H 6.58.

17 (*S,R*), yield 99%, crystallizing on standing, ^{1}H NMR ($CDCl_3$): 7.67-7.25 (m, 10H, Ph); 4.58-4.54 (m, 1H, *CH); 3.01 (d, 1H, J=1.08Hz, CH_AH_B); 2.99 (s, 1H, CH_AH_B); 2.03 (s, 2H, NH_2); IR (CCl_4): 3372, 3060, 2970, 1616, 1450, 1080, 1025; $[\alpha]_D^{20}$ = 164.8° (0.54, $CHCl_3$); R_f=0.48 (*t*-BuOMe:$CHCl_3$:MeOH, 1.5:1:1); Anal. calcd. for: $C_{14}H_{15}NOS$ (245.34): C 68.54, H 6.16; found: C 68.49, H 6.14.

18 (*S,R*), yield 98%, crystallizing on standing, ^{1}H NMR ($CDCl_3$): 7.67-7.27 (m, 5H, Ph); 3.25-3.19 (m, 1H, *CH); 2.82 (dd, 1H, J_1=13.0, J_2=2.40Hz, CH_AH_B); 2.61 (dd, 1H, J_1=13.0, J_2=10.85Hz, CH_AH_B); 1.73-1.62 (m, 1H, CH); 1.57 (br s, 2H, NH_2); 0.90 (dd, 6H, J_1=11.5, J_2=6.8Hz, Me_2); IR (CCl_4): 3386, 3063, 2962, 2874, 1584, 1478, 1444, 1088, 1045; $[\alpha]_D^{20}$ = 240.1° (1.52, $CHCl_3$); Anal. calcd. for: $C_{11}H_{17}NOS$ (211.32): C 62.52, H 8.11; found: C 62.50, H 8.13.

19 (*R,R*), yield 97%, oil, ^{1}H NMR ($CDCl_3$): 7.64-7.60 (m, 2H, Ph); 7.50-7.48 (m, 3H, Ph); 7.29- 7.15 (m, 5H, Ph); 3.60-3.56 (m, 1H, *CH); 2.91 (dd,1H, J_1=13.1, J_2=7.7Hz, CH_2); 2.89 (dd, 1H, J_1=13.1, J_2=5.3Hz, CH_2); 2.78 (dd,1H, J_1=13.1, J_2=4.6Hz, CH_AH_B); 2.72 (dd, 1H, J_1=13.1, J_2=4.6Hz, CH_AH_B); 1.55 (s, 2H, NH_2); IR

(CCl_4): 3372, 3064, 2970, 2880, 1610, 1438, 1070, 1030; $[\alpha]_D^{20} = 116.0°$ (0.63, $CHCl_3$); Anal. calcd. for: $C_{15}H_{17}NOS$ (259.37): C 69.46, H 6.61; found: C 69.42, H 6.59.

20 (*S,S*), yield 98%, m.p. 91-93 °C ($CHCl_3$/hexane), ^1H NMR ($CDCl_3$): 7.66-7.26 (m, 10H, Ph); 4.60-4.56 (m, 1H, *CH); 3.19 (dd,1H, J_1=13.06, J_2=8.43Hz, CH_AH_B); 2.92 (dd,1H, J_1=13.06, J_2=5.12Hz, CH_AH_B); 1.91 (s, 2H, NH_2); IR (KBr): 3328, 3142, 2870, 1616, 1443, 1085, 1032; $[\alpha]_D^{20} = -93.5°$ (1.36, $CHCl_3$); R_f=0.43 (*t*-BuOMe:$CHCl_3$:MeOH, 1.5:1:1); Anal. calcd. for: $C_{14}H_{15}NOS$ (245.34): C 68.54, H 6.16; found: C 68.50, H 6.13.

21 (*S,S*), yield 97%, oil, ^1H NMR ($CDCl_3$): 7.63-7.43 (m, 5H, Ph); 3.06-3.00 (m, 1H, *CH); 2.79 (dd, 1H, J_1=13.16, J_2=8.73Hz, CH_AH_B); 2.71 (dd, 1H, J_1=13.16, J_2=3.87Hz, CH_AH_B); 1.70-1.59 (m, 1H, CH); 1.57 (s, 2H, NH_2); 0.83 (dd, 6H, J_1=9.76, J_2=6.83Hz, Me_2); IR (CCl_4): 3380, 3060, 2963, 2876, 1586, 1480, 1440, 1080; $[\alpha]_D^{20} = -129.8°$ (1.04, $CHCl_3$); Anal. calcd. for: $C_{11}H_{17}NOS$ (211.32): C 62.52, H 8.11; found: C 62.50, H 8.10.

Introduction of the phthaloyl function to the amino group:

The solution of 10.0 mmol of o-methoxycarbonylbenzoyl chloride (1.99 g) in THF (50 ml) was added dropwise to the cold solution of 10.0 mmol of aminosulfoxide and 12.0 mmol Et_3N (1.7 ml) in THF (100 ml). The solution was stirred for 1 hr in 0°C. After that the solution was poured to the ice - water mixture (about 200 ml) and left overnight. The water solution was extracted with ethyl acetate (4×50 ml). Organic solution was washed with brine and dried over anhydrous Na_2SO_4. After evaporation under reduced pressure the crude product was purified by crystallization from toluene.

22 (*S,R*), yield 70%, oil, ^1H NMR ($CDCl_3$): 7.85-7.26 (m, 15H, Ar, NH); 5.92 (dd 1H, J_1=12.34, J_2=4.04Hz, *CH); 4.50 (t, 1H, J=3.34Hz, CH_AH_B); 3.91 (s, 3H, Me); 3.30 (dd 1H, J_1=13.34, J_2=4.04Hz, CH_AH_B); IR (CCl_4):3340, 3063, 2955, 2890, 1732, 1638, 1550, 1262, 1080, 1040; $[\alpha]_D^{20} = 39.0°$ (1.0, $CHCl_3$); Anal. calcd. for: $C_{23}H_{21}NO_4S$ (407.48): C 67.79, H 5.19; found: C 67.70, H 5.17.

23 (*S,R*), yield 73%, m.p. 148-150 °C ($CHCl_3$/hexane), ^1H NMR ($CDCl_3$): 7.88-7.52 (m, 9H, Ar); 6.98 (d, 1H, J=8.5Hz, NH); 4.33-4.27 (m, 1H, *CH); 3.87 (s, 3H, Me); 3.17 (d, 2H, J=5.3Hz, CH_2); 2.46-2.39 (m, 1H, CH); 1.13 (dd, 6H, J_1=6.57, J_2=5.73Hz, Me_2); IR (KBr): 3332, 3065, 2957, 2890, 1733, 1638, 1291, 1043; $[\alpha]_D^{20} = 155.50°$ (0.85, $CHCl_3$); Anal. calcd. for: $C_{20}H_{23}NO_4S$ (373.47): C 64.32, H 6.21; found: C 64.28, H 6.19.

24 (*S,S*), yield 91%, oil, ^1H NMR ($CDCl_3$): 7.67-7.26 (m, 14H, Ar); 6.00-5.96 (m, 1H, *CH); 4.37 (dd, 1H, J_1=13.96, J_2=9.75Hz, CH_AH_B); 3.70 (dd 1H, J_1=13.96, J_2=4.68Hz, CH_AH_B); IR (CCl_4): 3065, 2929, 1780, 1717, 1385, 1361, 1088, 1051; $[\alpha]_D^{20} = -96.25°$ (1.6, $CHCl_3$); Anal. calcd. for: $C_{22}H_{17}NO_3S$ (375.44): C 70.38, H 4.56; found: C 70.36, H 4.55.

25 (*S,S*), yield 86%, m.p. 127.5-128.5 °C ($CHCl_3$/hexane), ^1H NMR ($CDCl_3$): 7.74-7.65 (m, 4H, Pht); 7.54 (d, 2H, J=7.7Hz, H_o); 7.30 (t, 2H, J=7.7Hz, H_m); 7.15 (t, 1H, J=7.5Hz, H_p); 4.39 (m, 1H, *CH); 3.92 (dd,1H, J_1=14.2, J_2=10.8Hz, CH_AH_B); 3.29 (dd,1H, J_1=14.2, J_2=2.55Hz, CH_AH_B); 2.42-2.27 (m, 1H, CH); 0.91 (dd, 6H, J_1=40.0, J_2=6.7Hz, Me_2); IR (KBr): 3050, 2957, 2868, 1770, 1710, 1389, 1364, 1080, 1039; $[\alpha]_D^{20} = -77.0°$ (1.0, $CHCl_3$); R_f=0.50 (*t*-BuOMe:$CHCl_3$,2.5:2.0); Anal. calcd. for: $C_{19}H_{19}NO_3S$ (341.41): C 66.83, H 5.61; found: C 66.72, H 5.64.

Hydrolysis of **23**:

The ester **23** (1 mmol) was dissolved in methanol (5 ml) and stoichiometric amount of KOH (0.056 g) was added. The solution was stirred overnight at room temperature. Then the solvent was evaporated and the residue

was dissolved in water. The solution was acidified with citric acid and extracted with chloroform (4 × 5 ml). The organic solution was dried over anhydrous Na_2SO_4. After evaporation the crude acid **26** (92% yield) was spectroscopicaly tested.

26 (*S,R*), m.p. 155-157 °C; ^{1}H NMR (DMSO): 12.90 (br s, 1H, COOH); 8.48 (d, 1H, J=7.47Hz, NH); 7.77-7.50 (m, 9H, Ar); 4.29-4.20 (m, 1H, *CH); 3.09 (dd, 1H, J_1=13.1, J_2=11.9 Hz, CH_AH_B); 2.80 (dd, J_1=13.1, J_2=2.65Hz, CH_AH_B); 1.99-1.96 (m, 1H, CH); 0.89 (dd, 6H, J_1=6.8, J_2=3.07Hz, Me_2); IR (KBr): 3288, 3056, 2964, 2928, 1708, 1636, 1539, 1271, 1084, 990; $[\alpha]_D^{20}$ = 109.5° (1.0, MeOH); Anal. calcd. for: $C_{19}H_{21}NO_4S$ (359.44): C 63.49, H 5.89; found: C 63.46, H 5.87.

REFERENCES

1. Carreno, C. M. *Chem. Rev.*, **1995**, *95*, 1717.
2. Ronan, B.; Marchalin, S.; Samuel, O.; Kagan, H. B. *Tetrahedron Lett.*, **1988**, *29*, 6101; Ruano, J. L. G.; Lorente, A.; Rodriguez, J. H. *Tetrahedron Lett.*, **1992**, *33*, 5637; Pyne, S. G.; Hajipour, A. R. *Tetrahedron*, **1994**, *50*, 13501; Bravo, P.; Crucianelli, M.; Zanda, M. *Tetrahedron Lett.*, **1995**, *36*, 3043.
3. For preliminary communication, see: Siedlecka, R; Skarżewski, J. *Synlett*, **1996**, 757.
4. Solladie, G.; Greck, C.; Demailly, G.; Solladie-Cavallo, A. *Tetrahedron Lett.*, **1982**, *23*, 50437; Solladie, G.; Frechau, C.; Demailly, G.; Greck, C. *J. Org. Chem.*, **1985**, *50*, 1552; Carreno, M. C.; Ruano, J. L. G.; Martin, A. M.; Pedregal, C.; Rodriguez, J. H.; Rubia, A.; Sanchez, J.; Solladie, G. *J. Org. Chem.*, **1990**, *55*, 2120; Arnone, A.; Bravo, P.; Capelli, S.; Fronza, G.; Meille, S. V.; Zanda, M. *J. Org. Chem.*, **1996**, *61*, 3375.
5. Brunet, E.; Gallego, M. T.; Ruano, J. L. G.; Alcudia, P. *Tetrahedron*, **1986**, *42*, 423.
6. Alvarez-Ibara, C.; Cuervo-Rodriguez, R.; Fernandez-Montreal, M. C.; Ruiz, M. P. *J. Org. Chem.*, **1994**, *59*, 7284.
7. Lewanowicz, A.; Roszak, S.; Siedlecka, R. *Mol. Phys. Reports* **1996**, *16*, 9.
8. Nakagawa, I.; Hata, T. *Tetrahedron Lett.*, **1975**, 1409; Nakagawa, I.; Aki, K.; Hata, T. *J. Chem. Soc., Perkin Trans. I*, **1983**, 1315; Kotsuki, H.; Matsumoto, K.; Nishizawa, H. *Tetrahedron Lett.*, **1991**, *32*, 4155.
9. Cran, G. A.; Gibson, C. L.; Handa, S. *Tetrahedron Asymmetry* **1995**, *6*, 1553.
10. Hoogwater, D. A.;Reinhoudt, D. N.; Lie, T. S.; Gunnenweg, J. J.; Beyerman, H. C.; *Recueil* **1973**, *92*, 819.
11. Mislow, K.; Green, M. M.; Laur, P.; Melillo, J. T.; Simmons,T.; Ternay, A. L. *J. Am. Chem. Soc.*, **1965**, *87*, 1958.
12. Jones, D. N.; Green, M. *J. C. Chem. Soc. (C)*, **1967**, 532.
13. Kaźmierczak, F.; Gawrońska, K.; Rychlewska, U.; Gawroński, J. *Tetrahedron: Asymmetry* **1994**, 5, 527 and references cited therein.
14. Sheldrick, G. M. (1985). *SHELXS*86. *Program for the Solution of Crystal Structures.* University of Göttingen, Germany.
15. Dewar, M. J. S.; Thiel, W. *J. Am. Chem. Soc.*, **1977**, *99*, 4899.
16. Karplus, M. *J. Chem. Phys.*, **1959**, *30*, 11; Karplus, M. *J. Am. Chem. Soc.*, **1963**, *85*, 2870.
17. Acton, N.; Komoriya, A. *Org. Prep. Proc. Int.*, **1982**, *14*, 381.
18. Koga, K.; Matsuo, H.; Yamada, S. *Chem. Pharm. Bull.*, **1966**, *14*, 243.
19. Iwakura, Y.; Hayashi, K.; Iwata, K. *Macromol. Chem.*, **1967**, *104*,46.
20. O'Brien, P. M.; Sliskovic, D. R.; Blankley, C. J.; Roth, B. D.; Wilson, M. W.; Hamelehle, K. L.; Krauze, B. R.; Stanfield, R. L. *J. Med. Chem.*, **1994**, *37*, 1810.
21. Reihlen, H.; Knopfle, L.; Sapper, W. *Liebigs Ann. Chem*; **1938**, *543*, 247.
22. Furukawa, N.; Yoshimura, T.; Ohtsu, M.; Akasaka, T.; Oae, S. *Tetrahedron*, **1980**, *36*, 73.
23. Bates, R. B.; Janda, K. D. *Synthesis*, **1984**, 310.
24. Kano, S.; Yokomatsu, T.; Shibuya, S. *J. Org. Chem.*, **1989**, *54*, 513.