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The Effect of Molecular Structure on Optical Properties of Sulfoxide Systems. Benzylsulfinylacetic Acids and Some of Their Derivatives. IV *

Wpływ budowy cząsteczkowej na własności optyczne układów sulfotlenkowych. Kwasy benzylosulfinylooctowe i niektóre ich pochodne. IV

Влияние молекулярной структуры на оптические свойства сульфоокислых систем. Бензилсульфинилуксусные кислоты и некоторые их производные. IV

The problem of the effect of position isomerism of certain substituents and functional groups in arene nuclei on optical properties of aromatic-aliphatic systems containing carbon and heteroatomic chirality centres has been studied in our laboratory in the case of the group of compounds in which the asymmetric atoms are bonded directly to the aromatic fragments of the molecules [1-7]. The results prompted us to further studies on systems in which the chirality centres are separated from the arene fragments by methylene, and vinyl groups or heteroatoms. In general, on the basis of the Czugajew [8] distance rule it could be expected that the optical effects would decrease with increasing distance between the aromatic fragment bonded to the substituent and the chirality centre. The effect

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of the substituents should be transmitted much strongly by unsaturated groups and heteroatoms than by saturated carbon chains. The elucidation of optical relationships, particularly in the group of compounds containing heteroatomic chirality centres, which are not yet well known, could lead to very interesting conclusions.

We have started our studies by comparing the principal chiralooptical properties of isomeric bromophenyl-sulfinylacetic acids and their homologues in which the asymmetric sulfur atom was bonded to benzene ring via methylene group, i.e. isomeric bromobenzylcarboxymethylsulfoxides.

In the case of bromoberzylsulfinylacetic acids we assumed unsubstituted benzylsulfinylacetic acid as the reference system having the character of configurational standard as well as a standard for comparing the measured rotation values. We have arbitrarily assigned configuration D(+) to the dextrorotatory antimer of this acid, which can be represented by the following spatial formula:

 $-CH_2 - \frac{5}{5} - CH_2 - COOH$

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We have accepted the Freudenberg shift rule and the structures of ORD and CD spectra as the criteria of configurational comparison of benzylsulfinylacetic acids and their derivatives containing substituents in the arene nucleus. We have not yet completed our attempts aimed at the determination beyond any doubt of absolute spatial configurations of the configurational standards.

In the present communication we are reporting the results of the experiments leading to the synthesis and the determination of principal optical properties of enanticmeric benzylsulfinylacetic acids and their dextrorotatory amides and esters.



The starting material was known [9] racemic benzylsulfinylacetic acid 2 which was obtained in our laboratory in a good yield by oxidation of mercaptoacid 1 with 30% hydrogen peroxide in glacial acetic acid at room temperature. When an aqueous solution of sodium salt of mercaptoacid 1 was treated with an excess of the oxidizing agent at elevated temperature, a good yield of readily crystallizing sulfone 17 was obtained, the IR spectra confirming the structures of the two oxidation pro-

ducts are shown in the Experimental Part . Racemic acid 2 was characterized as its amide 4 and p-bromophenacyl 5, p-phenylphenacyl 6 and p-nitrobenzyl 7 esters.

In our further studies we have resolved racemic acid 2 by crystallization of its diastereomeric salts with alkaloids. The neutral cinchonidine salt crystallizing from ethyl acetate was found to be the most suitable for the isolation of dextrorotatory enantiomer 9. After four crystallizations it was obtained in the form of a homogeneous substance m. p. $122^{\circ}C[d_{n}]_{p}^{20} = -20.0^{\circ}$ (ethanol). Our search for an optically active base suitable for the isolation in front fractions of the second enantiomer. i.e. the laevorotatory acid, did not give positive results. This acid was obtained from the mother liquors remaining after the crystallization of cinchonidine salt of the dextrorotatory acid. Cinchonidine salt of the laevorotatory acid obtained from the mother liquors was purified by crystallization from ethyl acetate. The product had m. p. $152^{\circ}C$, $[\mathcal{A}]_{D}^{20} = -143.0^{\circ}$ (ethanol). The laevorotatory enantiomer 11 isolated from this salt was identical with the dextrorotatory enantiomer 9, from which it differed only in the direction of rotation of polarized light (m. p. 145-146°C. with decompn. $[\alpha]_{p}^{20} = -90.1^{\circ}$ (ethanol).

Crystallization of an equimolar mixture of the enantiomers gave racemic acid 2. The m. p. of racemate 2 was lower from that of the antimers ($\Delta t = 19^{\circ}$ C). The IR spectrum of racemic acid 2 was different in the "fingerprint region" from the spectra of enantiomers 9 and 11, which were identical. Pronounced differences were also observed in the carbonyl group stretching vibrations band; in the case of racemate 2 there we only one sharp band at 1700 cm⁻¹, whereas in the case of the enantiomers there was a doublet with maxima at 1730 and 1740 cm⁻¹. A similar cleavage of the carbonyl stretching band was observed by us in the case of 2-naphthylsulfinylacetic[10] and 2-dibenzofurylsulfinylacetic acids[11]. The physical differences mentioned above indicate that optically inactive acid 2 is a true racemate.

Optically active benzylsulfinylacetic acids 9 and 11 are very resistant to racemization in alkaline media but are readily racemized in organic solvents in the presence of concentrated hydrochloric acid. In our laboratory the racemization processes were studied using a mixture (2:1 v/v) of dioxane and dilute (7:1 v/v, d = 1.15) hydrochloric acid as solvent [12]. In these conditions the racemization of optically active acids 9 an 11 took place according to the kinetic equation for the first order reactions $(K = \frac{1}{t} \ln - \frac{\mathcal{L}_0}{\mathcal{K}})$. The racemization constants (K), the activation enthalpies $(\Delta H^{\#})$ and the activation entropies $(\Delta S^{\#})$ calculated for four temperatures after averaging the kinetic measurements by the least squares method are shown in Table 1. The activation parameters of the racemization processes have been determined by the classical kinetic methods on the basis of the Eyring equation [13].

Table 1. Thermodynamic characterization of racemization of optically active benzylsulfinylacetic acids

Racemization temperature o _C	Racemization constants K x 10 ⁵ sec ⁻¹	Activation entropy $(\Delta S^{+})e.u.$	Activation enthalpy(\(\(\Delta\) H") K cal/mole
12	7.68 - 1.15	-7.88 ± 0.98	19.81 ± 0.09
16	10.81 + 1.29	-7.90 ± 0.78	19.81 ± 0.07
20	19.30 ± 1.73	-7.93 - 0.59	19.80 = 0.05
24	33.56 - 2.27	-7.96 - 0.45	19.79 - 0.04
28	47.67 - 3.32	-7.99 - 0.46	19.78 ± 0.04

The activation energy (Ea) and the preexponential factor $(A = K_{max})$ have been determined from the empirical Arrhenius equation: $(K = A \cdot e^{-Ea/RT}, Ea = 20.38 \text{ Kcal/mole}, A = 3.089 \text{ x } 10^{11} \text{ sec}^{-1})$. The negative values of the activation entropy $(\Delta S^{\#} \langle 0)$ indicate that in the transition state of the racemization process additive compounds or intermediate compounds, previously proposed for arylalkylsulfoxides by German [14-16] and American [12-17] authors, are formed.

= 0.5 70 c = 0,01; Table 2a. Optical rotatory dispersion of bensylsulfinylacetic acid

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142.73 51.54 (55.13) 190.31 231.86 (68. 788) 987.23 (988.53) 705.73 282.27) À =340 -41.63 -146.69 289.43 888.11 **≥=520** λ =546.1 45.59 158.59 205.05 681.94 (684.30) 785,03 218.06 (213.02) 130.83 543.17 (540.02) -41.63 122.90 A =360 43.61 (44.36) 194.27 420.26 (428.55) 166 52 (167 . 33) 154.62 -33.70 551.10 (626.07) (118.74) 622.47 118.94 **) =560** -109.03 À =380 138.76 (143.78) 178.41 107.04 (108.26) (40.35) 519.38 352.86 138.56 (135.48) 459.91 (449.53) -33.70 37.66)=579.1 X=400 -91.19 20 Molar rotation [M] 134.80 (137.28) 99.11 (103.26) 35.68 (38.44) 174.45 (166.44) 333.04 388.55 261.67 (256.56) 103**.08** (98.17) A ₩35,8 -31.71 **入=589.3** -67.40 166.52 (158.99) 35.70 126.87 (130.96) -23.78 380.62 (378.70) 95.15 329.07 253.74 (248.27) 95.15 À =440 -63.41 A =600 λ =623 • 4 31.71 (33.00) 138.76 (144.42) 114.97 88.54) 245.81 (244.74) 297.35 186.34 (186.92) 63.43 87.22 -23.78 λ**=**480 -51.54 Chloroform Chloroform Methanol Methanol Solvent Acetone Dioxane Acetone Ethanol Ethanol Dioxane Compound benzyl--Ivillus benzylrotatory Sulfinyl. rotatory Der tro-Dextroscetic acetic acid scid

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Daniantin	Calmont	Concn.	C A BES	Molar r	otation [M	PAC	5 2 2
ATTAATJAA	THATOC	g/100 ml.	λ=623.4	λ =589.3	X=579.1	λ=546.1	λ=435.8
- AND	Methanol	0.083	136.04	149.55	156.55	179.34	388.70
	Ethanol	0.083	161.70	180.22	187,88	216.78	453.52
Amide	Acetone	0.083	137.95	152.30	157.82	183.97	395.24
1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	Chloroform	0.083	-53.26	-59.50	-61.65	-71.73	-154.80
Yal	Dioxane	0*083	53.46	60.76	63.78	73.56	158.88
1428	Methanol	0.083	206.25	233.82	245.37	283.45	612.23
p-Bromo-	Ethanol	0.083	228.64	259.72	271.18	306.86	680.58
phenacyl	Acetone	0.083	221.94	252.64	264.86	305.47	659.78
ester	Chloroform	0.083	127.47	144.15	151.13	175.44	378-93
p-Nitro-	Methanol .	0.010	10.00	23.33	23,33	33.33	73.34
benzyl	Ethanol	0.010	6.66	16.66	17.33	26.66	56.67
ester	Chloroform	0.010	-193.35	-233.35	-240.02	-266.69	-513.38
	Dioxane	0.010	-146.68	-176.68	-180,01	-200.01	-380.03
p-Phenyl-	Methanol	0.062	214.28	240.05	252.04	292,80	628,80
phenacyl	Ethanol	0.062	289.07	317.98	333.90	384.78	833.16
ester	Acetone	0.062	228.16	251.12	263.55	308.73	660.24
-	Chloroform	0.083	162.42	180,31	189,31	218.16	468.17

In order to obtain a larger comparable material for chiralcoptical studies we have prepared the following derivatives of dextrorotatory acid 9: amide 13, p-bromophenacyl ester 14, p-phenylphenacyl ester 15 and p-nitrobenzyl ester 16. The syntheses of these compounds were first elaborated for the optically inactive material. It can be assumed that the mild conditions in which the reactions were carried out did not cause racemization at the asymmetric sulfur atom. The molar rotations of dextrorotatory acid 11 were determined in Perkin-Elmer spectropolarimeter 241-MC in the region $340 < \lambda < 623$ nm and those of amide 13 and esters 14, 15 and 16 in the previously described apparatus [18] at wave lengths shown in the table, using methanol M , ethanol (E), acetone (A), dioxane (D) and chloroform (Ch) as solvents.

The results are shown in Tables 2a and 2b. Comparison of numerical values shown in these Tables indicates that the nature of solvent has a considerable effect on the value of molar rotation. In the visible part of the spectrum the effects of the solvents can be arranged in the following order according to decreasing numerical values of molar rotation: a) for free acid 11 : $E \rangle M \rangle A \rangle D \rangle Ch$; b) for acid amide 13: $E \rangle A \rangle M \rangle D \rangle Ch$; c) for p-bromophenacyl ester 14 and p-phenylphenacyl ester 15: E A M Ch; d for p-nitrobenzyl ester 16: M E D Ch. The decreases of the numerical value of molar rotation accompanying the change of solvents in the order given by the above sequences are moderate. Only in the case of free acid 11, its amide 13 and esters 14, 15 and 16 in dioxane and chloroform the change is very pronounced. It should be stressed that free acid 11. amide 13 and p-nitrobenzyl ester 16 in chloroform (ester 16 also in dioxane) change the direction of rotation of the plane of polarized light.

Analysis of the numerical data collected in Tables 2a and 2b shows that the curves representing function $\frac{1}{\mathcal{K}}(\lambda^2)$ in the region $440\langle\lambda\langle 623 \rangle$ for dextrorotatory acid 9 and its deriva-

tives 13, 14, 15 and 16 are almost straight lines, which leads to the conclusion that the optical rotatory dispersion of the examined compounds in the visible part of the spectrum has the character of normal dispersion. It should be stressed that in the region 440 $\langle \lambda \langle 623 \rangle$ the molar rotations of dextrorotatory acid 9 are considerably higher in all the solvents used in the measurements than those of its p-nitrobenzyl ester 16 and considerably lower than those of its p-bromophenacyl ester 14 and phenylphenacyl ester 15.

In order to determine exactly the analysed optical properties of benzylsulfinylacetic acids we have calculated, on the basis of the data collected in Table 2a, functions $[M](\lambda)$ for dextrorotatory enantiomer 9 in four solvents. These functions have the character of the following two-term equations^{*}:

a) in methanol:

$$\left[\mathbb{M}\right]_{\lambda}^{20} = \frac{294 \times 10^{6}}{\lambda^{2} - (225.0)^{2}} - \frac{258 \times 10^{6}}{\lambda^{2} - (211.0)^{2}}$$

b) in ethanol:

c) in acetone:

$$[M]_{\lambda}^{20} = \frac{273 \times 10^{6}}{\lambda^{2} - (223.4)^{2}} - \frac{228 \times 10^{6}}{\lambda^{2} - (208.6)^{2}}$$

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$$[\mathbb{M}]_{\lambda}^{20} = \frac{244 \times 10^{6}}{\lambda^{2} - (224.6)^{2}} - \frac{219 \times 10^{6}}{\lambda^{2} - (209.4)^{2}}$$

d) in dioxane: $[M]_{\lambda}^{20} = \frac{121 \times 10^{6}}{\lambda^{2} - (226.4)^{2}} - \frac{111 \times 10^{6}}{\lambda^{2} - (213.8)^{2}}$

The values of molar rotations calculated by means of the above equations are shown in brackets in Table 2a. The agreement

*The equations were derived by the least squares method using the algorithm of coupled gradients for finding the function of many variables (computer ODRA-1013).

between the calculated values and those determined experimentally is fairly good. Functions $[M](\lambda)$ describing in the reclangularsystem of coordinates (λ is the independent variable) the optical properties of dextrorotatory benzylsulfinylacetic acid do not change the sign and each of them has one negative maximum within the limits $\lambda_2 < \lambda < \lambda_1$. Their asymptotes are the λ axis and the straight lines perpendicular to it at points λ_1 and λ_2 .

In order to confirm the validity of the above equations we have determined the circular dichroism (CD) and the (UV)spectrum (UV) of laevorotetory enantiomer 11 in methanol in the region $200 < \lambda < 300$ nm.

The circular dichroism curve (Fig. 1) shows at $\lambda = 211$ nm a weak positive maximum $\begin{bmatrix} 0 \end{bmatrix}_{211} = +8218$ and at $\lambda = 225$ nm a strong negative maximum ($\begin{bmatrix} 0 \end{bmatrix}_{225} = -46682.6$). The electronic spectrum shows in the examined region a very strong adsorption band at $\lambda = 218$ nm ($\xi_{218} = 10666.46$). The non-symmetric shape of this band indicates that it was formed as a result of overlap of two bands situated in this region close to one another. It is significant that the wave lengths of the characteristic points on the circular dichroism curve (θ_{max}) and the dispersion constants in the two-term equation determining function $[M](\lambda)$ have exactly the same values.

Analysis of the results of optical measurements leads to the conclusion that the laevorotatory benzylsulfinylacetic acid shows in the examined spectral range one negative and one positive Cotton effect situated in the region $\lambda = 225$ and 211 nm.

Studies on optical effects caused by reconstructions of chiral systems are justifiable in the range of λ values where the dispersion of optical rotation has the character of normal dispersion. The compared systems should also have identical spatial configurations. We have not yet unambiguously determined the spatial configuration of optically active benzylsulfinylacetic acids. In the comparison of their molar rotations with those of optically active phenylsulfinylacetic acids we had to use only



Fig. 1. Optical rotatory dispersion (ORD) of dextrorotatory benzylsulfinylacetic acid and circular dichroism (CD) as well as UV spectrum (UV) of laevorotatory benzylsulfinylacetic acid ORD : (c= 0.007 g/100 ccm, d = 0.1 dcm) pk. $[M]_{236 \text{ rm}}^{26}$ = = + 22091.8° ($darma = +0.078^{\circ}$); z $[M]_{227 \text{ rm}}^{26} = 0.0^{\circ}(darma = 0.000^{\circ})$ in 96% ethanol. . CD : (c = 0.0005019 mole/dcm³, d = 0.1 cm) (θ)_{225 rm} = - 46682.6; $\Delta A = 710 \times 10^{-6}$; (θ)_{211 rm} = + 8218.7; $\Delta A = 125 \times 10^{-6}$ (in methanol). UV : (c = 0.0000504 mole/dcm³, d = 1 cm); $\xi_{218 \text{ rm}}$ =

= 10666.46 (A = 0.53759) (in methanol).

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the absolute values. The comparison of the absolute numerical values of molar rotations (determined in solvents not causing the change of direction of rotation of polarized light plane) leads to the conclusion that the rotations of benzylsulfinylacetic acids are much lower than those of phenylsulfoxyacetic acids. The relative per cent decreases ($\% \Delta R_{mol}$) [1] vary from 50% to 90% according to the character of the solvent.

We have observed similar optical rules in the case of 1- and 2-naphthylmethylsulfinylacetic acids 19, 20 which had been compared with 1- and 2-naphthylsulfinylpropionic acids.

The observed decrease of molar rotations accompanying the reconstruction of the systems could be due to the decrease of the interaction of free π electrons of the arene nucleus with the sulfinylic chirality centre. It is not improbable that in the case of systems in which the chirality centres are situated in the aliphatic chain further from the arene nucleus, the effect of substituents having strong mesomeric effects on molar rotation is smaller.

EXPERIMENTAL PART

The melting points are uncorrected. The polarimetric measurements were carried out in the previously described apparatus [18] and in Perkin-Elmer 241-MC spectropolarimeter in the solvents listed in the text. The IR and UV spectra were determined by means of SP-200 and SP-700 spectrophotometers. The ORD spectra were obtained in JASCO (ORD/CD/UV/5) apparatus and the CD spectra in Rouseel-Jouen III dichrograph. The IR spectra were obtained for suspensions of the examined compounds in paraffin oil and for their solutions in the solvents listed in the text.

1. Benzylthioglycolic acid 1

63 g of benzyl chloride in 350 ccm of 96% ethanol was introduced to a solution of 40.5 g thioglycolic acid in 400 ccm of 15% NaOH cooled with ics water. The mixture was stirred at room temperature for 20 min and was refluxed on water bath for 1 hr. Then

it was allowed to stand at room temperature for 12 hrs and after cooling to 0°C it was acidified to Congo with dilute (1:1 V/V) hydrochloric acid. A fine crystalline precipitate separated. It was filtered off (40 g) and after washing with water and drying in a vacuum desiccator over CaCl₂ it was crystallized from petroleum ether (750 ccm). Rods, m. p. 61-62°C (lit[9] m. p. 60-61°C). Yield 32 g. The compound is readily soluble in the commonly used organic solvents and is fairly soluble in petroleum ether:

IR (cm⁻¹): 680 $\sqrt{C-S}$; 690, 760, 1070, 1130, 1150 δC_{Ar} -H (subst. 1), 1458, 1500, 1570, 1600 $\sqrt{C_{Ar}}=C_{Ar}$; 940 δ OH; 1220, 1315, 1410 δ OH and $\sqrt{C-O}$; 1690 $\sqrt{C=O}$ (COOH).

2. Racemic benzylsulfinylacetic acid 2

9.1 g of acid 1 was dissolved in 400 ccm of acetone. The solution was treated with 5.5 ccm of $30\% H_2O_2$ and was allowed to stand at room temperature until the time when all the solvent evaporated. The dry residue (9.2 g)was crystallized from a mixture of benzene (250 ccm) and methanol (22 ccm). Needles, m.p. 126-127°C (lit.[9] m. p. 126-127°C). Yield 6 g. The compound is readily soluble in acetone, methanol and 96% ethanol and is spezingly soluble in petroleum, ether and benzene. IR (cm⁻¹): 680 VC-S; 690, 750, 1065, 1118, 1150 δC_{Ar} -H

(aubst. 1); 1460, 1570, 1580, 1605, $VC_{Ar} = C_{Ar}$; 985 VS = 0; 920 δOH ; 1230, 1310, 1438 δOH and VC = 0; 1700 VC = 0(COOH).

3. Amide of racemic benzylsulfinylacetic acid 4

A solution of diazomethane in ether (prepared from 1.1 g of N,N-nitrosomethylurea)[21] was added dropwise with stirring to a solution of 4 g of racemic acid 2 in 70 ccm of methanol cooled externally with ice water until a permanent coloration of the liquid appeared. At the end of the vigorous esteri-

fication reaction, the ethereal solution was washed with 2% NaHCQ $(2 \times 20 \text{ ccm})$ and then with water $(2 \times 30 \text{ ccm})$. The solvent was removed by distillation under reduced pressure (12 mm Hg, water bath). The oily light yellow residue was suspended in 50 ccm of conc. ammonia (d = 0.88) and was mechanically shaken for 2.5 h at room temperature. A fine crystalline precipitate separated. It was filtered (4 g) and, after drying in a vacuum desiccator over conc. H_2SO_4 , it was crystallized from ethyl acetate (25 ccm). Fine needles m. p. $178^{\circ}C$ with decompn. Yield 3 g. The amide is readily soluble in chloroform, fairly soluble in acetone and 96% ethanol and insoluble in petroleum ether.

Analysis:

For the formula $C_{9}H_{11}NO_{2}S$ (197.27):

calculated: 7.10% N; found: 6.95% N.

4. p-Bromophenacyl ester of racemic benzylsulfinylacetic acid 5

2 g (0.01 mole) of powdered racemic acid 2 was added to a solution of 0.4 g (0.01 mole) of NaOH in 10 ccm of water. Then 2 g (0.007 mole) of p-phenacyl bromide and 35 ccm of 96% ethanol were added. The mixture was refluxed for 1 h on water bath. A fine crystalline precipitate separated. It was filtered and was dissolved in chloroform (30 ccm). The solution was washed with 5% Na₂CO₃ solution (1 x 30 ccm) and then with water (2 x 10 ccm) and was dried with anhydrous MgSO₄. Finally it was treated with petroleum ether (80 ccm). A fine crystalline precipitate soon separated. It was filtered (2.0 g) and was crystallized from ethyl acetate (70 ccm). Colourless needles m. p. 168°C with decompn. Yield 1.6 g. The ester is readily soluble in chloroform, fairly soluble in acetone and 96% ethanol and insoluble in petroleum ether.

> Analysis: For the formula: C₁₇H₁₅BrO₄S (395.27): calculated: 51.66% C, 3.82% H; found: 51.86% C, 3.96% H.

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5. p-Phenylphenacyl ester of racemic benzylsulfinylacetic acid 5

2 g (0.011 mole) of racemic acid 2 was added to a solution of 0.4 g (0.01 mole) of NaOH in 10 ccm of water. Then 2 g (0.007 mole) of p-phenylphenacyl bromide and 35 ccm of 96% ethanol were added. The mixture was refluxed for 1 hr. on water bath. A fine crystalline precipitate separated. It was filtered (2.7 g) and was dissolved in chloroform (40 ccm). The solution was washed with 5% Na₂CO₃ solution (2 x 20 ccm) and then with water (2 x 20 ccm) and was dried with anhydrous MgSO. Finally it was treated with petroleum ether (120 ccm). A fine crystalline precipitate soon separated. It was filtered (2.3)g and was crystallized from ethyl acetate (40 ccm). Colourless plates m. p. 168° C with decompn. Yield 1.6 g. The ester is readily soluble in chloroform, fairly soluble in acetone and 96% ethanol and insoluble in petroleum ether.

Analysis:

For the formula: $C_{23}H_{22}O_4S$ 492,47 calculated: 70.38 % C, 5.13 % H; found: 70.60 % C, 4.89 % H.

6. p-Nitrobenzyl ester of racemic benzylsulfinylacetic

acid 7

3 g of racemic acid 2 was suspended in 15 ccm of water and was neutralized to phenolphthalein with 3% NaOH. The solution was heated to 35° , 4 g of p-nitrobenzyl bromide in 45 ccm of 96% ethanol was added and the mixture was refluxed for 2 hrs. on water bath. Then it was filtered while still hot and was allowed to stand at room temperature. A light yellow oil separated and soon crystallized. It was filtered (2.9 g) and, after washing with water, it was dried in a vacuum desiccator over anhydrous CaCl₂ and was crystallized from a mixture of methanol (70 ccm) and petroleum ether (55 ccm). Plates m. p. 111-112°C.Yield 1.9g. The ester is readily soluble in chloroform, acetone and methanol, fairly soluble in benzene and carbon tetrachloride and sparingly soluble in petroleum ether.

Analysis:

For the formula: $C_{16}H_{15}NO_5S$ (333.36):

calculated: 4.20% N; found: 4.19% N.

7. Cinchonidine salt of dextrorotatory benzylsulfinylacetic acid 8

19.8 g (0.1 mole) of powdered racemic acid 2 was mixed with 29.4 g (0.1 mole) of cinchonidine and was 'dissolved in 350 ccm of boiling ethyl acetate. The solution was filtered and was allowed to crystallize at room temperature. The first fraction of the salt was filtered after 24 hrs. Needles m. p. $109^{\circ}C_{f}C_{D}^{20} =$ = -72.0° (c = 0.25, d = 4, $\mathcal{K} = -0.72$) in 96% ethanol. After three crystallizations the salt had physical properties which were not changing during further purification. Needles m. p. 122°C $[\mathcal{K}_{D}^{20} = -20.0^{\circ}$ (c = 0.25, d = 4, $\mathcal{K} = -0.20$) in 96% ethanol. Yield 11 g. The salt of the dextrorotatory enantiomer is readily soluble in benzene, chloroform and 96% ethanol and is insoluble in petroleum ether.

Analysis:

For the formula: $C_{28}H_{32}N_2O_4S$ (492.64):

calculated: 5.60% N; found: 5.94% N.

8. Dextrorotatory benzylsulfinylacetic acid 9

10 g (0.02 mole) of powdered salt 8 (m. p. $122^{\circ}C$, $[A]_{D}^{20} = = -20.0^{\circ}$) was suspended in 40 ccm of water and was acidified with 10 ccm (0.05 mole) of 18% hydrochloric acid. The mixture was stirred for 2 hrs at room temperature. Free acid 9 precipitated. It was mixed with 50 ccm of water and the pH was ad-

Table 3. Fractional crystallization of cinchonidine salt of dextrorotatory benzylsulfinylacetic acid (crystallization time 24 hrs.)

Fraction No.	Volume of ethyl acetate (ccm)	Weight of salt (g)	Specific rotation in 96% ethanol [A] ²⁰	M. p. of salt oc
1.	350	33	-72.00	110
1.1.	200	23	-64.0°	115
1.1.1.	150	15	-23.5°	119
1.1.1.1.	100	0	-20.0°	122
1.1.1.1.1.	80	8	-20.0°	122

justed to 10 with 20% NaOH. The solution of the sodium salt was extracted with chloroform (5 x 50 ccm). Chloroform dissolved in the aqueous layer was removed by distillation under reduced pressure (12 mm Hg, water bath at 40°). The remaining aqueous solution was acidified to Congo with 15% hydrochloric acid. A fine orystalline precipitate separated immediately. It was filtered (4 g) and after washing with water (2 x 20 ccm) it was dried in a vacuum desiccator over anhydrous CaCl₂. The crude acid (4 g, m. p. 145°C, $[\&]_D^{20} = +89.0°$) was crystallized from ethyl acetate (75 ccm). Large blocks m.p. 146° with decompn., $[\&]_D^{20} = +89.5°$ (c = 0.25, d = 4, & = +0.895°) in 96% ethanol. Yield 3 g. The dextrorotatory enantiomer is readily soluble in chloroform, fairly soluble in acetone and 96% ethanol and insoluble in petroleum ether.

Analysis:

For the formula: $C_9H_{10}O_3S$ (198.26) :

calculated: 54.52% C, 5.08% H; found: 54.26% C, 5.29% H.

IR (cm^{-1}) : 670 VC-S; 700, 770, 1080, 1120, 1150 δC_{Ar} -H (subst. 1), 1460, 1520, 1610, $V C_{Ar} = C_{Ar}$; 1020 VS=0; 920 δOH ; 1250, 1310, 1438 δOH and V C=0; 1730, 1740 V C=0 (COOH).

9. Cinchonidine salt of laevorotatory benzylsulfinylacetic acid 10

The mother liquors remaining after the filtration of the first fraction of cinchonidine salt of dextrorotatory acid 9 were evaporated under reduced pressure (12 mm Hg, water bath at $40^{\circ}C$) to 160 ccm and were allowed to stand at room temperature. They were soon filled with a fine crystalline precipitate. It was filtered after 24 hrs. The salt (12 g) had the form of fine needles m. p. $151^{\circ}C$, $[\&]_{D}^{20} = -138.0^{\circ}$ (c = 0.25, d = 4, $\&]_{=}-1.38^{\circ}$) in 96% ethanol. On recrystallization from boiling ethyl acetate (90 ccm) it appeared in the form of regular needles (8 g) m. p. $152^{\circ}C$, $[\&]_{D}^{20} = -143.0^{\circ}$ (c = 0.25, d = 4, $\&]_{=}-1.43^{\circ}$) in 96% ethanol. Its physical properties remained unchanged by further purification. The salt is readily soluble in benzene, chloroform and 96% ethanol, fairly soluble in ethyl acetate and insoluble in petroleum ether.

Analysis:

For the formula: $C_{28}H_{32}O_4N_2S$ (492.62) :

calculated: 5.69% N; found: 5.97% N.

10. Laevorotatory benzylsulfinylacetic acid 11

5 g (0.01 mole) of powdered cinchonidine salt 10 (m. p. 152°C, $[\pounds]_D^{20} = -143.0^\circ$) was converted into the free acid as in section 8. The crude laevorotatory enantiomer (2 g, m. p. 144° with decompn. $[\pounds]_D^{20} = -90.0^\circ$) was crystallized from ethyl acetate (35 ccm). Regular blocks m. p. 145°C with decompn., $[\pounds]_D^{20} =$ $= -90.1^\circ$ C (c = 0.25, d = 4, $\pounds = -0.901^\circ$) in 96% ethanol. Yield 1 g. The laevorotatory enantiomer is readily soluble in

chloroform, fairly soluble in acetone and 96% ethanol and insoluble in petroleum ether.

Analysis:

For the formula: C29H1003S (198.26) :

calculated: 54.52% C, 5.08% H; found: 54.39% C. 4.86% H.

11. Amide of dextrorotatory benzylsulfinylacetic acid 13

2 g (0.01 mole) of dextrorotatory acid 9 (m. p. 146° C with decompn., $[\pounds]_{D}^{20} = +89.5^{\circ}$) was converted into its amide under the conditions described in section 3. The orude product (1.7 g, m. p. 177° C, $[\pounds]_{D}^{20} = +91.1^{\circ}$) was crystallized from a mixture of chloroform (210 ccm) and petroleum ether (600 ccm). Fine irregular lumps m. p. 178° C, $[\pounds]_{D}^{20} = +91.4^{\circ}$ (c = 0.125, d = 4. \pounds = $\pm +0.457^{\circ}$) in 96% ethanol. The amide is readily soluble in chloroform, fairly soluble in acetone and methanol and insoluble in petroleum ether.

Analysis:

For the formula: C₉H₁₁NO₂S (197.27) : calculated: 7.10% N; found: 7.25% N.

12. p-Bromophenacyl ester of dextrorotatory benzylsulfinylacetic acid 14

1.2 g of dextrorotatory acid 9 (m. p. $146^{\circ}C$, $[\Box_{D}]_{D}^{20} = +89.5^{\circ}$) and 1.3 g of p-bromophenacyl bromide dissolved in 30 ccm of 96% ethanol were converted into the ester under the conditions described in section 4. The crude product (2.7 g) was dissolved in 35 ccm of chloroform. The solution was washed with 5% Na₂CO₃ solution (2 x 15 ccm) and water (2 x 20 ccm) and after drying with anh. MgSO₄ it was treated with petroleum ether (90 ccm). A fine orystalline precipitate soon separated. It was filtered and was crystallized from a mixture of chloroform (20 ccm) and

petroleum etner (75 ccm). Fine needles m. p. 157° C, $\int_{D}^{20} = +65.7^{\circ}$ (c = 0.083, d = 4, & = +0.219°) in 96% ethanol. Yield 1 g. The ester is readily soluble in chloroform, fairly soluble in acetone and methanol and insoluble in petroleum ether.

Analysis:

For the formula: C₁₇H₁₅BrO₄S (395.27) : calculated: 51.66% C, 3.82% H; found: 51.39% C. 3.88% H.

13. p-Phenylphenacyl ester of dextrorotatory benzylsulfinylacetic acid 15

1.2 g of dextrorotatory acid 9 (n. p. $146^{\circ}C, [\Lambda]_{D}^{20} = +89.5^{\circ}$) and 1.3 g of p-phenylphenacyl bromide dissolved in 35 ccm of 96% ethanol was converted into the ester as in section 5. The product was dissolved in 40 ccm of chloroform. The solution was washed with 5% Na₂CO₃ solution (2x15 ccm) and then with water (2 x 20 ccm) and after drying with anh. MgSO₄ it was treated with hot petroleum ether (100 ccm). An amorphous precipitate soon separated. It was filtered (1.4 g) and was crystallized from ethyl acetate (22 ccm). Plates m. p. $160^{\circ}C$, $[\Lambda_{D}^{20} = +80.8^{\circ}$ (c = 0.0625, $1 = 4, \Lambda = +0.202^{\circ}$) in 96% ethanol. Yield 1 g. The ester is readily soluble in chloroform, fairly soluble in acetone and insoluble in petroleum ether.

Analysis:

For the formula: C₂₃H₂₀O₄S (392.47) : calculated: 70.39% C, 5.14% H; found: 70.61% C, 4.98% H.

14. p-Nitrobenzyl ester of dextrorotatory benzylsulfinylacetic acid 16

3 g of dextrorotatory acid 9 (m. p. $146^{\circ}C$, $[\&]_{D}^{20} = +89.5^{\circ}$) was converted into its p-nitrobenzyl ester as in section 6. The product (2 g) was crystallized from 60% ethanol (40 ccm).

Plates m. p. $104-105^{\circ}$ (c = 0.5, d = 2, f. = 0.035) in 96% ethanol. Yield 1.3 g. The ester is readily soluble in methanol and 96% ethanol. It is sparingly soluble in petroleum ether.

Analysis:

For the formula: C₁₆H₁₅NO₅S (333.36) : calculated: 4.20% N; found: 4.14% N.

15. Benzylsulfonylacetic acid 17

4 g (0.02 mole) of acid 2 was suspended in 10 ccm of water and the pH was adjusted to 12.0 with 5% NaOH. The solution of the sodium salt was heated on water bath and was treated in 2 h intervals with five 2 ccm portions of 29% H_2O_2 . After the last portion the solution was allowed to stand for 24 hrs. at room temperature and was acidified to Congo with 10% hydrochloric acid. An amorphous precipitate scon separated. It was filtered (3 g) and was crystallized from a mixture of chloroform 10 ccm and petroleum ether (35 ccm). Fine needles m. p. 139°C lit. 9 m. p. 137-138°C Yield 2 g. IR (cm⁻¹): 680 VC-S; 760, 1070, 1120, 1140 δC_{Ar} -H (subst. 1); 1460, 1500, 1565 $V C_{Ar} = C_{Ar}$; 1145 $V sSO_2$; 1330 $asSO_2$; 920 δOH ; 1225, 1320, 1428 δOH and V C=0; 1700 V C=0 (COOH).

16. Racemization of laevorotatory benzylsulfinylacetic acid

Racemization of acid 11 was carried out in thermostated polarimetric tubes (ultrathermostat UTP Kraków, temperature sensitivity range -0.03) (d = 0.5) fitted to Perkin-Elmer 241-MC polarimeter. The solvent was a mixture of dioxane and dil. HCl (2:1 V/V) (the acid was a mixt. 7:1 V/V conc. HCl/H₂O, d = 1.15). The concentration of the optically active acid 11 was c = 0.5. The rotation angle d_{c} was determined every 300 sec immediately after dissolving acid 11 in the mixture of dioxane and dil. hy-

drochloric acid and filling the polarimetric tube with the solution. The measurements were carried out until the time when the initial value of the rotation angle & decreased by 90%. Before the experiment the solvent and the polarimetric tube were heated to the racemization temperature. The racemization was studied at 12, 16, 20, 24 and 28°C. The polarimetric measurements were carried out using sodium light ($\lambda = 589$ nm). The compound recovered from the control solutions in dioxane and dil. hydrochloric acid after the complete disappearance of optical activity (i.e after the complete racemization of acid 11) was found to be, in every case, racemic acid 2. The calculations of the racemization parameters and experimental errors were carried out by means of a digital calculating machine ODRA-1013.

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STRESZCZENIE

Opisano syntezę i podstawowe własności kwasów benzylosulfinylo-i sulfonylo-octowych. Racemiczny sulfotlenek rozszczepiono w drodze krystalizacji frakcyjnej jego soli cynchonidynowej z octanu etylu na enancjomery. Poszczególnym enancjomerom przypisano względne konfiguracje przestrzenne. Zdefiniowano w widzialnej części widma dyspersję rotacji optycznej prawoskrętnego antymeru, jego amidu oraz estrów: p-bromofenacylowego, p-fenylofenacylowego i p-nitrobenzylowego. Wyznaczono dwuczłonowe równania opisujące rotację optyczną prawoskrętnego enancjomeru w widzialnej i nadfioletowej części widma. Określono stałe racemizacji (K) oraz parametry aktywacji (Ea, $\Delta H^{\pm} i \Delta S^{\pm}$)dla procesu racemizacji lewoskrętnego kwasu benzylosulfinylooctowego w oparciu o metody kinetyki klasycznej.

PESIOME

В данной работе описан синтез и основные свойства бензилсульфиныло и сульфонилоуксусных кислот. Рацемическую сульфоокись расщепливали путем фракционной кристаллизации ее цинхонидной соли из ацетата этила на оптических энантиомерах. Отдельным энантиомерам приписывают относительную пространственную конфигурацию. Определено в видимой части спектра дисперсию оптического вращения правовращающегося антимера, его амида, а также сложных эфиров: п-бромофенацилового, п-фенилофенацилового и п-нитробенаилового. Установлено двутермовые уравнения представляющие оптическое вращение правовращающегося энантиомера в видимой и ультрафиолетовой части спектра. Определено постоянные рацемизации (К), а также параметры активации (Ка, $\Delta H^{\#}$ и $\Delta S^{\#}$) для процесса рацемизации левовращающейся бензилосульфинилоуксусной кислоты, опираясь на методы классической кинетики.

