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The Effect of Molecular Structure on the Optical Properties of Sulfoxide Systems. The o-Bromophenylsulfinylacetic Acids and Some of Their Derivatives. VI *

Wpływ budowy cząsteczkowej na własności optyczne układów sulfotlenkowych. Kwasy o-bromofenylosulfinylooctowe i niektóre ich pochodne. VI

Влияние молекулярного строения на оптические свойства сульфоокислых систем. о-бромофенилосульфинилоуксусные кислоты и некоторые их производные. VI

The problem of the effect of halogen atom position isomerism in benzene ring on the optical properties of aromatic-aliphatic compounds, containing sulfinylic chirality centers, is being studied in our laboratory which is exemplified by bromo derivatives of phenyl- and benzylsulfinylacetic acids. In the previous communications [1, 2] we have described the synthesis and the principal chiraloptical properties of enantiomeric phenylsulfinylacetic acids and of their meta- and para- bromo derivatives. Continuing our studies we are now examining the o-bromophenylsulfinylacetic acids.

In the present communication we describe the results of studies on the synthesis and the principal optical and stereochemical properties of enantiomeric o-bromophenylsulfinylacetic acids.

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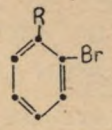

1: R=SH
2: R=SCH_2COOH
3: R=$\overset{(\pm)}{S}O \cdot CH_2COOH$
4: R=$\overset{(\pm)}{S}O \cdot CH_2 \cdot CO \cdot OCH_3$
5: R=$\overset{(\pm)}{S}O \cdot CH_2 \cdot CO \cdot NH_2$
6: R=$\overset{(\pm)}{S}O \cdot CH_2 \cdot CO \cdot OCH_2 \cdot C_6H_4 \cdot NO_2$
7: R=$\overset{(\pm)}{S}O \cdot CH_2 \cdot CO \cdot OCH_2CO \cdot C_6H_4Br$
8: R=$\overset{(+)}{S}O \cdot CH_2 \cdot COOH$ · Strych. *
9: R=$\overset{(+)}{S}O \cdot CH_2 \cdot COOH$
10: R=$\overset{(-)}{S}O \cdot CH_2 \cdot COOH$ · Cynch. **
11: R=$\overset{(-)}{S}O \cdot CH_2 \cdot COOH$
12: R=$\overset{(-)}{S}O \cdot CH_2 \cdot COOCH_3$
13: R=$\overset{(-)}{S}O \cdot CH_2 \cdot CO \cdot NH_2$
14: R=$\overset{(-)}{S}O \cdot CH_2 \cdot CO \cdot OCH_2 \cdot C_6H_4NO_2$
15: R=$\overset{(-)}{S}O \cdot CH_2 \cdot CO \cdot OCH_2CO \cdot C_6H_4Br$
16: R=$SO_2 \cdot CH_2 \cdot COOH$

The starting material in our studies was the already known [3] o-bromophenylthioglycolic acid (2), which we obtained in considerable yield by coupling o-bromothiophenol (1) with chloroacetic acid in an alkaline solution. The structure of acid 2 was confirmed by its IR spectrum (the characteristic bands are given in the Experimental Part). The racemic o-bromophenylsulfinylacetic acid (3), which was necessary for our chiraloptical studies, was prepared by oxidation of compound 2 with 30% hydrogen peroxide at room temperature in glacial acetic acid. When an excess of the oxidizing agent was used, sulfone 16 was formed (the IR spectra confirming the structures of the oxidation products are given in the Experimental Part). The compound 3 was characterized as its amide (5) and methyl (4), p-nitrobenzyl (6) and p-bromophenacyl (7) esters.

The racemic acid 3 was resolved by crystallization of diastereomeric salts with optically active bases. For this purpose the neutral salts of strychnine and cinchonine were the most suitable. During the fractional crystallization of the strychnine salt the first fractions contained the salt of the dextrorotatory acid, whereas the laevorotatory enantiomer could be separated from the racemate by crystallization of the cinchonine salt. After the liberation from the alkaloids and crystallization from benzene the antimeric acids 9 and 11 had high specific rotations: $[\alpha]_D^{20} = +320.0°$ and $-321.3°$ (ethanol). On mixing acids 9 and 11 in equimolar proportions and crystallizing the mixture, the racemic acid 3 was recovered. The melting point of the racemate 3 is by 11° lower than that of the antipodes 9 and 11. In the "finger print" region the IR spectrum of the racemic acid 3 is different from the spectra of the enantiomers, which are identic-

* Strych. — strychnine.
** Cynch. — cinchonine.

al. Since the racemic acid 3 is not readily resolved, it is probably a true racemate. This conclusion is confirmed by the above mentioned physical differences.

Optically active o-bromophenylsulfinylacetic acids 9 and 11 are resistant to racemization in alkaline media but are readily racemized in organic solution in the presence of concentrated hydrochloric acid. The racemization was studied in a solvent consisting of dioxane and dilute ($d=1.15$) hydrochloric acid (2:1 v/v) [1, 4]. Under these conditions the racemization was obeying the kinetic equation of the first order reactions: $K=(1/t)\ln(\alpha_0/\alpha)$. The racemization constants (K), the activation enthalpies ($\Delta H^{\#}$) and the activation entropies ($\Delta S^{\#}$), calculated at five temperatures and averaged by the least squares method, are shown in Table 1. The activation parameters were calculated by means of the Eyring equation [5].

Table 1. Thermodynamic characteristics of racemization of optically active o-bromophenylsulfinylacetic acids

Racemization temperature +°C	Racemization constant $K \cdot 10^5$ sec^{-1}	Activation entropy $\Delta S^{\#}$ eu	Activation enthalpy $\Delta E^{\#}$ kcal/mole
12	1.20 ±0.19	−3.21 ±1.01	22.25 ±0.09
16	1.52 ±0.19	−3.23 ±0.82	22.24 ±0.07
20	3.03 ±0.20	−3.26 ±0.43	22.23 ±0.04
24	5.10 ±0.20	−3.28 ±0.26	22.23 ±0.02
28	9.59 ±0.24	−3.31 ±0.16	22.22 ±0.01

The activation energy (E_a) and the preexponential factor ($A=K_{max}$) were calculated by means of the empirical Arrhenius equation ($K=A\cdot e^{-Ea/RT}$); $E_a=22.816$ kcal/mole, $A=3.24.10^{12}$ sec^{-1}. The negative values of the activation entropy suggest that the transition states in the racemization reaction, have the character of additive compounds or that they are the compounds which have been suggested by the American [9] and German [6—8] authors in the case of arylalkylsulfoxides.

In order to obtain the sufficient material for chiralooptical studies we have prepared the following derivatives of laevorotatory acid 11: amide (13), methyl ester (12), p-nitrobenzyl ester (14) and p-bromophenacyl ester (15). The syntheses of these compounds were, at first, carried out on optically inactive material. Since the reactions were carried out under mild conditions, the racemization on the asymmetric sulfur atom was unlikely. The molar rotation of laevorotatory acid 11 was determined in Perkin-Elmer 241-MC spectropolarimeter in the region $320<\lambda<623$ nm, and those of its amide and esters in the previously described apparatus [10] at wave lengths given in the tables using methanol (M), ethanol (E), acetone (A), dioxane (D) and chloroform (Ch) as solvents. The results are shown in Tables 2 and 3.

Table 2. Rotatory dispersion of laevorotatory o-bromophenylsulfinylacetic acid

Compound	Solvent	Molar rotation $[M]_\lambda^{20}$							
		623.4 nm	600.0 nm	589.3 nm	579.1 nm	560.0 nm	576.1 nm	520.0 nm	480.0 nm
Laevorotatory o-bromophenylsulfinyl acetic acid	Methanol	768.3 (770.2)	842.0 (846.4)	884.1 (885.3)	920.9 (925.2)	999.8 (1008.2)	1063.0 (1076.6)	1226.1 (1227.4)	1541.9 (1538.4)
	Ethanol	757.8 (764.1)	(842.0) (839.8)	878.8 (878.5)	915.6 (918.2)	989.3 (1000.8)	1057.7 (1068.8)	1210.3 (1219.1)	1526.1 (1529.1)
	Acetone	799.9	878.8	920.9	957.7	1047.2	1120.9	1273.5	1612.9
	Dioxane	792.0 (799.1)	876.2 (879.9)	915.6 (921.3)	955.1 (963.8)	1047.2 (1052.5)	1120.9 (1125.7)	1289.6 (1288.0)	1628.1 (1625.1)
	Chloroform	678.8 (680.9)	747.2 (749.9)	765.7 (785.3)	810.4 (821.6)	894.6 (897.4)	963.0 (960.0)	1102.5 (1098.9)	1397.2 (1388.2)

	Molar rotation $[M]_\lambda^{20}$						
Solvent	440.0 nm	435.8 nm	400.0 nm	380.0 nm	360.0 nm	340.0 nm	320.0 nm
Methanol	2020.7 (2009.5)	2083.9 (2073.1)	2807.5 (2796.0)	3425.8 (3419.7)	4320.4 (4336.6)	5788.6 (5794.9)	8398.7 (8394.1)
Ethanol	2010.2 (1999.6)	2706.0 (2063.3)	2807.5 (2787.2)	3420.5 (3413.4)	4323.0 (4336.4)	5793.8 (5808.8)	8451.3 (8444.1)
Acetone	2115.5	2194.4	2983.8	3654.7	4657.2	6246.4	—
Dioxane	2147.0 (2141.2)	2220.7 (2211.5)	3031.1 (3015.8)	3728.4 (3719.3)	4762.4 (4768.6)	6456.9 (6474.6)	9640.6 (9633.8)
Chloroform	1841.8 (1833.1)	1894.4 (1893.8)	2599.6 (2592.3)	3215.3 (3207.6)	4125.7 (4131.9)	5636.0 (5647.3)	8482.9 (8478.2)

c=0.1 g/100 ml

Table 3. Rotatory dispersion of some derivatives of laevorotatory o-bromophenylsulfinylacetic acid

Compound	Solvent	Conc.	Molar rotation $[M]_\lambda^{20}$				
			623.4 nm	589.3 nm	579.1 nm	546.1 nm	435.8 nm
Methyl ester of laevorotatory o-bromophenylsulfinylacetic acid	Methanol	0.4	796.8	911.1	949.2	1080.3	2040.5
	Ethanol	0.4	817.6	918.0	952.7	1100.1	2092.4
	Acetone	0.4	838.4	938.8	970.0	1136.4	2127.1
	Dioxane	0.4	786.4	900.7	938.8	1077.4	2030.1
	Chloroform	0.4	845.3	945.8	1008.1	1164.0	2134.0
Amide of laevorotatory o-bromophenylsulfinylacetic acid	Methanol	0.3	862.8	942.1	990.5	1148.9	2135.1
	Ethanol	0.3	859.0	928.9	959.3	1105.5	2121.9
	Acetone	0.3	871.6	950.9	999.3	1162.2	2139.5
	Dioxane	0.3	810.0	876.0	911.3	1047.7	2033.8
	Chloroform	—	—	—	—	—	—
p-Bromophenacyl ester of laevorotatory o-bromophenylsulfinylacetic acid	Methanol	0.3	881.9	1104.4	1119.7	1219.4	2038.4
	Ethanol	0.3	797.6	1073.7	1081.4	1173.4	2239.4
	Acetone	0.4	920.3	1115.9	1127.4	1248.2	2392.8
	Dioxane	0.4	1012.3	1150.4	1179.1	1397.7	2576.9
	Chloroform	0.4	1035.4	1167.6	1173.4	1426.5	2651.6
p-Nitrobenzyl ester of laevorotatory o-bromophenylsulfinylacetic acid	Methanol	0.4	861.2	1015.5	1050.4	1219.6	2245.1
	Ethanol	0.4	935.9	1030.5	1060.3	1239.5	2289.9
	Acetone	0.4	950.8	1040.4	1075.3	1254.5	2314.8
	Dioxane	0.4	1005.6	1075.3	1120.1	1289.3	2399.4
	Chloroform	0.4	1090.2	1179.8	1244.5	1354.6	2678.2

The data collected in Tables 2 and 3 show that the molar rotations are solvent dependent. In the visible part of the spectrum the absolute values of molar rotations in the examined solvents decrease in the following order: a) free acid: A>D>M>E>Ch; b) acid amide: A>M>E>D; c) methyl ester: Ch>A>E>M>D; p-nitrobenzyl ester: Ch>D>A>E>M; p-bromophenacyl ester: Ch>D>A>M>E.

In all the solvents the difference between the molar rotation of free acid 11 and its p-nitrobenzyl ester 14 was fairly large in the region 546—623 nm. The molar rotations of the ester were much lower than those of the free acid. In case of the amide this difference was much less pronounced in all the solvents with the exception of dioxane. It should be mentioned that the molar rotations of p-bromophenacyl ester were much lower than those of the free acid.

An analysis of the numerical values shown in Tables 2 and 3 indicates that the curves representing the function $(1/\alpha)(\lambda^2)$, in the region $423<\lambda<623$ nm for the laevorotatory acid and its derivatives 12, 13, 14 and 15 are almost linear, which leads to the conclusion that in this region the optical rotatory dispersion of the examined compounds is normal.

The rotational relationships presented above make it possible to determine the configurations of the optically active o-bromophenylsulfinylacetic acids, on the basis of the Freudenberg shift rule and on the basis of the solvent effect on the examined compounds and the reference system. In the first case, the configurational standards were laevorotatory phenylsulfinylacetic acid [2] and its 4-bromo derivative as well as laevorotatory 1,4-bromonaphthylsulfinylacetic acid [11], which have the spatial structure S(−), and also their amides and p-nitrobenzyl esters. In the second case, the standards were p-bromophenacyl esters of laevorotatory phenylsulfinylacetic acid [2] and its 3-bromoderivative [2] as well as the esters of laevorotatory 1-naphthylsulfinylacetic acid [10] and its 2-bromoderivative [12], which also have the configuration S(−).

Table 4. Molar rotations $[M]_D^{20}$ of laevorotatory phenylsulfinylacetic (A), 1,4-bromonaphthylsulfinylacetic (D)

Compound	Methanol			Ethanol		
	a	b	c	a	b	c
A	463.0	407.7	377.6	455.0	380.2	353.7
B	1075.5	942.1	884.1	1030.5	928.9	878.8
C	578.0	458.0	437.0	518.0	426.0	408.0
D	1296.6	1231.3	1112.5	1297.4	1229.8	1086.7

a — p-nitrobenzyl ester, b — amide, c — acid.

A comparison of the optical shifts collected in Table 4 shows that laevorotatory phenylsulfinylacetic acid, 2- and 4-bromophenylsulfinylacetic acids and 1,4-bromonaphthylsulfinylacetic acid have the same spatial structure, which means that the laevorotatory 1,2-bromophenylsulfinylacetic acid has the configuration S(−). The correctness of the spatial structures assigned to acids 11 and 9, is confirmed by the shifts of molar rotations caused by the solvent effect which are collected in Table 5.

Table 5. Effect of solvent on molar rotation of p-bromophenacyl esters of laevorotatory phenylsulfinylacetic (A), 1,2-bromophenylsulfinylacetic (B), 1,3-bromophenylsulfinylacetic (C), 1-naphthylsulfinylacetic (D) and 2-bromo-7-naphthylsulfinylacetic (E) acids

Solvent	Molar rotation $[M]_D^{20}$				
	Ester of acid A	Ester of acid B	Ester of acid C	Ester of acid D	Ester of acid E
Dioxane	428.9	1150.4	454.4	1290.9	401.9
Acetone	400.3	1115.9	383.4	1213.3	355.6
Methanol	386.0	1104.4	287.6	1155.5	324.7
Ethanol	343.2	1073.7	264.6	954.1	—

On the basis of the data collected in Table 2 we have determined the functions $[M](\lambda)$ for dextrorotatory 1,2-bromophenylsulfinylacetic acid 9 in four solvents. The functions have the character of three-term equations which we give below.

a) In methanol:

$$[M]_{\lambda}^{20}=\frac{3.8056322\times10^{9}}{\lambda^{2}-(200.9940)^{2}}-\frac{4.513964\times10^{9}}{\lambda^{2}-(209.1226)^{2}}+\frac{9.5537173\times10^{8}}{\lambda^{2}-(250.0379)^{2}}$$

b) In ethanol:

$$[M]_{\lambda}^{20}=\frac{3.8077284\times10^{9}}{\lambda^{2}-(202.0051)^{2}}-\frac{4.6401894\times10^{9}}{\lambda^{2}-(210.1574)^{2}}+\frac{9.9707452\times10^{8}}{\lambda^{2}-(250.0574)^{2}}$$

1,2-bromphenylsulfinylacetic (B), 1,4-bromophenylsulfinylacetic (C), acids and some of their derivatives

Acetone			Chloroform		
a	b	c	a	b	c
518.9	419.1	333.2	475.0	361.8	357.4
1040.4	950.9	920.9	1179.8	—	765.7
597.0	462.0	453.0	548.0	399.0	358.0
1399.4	—	1138.1	1629.3	—	1195.7

c) In dioxane:

$$[M]_{\lambda}^{20}=\frac{1.6331330\times10^{9}}{\lambda^{2}-(209.3411)^{2}}-\frac{2.0845212\times10^{9}}{\lambda^{2}-(219.3577)^{2}}+\frac{7.0124613\times10^{8}}{\lambda^{2}-(260.0138)^{2}}$$

d) In chloroform:

$$[M]_{\lambda}^{20}=\frac{1.9644731\times10^{9}}{\lambda^{2}-(209.1757)^{2}}-\frac{2.5147344\times10^{9}}{\lambda^{2}-(219.3775)^{2}}+\frac{7.6327287\times10^{8}}{\lambda^{2}-(258.0527)^{2}}$$

The molar rotation values calculated by means of the above equations are given in Table 2 in brackets. The agreement between these values and the experimental data is fairly good. Functions $[M](\lambda)$ describing in the rectangular system of coordinates (λ is the independent variable) the optical properties of dextrorotatory o-bromophenylsulfinylacetic acid do not change the sign, have no inflexion points and have the extrema within the range $\lambda_3<\lambda<\lambda_1$. Their asymptotes are the λ axis and the straight lines perpendicular to it at points λ_1, λ_2 and λ_3.

The circular dichroism curve determined in methanol for the laevorotatory o-bromophenylsulfinylacetic acid 11 has one positive maximum at $\lambda=209$ nm ($[\Theta]=+39902.2$), one negative maximum at 246 nm ($[\Theta]=-78106.5$) and two positive inflexions at 218 nm ($[\Theta]=+22922.6$) and

200 nm ([Θ]=+32261.4) as well as one negative inflexion at 275 nm ([Θ]=−19526.6). These extrema suggest that the compound has two strong Cotton effects (one negative at 246 nm and one positive at 209 nm). These effects are localized in the regions corresponding to the dispersion constants of the three-term equations, describing the functions [M](λ). However, the dispersion constant of the third term (λ=209 nm) of high rotation constant indicates that the inflexion at 200 nm, which is screened by the strong band in the 209 nm region, signals the presence of the third Cotton effect. For comparison, we would like to mention that the circular dichroism curve determined in acetonitrile for laevorotatory p-bromophenylsulfinylacetic acid [1], has one positive maximum at 225 nm ([Θ]=+110040.0), one negative maximum at 254 nm ([Θ]=−84030.5), one positive inflexion at 210 nm ([Θ]=+58021.1) and two negative inflexions at 275 nm ([Θ]=−40014.5) and 280 nm ([Θ]=−17606.4).

Circular dichroism curves of laevorotatory phenylsulfinylacetic and o-bromophenylsulfinylacetic acids are very similar, which confirms our hypothesis that enantiomers, rotating polarized light (in the visible part of the spectrum) in the same direction, have the same spatial structures.

The UV spectrum of laevorotatory o-bromophenylsulfinylacetic acid 11 in methanol has two groups of bands. The first of them, appearing in the region $200<\lambda<235$ nm, has two bands at 208 nm (ε=9158.0) and 216 nm (ε=9052.6) as well as one inflexion at 200 nm (ε=8210.5). The second group appears in the region $235<\lambda<285$ nm. It consists of one maximum at 245 nm (ε=3157.9) and two inflexions at 273 nm (ε=1157.9) and 280 nm (ε=842.1). The wave lengths of the optically active bands at 208 and 245 nm and of the inflexion at 200 nm are in fairly good agreement with the values of dispersion constants, appearing in the three-term equations describing the optical rotation of dextrorotatory enantiomer 9.

The optical effects caused by the introduction of bromine atom to the ortho position of benzene ring of phenylsulfinylacetic acid molecule in the region of λ values, for which optical rotatory dispersion is normal, are not difficult to determine in spite of the pronounced and diverse solvent effect. Both the laevorotatory o-bromophenylsulfinylacetic acid 11 and all its derivatives examined by us (12, 13, 14 and 15) in all the solvents, showed molar rotations higher than those of the corresponding unsubstituted compounds and of the corresponding compounds containing bromine atoms in the para or meta positions. Thus, the introduction of bromine atom to the ortho position, with respect to the asymmetry center, causes the greatest increase of the molar rotation. Unambiguous interpretation of our observations is difficult. It is probable that the

observed relationships could be connected with changes in charge density in the vicinity of the sulfinylic chirality center, which are caused by the mutually opposing mesomeric (+M) and inductive (−I) effects of the halogen atom on the free π electrons of the aromatic ring. It is also probable that the molar rotations of the ortho-substituted acids are higher than those of their position isomers as a result of steric crowding, which may cause a deviation of the substituent from the plane of the aromatic ring or as a result of the polar effect of bromine atom, which is situated close to the asymmetry center.

Unambiguous interpretation of the observed phenomena requires further systematic stereochemical studies.

EXPERIMENTAL

The melting points are uncorrected. The IR and UV spectra were obtained by means of SP-200 and SP-700 spectrophotometers using suspensions in paraffin oil (IR) and solutions in methanol (UV). The ORD spectra were obtained in Perkin-Elmer 241-MC spectropolarimeter and the CD spectra in Roussel-Jouan III dichrograph using the solutions specified in the text.

1. o-Bromophenylthioglycolic acid (2)

A solution of 31 g of o-bromothiophenol (b. p. 238—239°, lit. [13] b. p. 238—239°) in 45 ccm of 96% ethanol was treated with 60 ccm of 20% NaOH and was heated for 15 min. on water bath. The mixture was cooled to room temperature and a solution of 16 g of chloroacetic acid in 210 ccm of water neutralized with solid Na_2CO_3 was added. Then the mixture was heated for 30 min. on water bath and after filtering it was acidified to Congo with dilute (1:1 v/v) hydrochloric acid. A fine crystalline precipitate separated immediately. It was filtered (30 g) and after drying in a vacuum desiccator (H_2SO_4) it was crystallized from carbon tetrachloride (240 ccm). Plates m. p. 117° (lit. [3] m. p. 117—118°). Yield 25 g. The product is readily soluble in dioxane, acetone, methanol and 96% ethanol, fairly soluble in carbon tetrachloride and sparingly soluble in benzene and chloroform.

IR (cm^{-1}): 650νC−Br; 710νC−S; 750, 1020, 1105, 1195δC_{Ar}−H (subst. 1, 2); 1450, 1510, 1570$\nu C_{Ar}=C_{Ar}$; 910δOH(COOH); 1250, 1280, 1430δOH and νC−O(COOH); 1700νC=O(COOH).

2. Racemic o-bromophenylsulfinylacetic acid (3)

15 g of powdered acid 2 was suspended in 46 ccm of the glacial acetic acid. The suspension was cooled to 10° in ice bath and was treated with 4.5 ccm of 30% H_2O_2. The mixture was shaken mechanically at room temperature for 12 hrs. Then it was treated in 12 hrs. intervals with two portions of 1.2 ccm of 30% H_2O_2 and was shaken mechanically for 24 hrs. The product was filtered (13 g) and, after washing with ether, it was crystallized from benzene (390 ccm). Plates m. p. 129—130°. Yield 7 g. The racemic acid is readily soluble in acetone, methanol and 96% ethanol and fairly soluble in benzene and carbon tetrachloride.

Analysis:

For the formula: $C_8H_7BrO_3S$ (263.12) calculated: 36.5% C, 2.7% H;
found: 36.4% C, 2.6% H.

IR (cm^{-1}): 650 $\nu C-Br$; 715 $\nu C-S$; 765, 1020, 1100, 1180 $\delta C_{Ar}-H$ (subst. 1, 2); 1450, 1570, 1610 $\nu C_{Ar}=C_{Ar}$; 1040 $\nu S=O$; 900 $\delta OH(COOH)$; 1245, 1290, 1435 δOH, $\nu C-O(COOH)$; 1720 $\nu C=O(COOH)$.

3. Methyl ester of rac. o-bromophenylsulfinylacetic acid (4)

3 g of rac. acid 3 was converted into its methyl ester as in ref. 1. The crude product (1.8 g) was crystallized from petroleum ether (30 ccm). Rods m. pt. 60—61°. Yield 1.2 g. The ester is readily soluble in benzene, dioxane, methanol and 96% ethanol and fairly soluble in petroleum ether and carbon tetrachloride.

Analysis:

For the formula: $C_9H_9BrO_3S$ (277.14) calculated: 38.7% C, 3.3% H;
found: 38.9% C, 3.4% H.

4. Amide of rac. o-bromophenylsulfinylacetic acid (5)

0.8 g of powdered ester 4 was suspended in 40 ccm of 14% ammonia and was shaken mechanically at room temperature for 2 hrs. The product was filtered (0.45 g) and was crystallized from methanol (12 ccm). Needles m. p. 190—191°. Yield 0.25 g. The amide is fairly soluble in acetone, methanol and 96% ethanol and is sparingly soluble in benzene and chloroform.

Analysis:

For the formula: $C_8H_8BrNO_2S$ (262.13) calculated: 5.3% N;
found: 5.6% N.

5. p-Nitrobenzyl ester of rac. o-bromophenylsulfinylacetic acid (6)

2 g of rac. acid 3 was converted into its p-nitrobenzyl ester according to ref. 1, using 2 g of p-nitrobenzyl bromide. The esterification was carried out in 82% methanol (55 ccm). The crude product (0.8 g) was crystallized from 96% ethanol (10 ccm). Rods m. p. 112—113°. Yield 0.5 g. The ester is readily soluble in chloroform and acetone, fairly soluble in methanol and 96% ethanol and sparingly soluble in benzene.

Analysis:

For the formula: $C_{15}H_{13}BrNO_5S$ (398.19) calculated: 3.5% N;
found: 3.7% N.

6. p-Bromophenacyl ester of rac. o-bromophenylsulfinylacetic acid (7)

2.6 g of rac. acid 3 was converted into its p-bromophenacyl ester according to ref. 1, using 2 g of p-bromophenacyl bromide. The esterification was carried out in 95% methanol (95 ccm). The product (3 g) was crystallized from 96% ethanol (39 ccm). Needles m. p. 136—137°. Yield 2.3 g. The ester is readily soluble in chloroform and acetone, fairly soluble in methanol and 96% ethanol and sparingly soluble in benzene.

Analysis:

For the formula: $C_{16}H_{12}Br_2O_4S$ (460.16) calculated: 41.8% C, 2.6% H;
found: 41.9% C, 2.5% H.

7. Strychnine salt of the dextrorotatory o-bromophenylsulfinylacetic acid (8)

10.52 g (0.04 mole) of powdered rac. acid 3 was mixed with 13.38 g (0.04 mole) of strychnine and was dissolved in 800 ccm of boiling acetone and 50 ccm of water. The hot solution was filtered and was allowed to stand at room temperature. After 48 hrs. the first fraction of the salt was filtered. Needles (5 g) m. p. 215° with decomposition, $[\alpha]_D^{20} = +131.3°$ ($c=0.4$, $d=2$, $\alpha=+1.05$) in 96% ethanol. The salt (5 g) was crystallized from 300 ccm of boiling acetone and 30 ccm of water. The crystallization time was 48 hrs. The product remained unchanged by further crystallization. Needles m. p. 208—209° with decomposition, $[\alpha]_D^{20} = +137.5°$ ($c=0.4$, $d=2$, $\alpha=+1.10°$) in 96% ethanol. Yield 1.3 g. The salt is readily soluble in methanol and 96% ethanol, fairly soluble in acetone and sparingly soluble in benzene.

Analysis:
For the formula: $C_{29}H_{29}BrN_2O_5S$ (597.54) calculated: 4.7% N;
found: 4.8% N.

8. Dextrorotatory o-bromophenylsulfinylacetic acid (9)

2 g of powdered strychnine salt 8 was converted into the free acid according to ref. 1. The product (0.5 g) was crystallized from benzene (20 ccm). Plates m. p. 140—141° with decomposition, $[\alpha]_D^{20} = +320.0°$ ($c = 0.4$, $d = 2$, $\alpha = +2.56°$) in 96% ethanol. Yield 0.3 g. The acid is readily soluble in methanol and 96% ethanol and is fairly soluble in benzene and chloroform.

Analysis:
For the formula: $C_8H_7BrO_3S$ (263.12) calculated: 36.5% C, 2.7% H;
found: 36.7% C, 2.8% H.

9. Cinchonine salt of laevorotatory o-bromophenylsulfinylacetic acid (10)

10.52 (0.04 mole) of powdered rac. acid 3 was mixed with 11.8 g (0.04 mole) of cinchonine and was dissolved in 1300 ccm of boiling acetone and 20 ccm of water. The hot solution was filtered and was allowed to stand at room temperature. After 24 hrs., the first fraction of the salt was filtered. Needles m. p. 192—194° with decomposition, $[\alpha]_D^{20} = -15.0°$ ($c = 0.333$, $d = 2$, $\alpha = -0.18°$) in 96% ethanol. The salt (6 g) was recrystallized from dilute acetone (400 ccm of acetone and 11 ccm of water). The product remained unchanged by further crystallization. Needles m. p. 198° with decomposition, $[\alpha]_D^{20} = -30.0°$ ($c = 0.333$, $d = 2$, $\alpha = -0.20°$) in ethanol. Yield 2 g. The salt is readily soluble in chloroform, methanol and 96% ethanol, fairly soluble in acetone and sparingly soluble in benzene.

Analysis:
For the formula: $C_{27}H_{28}BrN_2O_4S$ (537.49) calculated: 5.0% N;
found: 5.2% N.

10. Laevorotatory o-bromophenylsulfinylacetic acid (11)

2 g of cinchonine salt 10 (t.t. 198°, $[\alpha]_D^{20} = -30.0°$) was converted into the free acid as in section 8. The product (0.9 g) was crystallized from a mixture of benzene (17 ccm) and methanol (0.5 ccm). Plates m.p. 141—

141.5° with decomposition, $[\alpha]_D^{20} = -321.3°$ ($c = 0.333$, $d = 2$, $\alpha = -2.14°$) in 96% ethanol. Yield 0.5 g. The laevorotatory o-bromophenylsulfinylacetic acid is readily soluble in dioxane, acetone, methanol and 96% ethanol, fairly soluble in chloroform and sparingly soluble in benzene.

Analysis:

For the formula: $C_8H_7BrO_3S$ (263.12) calculated: 36.5% C, 2.7% H;
found: 36.6% C, 2.6% H.

IR (cm^{-1}): 650 νC—Br; 715 νC—S; 760, 1010, 1095, 1170 δC_{Ar}—H (subst. 1, 2); 1460, 1570 $\nu C_{Ar} = C_{Ar}$; 1450 νS=O; 900 δOH; 1250, 1265, 1435 δOH, νC—O(COOH); 1720 νC=O(COOH).

11. Methyl ester of laevorotatory o-bromophenylsulfinylacetic acid (12)

2.5 g of laevorotatory acid 11 was converted into its methyl ester as in section 3. The crude product (1.7 g) was crystallized from petroleum ether (90 ccm). Rods m. p. 50—51°, $[\alpha]_D^{20} = -331.3°$ ($c = 0.4$, $d = 2$, $\alpha = -2.65°$) in 96% ethanol. Yield 1.1 g. The ester is readily soluble in chloroform, aceton and methanol, fairly soluble in petroleum ether and sparingly soluble in carbon tetrachloride.

Analysis:

For the formula: $C_9H_9BrO_3S$ (277.14) calculated: 38.7% C, 3.3% H;
found: 38.9% C, 3.1% H.

12. Amide of laevorotatory o-bromophenylsulfinylacetic acid (13)

1 g of laevorotatory methyl ester 12 was converted into the corresponding amide as in section 4. The crude product (0.6 g) was crystallized from methanol (15 ccm). Needles m. p. 214—215° $[\alpha]_D^{20} = -351.7°$ ($c = 0.3$, $d = 2$, $\alpha = -2.11°$) in 96% ethanol. Yield 0.3 g. The amide is fairly soluble in dioxane, acetone, methanol and 96% ethanol and is sparingly soluble in chloroform.

Analysis:

For the formula: $C_8H_8BrNO_2S$ (262.13) calculated: 5.3% N;
found: 5.5% N.

13. p-Nitrobenzyl ester of laevorotatory o-bromophenylsulfinylacetic acid (14)

2 g of laevorotatory acid 11 was converted into its p-nitrobenzyl ester as in section 5, using 2 g of p-nitrobenzyl bromide. The esterification was

carried out in 82% ethanol (55 ccm). The crude product (1.2 g) was crystallized from carbon tetrachloride (25 ccm). Bars m. p. 114—115°, $[\alpha]_D^{20} = -258.8°$ ($c=0.4$, $d=2$, $\alpha=-2.07°$) in 96% ethanol. Yield 0.7 g. The ester is readily soluble in chloroform and acetone, fairly soluble in dioxane, methanol and 96% ethanol and sparingly soluble in benzene.

Analysis:

For the formula: $C_{15}H_{12}BrNO_5S$ (398.19) calculated: 3.5% N;
found: 3.7% N.

14. p-Bromophenacyl ester of laevorotatory o-bromophenylsulfinylacetic acid (15)

1 g of laevorotatory acid 11 was converted into its p-bromophenacyl ester as in section 6 using 1 g of p-bromophenacyl bromide. The esterification was carried out in 80% ethanol (30 ccm). The crude product (1.4 g) was crystallized from 96% ethanol (25 ccm). Needles m. p. 120°, $[\alpha]_D^{20} = -233.3°$ ($c=0.3$, $d=2$, $\alpha=-1.40°$) in 96% ethanol. Yield 0.9 g. The ester is readily soluble in dioxane, chloroform and acetone and fairly soluble in methanol and 96% ethanol.

Analysis:

For the formula: $C_{16}H_{12}Br_2O_4S$ (460.15) calculated: 41.7% C, 2.6% H;
found: 41.5% C, 2.8% H.

15. o-Bromophenylsulfonylacetic acid (16)

2.63 g of powdered rac. acid 3 was suspended in 15 ccm of glacial acetic acid and three portions of 30% H_2O_2 (4 ccm, 4 ccm and 2 ccm) were added in 12 hrs. intervals. The mixture was shaken mechanically at room temperature for 36 hrs. Then it was evaporated in a vacuum desiccator over KOH to a small volume. A fine crystalline precipitate separated. It was filtered (2.1 g) and was crystallized from benzene (80 ccm). Needles m. p. 125—126°. Yield 1.9 g. The sulfone is readily soluble in chloroform, acetone, methanol and 96% ethanol and is sparingly soluble in carbon tetrachloride.

Analysis:

For the formula: $C_8H_7BrO_4S$ (279.12) calculated: 34.4% C, 2.5% H;
found: 34.6% C, 2.4% H.

IR (cm^{-1}): 650 νC—Br; 700 νC—S; 760, 1025, 1095, 1180 δC_{Ar}—H (subst. 1, 2); 1450, 1575 $\nu C_{Ar}=C_{Ar}$; 1140 νsSO_2; 1320 ν $asSO_2$; 915 δOH(COOH); 1245, 1280, 1430 δOH, νC—O(COOH); 1730 νC=O(COOH).

16. The racemization of laevorotatory o-bromophenylsulfinylacetic acid

The racemization of acid 11 was carried out in thermostated (ultrathermostat UTP-Kraków, sensitivity range $\pm 0.03°$), polarimetric tubes ($d=0.5$ dcm) fitted to Perkin-Elmer 241-MC polarimeter. The solvent was a mixture of dioxane and dilute ($d=1.15$) hydrochloric acid (2:1 v/v). The concentration of acid 11 was 0.5/100 ccm. The rotation angle α was determined every 5 min. immediately after dissolving acid 11 in the solvent and filling the polarimetric tube. The measurements were carried out until the time when the initial value of α decreased by 90%. Before the experiment the solvent and the polarimetric tube were preheated to the racemization temperature. The racemization was studied at 12, 16, 20, 24 and 28°. In the polarimetric measurements sodium light ($\lambda=589$ nm) was used. The compound, regenerated from control solutions in dioxane and dilute hydrochloric acid after the complete disappearance of optical activity (i.e. after the complete racemization of acid 11), was always found to be racemic acid 3. The racemization parameters and the experimental errors were calculated by means of digital computer ODRA-1013.

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STRESZCZENIE

Opisano syntezę i podstawowe własności kwasów o-bromofenylo-sulfinylooctowych i sulfonylooctowych. Racemiczny sulfotlenek rozszczepiono w drodze krystalizacji frakcyjnej jego soli strychninowej i cynchoninowej z acetonu na enancjomery. Poszczególnym enancjomerom przypisano bezwzględne konfiguracje przestrzenne. Zdefiniowano w widzialnej części widma dyspersję rotacji optycznej lewoskrętnego antymeru, jego amidu oraz estrów: metylowego, p-nitro-benzylowego i p-bromofenacylowego. Wyznaczono trójczłonowe równania opisujące rotację optyczną prawoskrętnego enancjomeru w widzialnej i nadfioletowej części widma. Określono stałe racemizacji (K) oraz parametry aktywacji (E_a, ΔH#, ΔS#) dla procesu racemizacji enancjomerycznych kwasów o-bromofenylosulfinylooctowych w oparciu o metody kinetyki klasycznej.

РЕЗЮМЕ

Описано синтез и основные свойства о-бромофенилосульфинилоуксусных и сульфонилоуксусных кислот. Рацемическую сульфоокись разщеплено путем фракционной кристаллизации ее стрихниновой и цинхониновой солей с ацетона на энанциомеры. Отдельным энанциомерам приписано относительные пространственные конфигурации. Определено в видимой части спектра дисперсию оптического вращения левовращающего антимера, его амида и таких эстров как: метилового, р-нитробензилового и р-бромофенацилового. Установлено тричленистое уравнение, представляющее оптическое вращение правовращающего энанциомера в видимой и ультрафиолетовой частях спектра. Определено постоянные рацемизации (К) и параметры активации (E_a, ΔH# и ΔS#) энанциомерических о-бромофенилосульфинилоуксусных кислот, опираясь на методы классической кинетики.