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Synthesis and hydrolysis of optically active naphthyl-phenyl-bis(acyloxy)spiro-λ⁴-sulfane: absolute configurations of spiro-λ⁴-sulfanes, related sulfonium salts and naphthyl phenyl sulfoxides determined by CD spectroscopy using exciton chirality and empirical rules

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Abstract—(*S*)-(+)- and (*R*)-(−)-enantiomers of naphthyl-phenyl-bis(acyloxy)spiro-λ⁴-sulfane **2** were prepared from the precursors (*R*)-(−)- and (*S*)-(+)-naphthyl phenyl sulfoxide dicarboxylic acid **2a** with acetic anhydride. The hydrolysis of spiro-λ⁴-sulfane (*R*)-(−)-**2** in acidic and basic solutions gave as major products sulfoxide (*S*)-(+)-**2a** and (*R*)-(−)-**2a**, respectively. The selectivity of the reactions was interpreted with the different reactivities of the *ortho* and *peri* neighboring carboxylic groups of the sulfoxide **2a**, and with the different ability of the five and six-membered rings to be cleaved in spiro-λ⁴-sulfane **2**. The absolute configurations of the enantiomeric spiro-λ⁴-sulfanes **2** and sulfoxides **2a** were determined by CD spectroscopy. Exciton coupling was observed in the spectrum of spiro-λ⁴-sulfane **2** between the benzene ^1L_a and naphthalene ^1B_b transitions, which results in a negative couplet for (*R*)-(−)-**2**. Exciton coupling can be expected only for the ^1B_b transitions of the *S*-phenyl and *S*-naphthyl rings of the sulfoxides, which define a positive couplet for (*S*)-(+)-**2a**. Empirical rules were found to be valid for the determination of configuration of spiro-λ⁴-sulfanes and related sulfonium compound derivatives with a trigonal bipyramidal structure, and for that of naphthyl-phenyl-sulfoxides. Both spiro-λ⁴-sulfanes and sulfoxides should be viewed from the side of the lone pair; the axial substituents in the former case and the downwards oriented S=O bond in the latter case are placed in a vertical plane. Rings and substituents in the upper-right and lower-left sectors define positive exciton couplets, while the opposite case is characterized by negative exciton-coupled circular dichroism (EC-CD).

1. Introduction

Enantiomers of optically active diaryl(acyloxy)(alkoxy)- and diaryl(acylamino)(acyloxy)-spiro-λ⁴-sulfanes **1** bearing *S*-phenyl and *S*-naphthyl rings were prepared either from optically active precursor diaryl sulfoxides **1a**[1–3] by dehydration or from spiro-λ⁴-sulfane racemates by using the method of chromatographic resolution.[4] The stereospecificity of sulfoxide dehydration (**1a**→**1**) could be related to the different reactivities of the carboxyl, hydroxymethyl and *N*-methylcarbamoyl substituents of the aryl groups, lying in the neighborhood of the central sulfur atom. In other experiments optically active spiro-λ⁴-sulfanes **1** and sulfoxide carboxylic acids **1a** were methylated to obtain sulfonium salts **1b** and sulfoxide carboxylic acid methyl esters **1c**, respectively[3,5,6] without loss of the optical activity. X-Ray crystallographic investigations proved that spiro-λ⁴-sulfanes (**1**) and their sulfonium salt derivatives **1b** possess trigonal bipyramidal structure,[7–14] and the geometry of the sulfonium salts is stabilized by an S···O close contact. Methods for syntheses of diaryl spiro-λ⁴-sulfanes **1**, sulfonium salts **1b** and sulfoxide carboxylic acid methyl esters **1c** from sulfoxide carboxylic acids **1a** are shown in Scheme 1 (Z–Y = CH_2–O, CO–NMe or CO–O; Ar = phenyl or naphthyl ring).

The hydrolysis of optically active diaryl(alkoxy)-(acyloxy)- and diaryl(acylamino)(acyloxy)spiro-λ⁴-sulfanes with *S*-phenyl and *S*-naphthyl rings **1** leading to optically active sulfoxides **1a** and **1a*** as shown in Scheme 2 were also investigated earlier in detail.[3,5] Due to the different reactivities of the axial groups, the

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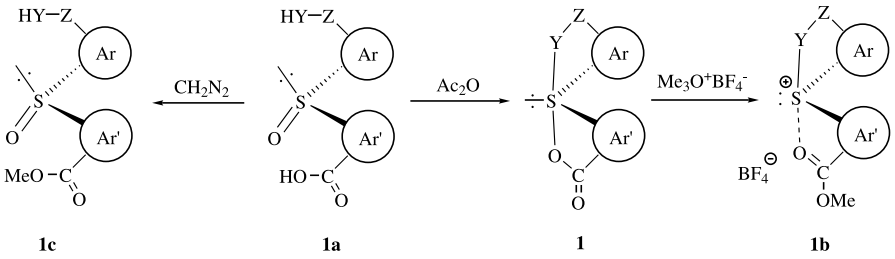
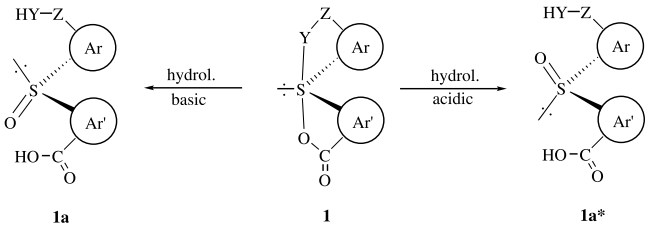


Scheme 1.



Scheme 2.

hydrolysis reaction proved to be stereospecific. Nevertheless, the configuration of the sulfoxide products was found to depend on the pH of the media pointing to reaction pathways which differ in the order of the opening of the spiro rings. Kinetic measurements showed that the rate of the hydrolysis of spiro-λ^4-sulfanes is influenced by the structure of the nucleophile (H_2O or OH^-), the leaving group ability of the axial groups and the size of the spiro rings.[15,16] The key steps in the hydrolysis mechanism of the spiro-λ^4-sulfanes are the equilibrium opening of the first spiro ring and the nucleophilic attack on the resulted monocyclic sulfonium centre. Sulfonium salt intermediates with a six-membered ring were found to react much more slowly than those with a five-membered ring.[16]

The absolute configurations of the optically active compounds were investigated by CD spectroscopy,[1,2,5,6,17] stereospecific syntheses[1,3,5] and in a few cases by X-ray analysis.[1,2] In CD studies molecules of known absolute configurations were used as references.

Herein we report the synthesis of the enantiomers of an optically active naphthyl-phenyl-bis(acyloxy)spiro-λ^4-sulfane, starting from optically active sulfoxide dicarboxylic acid enantiomers. The selectivity of the dehydration reactions is associated with the different reactivities of the carboxylic groups, linked to the *ortho* and *peri* positions of the *S*-phenyl and *S*-naphthyl rings in the precursor sulfoxide. The reverse reaction yielding optically active sulfoxide dicarboxylic acids was also studied in order to clear up the role of the acyloxy spiro rings with different ring size. The absolute configurations of the model compounds were investigated by CD spectroscopy, considering the coupling of the electric transition dipole moments. Empirical rules[14] were found to be valid for predicting the absolute configurations of both trigonal bipyramidal diaryl-spiro-λ^4-sulfanes and diaryl-sulfonium salts with S···O close contact and for that of substituted naphthyl phenyl sulfoxides. For spiro-λ^4-sulfanes the Martin–Balthazor convention,[18] for sulfonium salts and sulfoxides the Cahn–Ingold–Prelog convention were used to designate the absolute configurations.

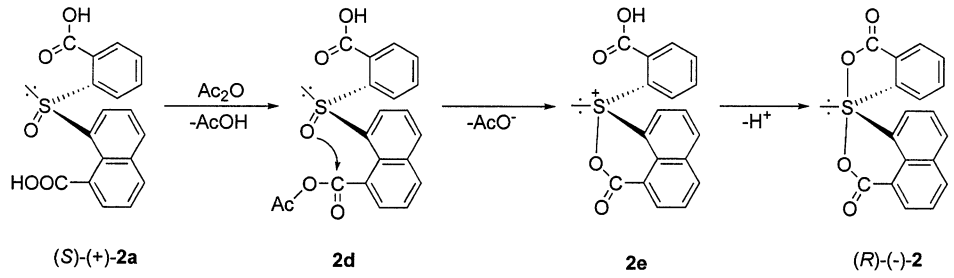
2. Results and discussion

2.1. Resolution of precursor sulfoxide 2a

The resolution of racemic 2-(8-carboxy-1-naphthylsulfinyl)benzoic acid **2a**[8] was carried out by an improved salting out selective extraction procedure published earlier.[19] To the aqueous solution of two equivalents of the dipotassium salt of sulfoxide were added one equivalent of (−)-quinine sulfate and chloroform, and the mixture was shaken until the partition equilibrium was reached. The partially resolved sulfoxide was isolated from both phases. (+)-**2a** and (−)-**2a** were found in 45 and 43% enantiomeric excess in the organic and the aqueous phases, respectively. The enantiomerically pure enantiomers were obtained by utilizing the different solubilities of the enantiomeric and racemic forms of **2a**. The enantiomers dissolve in dioxane, whereas the insoluble racemic form can be filtered off. Thus both (*S*)-(+)-**2a** and (*R*)-(−)-**2a** diaryl sulfoxide dicarboxylic acids were obtained in enantiomerically pure form from the dioxane solutions. (For the designation of configurations see Section 2.5.) The enantiomeric excess was determined by ^{1}H NMR spectroscopy using the complex formed from the corresponding dimethyl ester of (+)-**2a** and (−)-**2a** and the chiral shift reagent Eu(tfc)$_3$.

2.2. Formation of spiro-λ^4-sulfane (*R*)-(−)-2 and (*S*)-(+)-2

When (*S*)-(+)- and (*R*)-(−)-**2a** sulfoxide dicarboxylic acids were treated at room temperature with acetic anhydride in dichloromethane, (*R*)-(−)- and (*S*)-(+)-3*H*-2,1-benzoxathiole-1-spiro-1′-(3*H*-naphtho[1,8-*d*,*e*]-2,1-oxathiine)-3,3′-dione, i.e. (*R*)-(−)-**2** and (*S*)-(+)-**2**, respectively, were obtained. (For the designation of configurations see Section 2.4.) The mechanism of the conversion of sulfoxide (*S*)-(+)-**2a** into spiro-λ^4-sulfane (*R*)-(−)-**2** is shown in Scheme 3.



Scheme 3.

In an earlier paper[1] we described the stereospecific synthesis of diaryl(acyloxy)(alkoxy)spiro-λ^4-sulfane enantiomers starting from optically active diaryl sulfoxides having carboxyl and hydroxymethyl substituents on the aryl rings. As dehydrating agent acetyl chloride was used. The stereospecific ring closure was explained by the formation of an isolated unstable mixed anhydride intermediate which transforms stereospecifically into the given spiro-λ^4-sulfane enantiomer. In the same way we may suppose that the *peri*-carboxyl group in the naphthalene ring is acetylated selectively when one of the enantiomers of **2a** is treated with acetic anhydride, which leads to the reactive mixed anhydride intermediate **2d**. In the following step the sulfinyl-oxygen attacks the carbon atom of the acetylated carboxyl group and one of the spiro ring is formed (**2d**→**2e**). Finally the second spiro ring is closed by the attack of the free *ortho*-carboxyl group on the positive sulfur atom as shown in Scheme 3.

The selective acetylation of the *peri*-carboxyl group can be attributed to the conformation of the precursor sulfoxide **2a**. It is known that phenyl sulfoxides with *ortho*-carboxyl group are stabilized by an effective S···O close contact of 1,5 type.[20] On the other hand, the *peri*-carboxyl group could participate only in a less effective S···O interaction of 1,6 type, so its acetylation is presumably more favorable. Conclusions about the enantiomeric purity of spiro-λ^4-sulfane **2** enantiomers were drawn from hydrolysis experiments (see Section 2.3).

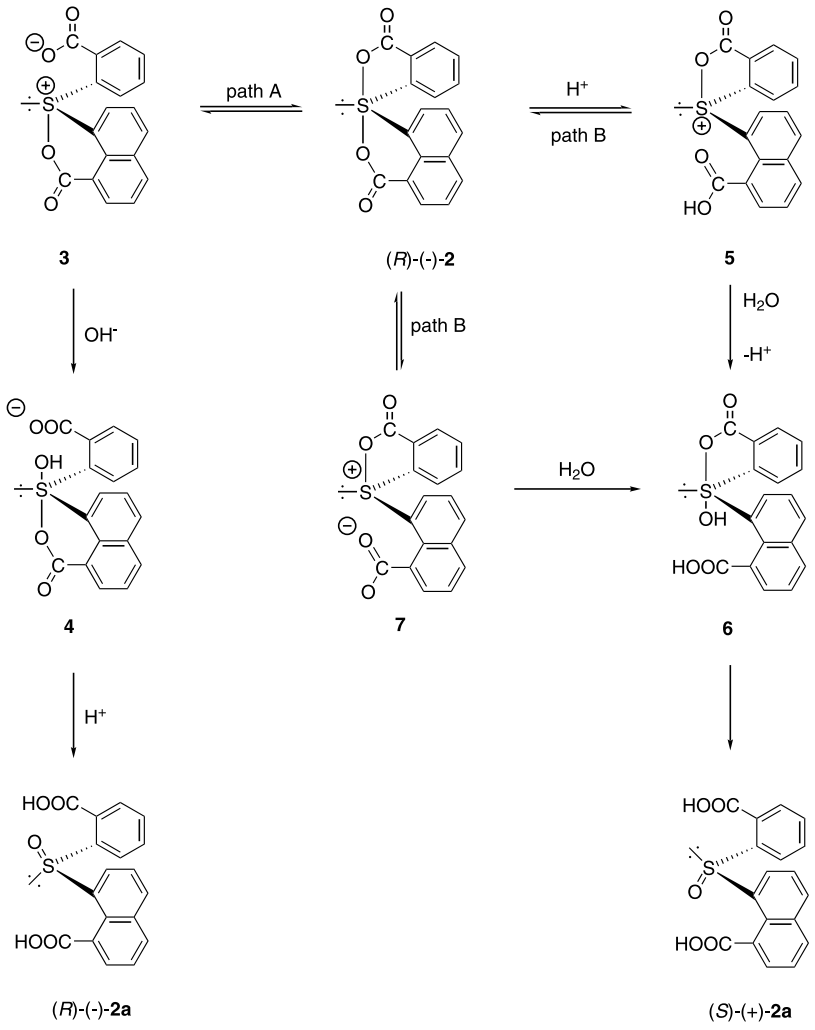
2.3. Hydrolysis of spiro-λ^4-sulfane (*R*)-(−)-2

Previous experiments showed that the hydrolysis of racemic diaryl-bis(acyloxy)spiro-λ^4-sulfane **2** takes place very rapidly,[15] even in a solvent containing only a few percent of water. Both the opening of the spiro ring and the hydrolysis of the monocyclic acyloxysulfonium salt[21] are fast reactions. We investigated now an optically active starting material, spiro-λ^4-sulfane (*R*)-(−)-**2**, and found that the enantiomeric distribution of the sulfoxide product depends on the pH of the medium, similar to the case of diaryl(alkoxy)(acyloxy)- and diaryl-(acylamino)(acyloxy)spiro-λ^4-sulfanes.[3,5] In basic medium sulfoxide (*R*)-(−)-**2a** was formed in 66% e.e., whereas in neutral and acidic solvents (*S*)-(+)-**2a** in 61 and 41% e.e., respectively. On the basis of the present experimental data and earlier findings[3,5,15,16] obtained for the hydrolysis of spiro-λ^4-sulfanes with different axial substituents, we propose two ways of mechanism (path A and path B) to explain the formation of sulfoxide enantiomers in the hydrolysis of spiro-λ^4-sulfane (*R*)-(−)-**2** (Scheme 4).

Path A (basic medium). By an equilibrium splitting of the hypervalent bonds in compound (*R*)-(−)-**2**, one of the spiro rings can be opened, resulting in the formation of monocyclic acyloxysulfonium–carboxylate zwitterion intermediates **3** and **7** (path A and path B). It seems very likely that the equilibria may be shifted toward **3** (with the conservation of the six-membered ring), because in compound **2** the S–O hypervalent bond in the five-membered ring is longer (1.869 Å) and weaker than in the six-membered one (1.839 Å).[8] Although the sulfonium centre built in a six-membered ring (as in **3**) is known to be less reactive[16] than its five-membered analogue (as in **7**), the hydroxide ions in basic medium are strong enough nucleophiles to attack effectively the less reactive sulfonium centre in **3** which can be present in greater concentration than **7**. The reaction of **3** leads to a monocyclic (hydroxy)(acyloxy)-λ^4-sulfane **4** from which (*R*)-(−)-**2a** is formed by ring-opening associated with proton-transfer.

Path B (neutral and acidic media). In neutral and acidic media water molecule as a poor nucleophile can not cleave the six-membered hetero ring in cyclic acyloxysulfonium-carboxylate **3**, but can react with the more reactive sulfonium centre in the analogous intermediates **7** or **5** having five-membered hetero ring.

Path A and path B describe two different stereospecific ways of enantiomeric sulfoxide formation. Because the reactivity of the two acyloxysulfonium-carboxylate **3** and **7**, formed as key intermediates from the starting spiro-λ^4-sulfane (*R*)-(−)-**2**, are not extremely different, the two ways of reaction take place parallel, and so the complex reaction cannot be regarded stereospecific. Nevertheless, path A dominates in basic conditions while path B in neutral and acidic conditions. Unfortunately, from these results we cannot determine exactly the enantiomeric excess of the starting spiro-λ^4-sulfane **2** enantiomers, and can only assert that it may be not less than 66%.



Scheme 4.

2.4. Configuration of diaryl-spiro-λ⁴-sulfanes and related sulfonium salts

The absolute configurations of spiro-λ⁴-sulfanes **8** and **13** were determined by X-ray crystallography,[1] while that of the other spiro-λ⁴-sulfanes **9**–**12** and **14**–**16** and sulfonium salts **8b**, **11b** and **13b**–**16b**, were obtained by comparative analysis of the CD spectra[6,17] (see Table 1 and Figure 1).

The bands in the UV and CD spectra were assigned to the ^1B_b, ^1L_a, and ^1L_b transitions of the aromatic rings. The n→σ* band due to the excitation of the electron in the sulfur lone pair cannot be found in the UV spectrum as it is blue shifted because of the high positive charge of the sulfur atom.[17] An exciton coupling between the ^1L_a transition of the benzene rings or that of the ^1L_a and ^1B_b transitions of the benzene and naphthalene rings, respectively, was observed in the CD spectra of these compounds. It must be mentioned, however, that in some cases the couplet is rather unsymmetric, the intensity of the short wavelength band may be smaller (compounds **10**, **11** and **15**) or it may even be missing (compounds **12** and **13**) from the CD spectra. The sign of the exciton couplet is characteristic for the absolute configuration of the compounds and it can be determined[17] from the orientation of the coupled electric transition dipole moments of the two aromatic rings. The sign of the couplet comes from that of the long wavelength band of the exciton couplet, found at about 240 nm (Table 1). The similarity between the CD spectra of spiro-λ⁴-sulfanes and their sulfonium salt derivatives is the consequence of their analogous trigonal bipyramidal arrangement about the central sulfur atom.

For the definition of a new empirical rule we concluded from the structure of spiro-λ⁴-sulfanes and related sulfonium salts of known absolute configuration that if the molecule of trigonal bipyramidal geometry is viewed from the side of the equatorial lone pair, 'apical axis' is vertical and the hetero rings fused with the aromatic rings or the substituents involved in the S···O close contact are in the upper-right and the lower-left sector,

Table 1. Wavelength and $\Delta\varepsilon$ values ($dm^3\ mol^{-1}\ cm^{-1}$, in acetonitrile) of the long wavelength bond of the exciton couplet for spiro-λ^4-sulfanes and sulfonium salts of trigonal bipyramidal geometry. Formulas are given in Figure 1.

Compound	Formula	U–V–S	Z–Y	λ/nm	$\Delta\varepsilon$	Ref.
(*R*)-(−)-**2**	D	CO–O–S	CO–O	236	−61.8	[a]
(*S*)-(+)-**2**	C	CO–O–S	CO–O	236	86.6	[a]
(*S*)-(−)-**8**	A, X = H	CO–O–S	CH_2–O	234.5	52.3	17
(*R*)-(+)-**8**	B	CO–O–S	CH_2–O	234.5	−52.3	1,6,17
(*S*)-(−)-**8b**	B	$C(OCH_3)$=O···S^+	CH_2–O	243	−22.8	5,6
(*S*)-(+)-**9**	A, X = H	CO–O–S	CO–O	236	53.5	17
(*S*)-(+)-**10**	A, X = Cl	CO–O–S	CO–O	242	83.9	17
(*S*)-(+)-**11**	A, X = H	CO–O–S	CO–NMe	238.5	42.4	6,17
(*R*)-(+)-**11b**	A, X = H	$C(OCH_3)$=O···S^+	CO–NMe	239	42.1	6
(*S*)-(+)-**12**	A, X = Cl	CO–O–S	CO–NMe	243	27.2	17
(*R*)-(+)-**13**	C	CO–O–S	CH_2–O	237.5	75.4	1,6,17
(*S*)-(−)-**13**	D	CO–O–S	CH_2–O	237.5	−75.4	17
(*S*)-(+)-**13b**	C	$C(OCH_3)$=O···S^+	CH_2–O	242	29.9	6
(*R*)-(−)-**13b**	D	$C(OCH_3)$=O···S^+	CH_2–O	242	−29.9	5
(*R*)-(+)-**14**	C	CO–O–S	CO–NMe	236	71.0	6
(*S*)-(+)-**14b**	C	$C(OCH_3)$=O···S^+	CO–NMe	237.5	89.9	6
(*S*)-(+)-**15**	E	CO–O–S	CH_2–O	237.5	125	1,6,17
(*R*)-(−)-**15b**	E	$C(OCH_3)$=O···S^+	CH_2–O	227	60.5	5,6
(*S*)-(+)-**16**	E	CO–O–S	CO–NMe	235	80.4	6
(*R*)-(+)-**16b**	E	$C(OCH_3)$=O···S^+	CO–NMe	235.5	103	6

[a] This work.

then the sign of the exciton couplet is positive (Formulas A, C and E in Fig. 1 and Table 1). On the other hand, the sign of the couplet is negative if the hetero rings or the given substituents are in the upper-left and lower-right sectors (Formulas B and D in Fig. 1, Table 1). The sign of the sectors is opposite to that used for the octant rule of ketones.[22] The rule was found to be valid for the sign of the Cotton effect of the band near to 240 nm even in those cases when the short wavelength band of the couplet was missing from the CD spectrum (e.g. in the case of compounds **12** and **13**, Table 1). The sign of the couplet is related to the configuration of the molecules and does not have any connection with the stereochemical descriptors (*R*) and (*S*), which are based on a priority convention and do not express any stereochemical analogy. It is remarkable that spiro-λ^4-sulfanes and their sulfonium salt derivatives, with different chemical bonds but with the same spatial arrangement, give rise to couplets with the same sign. Besides, the first eluted enantiomer of spiro-λ^4-sulfanes on an HPLC column with the chiral sorbent Kromasil CHI DMB shows a positive exciton couplet[4,6,17] and therefore a structure analogous to those given in formulas A, C or E in Figure 1.

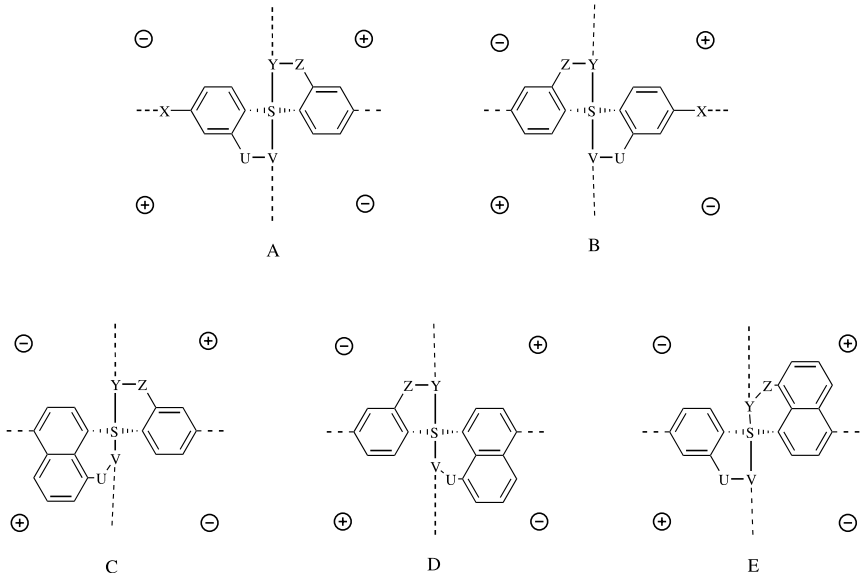


Figure 1. Schematic representation of the empirical rule for prediction of the sign of the exciton couplet for spiro-λ^4-sulfanes and related sulfonium salts of trigonal bypyramidal structure. The molecules are viewed from the side of the equatorial lone pair (not shown in the Figure as being in overlap with the central sulfur atom); Z–Y and U–V–S symbols are explained in Table 1.

Data obtained from the CD and UV spectra of naphthyl-phenyl-bis(acyloxy)spiro-λ^4-sulfanes enantiomers **2** are given in Table 2.

The ^1L_a and ^1L_b transitions of the naphthalene and the ^1L_b transition of the benzene ring show Cotton effects of small intensity between 260 and 330 nm. One can find, however, a high intensity negative exciton couplet at 236 and 216 nm in the CD spectrum of the (−)-**2** (Fig. 2) and a positive one for the (+) enantiomer (Table 2). This couplet can be assigned to the coupled electrical transition dipoles of the ^1B_b transition of the naphthalene (long-axis polarization) and the ^1L_a transition of the benzene ring (polarization direction along the aromatic *para*-carbon and the carbonyl-carbon atoms). As shown in Figure 3 the given transition dipole moments define a negative projection angle for the (*R*)-enantiomer, so this configuration can be assigned to (−)-**2**, exhibiting a negative couplet in the CD spectrum.

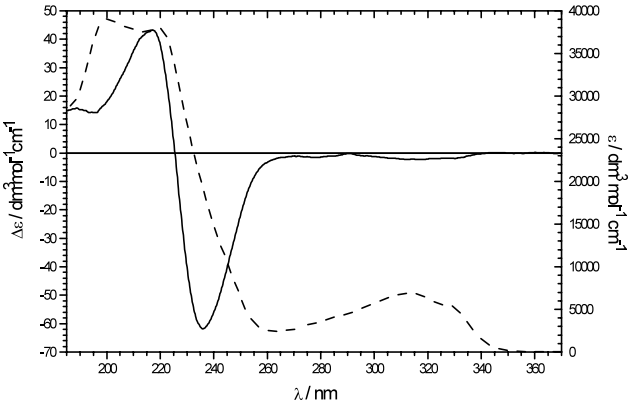


Figure 2. CD (—) and U V (- - -) spectra of (*R*)-(−)-**2** (in acetonitrile).

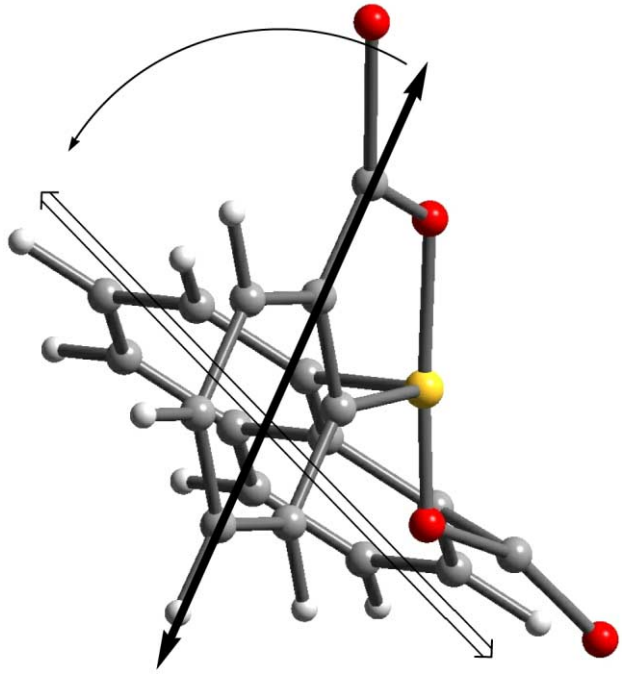


Figure 3. Orientation of the benzene ^1L_a and naphthalene ^1B_b transition dipole moments of (*R*)-(−)-**2**, which define negative chirality.

Table 2. Spectral data of naphthyl-phenyl-bis(acyloxy)spiro-λ^4-sulfane **2**, (8-carboxy-1-naphthylsulfinyl)benzoic acid **2a** and (8-carboxy-1-naphthylsulfinyl)benzoic acid methyl ester **2c**. Solvent: acetonitrile; for **2c** acetonitrile and ethanol

Compound	Spectrum	λ/nm (CD: $\Delta\varepsilon$/dm^3 mol^{-1} cm^{-1}; UV: $\varepsilon/10^3$ dm^3 mol^{-1} cm^{-1})
(*R*)-(−)-**2**[a]	CD	217 (43.3)[h] 236 (−61.8)[h] 274 (−1.4)[i] 312 (−2.3)[i] 330 (−1.9)[i]
	UV	200 (39.1)[g] 219 (38.0)[h] 313 (6.9)[i] ~333(4.3)[i]
(*S*)-(+)-**2**[b]	CD	216 (−61.3)[h] 236 (86.8)[h] 273 (2.7)[i] 311 (3.5)[i] 328 (3.3)[i]
	UV	200 (43.1)[g] 219 (42.1)[h] 313 (7.6)[i] ~327 (6.1)[i]
(*R*)-(−)-**2a**[c]	CD	198 (48.0)[g] 230.5 (−47.0)[h] 257.5 (−43.6)[h] ~278 (−7.6)[i] 301 (11.2)[i]
	UV	200 (37.0)[g] 227 (47.5)[h] 294 (8.1)[i]
(*S*)-(+)-**2a**[d]	CD	198 (−48.8)[g] 232 (48.0)[h] 257.5 (45.2)[h] ~281 (7.4)[i] 304 (−11.6)[i]
	UV	200 (36.8)[g] 227 (47.3)[h] 294 (7.9)[i]
(*S*)-(+)-**2c**[e]	CD	198 (−48.8)[g] 232 (36.3)[h] 257 (36.5)[h] ~283 (3.0)[i] 301 (−8.6)[i]
	UV	199 (39.4)[g] 227 (52.5)[h] 294 (8.8)[i]
(*S*)-(+)-**2c**[f]	CD	198 (−61.1)[g] ~223.5 (38.5)[j] 234 (47.9)[h] 257 (45.8)[h] ~282 (6.5)[i] 302 (−9.1)[i]
	UV	199 (41.7)[g] 227 (55.6)[h] 295 (9.4)[i]

Structures:
[a] Formula D, Fig. 1; U–V–S=CO–O–S, Z–Y=CO–O.
[b] Formula C, Fig. 1; U–V–S=CO–O–S, Z–Y=CO–O.
[c] Formula F, Fig. 7; X=Y=COOH.
[d] Formula G, Fig. 7; X=Y=COOH.
[e] Formula G, Fig. 7; X=Y=COOMe; solvent: acetonitrile.
[f] Formula G, Fig. 7; X=Y=COOMe; solvent: ethanol.
Assignments:
[g] ^1B_b transition of the benzene ring.
[h] ^1B_b transition of the naphthalene ring and ^1L_a transition of the benzene ring.
[i] ^1L_a and ^1L_b transitions of the naphthalene ring and ^1L_b transition of the benzene ring.
[j] n→σ* transition of the sulfur lone pair.

The same result is obtained with the application of the empirical rule. On the basis of the sign of the bands at 236 nm in the CD spectrum (Table 1) the structures D and C (Fig. 1) and therefore configuration (*R*) and (*S*), respectively, can be proposed for the (−)- and (+) enantiomers of **2**.

2.5. Configuration of naphthyl phenyl sulfoxides

The CD spectra of dialkyl, alkyl phenyl and diphenyl sulfoxides are widely discussed in the literature.[23–25] Three bands can be found in the UV spectra of naphthyl-phenyl-sulfoxides substituted with two carboxyl groups (compound **2a**) at about 200, 230 and 295 nm. In the CD

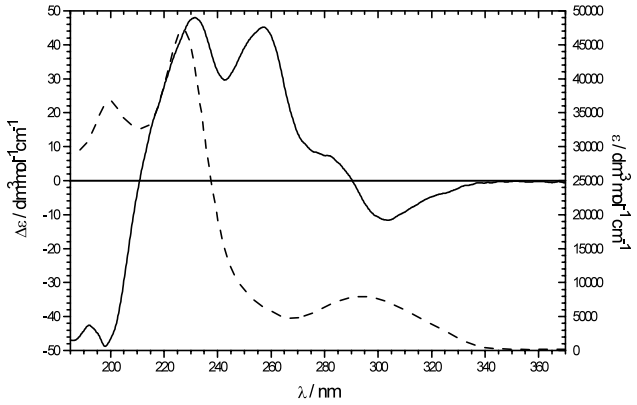


Figure 4. CD (—) and UV (- - -) spectra of (*S*)-(+)-**2a** (in acetonitrile).

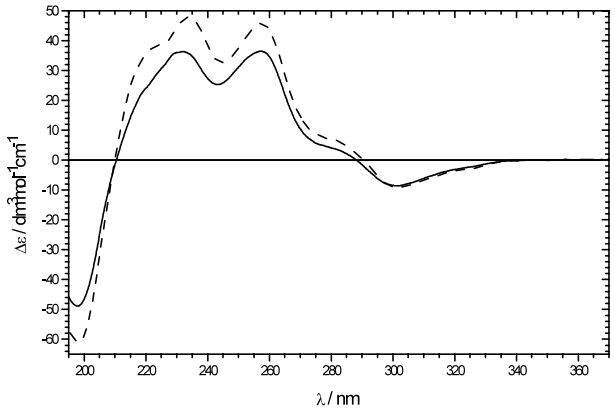


Figure 5. CD spectra of (*S*)-(+)-**2c** in acetonitrile (—) and ethanol (- - -).

spectrum (Fig. 4) two additional Cotton effects are present in the vicinity of 260 and 280 nm. The CD bands at 200 and 300 nm are of opposite sign as the others. These bands can be assigned to the ^1B_b, ^1L_a and ^1L_b electronic transitions of the naphthalene and benzene rings as given in Table 2.

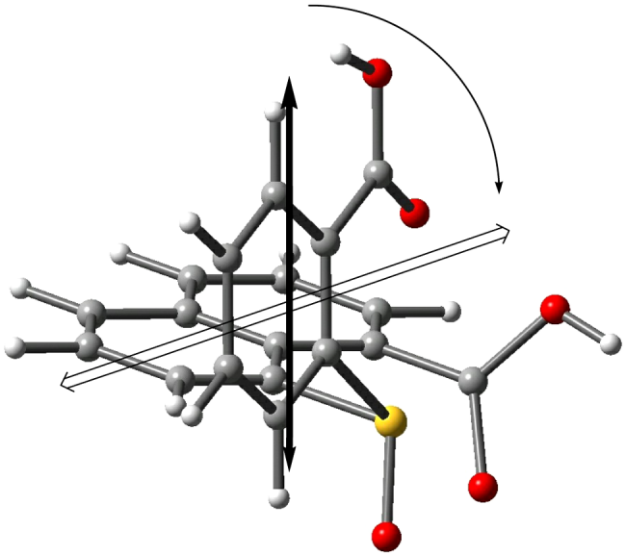


Figure 6. Orientation of the ^1B_b transition dipole moments of benzene and naphthalene rings in (*S*)-(+)-**2a**, which define positive chirality.

The CD spectrum of (+)-**2c**, the dimethyl ester of sulfoxide-(+)-**2a**, (Fig. 5) recorded in acetonitrile is very similar to that of sulfoxide dicarboxylic acid (+)-**2a** (Fig. 4). Intramolecular hydrogen bonds seems to have no effect on the electronic transitions of the sulfoxide **2a**. Comparing the curves of (+)-**2c** in acetonitrile and ethanol, a shoulder can be seen at 223.5 nm in the latter solvent. This can be assigned to the $n\rightarrow\sigma^*$ transition of the sulfur atom, which is blue shifted in the protic solvent. The CD spectra of the enantiomers of (+)-**2a**, (+)-**2c** and (−)-**2a** are analogous to those of (*S*)-(+)-**13a**, (*S*)-(+)-**15a** (configuration determined by X-ray diffraction[1]) and (*S*)-(+)-**16a**[6] and to that of (*R*)-(−)-**14a**[6] of known absolute configuration, respectively (Table 3). This suggests (*S*) configuration for (+)-**2a** and (+)-**2c**, while (*R*) configuration for (−)-**2a**.

X-Ray diffraction studies[2] proved that the S=O bond and the benzene ring are nearly in the same plane in the

Table 3. λ/nm (Δε) values (in acetonitrile) of the Cotton effect of the ^1B_b transition of the naphthalene ring and ^1L_a transition of the benzene ring in naphthyl phenyl sulfoxides. Formulas are given in Figure 7

Compound	Formula	Y	X	λ/nm (Δε)	Ref.
(*R*)-(−)-**2a**	F	COOH	COOH	230.5 (−47.0) 257.5 (−43.5)	b
(*S*)-(+)-**2a**	G	COOH	COOH	232 (48.0) 257.5 (45.2)	b
(*S*)-(+)-**2c**	G	COOMe	COOMe	232 (36.3) 257 (36.5)	b
(*R*)-(−)-**13a**	F	CH_2OH	COOH	233 (−77.5)	6
(*S*)-(+)-**13a**	G	CH_2OH	COOH	233 (77.5)	1
(*R*)-(−)-**13c**	F	CH_2OH	COOMe	234 (−48.2)	6
(*R*)-(−)-**14a**	F	CONHMe	COOH	230 (−40.4), 254 (−43.4)	6
(*R*)-(−)-**14c**	F	CONHMe	COOMe	229 (−31.8), 253.5 (−51.6)	6
(*S*)-(+)-**15a**	G	COOH	CH_2OH	232 (65.3), 259 (15.2)	1,6
(*S*)-(+)-**15c**	G	COOMe	CH_2OH	231 (46.6), 254 (10.8)	6
(*S*)-(+)-**16a**	G	COOH	CONHMe	230 (49.9), 255.5 (23.7)	6
(*S*)-(+)-**16c**	G	COOMe	CONHMe	229.5 (78.4), 256 (35.6)	6
(*S*)-(+)-**17**[a]	–	–	–	242 (−7.1)	24

[a] (2-Naphthyl) (4-tolyl) sulfoxide.
[b] This work.

energetically most favored conformation of the naphthyl-phenyl-sulfoxides, and the naphthalene ring is by about 110° twisted with respect to this plane (Fig. 6).

The aromatic rings together with their C-substituents are placed in the region opposite to the S→O bond direction and there is a close contact between the sulfur atom and the oxygen atom of the carbonyl group bound to the benzene ring. It seems from the CD spectra (+)-**2a** and (+)-**2c** that exciton coupling occurs in these compounds between the ^1B_b bands of the benzene and naphthalene rings, as an EC-CD spectrum can be observed (Table 2, Figs. 4 and 5). Though the true directions of the two ^1B_b transitions dipoles of the disubstituted aromatic rings are not known, they seem to define positive chirality and a positive couplet in the given conformation for compounds (+)-**2a** with an (*S*)-configuration (Fig. 6).

An empirical rule can also be used for the determination of the configuration of naphthyl-phenyl-sulfoxides. The molecules of the given type should be viewed from the direction of the lone pair with the S=O bond placed downwards in a vertical plane (Fig. 7).

If the naphthalene ring is in the upper-right or lower-left sector then the sign of the Cotton effect found between 230 and 250 nm and assignable to the naphthalene ^1B_b and benzene ^1L_a transitions is positive. If the naphthalene ring is situated in the upper-left or lower-right sector then the Cotton effect is negative (Fig. 7, Table 3). The signs of the sectors is the same as those for spiro-λ^4-sulfanes and sulfonium salts. The rule proved to be valid for determining the configuration of (*S*)-(+)-(2-naphthyl) (4-tolyl) sulfoxide **17**[24] (Table 3) as well as (*S*)-alkyl-phenyl- and (*S*)-alkyl-naphthyl-sulfoxides.[25] For alkyl aryl sulfoxides the position of the aromatic ring defines the sign of the couplet.

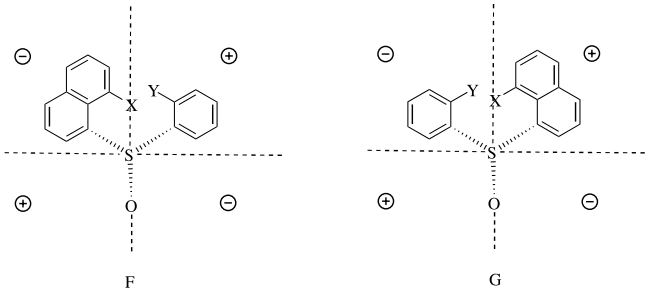


Figure 7. Schematic representation of the empirical rule for prediction of the sign of the exciton couplet for naphthyl phenyl sulfoxides. The molecules are viewed from the direction of the lone pair (not shown in the Figure as being in overlap with the central sulfur atom) with the S=O bond placed downwards in a vertical plane; X and Y symbols are explained in Table 3.

3. Experimental

3.1. CD measurements

CD spectra of the samples were measured on a Jasco J 810 Dichrograph. Circular dichroism is expressed as $\Delta\varepsilon$, in units of $dm^3\ mol^{-1}\ cm^{-1}$. Measurements were carried out at rt in 0.05 cm cells. Acetonitrile and ethanol were used as solvents. The concentration of the samples ranged between 3.5 and 3.8 mM.

3.2. (*R*)-(−)- and (*S*)-(+)-2-(8-Carboxy-1-naphthylsulfinyl)benzoic acid 2a

To a solution of $KHCO_3$ (6 g, 60 mmol) in water (100 mL) was added racemic sulfoxide **2a** (6.8 g, 20 mmol) and stirred to afford a clear solution. Then it was transferred into a separatory funnel and mixed with (−)-quinine sulfate dihydrate (7.82 g, 10 mmol) and chloroform (250 mL). The mixture was shaken until two clear liquid phases were formed at 25°C equilibrium temperature (~300 shakings). The water layer was separated and washed with chloroform (3×10 mL), then acidified with 1N H_2SO_4 (~45 mL) at 5°C to yield a solid precipitate. It was kept in ice-bath for 1 h, then filtered off and washed free from H_2SO_4 with distilled water to give sulfoxide (−)-**2a** monohydrate (3.59 g); $[\alpha]_{578}=-222$ ($c=0.5$, DMF, 25°C); e.e.=43%. The above sulfoxide monohydrate (2.52 g, 7.04 mmol of $[\alpha]_{578}=-222$) was stirred with dioxane (50 mL) at rt for 1 h. The crystalline precipitate was filtered off and washed with dioxane (3×5 mL) and dried to afford 1.82 g of the racemic sulfoxide **2a**–dioxane 1:1 complex. The dioxane solution was treated with charcoal at rt for 1 h, then filtered and evaporated in vacuo at 35–40°C. The resulting oil was dissolved in 0.5N $KHCO_3$ (20 mL) and about 5 mL of the solvent was removed in vacuo. The dioxane-free solution obtained was acidified at 10°C by 1N H_2SO_4 (pH 2). The white crystalline product was filtered off and washed with water and dried over KOH in a vacuum desiccator to yield enantiomerically pure sulfoxide (−)-**2a** monohydrate (1.01 g); $[\alpha]_{578}=-508$ (c 0.5, DMF, 25°C); e.e. >98%; mp 235–250°C (dec.); IR ν_{max} (KBr)/cm^{-1} 3537s (OH, H_2O), 3300–2200br (OH, COOH), 1695vs (C=O), 989vs (S=O). ^1H NMR (250 MHz, DMSO-d_6) δ 13.38 (br, 2H, COOH), 7.40–8.52 (m, ArH).

To prepare the (+)-enantiomer of **2a** the chloroform phase was extracted with 1N Na_2CO_3 solution (3×50 mL) and acidified with 5N H_2SO_4 (30 mL) at 5°C. The precipitate was collected by filtration, washed with water and dried to yield compound (+)-**2a** monohydrate (3.46 g); $[\alpha]_{578}=+232$ (c 0.5, DMF, 25°C); e.e.=45%. To obtain the enantiomerically pure enantiomer of (+)-**2a** a similar procedure was applied as described for the purification of (−)-**2a** (1.0 g); $[\alpha]_{578}=+510$ (c 0.5, DMF, 25°C); e.e.>98%.

3.3. (*R*)-(−)- and (*S*)-(+)-3*H*-2,1-benzoxathiole-1-spiro-1′-(3*H*-naphtho[1,8-*d*,*e*]-2,1-oxathiine-3,3′-dione 2

Sulfoxide (*S*)-(+)-**2a** (0.18 g, 0.50 mmol) was dried by azeotropic distillation of dioxane in vacuo at 40°C

(3×10 mL). The residue was dissolved in dry pyridine (2 mL) and to this solution was added a mixture of 1:9 dichloromethane-acetic anhydride (0.5 mL). After stirring for 10 min at rt diethyl ether (4 mL) was added and the crystals precipitated was filtered off, washed with diethyl ether (3x2 mL) and dried to afford (*R*)-(−)-**2** (0.12 g, 75%); $[\alpha]_{578} = -416$ (*c* 0.5, DMF, 25°C); mp 249–256°C (dec.); IR ν_{max} (KBr)/cm^{-1} 1724vs, 1695vs (C=O); ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.56–8.76 (m, ArH).

Spiro-λ^4-sulfane (*S*)-(+)-**2** was prepared by a similar procedure starting from sulfoxide (*R*)-(−)-**2a**. Yield: 0.13 g (80%); $[\alpha]_{578} = +387$ (*c* 0.5, DMF, 25°C).

3.4. Hydrolysis of spiro-λ^4-sulfane (*R*)-(−)-2

(A) The mixture of spiro-λ^4-sulfane (*R*)-(−)-**2** (0.1 g, 0.31 mmol), acetone (2 mL) and aqueous Na_2CO_3 (1 M, 2 mL) was stirred at rt for 15 min then acidified with HCl (2 M, 2 mL). Acetone was removed in vacuo, the crystals were collected by filtration, washed with water and dried. Yield: 0.087 g, (83%). (*R*)-(−)-**2a**; $[\alpha]_{578} = -342$ (*c* 0.5, DMF, 25°C), e.e. 66%.

(B) The mixture of spiro-λ^4-sulfane (*R*)-(−)-**2** (0.1 g, 0.31 mmol), acetone (2 mL) and water (2 mL) was stirred at rt for 15 min. Acetone was removed in vacuo, the crystals were collected by filtration, washed with water and dried. Yield: 0.086 g, (82%). *(S)*-(+)-**2a**; $[\alpha]_{578} = +316$ (*c* 0.5, DMF, 25°C), e.e. 61%.

(C) The mixture of spiro-λ^4-sulfane (*R*)-(−)-**2** (0.1 g, 0.31 mmol), acetone (2 mL) and aqueous HCl (1 M, 1 mL) was stirred at rt for 15 min. Acetone was removed in vacuo, the crystals were collected by filtration, washed with water and dried. Yield: 0.089 g, (85%). *(S)*-(+)-**2a**; $[\alpha]_{578} = +212$ (*c* 0.5, DMF, 25°C), e.e. 41%.

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