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Synthesis of Racemic p-Methylbenzylsulfoxyacetic Acid and Its Resolution into Optical Antipodes

Synteza racemicznego kwasu p-metylobenzylosulfinylooctowego i jego rozdział na antypody optyczne

Синтез рацемической р-метилбензилсульфинилуксусной кислоты и ее разделение на оптические антиподы

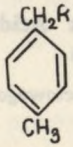
The problem of the effect of alkyl substituents with straight and branched carbon chains on the optical properties of arylalkylsulfoxyaliphatic systems is now being studied in our laboratory on the example of suitable derivatives of benzylsulfoxyacetic acid. So far we have carried out the synthesis of enantiomeric m-methylbenzylsulfoxyacetic acids [1] and have determined their principal optical properties. These compounds and also their esters and amides have normal rotatory dispersion in the visible part of the spectrum and show fairly high molar rotation. However, their molar rotations are considerably lower than those of the structurally corresponding systems containing the sulfinylic group bonded directly to the aromatic ring. The observed decrease of molar rotation is undoubtedly connected with the decrease of the interaction between free π electrons of the aromatic ring and the asymmetric sulfoxide system [2].

In order to collect further data we have investigated the

optical properties of other alkyl derivatives of the carboxymethylbenzylsulfoxide system.

In the present communication we are reporting the results of our experiments carried out in order to elaborate the synthesis of racemic p-methylbenzylsulfoxyacetic acid and its resolution into optical antipodes.

The starting material was known p-methylbenzyl bromide 1. On treatment with sodium thioglycolate in an alkaline medium, it gave p-methylbenzylthioglycolic acid in fairly good yield. The acid was characterized as its anilide. Its structure was confirmed by IR spectra; the characteristic bands are quoted in the experimental part.



1: R = Br

2: R = $S \cdot CH_2 \cdot COOH$

3: R = $S \cdot CH_2 \cdot CO \cdot NH \cdot C_6H_5$

4: R = $\overset{(+)}{S}O \cdot CH_2 \cdot COOH$

5: R = $\overset{(+)}{S}O \cdot CH_2 \cdot CO \cdot NH_2$

6: R = $\overset{(+)}{S}O \cdot CH_2 \cdot CO \cdot O \cdot CH_2 \cdot CO \cdot C_6H_4Br$

7: R = $\overset{(+)}{S}O \cdot CH_2 \cdot CO \cdot O \cdot CH_2 \cdot CO \cdot C_6H_4 \cdot C_6H_5$

8: R = $\overset{(+)}{S}O \cdot CH_2 \cdot COOH \cdot HCND^*$

9: R = $\overset{(-)}{S}O \cdot CH_2 \cdot COOH$

10: R = $\overset{(+)}{S}O \cdot CH_2 \cdot COOH \cdot CND^{**}$

11: R = $\overset{(+)}{S}O \cdot CH_2 \cdot COOH$

12: R = $\overset{(+)}{S}O \cdot CH_2 \cdot CO \cdot NH_2$

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*HCND - hydrocinchonidine.

**CND - cinchonidine.

13: R = $\overset{(+)}{S}O \cdot CH_2 \cdot CO \cdot O \cdot CH_2CO \cdot C_6H_4Br$

14: R = $\overset{(+)}{S}O \cdot CH_2 \cdot CO \cdot O \cdot CH_2 \cdot CO \cdot C_6H_4 \cdot C_6H_5$

15: R = $SO_2 \cdot CH_2 \cdot COOH$

Racemic p-methylbenzylsulfoxyacetic acid 4 was prepared by oxidation of acid 2 with 30% H_2O_2 at room temperature in glacial acetic acid. Its amide 5 crystallized readily. We have also prepared its p-bromophenacyl ester 6 and p-phenylphenacyl ester 7. Its methyl ester could not be obtained in the crystalline state. Its IR spectrum (the characteristic bands are quoted in the experimental part) was in complete agreement with the assigned structure. It should be mentioned that the sodium salt of 4 could be readily converted into sulfone 15 by oxidation under drastic conditions (at 100°C in aqueous medium in the presence of an excess of the oxidizing agent).

In our further studies we have resolved racemic acid 4 by crystallization of its diastereomeric salts with optically active alkaloids. Neutral hydrocinchonidine salt, which crystallises from ethyl acetate, was the most suitable for the isolation of laevorotatory antipode 9. After six crystallizations it was optically homogeneous. It forms regular needles m. p. 133°C, $[\alpha]_D^{20}$ = +54.7° in 96% ethanol.

In order to prepare the dextrorotatory enantiomer we carried out a crystallization of the cinchonidine salt of racemic acid 4 from ethyl acetate. After six crystallizations it was optically pure. It had m. p. 128°C and $[\alpha]_D^{20}$ = -25.3° in 96% ethanol. The relatively easy resolution of the racemate by means of the bases having the same spatial configurations does not confirm the known and often used Winther rule [3].

Antimeric acids 9 and 11 obtained by liberation from the alkaloids salts and crystallization from ethyl acetate melted at 156-157°C and had relatively low optical activity $[\alpha]_D^{20}$ = =+79.1° and -79.8° in 96% ethanol. Mixing of the antipodes in

1:1 ratio followed by crystallization gave racemic acid 4. The melting point of the racemate is much lower than that of the antipodes $(\Delta t = 17^{\circ})$. The IR spectrum of the racemic acid is not significantly different from those of the enantiomers, which are identical. Since the racemic acid does not separate readily into the antipodes, it is probably a system of pseudoasymmetric mixed crystals. This conclusion is corroborated by the physical properties of the individual compounds quoted above.

In order to obtain further comparable data for polarimetric studies we have prepared amide 12, p-bromophenacyl ester 13 and

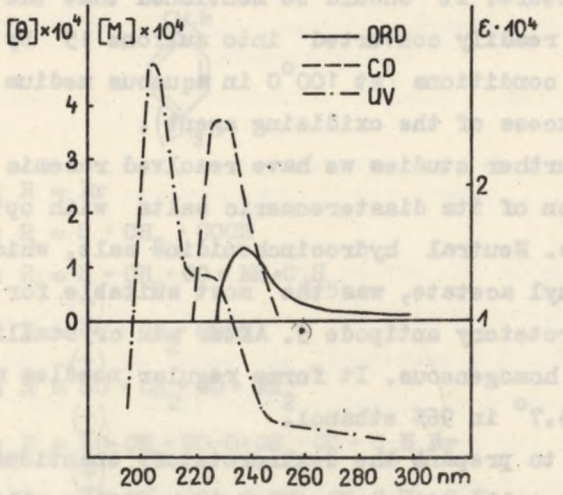

Fig. 1. Optical rotatory dispersion (ORD), circular dichroism (CD) and ultraviolet spectrum (UV) of dextrorotatory p-methylbenzylsulfoxyacetic acid in 96% ethanol

ORD $(c = 0.007$ g/100 ccm, $d = 0.1$ dm$)$; $\lambda_{pk} = 237$ nm, $\lambda_{z_0} = 228$ nm; $[M]^{26}_{237} = 13646^{\circ}$ $(\alpha = 0.045^{\circ})$.

CD $(c = 0.00033$ mole/dm^3, $d = 1$ cm$)$; $\lambda_{\Theta max} = 229$ nm; $[\Theta]_{229} = 35524$ $(\Delta A = 0.00355)$.

UV $(c = 0.000032799$ mole/dm^3, $d = 1$ cm$)$; $\lambda_{max} = 203$ nm, 227 nm; $\varepsilon\lambda_{203} = 29226$ $(A = 0.9586)$; $\varepsilon\lambda_{227} = 5228$ $(A = 0.1715)$.

p-phenylphenacyl ester 14 of dextrorotatory enantiomer 11. Since these preparations were carried out under mild conditions, acid 11 probably did not undergo racemization during the reactions. Attempted preparations of methyl and p-nitrobenzyl esters of acid 11 failed. In both cases the products were oils which were extremely difficult to purify to the state required for polarimetric measurements.

We have completed the above studies by determining rotatory dispersion in the region 200-300 nm as well as circular dichroism and electronic spectra of enantiomer 11.

The optical rotatory dispersion curve (ORD) shown in Fig.1 has a peak at 237 nm corresponding to molar rotation $[M]_{237}$ = 13.646° and at λ = 228 nm it cuts the axis of zero rotations. Analogously the circular dichroism (CD) curve has a pronounced positive maximum at 229 nm where the molar ellipticity is $[\theta]$ = 35.524°. The electronic spectrum curve has in the examined region, two absorption bands at 203 and 227 nm (ε_{203} = 29226, ε_{227} = 5228). It is significant that the characteristic points on the ORD (λ_{z_o}), CD ($\lambda_{\theta max}$) and UV ($\lambda_{\varepsilon max}$) curves show only a slight scatter. Analysis of the results of optical measurements leads to the conclusion that dextrorotatory acid 11 has in the examined spectral region (200-300 nm) only one positive Cotton effect localized in the range λ = 228-229 nm.

It should be mentioned that chiral-optical properties of dextrorotatory m-methylbenzylsulfoxyacetic and 1, 2, 3, 4-tetrahydro-5- and 6-naphthylmethylsulfoxyacetic acids[4,5] are very similar to those of dextrorotatory p-methylbenzylsulfoxyacetic acid. In the examined spectral region (200-300 nm), the compounds of the m-methylbenzyl and tetrahydro-5- and 6-naphthylmethyl series also show only one Cotton effect which is slightly shifted in the direction of longer waves. The characteristic points on the ORD and CD curves of m-methylbenzylsulfoxyacetic and 1, 2, 3, 4-tetrahydro-5- and 6-naphthylmethylsulfoxyacetic acids are as follows: λ_{z_o} = 228, 233 and 234 nm,

$\lambda_{\Theta max}$= 234, 233 and 233 nm. It should be stressed that dextrorotatory para and meta acids of the benzyl and tetrahydro-5- and 6-naphthylmethyl series change the direction of molar rotation in certain solvents ($CHCl_3$), which is not observed in the case of isomeric compounds containing the sulfoxy group connected directly with the aromatic or hydroaromatic ring.

The measurements of molar rotations of p-methylbenzylsulfoxyacetic acids and some of their derivatives in various solvents in a wide spectral range will be carried out in the near future.

Further studies on the effect of alkyl substituents of straight and branched carbon chains on the rotation of sulfoxy chirality centres will be continued by one of us (M. J.).

EXPERIMENTAL PART

The melting points are uncorrected. The polarimetric measurements were carried out in the previously described [6] apparatus in the solvents quoted in the text. The IR spectra were determined by means of SP-200 spectrophotometer. The ORD, CD and UV spectra were obtained in JASCO ORD/CD/UV/5 apparatus. The spectra were obtained for a suspension in paraffin oil (IR) and for ethanolic solutions (ORD, CD and UV).

1. p-Methylbenzyl Bromide 1

150 g of purified p-xylene was converted into p-methylbenzyl bromide under the previously described [1] conditions, using 240 g of bromine dried over H_2SO_4. The product was distilled under reduced pressure and the fraction boiling in the range 104 -106°C/13 mm Hg was collected. The distillate soon crystallized. The purified p-methylbenzyl bromide had m. p. 35°C (lit. [7] m. p. 35°C). Yield 152 g.

2. p-Methylbenzylthioglycolic acid 2

101 g (1.1 mole) of thioglycolic acid was dissolved in 60 ccm of water. The solution was stirred mechanically and cooled

externally with ice water. A solution of 88 g (2.2 mole) of NaOH in 132 ccm of water and then a solution of 185 g (1 mole) of p-methylbenzyl bromide in 140 ccm of 96% ethanol were added dropwise and the cooling bath was removed. The mixture was stirred at room temperature for 2 hrs. A fine crystalline precipitate separated. In order to dissolve it, 1.5 l of water was added. The solution was extracted with ether (3 x 200) ccm. The aqueous layer was freed from dissolved ether and was acidified with 10% HCl to pH = 1. An oil separated. It was extracted with ether (2 x 200 ccm). The extract was washed with water and then dried over anhydrous $MgSO_4$. The residue remaining after the removal of ether (water bath) was distilled under reduced pressure. The fraction boiling at 159-161°C/24 mm Hg was collected. The distillate soon crystallized. Needles from petroleum ether m. p. 65°C (lit.[8] m. p. 65°C). Yield 185 g.
IR: (cm^{-1}) : 825, 1020, 1120, 1170 δC_{Ar}-H (subst. 1,4); 1450, 1520, 1620 νC_{Ar}-C_{Ar}; 725 ν C-S; 940 δOH (COOH); 1245, 1300, 1418 δOH and ν C-O (COOH); 1700 ν C=O (COOH).

3. p-Methylbenzylthioglycolic acid anilide 3

10 g. (0.05 mole) of powdered acid 2 was added in small portions with stirring to 12 g (0.01 mole) of thionyl chloride. The suspension was refluxed ($CaCl_2$ tube) for 30 mins. The excess of thionyl chloride was removed by distillation under reduced pressure (12 mm Hg, water bath). The oily residue was introduced into a solution of 18 g (0.2 mole) of aniline in 50 ccm of benzene and the solution was shaken mechanically for 2 hrs. at room temperature. Then it was washed with dilute HCl (50 ccm of 10% HCl) and with water (2 x 100 ccm) and dried over anhydrous $MgSO_4$. The solid residue (6 g) obtained after the evaporation of benzene was crystallized from 72% methanol (100 ccm). Long needles m. p. 80.5°C. Yield 0.8 g. The anilide is readily soluble in benzene, chloroform, dioxane, acetone and 96% ethanol.

Analysis:
For the formula: $C_{16}H_{17}NOS$ 271.39 -
calculated: 5.16% N;
found: 5.16% N.

4. Racemic p-methylbenzylsulfoxyacetic acid 4

A solution of 47 g (0.24 mole) of acid 2 in 90 ccm of glacial acetic acid shaken mechanically and cooled externally with water at 10-12°C was treated with 29% hydrogen peroxide which was added every two hours in 4 portions of 7 ccm. Then the solution was allowed to stand at room temperature for 48 hrs. A fine crystalline precipitate separated (35 g). It was filtered and recrystallized from acetone (1.2 l). Colorless rods m. p. 140°C. Yield 34 g. Racemic acid 4 is readily soluble in chloroform, fairly soluble in acetone and methanol and insoluble in petroleum ether.

Analysis:
For the formula: $C_{10}H_{12}O_3S$ (212.26) -
calculated: 56.58% C. 5.70% H;
found: 56.82% C, 5.43% H.

IR: (cm^{-1}): 830, 1115, 1170 $\delta C_{Ar}-H$ (subst. 1,4); 1440, 1620 $\nu C_{Ar}=C_{Ar}$; 720 $\nu C-S$; 1010 νSO; 910 δOH(COOH); 1250, 1310, 1395 δOH and $\nu C-O$ (COOH); 1730 $\nu C=O$ (COOH).

5. Racemic p-methylbenzylsulfoxyacetic acid amide 5

A solution of 2.12 g (0.01 mole) of acid 4 in 30 ccm of anhydrous methanol was cooled externally with ice water and was treated dropwise with vigorous stirring with a solution of diazomethane prepared from 1.1 g of N,N- nitrosomethylurea until the solution became permanently colored [9]. After the vigorous methylation reaction, the solution was washed successively with 2% Na_2CO_3 (30 ccm) and water (2 x 40 ccm). The organic layer was separated. The remaining light yellow oil (12 g) obtained after the evaporation of the solvent (water bath) was suspended in 50 ccm of concd. ammonia (d = 0.88) and the mixture was shaken

mechanically at room temperature for 2.5 hrs. A fine crystalline precipitate separated. It was filtered (1.9 g) and recrystallized from methanol (30 ccm). Needles m. p. 190°C. Yield 1.3 g. The amide is readily soluble in chloroform, fairly soluble in benzene, acetone and methanol and insoluble in petroleum ether.

Analysis:

For the formula: $C_{10}H_{13}NO_2S$ (211.28) -

calculated: 6.63% N;

found: 6.80% N.

IR: (cm^{-1}): 830, 1020, 1105, 1170 δC_{Ar}-H(subst. 1,4); 1440,1520 $\nu C_{Ar}=C_{Ar}$; 720 νC-S; 1035 νSO; 1420 C-H; 1620 δN-H; 1655 νC=O ($CONH_2$); 3200, 3400 νN-H.

6. p-Bromophenacyl ester of racemic p-methylbenzylsulfoxyacetic acid 6

2.33 g (0.011 mole) of powdered racemic acid 4 was added to a solution of 0.4 g (0.01 mole) of NaOH in 10 ccm of water. The sulfoxide dissolved immediately. The solution was treated with 2 g (0,007 mole) of p-bromophenacyl bromide dissolved in 30 ccm of hot 96% ethanol and refluxed for 1 hr. Then it was filtered while still hot and allowed to stand at room temperature. A fine crystalline precipitate soon separated. It was filtered off and dissolved in chloroform (30 ccm). The solution was washed with 5% Na_2CO_3 (30 ccm) and then with water (2 x 50 ccm) and, after drying over anhydrous $MgSO_4$, it was treated with petroleum ether (100 ccm). Fine crystals soon separated. They were filtered off (2 g) and recrystallized from methanol (27 ccm). Plates m. p. 161°C. Yield 1.2 g. The ester is readily soluble in chloroform, fairly soluble in benzene and in methanol, and insoluble in petroleum ether.

Analysis:

For the formula: $C_{18}H_{17}BrO_4S$ (409.28) -

calculated: 52.82% C, 4.18% H;

found: 52.63% C, 4.47% H.

7. p-Phenylphenacyl ester of racemic p-methylbenzylsulfoxyacetic acid 7

2.33 g (0.011 mole) of powdered acid 4 was added to a solution of 0.4 g (0.01 mole) of NaOH in 10 ccm of water. The sulfoxide dissolved immediately. The solution was treated with 2 g (0.007 mole) of p-phenylphenacyl bromide in 35 ccm of 96 % ethanol and the mixture refluxed for 1 hr. Then the solution was cooled. The product (3 g) was filtered off and dissolved in chloroform (40 ccm). The solution was washed with 5% Na_2CO_3 solution (30 ccm) and then with water (2 x 50 ccm). Then the solution was dried over anhydrous $MgSO_4$ and treated with petroleum ether (150 ccm). A fine crystalline product was filtered off (1.8 g) and recrystallized from 96% ethanol (26 ccm). Small polyhedra m. p. 148°C. Yield 1 g. The ester is readily soluble in chloroform, fairly soluble in benzene and in 96% ethanol and insoluble in petroleum ether.

Analysis:

For the formula: $C_{24}H_{22}O_4S$ (406.48) -

calculated: 70.90% C, 5.45% H;
found: 70.87% C, 5.42% H.

8. Hydrocinchonidine salt of laevorotatory p-methylbenzylsulfoxyacetic acid 8

A mixture of 21.2 g (0.1 mole) of powdered acid 4 and 29.6 g (0.1 mole) of hydrocinchonidine was dissolved in 500 ccm of boiling ethyl acetate. The hot solution was filtered and allowed to stand at room temperature. After 24 hrs. the first fraction of crystals was filtered off. Needles m. p. 122°C and $[\alpha]_D^{20} = +113.0^\circ$ ($c = 0.25$, $d = 4$, $\alpha = +1.13^\circ$) in 96% ethanol. After additional crystallizations of the first fraction from ethyl acetate, its physical properties were no longer affected by further crystallizations. Needles m. p. 133°C and $[\alpha]_D^{20} = +54.7^\circ$ ($c = 0.25$, $d = 4$, $\alpha = +0.547$) in 96% ethanol. Yield 7 g. The salt of the laevorotatory enantiomer is readily

soluble in chloroform and in 96% ethanol and insoluble in petroleum ether.

Analysis:

For the formula: $C_{29}H_{36}N_2O_4S$ (508.65) -

calculated: 5.51% N;

found: 5.30% N.

Table 1. Fractional crystallization of hydrocinchonidine salt of laevorotatory p-methylbenzylsulfoxyacetic acid (crystallization time 24 hrs.)

Fraction No.	Volume of ethyl acetate ccm	Weight of salt g	Specific rotation in 96% ethanol $[\alpha]_D^{20}$	M.p. of salt °C
1.	500	31.0	+113.0°	122
1.1.	450	23.0	+ 91.0°	125
1.1.1.	300	15.0	+ 75.0°	127
1.1.1.1.	100	8.0	+ 66.0°	129
1.1.1.1.1.	50	7.5	+ 59.0°	132
1.1.1.1.1.1.	40	7.0	+ 54.7°	133
1.1.1.1.1.1.1.	25	5.0	+ 54.6°	133

9. Laevorotatory p-methylbenzylsulfoxyacetic acid 9

10 g (0.02 mole) of powdered salt 8 (m. p. 133°C, $[\alpha]_D^{20}$ = +54.7°) was suspended in 100 ccm of water and was acidified with 10 ccm of 18% HCl. The suspension was stirred for 2 hrs. at room temperature. The laevorotatory enantiomer separated and was filtered. It was suspended in 50 ccm of water and made alkaline with 2.6 g of NaOH dissolved in 10 ccm of water. The solution of sodium salt of the laevorotatory acid was extracted with chloroform (5 x 40 ccm). Chloroform dissolved in the alkaline

liquid was removed by distillation under reduced pressure (12 mm Hg, water bath) and the liquid acidified to Congo with 15% hydrochloric acid. A fine crystalline precipitate was filtered off and, after washing with water, was dried in a vacuum desiccator ($CaCl_2$). The crude sulfoxyacid (4 g) was recrystallized from ethyl acetate (200 ccm). Square plates m. p. 156°C, $[\alpha]_D^{20} = -79.1°$ (c = 0.125, d = 4, $\alpha = -0.385°$) in 96% ethanol. Yield 2.5 g. The laevorotatory enantiomer is readily soluble in chloroform, fairly soluble in acetone and methanol and insoluble in petroleum ether.

Analysis:

For the formula: $C_{10}H_{12}O_3S$ (212.26) -

calculated: 56.58% C, 5.70% H;

found: 56.74% C, 5.79% H.

10. Cinchonidine salt of dextrorotatory p-methylbenzylsulfoxyacetic acid 10

A mixture of 21.2 g (0.1 mole) of powdered acid 4 and 29.4 g (0.1 mole) of cinchonidine was dissolved in 1.5 l of hot ethyl acetate. The solution was filtered while still hot and allowed to stand at room temperature. After 24 hrs. the first fraction of the salt was filtered. Needles m. p. 130°C, $[\alpha]_D^{20} = -73.0°$ (c = 0.25, d = 4, $\alpha = -0.73°$) in 96% ethanol. After 5 additional crystallizations the salt had physical properties which were not changed after further crystallizations. Needles m. p. 128°C, $[\alpha]_D^{20} = -25.3°$ (c = 0.25, d = 4, $\alpha = -0.253°$) in 96% ethanol. Yield 7 g. The cinchonidine salt of the dextrorotatory enantiomer is readily soluble in chloroform and in 96% ethanol and insoluble in petroleum ether.

Analysis:

For the formula: $C_{29}H_{34}N_2O_4S$ (506.65) -

calculated: 5.53% N;

found: 5.28% N.

Table 2. Fractional crystallization of cinchonidine salt of dextrorotatory p-methylbenzylsulfoxyacetic acid (crystallization time 24 hrs.)

Fraction No.	Volume of ethyl acetate ccm	Weight of salt g	Specific rotation in 96% ethanol $[\alpha]_D^{20}$	M.p. of salt °C
1.	1500	40.0	-73.0°	130
1.1.	1500	39.0	-70.6°	130
1.1.1.	1500	33.0	-59.4°	129
1.1.1.1.	1400	28.0	-43.0°	128
1.1.1.1.1.	1000	15.0	-30.5°	128
1.1.1.1.1.1.	800	7.0	-25.0°	128
1.1.1.1.1.1.1.	600	5.0	-25.3°	128

11. Dextrorotatory p-methylbenzylsulfoxyacetic acid 11

20 g (0.04 mole) of powdered salt 10 (m. p. 128°C, $[\alpha]_D^{20}$ = -25.3°) was suspended in 200 ccm of water and after stirring was acidified with 14 ccm of 18% HCl. The suspension was stirred for 2 hrs. at room temperature. The resulting dextrorotatory enantiomer was filtered off and, after suspending in 50 ccm of water, was made alkaline with a solution of 4 g of NaOH in 15 ccm of water. The solution of sodium salt was extracted with chloroform (5 x 50 ccm). The alkaline liquid was freed from dissolved chloroform by distillation under reduced pressure (12 mm Hg, water bath) and then was acidified to Congo with 15% HCl. A fine crystalline precipitate immediately separated. It was filtered off and, after washing, dried in a vacuum desiccator H_2SO_4. The crude sulfoxyacid (8 g) was recrystallzed from ethyl acetate (420 ccm). Plates m. p. 157°C, $[\alpha]_D^{20}$ = +79.8°

(c = 0.125, d = 4, α = +0.399°) in 96% ethanol. Yield 5 g. The dextrorotatory enantiomer is readily soluble in chloroform, fairly soluble in acetone and methanol and insoluble in petroleum ether.

Analysis:

For the formula: $C_{10}H_{12}O_3S$ (212.26) -

calculated: 56.58% C, 5.70% H;

found: 56.33% C, 5.80% H.

IR: (cm^{-1}): 830, 1110, 1180 δC_{Ar}-H (subst. 1,4); 1440, 1520, 1580, 1620 $\nu C_{Ar}=C_{Ar}$; 720 νC-S; 1005, νS-O; 910 δOH (COOH); 1240, 1310, 1420 δOH and C-O (COOH); 1705 νC=O (COOH).

12. Dextrorotatory p-methylbenzylsulfoxyacetic acid amide 12

2.12 g (0.01 mole) of dextrorotatory acid 11 (m. p. 157°C, $[\alpha]_D^{20}$ = +79.8° was converted into its methyl ester according to the procedure described in section 5. 2.2 g of the ester (a light yellow non-solidifying oil) was suspended in 30 ccm of conc. ammonia (d = 0.88) and was shaken mechanically at room temperature. A fine crystalline precipitate separated. It was filtered off and, after washing with water, dried in a vacuum desiccator (H_2SO_4). The crude amide 1.7 g was crystallized from a mixture of chloroform (210 ccm) and petroleum ether (650 ccm). Small granules m. p. 192°C, $[\alpha]_D^{20}$ = +81.32° (c = 0.25, d = 4, α = +0.813°) in 96% ethanol. Yield 1.6 g. The amide is readily soluble in chloroform, fairly soluble in methanol and insoluble in petroleum ether.

Analysis:

For the formula: $C_{10}H_{13}NO_2S$ (211.29) -

calculated: 6.63% N;

found: 6.62% N.

IR: (cm^{-1}) : 830, 1020, 1160, 1170 δC_{Ar}-H (subst. 1,4); 1520 $\nu C_{Ar}=C_{Ar}$; 720 νC-S; 1020 νSO; 1420 C-N; 1630 δN-H; 1670 νC=O ($CONH_2$); 3160, 3400 νN-H.

13. p-Bromophenacyl ester of dextrorotatory p-methylbenzylsulfoxyacetic acid 13

1.3 g (0.006 mole) of powdered dextrorotatory acid 11 (m.p. 157°C, $[\alpha]_D^{20}$ = +79.8°) was dissolved in 0.2 g of NaOH (0.005 mole) in 5 ccm of water. The sulfoxide dissolved immediately. The solution was treated with 1.3 g of p-bromophenacyl bromide in 30 ccm of hot 96% ethanol and refluxed for 1 hr. Then it was allowed to stand at room temperature. A fine crystalline precipitate separated. It was filtered off and then dissolved in chloroform (35 ccm). The chloroform solution was washed first with a 5% Na_2CO_3 solution (130 ccm), then with water (2 x 60 ccm) and dried over anhydrous $MgSO_4$. The solution was treated with petroleum ether (90 ccm). A fine crystalline precipitate separated. The product was filtered off (1.5 g) and recrystallized from 40 ccm of 96% ethanol. Plates m. p. 157°C, $[\alpha]_D^{20}$ = +62.04° (c = 0.083, d = 4, α = +0.207°) in 96% ethanol. Yield 1 g. The ester is readily soluble in chloroform, fairly soluble in acetone and in 96% ethanol and insoluble in petroleum ether.

Analysis:

For the formula: $C_{18}H_{17}BrO_4S$ (409.28) -

calculated: 52.82% C, 4.18% H;

found: 52.94% C, 4.24% H.

14. p-Phenylphenacyl ester of dextrorotatory p-methylbenzylsulfoxyacetic acid 14

1.3 g (0.006 mole) of powdered dextrorotatory acid 11 (m. p. 157°C, $[\alpha]_D^{20}$ = +79.8°) was added to a solution of 0.2 g of NaOH (0.005 mole) in 5 ccm of water. The sulfoxide dissolved immediately. The solution was treated with 1.3 g of p-phenylphenacyl bromide suspended in 35 ccm of 96% ethanol and was refluxed for 1 hr. Then it was allowed to stand at room temperature. A fine crystalline precipitate separated. It was filtered

off and dissolved in chloroform (40 ccm). The solution was washed with a 5% Na_2CO_3 solution (30 ccm), then with water (2 x 60 ccm) and dried over anhydrous $MgSO_4$. On adding petroleum ether (100 ccm), a fine crystalline precipitate separated. It was filtered off (1.5 g) and recrystallized from ethyl acetate (20 ccm). Plates m. p. 145°C, $[\alpha]_D^{20} = +76.6^\circ$ ($c = 0.4$, $d = 4$, $\delta = +0.122^\circ$) in 96% ethanol. The ester is readily soluble in chloroform, fairly soluble in acetone and methanol and insoluble in petroleum ether.

Analysis:

For the formula: $C_{24}H_{22}O_4S$ (406.48) -

calculated: 70.90% C, 5.45% H;

found: 71.15% C, 5.18% H.

15. p-Methylbenzylsulfonylacetic acid 15

4.2 g (0.02 mole) of powdered racemic acid 4 was suspended in 10 ccm of water and neutralized to a pH of 10 with 25% NaOH solution. Then in was heated on water bath and 5 portions of 2 ccm of 29% hydrogen peroxide solution (0.018 mole) were added every 2 hrs. The solution was allowed to stand at room temperature for 24 hrs. and then acidified to Congo with 10% HCl. A fine crystalline precipitate separated. It was filtered off (3.5 g) and after drying in a vacuum desiccator (H_2SO_4), was recrystallized from a mixture of chloroform (50 ccm) and petroleum ether (180 ccm). Colorless plates m. p. 143°C. Yield 2.6 g. The sulfone is readily soluble in chloroform, fairly soluble in benzene and acetone and insoluble in petroleum ether.

Analysis:

For the formula: $C_{10}H_{12}O_4S$ (228.27) -

calculated: 52.62% C, 5.29% H;

found: 52.85% C, 5.14% H.

IR: (cm^{-1}): 824, 1050, 1138, 1195 $\delta C_{Ar}-H$ (subst. 1.4); 1440, 1490, 1570, 1610 $\nu C_{Ar}=C_{Ar}$; 720 $\nu C-S$; 1150 $\nu asSO_2$; 1350 νsSO_2;

930 δOH(COOH); 1240, 1310, 1400 δOH νC-O(COOH); 1750 νC=O (COOH).

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STRESZCZENIE

Opisano metodę syntezy oraz określono podstawowe własności fizyczne optycznie czynnych kwasów p-metylobenzylosulfoksyoctowych i ich niektórych pochodnych o charakterze amidowym i estrowym. Budowa strukturalna poszczególnych połączeń potwierdzona została na drodze badania widm oscylacyjnych. Określono dyspersję rotacyjną, dichroizm kołowy oraz widmo elektronowe w rejonie 200-300 nm prawoskrętnego enancjomeru. Tok syntez oraz stałe fizyczne nowo otrzymanych połączeń podano w tekście angielskim.

РЕЗЮМЕ

В данной работе представлено метод синтеза и определено основные физические особенности оптически активных р-метилбензилсульфинилуксусных кислот и их некоторые производные амидового и эстрового характера. Структуральное строение отдельных соединений подтвер дено путем исследования спектров колебания. Определено вращательную дисперсию, круговой дихроизм, а также электронный спектр в районе 200-300 нанометров правовращающего энантиомера. Ход синтеза и физические постоянные новополученных соединений представлено в тексте на английском языке.