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Kierownik: prof. dr Marian Janczewski

Marian JANCZEWSKI, Wit JANOWSKI

The Effect of Molecular Structure on Optical Properties of Sulfoxide Systems. LIX. Synthesis of Racemic o-Tolylsulfinyldimethylacetic Acid and Its Resolution into Optical Antipodes

Wpływ budowy cząsteczkowej na własności optyczne układów sulfotlenkowych. LIX. Synteza racemicznego kwasu o-tolilosulfinylodwumetylooctowego i jego rozszczepienie na antypody optyczne

Влияние молекулярного строения на оптические свойства сульфоокисных систем. LIX. Синтез рацемической о-толилсульфинилдвуметилуксусной кислоты и её расщепление на оптические антиподы

Although extensive studies on the effect of various substituents and functional groups on optical properties of sulfoxide systems have been carried out in our laboratory ,until the present time, we have not been interested in the effect of substituents consisting of straight chain and branched alkyls on the chirality centres in these systems [1].

On the basis of certain physical and chemical processes, it could have been expected that alkyl groups would cause two effects: hyperconjugation effect which in unsaturated systems have certain properties of the mesomeric effect (+M) and the inductive effect [2—5]. The latter seems to have negative values (—I) in saturated systems and positive values (+*I*) in unsaturated ones [6—9].

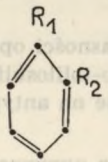
As a rule the inductive effect increases with increasing order of branching of carbon atoms directly bonded to the unsaturated system. This is accompanied by a steady decrease of the hyperconjugation effect. It is possible that these two effects have some influence on the rotation of unsaturated compounds as well as aromatic-aliphatic systems containing heteroatomic chirality centres.

In the course of our work on optical relationships in asymmetric tetra-

lene derivatives, we have unexpectedly encountered an optical order, the interpretation of which required the investigation of the effect of alkyl substituents on the optical rotation of sulfinylic chirality centres [10, 11]. We started this investigation by comparing optical properties of isomeric o-, m- and p-tolysulfoxydimethylacetic acids.

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

The starting material in these experiments was a known o-thiocresol [1] which was treated with sodium bromoisobutyrate in an alkaline medium. It gave a fairly good yield o-tolylmercaptodimethylacetic acid 2. The product was characterised by conversion into its amide 3, anilide 4 and p-bromophenacyl ester 5. The structure of acid 2 was confirmed on the basis of its IR spectrum. The characteristic absorption bands are given in the experimental part.



1: $R_1=CH_3$, $R_2=SH$;

2: $R_1=CH_3$, $R_2=S\cdot C(CH_3)_2\cdot COOH$;

3: $R_1=CH_3$, $R_2=S\cdot C(CH_3)_2\cdot CO\cdot NH_2$;

4: $R_1=CH_3$, $R_2=S\cdot C(CH_3)_2\cdot CO\cdot NH\cdot C_6H_5$;

5: $R_1=CH_3$, $R_2=S\cdot C(CH_3)_2\cdot CO\cdot OCH_2\cdot CO\cdot C_6H_4Br$;

6: $R_1=CH_3$, $R_2=\overset{(\pm)}{SO}\cdot C(CH_3)_2\cdot COOH$;

7: $R_1=CH_3$, $R_2=\overset{(\pm)}{SO}\cdot C(CH_3)_2\cdot CO\cdot OCH_3$;

8: $R_1=CH_3$, $R_2=\overset{(\pm)}{SO}\cdot C(CH_3)_2\cdot CO\cdot NH_2$;

9: $R_1=CH_3$, $R_2=\overset{(-)}{SO}\cdot C(CH_3)_2\cdot COOH\cdot HCND$;*

10: $R_1=CH_3$, $R_2=\overset{(-)}{SO}\cdot C(CH_3)_2\cdot COOH\cdot CND$;**

11: $R_1=CH_3$, $R_2=\overset{(-)}{SO}\cdot C(CH_3)_2\cdot COOH$;

12: $R_1=CH_3$, $R_2=\overset{(+)}{SO}\cdot C(CH_3)_2\cdot COOH\cdot HCND$;*

13: $R_1=CH_3$, $R_2=\overset{(+)}{SO}\cdot C(CH_3)_2\cdot COOH$;

14: $R_1=CH_3$, $R_2=\overset{(-)}{SO}\cdot C(CH_3)_2\cdot CO\cdot NH_2$;

15: $R_1=H$, $R_2=\overset{(\pm)}{SO}\cdot C(CH_3)_2\cdot COOH$;

16: $R_1=H$, $R_2=\overset{(-)}{SO}\cdot C(CH_3)_2\cdot COOH\cdot CND$;**

17: $R_1=H$, $R_2=\overset{(-)}{SO}\cdot C(CH_3)_2\cdot COOH$;

18: $R_1=H$, $R_2=\overset{(-)}{SO}\cdot C(CH_3)_2\cdot CO\cdot NH_2$;

* HCND=hydrocinchonidine

** CND=cinchonidine

We obtained racemic o-tolylsulfinyldimethylacetic acid 6 by oxidation of acid 2 with 30% hydrogen peroxide at room temperature in glacial acetic acid. The resulting sulfoxide 6 was converted into readily crystallizing amide 8 but we were unable to obtain its methyl ester 7 in the crystalline state. The IR spectrum of acid 6 (the characteristic absorption bands are given in the experimental part) fully confirmed its structure.

In our further studies we resolved racemic acid 6 by crystallization of its diastereomeric salts with optically active alkaloids. For the isolation of the laevorotatory antipode 11 the most suitable were neutral salts with hydrocinochonidine and with cinchonidine which crystallize from dilute acetone. After two crystallizations we obtained these salts in the homogenous state. The hydrocinchonidine salt of the laevorotatory enantiomer crystallized in regular needles m. pt. 134°C, $(\alpha)_D^{20} = -117°$ (in ethanol). The cinchonidine salt crystallized in needles m. pt. 145°C, $(\alpha)_D^{20} = -145°$ (in ethanol).

In order to obtain the second enantiomer we evaporated the mother liquors after the first crystallization of the hydrocinchonidine salt to dryness. The residue was dried under reduced pressure to constant weight and was crystallized from anhydrous acetone. Usually after one recrystallization the salt was optically homogenous. It crystallized in rods m. pt. 125°C, $(\alpha)_D^{20} = O°$ (in ethanol).

Optically active acids 11 and 13 were liberated from the diastereomeric hydrocinchonidine salts in the usual way. After crystallization from acetone they had m. pt. 98°C with decomposition and a relatively high optical activity $(\alpha)_D^{20} = \pm 131°$ (in ethanol).

The optical antipodes mixed in equimolar proportions and recrystallized gave the original racemic acid. The melting point of the racemate was considerably higher than that of the antipodes ($\Delta T = 16°$). Its vibrational spectrum did not significantly differ from those of the enantiomers which were identical.

The ease of resolution of the racemic acid and the differences as well as similarities between the properties of the enantiomers lead to the conclusion that the racemic acid was a system of pseudoracemic mixed crystals.

We completed the above studies by repeating the synthesis of the previously described [13] laevorotatory phenylsulfinyldimethylacetic acid which was used as the reference compound in comparison with the optical properties of isomers. It should be mentioned that the method of isolation of laevorotatory acid 17 from the racemate 15 used in our work was considerably simpler than that described in the literature [13].

In order to obtain a larger amount of material for comparative polarimetric studies we prepared amides 14 and 18 of laevorotatory o-tolysul-

finyldimethylacetic 11 and phenylsulfinyldimethylacetic 17 acids. Since the reactions were carried out under mild conditions it can be assumed that the laevorotatory enantiomers 11 and 17 were not racemised during these processes.

We were unable to obtain the corresponding methyl and p-nitrobenzyl esters. In both cases we obtained oily products which could not be purified to the degree of purity required in optical measurements.

The determination of molar rotations of laevorotatory o-tolysulfinyldimethylacetic 11 and phenylsulfinyldimethylacetic 17 acids and their amides 14 and 18 was carried out in the previously described [17] apparatus in methanol (M), ethanol (E), acetone (A), dioxane (D) and chloroform (Ch) at λ=6234, 5893, 5791, 5461 and 4358 Å. The results are shown in Table 1.

The data collected in Table 1 lead to the conclusion that the principal factor determining the molar rotation is the nature of the solvent. The solvents can be arranged in the following series according to the decreasing molar rotations:
for free acids:

11 — M>E>Ch>D>A; 17 — M>E>D>A>Ch;

for the amides:

14 — M>E>D>Ch>A; 18 — Ch>M>E>D>A.

It should be stressed that the solvent series are in principle similar, the only difference being the position of chloroform. It should be also stressed that the relation between the molar rotations of the examined systems and the wave length in the visible part of the spectrum obeys the one term Drude equation, which indicates that the dispersion of the specific rotation of these compounds is normal.

We investigated the relative spatial configurations of the optically active o-tolylsulfinyldimethylacetic acids and phenylsulfinyldimethylacetic acids by examination in the ultraviolet part of the spectrum rotatory dispersion, circular dichroism and electronic spectra of laevorotatory enantiomers 11 and 17. Both systems had almost identical chromophoric structure, which suggests that the similarity of optical spectra would indicate identity of relative configurations.

The results of optical measurements lead to the conclusion that laevorotatory enantiomers 11 and 17 exhibit double Cotton effects in the examined spectral region (220—300 nm). The effects observed at longer waves are negative and those observed at shorter waves are positive. Analogously each circular dichroism curve has two maxima. The negative maxima are localised at $\lambda_{\Theta max}$=250 nm — acid 17 and $\lambda_{\Theta max}$=258 nm — acid 11 and the positive ones at $\lambda_{\Theta max}$=215 nm — acid 17 and $\lambda_{\Theta max}$= =220 nm — acid 11. Electronic spectrum of acid 17 had in the examined

Table 1. Rotatory dispersion of laevorotatory phenylsulfinyldimethylacetic acid, o-tolysulfinyldimethylacetic acid and their amides

Compound	Solvent	Concn. g/100 ccm	Molar rotation $[M]_{\lambda}^{20}$				
			λ_1=623.4 nm	λ_2=589.3 nm	λ_3=579.1 nm	λ_4=546.1 nm	λ_5=435.8 nm
Laevorotatory phenylsulfoxydimethylacetic acid	Methanol	0.5	203.4	229.1	237.1	274.1	647.8
	Ethanol	0.5	182.8	197.4	207.2	238.2	552.8
	Dioxane	0.5	150.1	167.1	173.2	205.7	513.0
	Acetone	0.5	127.4	140.3	144.8	171.7	447.3
	Chloroform	0.5	91.3	100.6	107.8	129.1	341.6
Amide of laevorotatory phenylsulfoxydimethylacetic acid	Methanol	0.5	170.3	193.8	203.1	234.7	504.5
	Ethanol	0.5	162.5	183.6	190.4	217.9	422.9
	Dioxane	0.5	161.2	180.1	188.6	217.4	422.6
	Acetone	0.5	147.7	166.3	173.6	203.3	401.6
	Chloroform	0.5	189.3	212.1	224.2	260.2	580.9
Laevorotatory o-tolysulfoxydimethylacetic acid	Methanol	0.5	266.7	300.3	322.7	378.1	878.0
	Ethanol	0.5	259.9	294.0	318.4	376.9	841.8
	Dioxane	0.5	187.6	211.9	226.7	269.6	659.9
	Acetone	0.5	180.8	202.9	211.3	249.9	614.0
	Chloroform	0.5	198.9	222.6	237.9	282.5	682.3
Amide of laevorotatory o-tolysulfoxydimethylacetic acid	Methanol	0.5	242.8	284.0	301.6	344.0	766.4
	Ethanol	0.5	236.9	277.5	288.8	336.2	744.3
	Dioxane	0.5	236.5	274.8	284.6	335.1	733.2
	Acetone	0.5	214.5	243.4	253.1	300.4	610.7
	Chloroform	0.5	237.1	271.1	281.9	320.1	742.8

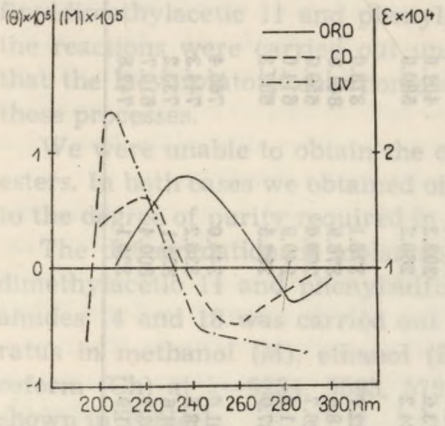


Fig. 1. Optical rotatory dispersion (ORD), circular dichroism (CD), and ultraviolet spectrum (UV) of the laevorotatory o-tolylsulfinyldimethylacetic acid in 96% ethanol

ORD (c=0.007 g/100 ccm, d=0.02 dcm);
tr $[M]^{26}_{285\ nm}$ = −29093°, (α = −0.018°);
z $[M]^{26}_{273\ nm}$ = 0°, (α = 0.000°);
pk $[M]^{26}_{237\ nm}$ = +80814°, (α = +0.050°).
Ampl. = 1099°.
CD (c=0.000309 mole/litre, d=0.2 cm);
$[\Theta]^{26}_{258\ nm}$ = −48058, (ΔA = 0.0009);
$[\Theta]^{26}_{220\ nm}$ = +61408, (ΔA = 0.00115).
UV (c=0.00003742 mole/litre, d= 1 cm);
$\varepsilon_{203\ nm}$ = 23680, (A = 0.8861).

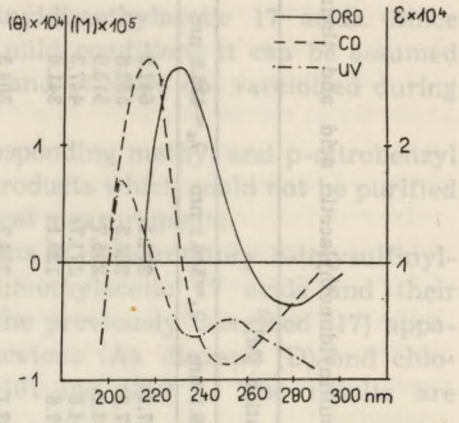


Fig. 2. Optical rotatory dispersion (ORD), circular dichroism (CD) and ultraviolet spectrum (UV) of the laevorotatory phenylsulfinyldimethylacetic acid in 96% ethanol

ORD (c=0.007 g/100 ccm, d=0.02 dcm);
tr $[M]^{26}_{278\ nm}$ = −36388°, (α = −0.024°);
z $[M]^{26}_{258\ nm}$ = 0°, (α = 0.000°);
pk $[M]^{26}_{227\ nm}$ = +169808°, (α = +0.112°);
z $[M]^{26}_{215\ nm}$ = 0°, (α = 0.000°);
Ampl. = 2062°.
CD (c=0.00033 mole/litre, d=0.2 cm);
$[\Theta]_{250\ nm}$ = −87500, (ΔA = 0.00175);
$[\Theta]_{215\ nm}$ = +177500; (ΔA = 0.00355).
UV (c=0.00005165 mole/litre, d=1 cm);
$\varepsilon_{252\ nm}$ = 5338, (A = 0.2757);
$\varepsilon_{204\ nm}$ = 17155 (A = 0.8861).

region two absorption bands at the wave length: $\lambda_{\varepsilon max}$ = 252 nm and 204 nm — and of acid 11 adsorption band at $\lambda_{\varepsilon max}$ = 203 nm.

It should be emphasized that the amplitude of the long wave Cotton effect of the unsubstituted acid 17 is two times higher than that of the acid having the methyl substituent in the ortho position 11. It is of importance that the characteristic points on the ORD curves (λ_z), CD curves ($\lambda_{\Theta max.}$) and UV curves ($\lambda_{\varepsilon max.}$) show only insignificant scatter along the wave length axis. The above experimental facts lead to the conclusion that the optically active acids having the same direction of molar rotation have the same configurations. It seems that these observations are confirmed by the Freudenberg optical shifts observed in the

case of conversion of laevorotatory acids 11 and 17 into their amides 14 and 18. The polarimetric measurements carried out in the visible part of the spectrum in the solvents shown in Table 1 indicate that the molar rotations of free o-methylphenylsulfinyldimethylacetic acids, and their amides are much higher than those of the corresponding unsubstituted acids, i.e. phenylsulfinyldimethylacetic acids and their amides having the same spatial structures. Thus the introduction of methyl group to the ortho position of phenylsulfinyldimethylacetic acid considerably increases the rotation of the system. It is possible that the observed increase of molar rotations is caused by the shift of aromatic π electrons in the direction of the sulfinylic chirality centre resulting from the hyperconjugation and the inductive effect of methyl group. There is no doubt that the observed increase of molar rotation is also due to the deviation from the benzene ring plane of tone of the two large substituents in the ortho position.

The studies on the effect of straight chain and branched alkyl substituents on the rotation of sulfinylic chirality centres will be continued.

EXPERIMENTAL

The melting points are uncorrected. The polarimetric measurements were carried out in the previously described [14] apparatus in the solvents indicated in the text. The IR spectrum was determined by means of Unicam SP-200 spectrophotometer. The ORD, CD and UV spectra were obtained in JASCO (ORD/CD/UV/5) apparatus. The IR spectra were obtained from the compounds which were suspended in paraffin oil and the ORD, CD and UV spectra from their solutions in ethanol.

1. o-Tolylmercaptodimethylacetic acid 2

31 g (0.25 mole) of o-thiocresol [12] and 42 g (0.25 mole) of α-bromoisobutyric acid [15] were introduced into 200 ccm of 96% ethanol. The resulting solution was cooled in an ice bath to 0°C and was treated carefully with stirring with 40 g of 50% NaOH. The mixture was allowed to stand at 0°C for 12 hours and then at room temperature for 24 hours. Finally it was refluxed for 8 hours, ethanol was distilled off by heating the mixture on water bath, the residue was treated with 200 ccm of water and was acidified to Congo with 50% sulfuric acid. Unreacted o-thiocresol was removed by steam distillation. The residue soon crystallized. It was filtered and after washing with 2×100 ccm of water, it was dried in a vacuume desiccator over solid KOH. The crude acid was crystallized from petroleum ether (50 ccm). Prisms m. pt. 63°C. Yield 22 g.

The product was very readily soluble in hexane, benzene, chloroform, acetone, 96% ethanol and glacial acetic acid, readily soluble in petroleum ether and insoluble in water.

Analysis:

For $C_{11}H_{14}O_2S$ (210.29) — calcd.: 62.82% C, 6.71% H;
found: 62.64% C, 6.57% H.

IR (cm^{-1}): 680 νC—S; 760, 1060, 1200 νC_{Ar}—H (subst. 1, 2); 1470, 1590 $\nu C_{Ar}=C_{Ar}$; 820, 1120, 1170 $\nu C(CH_3)_2$; 940 νOH(COOH); 1295, 1320, 1420 νOH and νC=O(COOH); 1700 νC=O(COOH).

2. o-Tolylmercaptodimethylacetic acid amide 3

10.5 g (0.05 mole) of powdered o-tolylmercaptodimethylacetic acid was added with stirring to 12 g (0.1 mole) of thionyl chloride. The mixture was refluxed for 20 minutes on water bath using a $CaCl_2$ guard tube. The excess of thionyl chloride was distilled off by heating the mixture on water bath. The oily residue was treated with 40 ccm of ammonia ($d=0.88$) and was mechanically shaken for 2 hours at room temperature. The finely crystalline reaction product was filtered and dried in a vacuum desiccator over H_2SO_4. The crude product (6 g) was crystallized from petroleum ether (170 ccm). Needles m. pt. 72°C. Yield 3 g.

The amide is readily soluble in benzene, chloroform, acetone, and 96% ethanol, fairly soluble in petroleum ether and sparingly soluble in water.

Analysis:

For $C_{11}H_{15}NOS$ (209.30) — calcd.: 6.69% N;
found: 6.47% N.

3. o-Tolylmercamptodimethylacetic acid anilide 4

11 g (0.05 mole) of o-tolylmercaptodimethylacetic acid chloride (prepared as described in section 2) was added to a solution of 18 g (0.2 mole) of aniline in 50 ccm of benzene and the mixture was mechanically shaken for 2 hours at room temperature. Then it was washed with dilute hydrochloric acid (50 ccm of 10% HCl) and water (2×100 ccm) and after drying with anhydrous $MgSO_4$, it was kept in the air until all the solvent evaporated. The amorphous residue (8 g) was crystallized from 90% methanol (68 ccm). Plates m. pt. 92°C. Yield 2 g.

The product was readily soluble in benzene, chloroform, acetone and 96% ethanol and sparingly soluble in water.

Analysis:

For $C_{17}H_{19}NOS$ (285.39) — calcd.: 4.90% N;
found: 4.77% N.

4. p-Bromophenacyl ester of o-tolymercaptodimethylacetic acid 5

4.2 g (0.02 mole) of powdered o-tolylmercaptodimethylacetic acid was suspended in 5 ccm of water and was neutralised to phenolphthalein with 10 g of 8% NaOH. The solution of the sodium salt was treated with 4 g (0.014 mole) of p-bromophenacyl bromide dissolved in 40 ccm of hot 96% ethanol. The mixture was refluxed on water bath for 1 hour. Then it was filtered (without cooling) and was allowed to stand at room temperature. A fine crystalline precipitate soon separated. The product (1.6 g) was filtered and after washing with water it was crystallized from 96% ethanol (17 ccm). Plates, m. pt. 62°C. Yield 1,4 g. The ester is readily soluble in chloroform, acetone and 96% ethanol, fairly soluble in petroleum ether and insoluble in water.

Analysis:

For $C_{19}H_{19}BrO_3S$ (407.32) — calcd.: 56.02% C, 4.70% H;
found: 55.80% C, 4.56% H.

5. Racemic o-tolylsulfinyldimethylacetic acid 6

52.5 g (0.25 mole) of o-tolylmercaptodimethylacetic acid was dissolved in 60 ccm of glacial acetic acid. The solution was cooled in water at 10—15°C and was treated at 12 hours intervals with 4×7.33 ccm portions of 29% hydrogen peroxide (0.24 mole). After the introduction of the last portion the solution was allowed to stand for 24 hours at room temperature. A finely crystalline precipitate separated (40 g). It was filtered and was dried in a vaccuum desiccator over solid KOH. The crude sulfoxide was crystallized from acetone (420 ccm). Rods, m. pt. 114°C with decomposition. Yield 20 g. The acid is readily soluble in benzene, chloroform, acetone and 96% ethanol, and is insoluble in petroleum ether.

Analysis:

For $C_{11}H_{14}O_3S$ (226.28) — calcd.: 58.38% C. 6.24% N;
found: 58.17% C, 6.17% H.

IR (cm^{-1}): 680 νC—S; 755, 1060, 1090, 1210 νC_{Ar}—H (subst. 1, 2); 1510, 1620 $\nu C_{Ar}=C_{Ar}$; 800, 1140, 1180 $\nu C(CH_3)_2$; 1010 νS=O; 960 νOH(COOH); 1270, 1320, 1400 νOH and νC=O(COOH); 1760 νC=O(COOH).

6. Racemic o-tolylsulfinyldimethylacetic acid amide 8

2.26 g (0.01 mole) of o-tolylmercaptodimethylacetic acid was dissolved in 30 ccm of methanol. The solution was cooled in a mixture of solid

carbon dioxide and acetone and was treated with equimolar (0.01 mole) amount of diazomethane dissolved in ether. The mixture was allowed to stand at room temperature for 20 minutes and the solvents were distilled off (bath temperature at 40°C) under reduced pressure (12 mm Hg). The oily residue (2.2 g) was added to 30 ccm of methanol saturated with ammonia. The mixture was mechanically shaken for 48 hours at room temperature. Then it was filtered and was allowed to evaporate at room temperature. The solid residue (1.5 g) was crystallized from a mixture of chloroform (10 ccm) and petroleum ether (50 ccm). Plates, m. pt. 124°C. Yield 1 g.

The amide is readily soluble in chloroform, acetone and 96% ethanol and is insoluble in petroleum ether.

Analysis:

For $C_{11}H_{15}NO_2S$ (225.30) — calcd.: 6.22% N;
found: 6.26% N.

7. Hydrocinchonidine salt of laevorotatory o-tolylsulfinyldimethylacetic acid 9

40 g (0.177 mole) of powdered racemic acid 6 was mixed with 52.4 g (0.177 mole) of hydracinchonidine and the mixture was dissolved in a hot mixture of 450 ccm of acetone and 45 ccm of water. The solution was filtered and allowed to crystallize at room temperature. After 14 hours the first fraction of the salt was filtered. Fine needles m. pt. 133°C, $(\alpha)_D^{20} = -100°$ ($c=0.5$, $d=2$, $\alpha=-1.00°$) in 96% ethanol. Yield 50 g. After second crystallization of the first fraction from dilute (350 : 30 vol/vol) acetone the product melted at 134°C (needles) and had $(\alpha)_D^{20} = -117°$ ($c=0.5$, $d=2$, $\alpha=-1.17°$) in 96% ethanol. It remained unchanged by further crystallizations. Yield 30 g.

The hydrocinchonidine salt 9 is readily soluble in chloroform and 96% ethanol, sparingly soluble in acetone and insoluble in petroleum ether.

Analysis:

For $C_{30}H_{38}N_2O_4S$ (522.68) — calcd.: 5.36% N;
found: 5.29% N.

8. Cinchonidine salt of laevorotatory o-tolylsulfinyldimethylacetic acid 10

22.6 g (0.1 mole) of powdered racemic acid 6 was mixed with 29.4 g (0.1 mole) of cinchonidine and the mixture was dissolved in a hot mixture of 480 ccm acetone and 45 ccm of water. The solution was filtered with-

out cooling and was allowed to crystallize at room temperature. After 24 hours the first fraction of the crystals was filtered off. Needles, m. pt. 142°C, $(\alpha)_D^{20} = -138°$ ($c = 0.5$, $d = 2$, $\alpha = -1.38°$) in 96% ethanol. Yield 18 g. Second crystallization of the first fraction from dilute (200 : 20 vol/vol) acetone gave the salt which remained unchanged by further crystallizations. Regular needles m. pt. 145°C, $(\alpha)_D^{20} = -145°$ ($c = 0.5$, $d = 2$, $\alpha = -1.45°$) in 96% ethanol. Yield 6 g.

The cinchonidine salt 10 is readily soluble in chloroform and 96% ethanol, fairly soluble in acetone and insoluble in petroleum ether.

Analysis:

For $C_{30}H_{36}N_2O_4S$ (520.77) — calcd.: 5.38% N;
found: 5.26% N.

9. Laevorotatory o-tolylsulfinyldimethylacetic acid 11

10 g of powdered hydrocinchonidine salt 9 (m. pt. 134°C, $(\alpha)_D^{20} = -117°$) was added to 20 ccm of water and was acidified to Congo with 4% hydrochloric acid. The mixture was stirred for 2 hours at room temperature and was filtered. The precipitate was suspended in 15 ccm of water and was neutralized to phenolphthalein with 2% NaOH solution. The mixture was extracted with chloroform (5×20 ccm). The aqueous layer was freed from dissolved chloroform by distillation under reduced pressure (12 mm Hg, water bath at 40°C) and was acidified to Congo with 15% hydrochloric acid. A finely crystalline precipitate separated immediately. Yield 2 g, m. pt. 96°C, $(\alpha)_D^{20} = -129°$. It was filtered and after washing with water, it was crystallized from acetone (10 ccm). The pure product crystallized in prisms m. p t.98°C with decomposition. $(\alpha)_D^{20} = -130°$ ($c = 0.5$, $d = 2$, $\alpha = -1.30°$) in 96% ethanol. Yield 0.8 g.

The laevorotatory enantiomer 11 is readily soluble in chloroform, acetone and 96% ethanol and is insoluble in petroleum ether.

Analysis:

For $C_{11}H_{14}O_3S$ (226.28) — calcd.: 58.38% C, 6.24% H;
found: 58.23% C, 5.98% H.

IR (cm^{-1}): 680 νC—S; 750, 1050, 1080, 1210 δC_{Ar}—H (subst. 1, 2); 1465, 1490, 1590 $\nu C_{Ar}=C_{Ar}$; 800, 1130, 1170 $(C(CH_3)_2)$; 1000 νS=O; 940 δOH(COOH); 1290, 1300, 1400 δOH and νC=O(COOH); 1725 νC=O(COOH).

10. Hydrocinchonidine salt of dextrorotatory o-tolylsulfinyldimethylacetic acid 12

The aqueous acetonic mother liquors remaining after the separation of the first fraction of hydrocinchonidine salt of laevorotatory o-tolylsulfinyldimethylacetic acid were evaporated under reduced pressure (3 mm Hg, water bath at 40°C) to a small volume. A finely crystalline precipitate separated. It was filtered and was dried in a vacuum desiccator over calcium chloride to constant weight. The product (60 g) was dissolved in 400 ccm of boiling acetone. The hot solution was filtered and allowed to crystallize at room temperature. A fine crystalline precipitate soon separated. After 24 hours it was filtered. Rods m. pt. 125°C, $(\alpha)_D^{20}=0°$ ($c=0.5$, $d=2$, $\alpha=0.00°$) in 96% ethanol. Yield 18 g. The product remained unchanged after further crystallizations.

The hydrocinchonidine salt 12 is readily soluble in benzene, chloroform and 96% ethanol, fairly soluble in acetone and insoluble in petroleum ether.

Analysis:

For $C_{30}H_{38}N_2O_4S$ (522.68) — calcd.: 5.36% N;
found: 5.60% N.

11. Dextrorotatory o-tolylsulfinyldimethylacetic acid 13

7 g (0.13 mole) of powdered hydrocinchonidine salt 12 (m. pt. 125°C, $(\alpha)_D^{20}=0°$) was added to 20 ccm of water, the mixture was treated with 40 g of 4% hydrochloric acid (0.04 mole) and was stirred for 2 hours at room temperature. The resulting precipitate was filtered and suspended in 15 ccm of water. 50 ccm of 2% sodium hydroxide solution was added and the mixture was extracted with chloroform (5×20 ccm). The alkaline aqueous layer was freed from dissolved chloroform by distillation under reduced pressure (12 mm Hg, water bath at 40°C) and was acidified to Congo with 15% hydrochloric acid. A fine crystalline precipitate immediately separated. It was filtered and after washing with water, it was dried in a vaccum desiccator. Yield 2.5 g, m. pt. 96°C, $(\alpha)_D^{20}=+130°$. The crude acid was crystallized from acetone (12 ccm). Prisms m. pt. 98°C with decomposition, $(\alpha)_D^{20}=+131°$ ($c=0.5$, $d=2$, $\alpha=+1.31°$) in 96% ethanol. Yield 1 g.

The dextrorotatory enantiomer 13 is readily soluble in chloroform, acetone and 96% ethanol and is insoluble in petroleum ether.

Analysis:

For $C_{11}H_{14}O_3S$ (226.28) — calcd.: 58.38% C, 6.24% H;
found: 58.33% C, 6.07% H.

12. Laevorotatory o-tolylsulfinyldimethylacetic acid amide 14

4.5 g of the laevorotatory acid 11 (m. pt. 98°C, $(\alpha)_D^{20} = -130°$) was dissolved in 30 ccm of anhydrous methanol and was converted into its methyl ester as in section 6. The light yellow oil (4.2 g) obtained after the removal of solvent by distillation (12 mm Hg, water bath at 40°C) was dissolved in 30 ccm of methanol saturated with ammonia. The solution was allowed to stand at room temperature for 48 hours. A small amount of the resulting amorphous precipitate was removed by filtration and the filtrate was evaporated by allowing it to stand at room temperature in an open vessel. The residue (4 g) was crystallized from a mixture of chloroform (24 ccm) and petroleum ether (80 ccm). Plates m. pt. 107°C, $(\alpha)_D^{20} = -123°$ ($c = 0.25$, $d = 4$, $\alpha = -1.23°$) in 96% ethanol. The laevorotatory acid amide 14 is readily soluble in chloroform, acetone and 96% ethanol and is insoluble in petroleum ether.

Analysis:

For $C_{11}H_{15}NO_2S$ (225.30) — calcd.: 6.22% N;
found: 6.42% N.

13. Racemic phenylsulfinyldimethylacetic acid 15

Racemic phenylsulfinyldimethylacetic acid 15 was prepared according to Piechulek and Suszko [13]. It crystallized from acetone in prisms m. pt. 122°C (lit. [13] m. pt. = 121—122°C).

IR (cm^{-1}): 680 νC—S; 700, 750, 1065, 1080, 1120 δC—H (subst. 1, 2); 1460, 1580, 1610 $\nu C_{Ar}=C_{Ar}$; 790, 1120, 1180 ($C(CH_3)_2$); 1010 νS=O; 930 δOH(COOH); 1280, 1310, 1400 δOH and νC—O(COOH); 1710 νC=O(COOH).

14. Cinchonidine salt of laevorotatory phenylsulfinyldimethylacetic acid 16

25 g of racemic acid 15 was dissolved in 400 cm^3 of boiling acetone and was mixed with a separately prepared solution of 34.7 g of cinchonidine in 2.4 l of hot acetone. The solution of the salt was filtered without cooling and was allowed to stand at room temperature for crystallization. After 24 hours the first fraction of the salt was filtered off. Needles, m. pt. 159°C, $(\alpha)_D^{20} = -85°$ ($c = 0.5$, $d = 2$, $\alpha = -0.85°$) in 96% ethanol. After two crystallizations of the first fraction from 96% ethanol, the salt remained unchanged by further crystallizations. Needles, m. pt. 163°C, $(\alpha)_D^{20} = -136°$ ($c = 0.5$, $d = 2$, $\alpha = -1.36°$) in 96% ethanol (lit. [13] m. pt. = 162—163°, $(\alpha)_D^{20} = -136°$).

Table 2. Fractional crystalization of cinchonidine salt of laevorotatory phenylsulfinyldimethylacetic acid (crystallization time = 24 hours)

Fraction No.	Volume of solvent in ccm	Yield of salt in g.	Specific rotation in 96% ethanol $(\alpha)_D^{20}$ in °	Melting point of salt in °C
1.	2800 acetone	39	−85	158
1.1.	620 96% ethanol	14	−127	160
1.1.1.	480 96% ethanol	9.8	−136	163
1.1.1.1.	370 96% ethanol	7	−136	163

15. Laevorotatory phenylsulfinyldimethylacetic acid 17

Laevorotatory phenylsulfinyldimethylacetic acid was prepared according to Piechulek and Suszko [13]. After crystallization from chloroform (25 ccm) and petroleum ether (100 ccm) mixture, it melted at 123°C and had $(\alpha)_D^{20} = -93°$ in 96% ethanol (lit. [13] m. pt. = 122—123°C, $(\alpha)_D^{20} = -94°$).

IR (cm^{-1}): 690 νC—S; 695, 758, 1075, 1080, 1130 δC_{Ar}—H (subst. 1, 2); 1440, 1490, 1610 $\nu C_{Ar} = C_{Ar}$; 800, 1130, 1170 $(C(CH_3)_2)$; 1000 νS=O; 940 δOH(COOH); 1290, 1320, 1400 δOH and νC—O(COOH); 1760 νC=O(COOH).

16. Amide of laevorotatory phenylsulfinyldimethylacetic acid 18

2.26 g of laevorotatory acid 17 (m. pt. 123°C, $(\alpha)_D^{20} = -93°$) was converted into its amide by the method described in section 6. The crude product (1.2 g, m. pt. 117°C) was crystallized from a mixture of chloroform (12 ccm) and petroleum ether (40 ccm). Needles m. pt. 118°C, $(\alpha)_D^{20} = -87°$ ($c = 0.25$, $d = 4$, $\alpha = -0.869°$) in 96% ethanol. Yield 1.5 g.

The amide is readily soluble in benzene, chloroform, acetone and 96% ethanol and is insoluble in petroleum ether.

Analysis:

For $C_{10}H_{13}NO_2S$ (211.27) — calcd.: 6.63% N;
found: 6.82% N.

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STRESZCZENIE

Grupy alkilowe przejawiają prawdopodobnie dwa zasadnicze efekty, a mianowicie efekt hiperkoniugacyjny, wykazujący w układach nienasyconych cechy efektu mezomerycznego (+M), oraz efekt indukcyjny [2—5], który w połączeniach o charakterze nasyconym wydaje się mieć wartości ujemne, a w układach nienasyconych wartości dodatnie [6, 9]. Nie jest wykluczone, że efekty te mogą wywierać pewien wpływ na rotację cząsteczkową połączeń nienasyconych oraz związków aromatyczno-tłuszczowych z heteroatomowymi węzłami chiralności. Jednoznacznych i dostatecznie uzasadnionych rozwiązań tego problemu należy szukać na drodze eksperymentalnej.

Przedmiotem bieżącego doniesienia jest porównanie własności optycznych lewoskrętnych kwasów fenylosulfinylodwumetylooctowego [6, 7] 17 i o-tolilosulfoksydwumetylooctowego 11 oraz ich pochodnych amidowych 18 i 14.

Niezbędne do dalszych badań enancjomeryczne układy sulfinylowe 17 i 11 otrzymaliśmy metodą krystalizacji frakcyjnej związków diastereomerycznych utworzonych przez wiązanie racematów 15 i 8 z optycznie czynnymi zasadami alkaloidowymi. Szczegółowy tok syntez układów racemicznych podano w tekście angielskim tej pracy. Badania krzywych rotacyjnych (ORD), krzywych dichroizmu kołowego (CD) i widm elektronowych (UV) w nadfioletowej części widma oraz przesunięć Freudenberga wskazują, iż konfiguracje sulfinylokwasów skręcających w widzialnej części widma płaszczyznę światła spolaryzowanego w tym samym kierunku są zgodne.

Oznaczenia rotacji cząsteczkowych lewoskrętnych sulfinylokwasów 17 i 11 i ich pochodnych amidowych 18 i 14 w widzialnej części widma wykonano w pięciu rozpuszczalnikach dla $\lambda = 6234$, 5843, 5791, 5461, 4358 Å. Uzyskany materiał cyfrowy zestawiono w tab. 1. Wynika z niego, że na wielkość skręcalności molowych znaczny wpływ wywiera charakter rozpuszczalnika oraz, że w widzialnej części widma dyspersja rotacyjna badanych układów ma charakter dyspersji normalnej. Z dwu badanych optycznie czynnych sulfinylokwasów 17 i 11 znacznie wyższe wartości rotacji molowych w widzialnej części widma we wszystkich stosowanych do pomiarów roz-

puszczalnikach wykazuje kwas o-tolilosulfinylodwumetylooctowy. Ogólnie można zatem stwierdzić, że wprowadzenie do układu niepodstawionego kwasu fenylosulfinylodwumetylooctowego grupy metylowej w położenie orto zwiększa w sposób zasadniczy rotację molową cząsteczki. Nie jest wykluczone, że wzrost rotacji molowej ma miejsce na skutek działania efektu hiperkoniugacyjnego i indukcyjnego na elektrony π rdzenia benzenowego. Hipoteza ta wymaga sprawdzenia na obszerniejszym materiale doświadczalnym. Badania będą kontynuowane (M. J.).

РЕЗЮМЕ

Алкиловые группы, вероятно, проявляют два основных эффекта — гиперконъюгационный эффект, проявляющий в ненасыщенных системах признаки мезомерного эффекта (+M), и индуктивный эффект [2—5], который в соединениях насыщенного характера может иметь отрицательные величины, а в соединениях ненасыщенного характера — положительные величины [6, 9]. Не исключено, что эти эффекты могут оказывать некоторое влияние на молекулярную ротацию ненасыщенных соединений и ароматическо-жирных соединений с гетероатомными узлами хиральности. Однозначных и достаточно обоснованных решений этой проблемы следует искать экспериментальным путем.

Предметом настоящей публикации является сравнение оптических свойств левовращающих фенилсульфинилдиметилуксусной [6, 7] 17 и о-толилсульфоксидиметилуксусной 11 кислот и их амидопроизводных 18 и 14.

Необходимые для дальнейших исследований энантиомерические сульфиниловые системы 17 и 11 мы получили методом фракционной кристаллизации диастереомерических соединений, образованных путем связывания рацематов 15 и 8 с оптически активными алкалоидными щелочами. Подробное описание синтеза рацемических систем дается в тексте на английском языке. Исследование ротационных кривых (ORD), кривых циркулярного дихроизма (CD) и электроновых спектров (UV) в ультрафиолетовой части спектра и смещений Фрейденберга указывает на то, что конфигурации сульфинокислот, вращающих в видимой части спектра плоскость поляризованного света в этом же направлении, совпадают.

Определение левовращающих молекулярных ротаций сульфинокислот 17 и 11 и их амидопроизводных 18 и 14 в видимой части спектра производилось в пяти растворителях для $\lambda=6234$, 5843, 5791, 5461, 4358 Å. Полученный цифровой материал представлен в табл. 1. Из него следует, что на величину молярного вращения влияет характер растворителя, а ротационная дисперсия изучаемых систем в видимой части спектра имеет характер нормальной дисперсии. Из двух оптически активных сульфинокислот 17 и 11 значительно высшие величины молярных ротаций в видимой части спектра во всех применяемых в измерениях растворителях обнаруживает о-толилсульфинилдиметилускусная кислота. Следовательно, можно утверждать, что введение в незамещенную систему фенилсульфинилдиметилуксусной кислоты метиловой группы в положение орто сильно увеличивает молярную ротацию молекулы. Не исключено, что рост молярной ротации происходит вследствие действия гиперконъюгационного эффекта и индуктивного эффектов на электроны π бензолового остова. Эта гипотеза требует проверки на более широком экспериментальном материале. Исследования будут продолжаться (М. Я.).