ANNALES
UNIVERSITATIS MARIAE CURIE-SKŁODOWSKA
LUBLIN — POLONIA
VOL. XXXVIII, 2 SECTIO AA 1983

Instytut Chemii UMCS
Zakład Stereo- i Spektrochemii
Kierownik: prof. dr hab. Marian Janczewski

Marian JANCZEWSKI, Krystyna KURYS

Effect of Molecular Structure on Optical Properties of Sulfoxide Systems. Part LXII *. 5-nitro-1-naphtylsulfinylacetic Acids and Some of Their Derivatives

Wpływ budowy cząsteczkowej na własności optyczne układów sulfotlenkowych. Część LXII. Kwasy 5-nitro-1-naftylosulfinylooctowe i ich niektóre pochodne

Влияние молекулярного строения на оптические свойства сульфоокисных систем. Часть LXII. Кислоты 5-нитро-1-нафтилсульфинилуксусные и некоторые их производные

The problem of the effect of position isomerism in arene nuclei of certain substituents displaying negative mesomeric (-M) and inductive (-I) effects on optical properties of aromatic-aliphatic systems containing heteroatomic chirality centers is studied in our laboratory on the example of 1-and 2-naphthylsulfinylacetic acid nitro derivatives.

In our previous communications [1,2] we described the synthesis and the principal chiraloptical properties of enan-

---

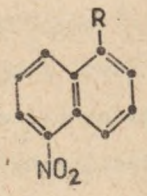
Part LXI: Janczewski M., Janowski W. Ann.Univ.Mariae Curie-Skłodowska, Lublin Sec AA, 18, 1 (1973).

The work was financed by the Polish Academy of Sciences, Grant No MR I.12.1.

tiomeric 1-naphthylsulfinylacetic acids and their 4-nitro derivatives. The results of these studies indicated that: (I) enantiomers rotating the plane of polarized light in the same direction have the same spatial configurations; (II) optically active acids have a normal optical rotatory dispersion in the visible part of the spectrum; (III) 4-nitro-1-naphthylsulfinylacetic acids and their derivatives have a lower molar rotation than that of the unsubstituted system.

We have suggested that the optical rotation of nitro acids was influenced by the mesomeric (-M) and the inductive (-I) effects of the nitro group on π electrons of the aromatic ring [2]. The observed optical and stereochemical relationships encouraged us to carry out further studies.

In the present communication we describe the synthesis and optical as well as stereochemical properties of enantiomeric 5-nitro-1-naphthylsulfinylacetic acids and of some of their derivatives.



1: R = NH_2

2: R = SCH_2COOH

3: R = SCH_2COOCH_3

4: R = $\overset{(\pm)}{S}OCH_2COOH$

5: R = $\overset{(\pm)}{S}OCH_2COOCH_3$

6: R = $\overset{(\pm)}{S}OCH_2CONH_2$

7: R = $\overset{(\pm)}{S}OCH_2COOCH_2C_6H_4NO_2$

8: R = $\overset{(\pm)}{S}OCH_2COOCH_2COC_6H_4Br$

9: R = $\overset{(+)}{S}OCH_2COOH \cdot$ Quind.

10: R = $\overset{(+)}{S}OCH_2COOH$

11: R = $\overset{(-)}{S}OCH_2COOH \cdot$ Hquind.

12: R = $\overset{(-)}{S}OCH_2COOH$

13: R = $\overset{(+)}{S}OCH_2COOCH_3$

14: R = $\overset{(+)}{S}OCH_2CONH_2$

15: R = $^{(+)}SOCH_2COOCH_2C_6H_4NO_2$ 17: R = SO_2CH_2COOH

16: R = $^{(+)}SOCH_2COOCH_2COC_6H_4Br$

Quind. = quinidine.

Hquind. = hydroquinidine.

The starting material in our studies was 5-nitro-1-naphthylthioglycolic acid (2) which we obtained in considerable yield by coupling 5-nitro-1-naphthyldiazonium chloride with thioglycolic acid in an acidic aqueous solution. The structure of acid 2 was confirmed by its elemental analysis and by its IR spectrum (the characteristic bands are quoted in the Experimental Part).

5-Nitro-1-naphthylsulfinylacetic acid (4) required for further studies was obtained by oxidation of compound 2 at room temperature in glacial acetic acid with 30% hydrogen peroxide. When an excess of peroxide was used and when the reaction was carried out at the boiling point of the solvent, sulfone 17 was formed in a satisfactory yield (the IR spectra confirming the structures of the oxidation products are given in the Experimental Part). The compound 4 was characterized as its amide (6) and methyl (5), p-nitrobenzyl (7) and p-bromophenacyl (8) esters.

The racemic acid 4 was resolved by crystallization of diastereomeric salts with optically active bases. For this purpose the neutral salts of quinidine and hydroquinidine were the most suitable. During the fractional crystallization of the quinidine salt the first fractions contained the salt of the dextrorotatory acid, whereas the laevorotatory enantiomer could be separated from the racemate by crystallization of the hydroquinidine salt.

Optically active 5-nitro-1-naphthylsulfinylacetic acids separated from alkaloid salts in the usual way showed relatively high specific rotation. After mixing the antimers in equimolecular relation and crystallization racemic acid 4 was obtained, its melting point was nearly equal ($\Delta t \sim 1^{\circ}C$) to that of the antimers 10 and 12. The IR spectrum of racemic acid 4 was different in the "finger print region" from the spectra of enantiomers 10 and 12 which were identical. A relatively difficult resolution of the optically inactiwe acid 4 as well as the physical differences mentioned above indicate that racemic acid 4 is a true racemate.

Optically active 5-nitro-1-naphthylsulfinylacetic acids (10 and 12) are resistant to racemization in alkaline media, but are readily racemized in organic solvents in the presence of hydrochloric acid. We have studied the racemization processes in the conditions previously described [2]. The racemization of acids 10 and 12 took place according to the kinetic equation for the first order reactions ($K = \frac{1}{t} \ln \frac{\alpha_o}{\alpha}$). The racemization constant (K), the activation enthalpies ($\Delta H^{\neq}$) and the activation entropies ($\Delta S^{\neq}$) calculated from the data obtained at six temperatures (averaged by the method of least squares) are shown in Tab. 1. The activation parameters were determined by the classical kinetic methods and by means of the Eyring equation [3].

The activation energy (E_a) and the pre-exponential factor ($A = K_{max}$) were determined from the empirical Arrhenius equation ($K = A. e^{-Ea/RT}$) : $E_a = 20{,}33$ kcal/mol, $A = 2{,}12 \times 10^{11} sec^{-1}$. It should be stressed that racemization constants of ana nitro-acids are considerably lower than that of isomeric para nitro

Tab. 1

Thermodynamic characteristic of racemization of optically active 5-nitro-1-naphthylsulfinylacetic acids

Racemization temperature °C	Racemization constant K x $10^5 sec^{-1}$	Activation entropy $\Delta S^{\neq}$, e.u.	Activation enthalpy $\Delta H^{\neq}$, kcal/mole
10	4,3 ± 0,2	- 8,6 ± 0,2	19,8 ± 0,2
14	7,0 ± 0,2	- 8,6 ± 0,2	19,8 ± 0,1
18	11,4 ± 0,2	- 8,7 ± 0,1	19,8 ± 0,1
22	18,0 ± 0,2	- 8,7 ± 0,1	19,7 ± 0,1
26	29,6 ± 0,3	- 8,7 ± 0,1	19,7 ± 0,1
30	46,2 ± 0,5	- 8,8 ± 0,1	19,7 ± 0,1

compound [2]. On the other hand the racemization entropy values of ana nitroacid show significant increase (in comparisson to that of para nitro compounds) conserving however their negative values. The negative values of the activation entropy suggest that in the transition state of the racemization process additive compounds or intermediate compounds are formed [2].

In order to obtain sufficient material for chiroptical studies we have prepared the following derivatives of dextrorotatory acid 10: amide (14), methyl ester (13), p-nitrobenzyl ester (15) and p-bromophenacyl ester (16). The syntheses of these compounds were first carried out on optically inactive material. The mild conditions under which the reactions were performed probably did not cause racemization on asymmetric sulfur atom. The results of determination of molar rotations of dextrorotatory acid 10 and its derivatives 15 and 16 in various solvents and in various wavelengths are shown in Tab. 2.

The data collected in Tab. 2 show that the molar rotations are solvent dependent. In the visible part of the spectrum the values of molar rotations in the examined solvents decrease in the following order: a) free acid (10): An > A > D > M > E; b) p-nitrobenzyl ester (15) : D > Ch > A > An > M; c) p-bromophenacyl ester (16): D > An > A > Ch. These sequences show that the solvent effect is diverse. The decreases in molar rotation observed in the above sequences are moderate.

An analysis of the numerical data shown in Table 2 shows that in the region $410 < \lambda < 600$ nm functions $\frac{1}{\alpha}\ (\lambda^2)$ for dextrorotatory acid (10) and its derivatives 15 and 16 are almost linear. It should be noted that in this spectral region molar rotations of acid 10 are much lower than those of its esters 15 and 16 in all the solvents used in the measurements.

The above rotational relationships make it possible to determine the spatial configurations of optically active 5-nitro-1-naphthylsulfinylacetic acids on the basis of Freundenberger's shift rule and on the basis of comparison of direction change of molar rotation under the influence of solvents in the reference systems and in the compounds examined. In the first case the configurational standards were 1-naphthylsulfinylacetic acid [1] and its 4-nitro derivative [2] which have the spatial structures R(+) and also their p-nitrobenzyl and p-bromophenacyl esters. In the second case the standards were the systems mentioned above as well as 4-bromo-1-naphthylsulfinylacetic acid [4] which also have the configuration R(+).

Tab.2

Optical rotatory dispersion of dextrorotatory 5-nitro-1-naphthylsulfinylacetic acid and some of its derivatives

Compound	Solvent[x]	Molar rotation/M/^{20}										
		=600nm	=589,3nm	=579,1nm	=560nm	=546,1nm	=520nm	= 480nm	= 440nm	=435,8nm	= 420nm	= 410nm
Dextrorotatory 5-nitro-1-naphthylsulfinylacetic acid	M	970,4 /972,0/	1018,4 /1018,7/	1068,3 /1066,9/	1166,2 /1168,2/	1250,1 / 1252,8/	1448,6 /1443,6/	1859,7 /1854,4/	2514,1 /2520,3/	2612,0 / 2614,2/	3028,7 /3026,8/	3350,3 / 3348,9/
	E	964,8 /964,0/	1006,8 /1010,1/	1051,5 /1057,6/	1160,6 /1157,8/	1244,5 / 1241,6/	1434,7 /1430,8/	1845,8 /1840,7/	2500,2 /2511,6/	2600,8 /2606,7/	3042,7 /3026,5/	3350,3 / 3355,7/
	A	998,4 /1011,3/	1059,9 /1058,9/	1107,4 /1108,0/	1213,7 /1211,9/	1300,4 / 1298,9/	1504,6 /1496,8/	1943,6 / 1930,9/	2654,0 /2658,2/	2749,1 /2762,8/	3224,5 /3228,6/	3607,6 / 3597,9/
	An	1029,1	1071,1	1127,0	1233,3	1328,4	1532,5	1974,4	2690,5	2788,2	3269,2	3641,2
	D	992,8 /1003,6/	1048,7 /1050,3/	1096,3 /1098,3/	1202,5 /1201,3/	1289,2 /1287,8/	1499,0 /1485,9/	1940,8 / 1929,0/	2684,7 /2693,2/	2791,1 /2805,0/	3308,4 / 3307,8/	3719,5 / 3711,5/
p-Nitrobenzyl ester of dextrorotatory 5-nitro-1-naphthylsulfinylacetic acid	M	1160,3	1230,7	1284,6	1413,0	1508,4	1756,9	2258,4	3087,2	3211,5	3746,0	4172,8
	A	1222,4	1301,2	1363,3	1495,9	1607,8	1856,4	2399,3	3286,1	3397,9	3990,5	4446,3
	An	1214,1	1272,2	1338,5	1471,1	1582,9	1827,4	2349,6	3203,2	3323,4	3862,1	-
	D	1346,7	1408,9	1475,2	1616,1	1740,4	2013,9	2614,8	3634,1	3770,9	4458,3	5043,0
	Ch	1334,3	1400,6	1462,8	1607,8	1719,7	2001,5	2581,6	3559,6	3688,0	4330,3	4877,3
p-Bromophenacyl ester of dextrorotatory 5-nitro-1-naphthylsulfinylacetic acid	A	957,4	1005,0	1052,6	1157,4	1243,1	1428,9	1829,0	2474,0	2562,5	2962,6	3272,2
	An	1033,6	1081,2	1138,4	1247,9	1343,2	1548,8	1986,2	2691,1	2791,1	3191,2	-
	D	1033,6	1095,5	1138,4	1252,7	1352,7	1676,6	2014,8	2767,3	2876,9	3386,5	3777,1
	Ch	943,1	1000,2	1043,1	1143,1	1228,9	1424,1	1819,5	2443,4	2538,7	2948,3	3172,2

c = 0,1 g/100ccm

x Solvents: A-acetone, An-acetonitrile, Ch-chloroform, D-dioxane, M-methanol, E-ethanol

Tab. 3

Molar rotations (M) $^{20}_{579,1}$ of dextrorotatory 1-naphthylsulfinylacetic, 4-and 5-nitro-1-naphthylsulfinylacetic acids and of some their derivatives

Compound	Dioxane			Acetonitril			Chloroform		
	p-Nitro-benzyl ester	p-Bro-mophe-nacyl ester	Acid	p-Nitro-benzyl ester	p-Bro-mophe-nacyl ester	Acid	p-Nitro-benzyl ester	p-Bromo-phenacyl ester	Acid
1-Naphthyl-sulfinyl-acetic acid	1393,4	1346,7	1164,3	-	-	-	1388,0	1333,2	1197,1
5-Nitro-1-naphthyl-sulfinyl-acetic acid	1475,2	1138,4	1096,3	1338,5	1138,4	1127,0	1462,8	1043,1	-
4-Nitro-1-naphthyl-sulfinyl-acetic acid	1292,9	1105,0	1005,4	1255,6	1214,6	1052,6	1297,0	1066,9	999,8

A comparison of the optical shifts collected in Tab. 3 shows that dextrorotatory 1-naphthylsulfinylacetic acid and its 4-and 5-nitro derivatives have the same spatial structure, which means that the dextrorotatory 5-nitro-1-naphthylsulfinylacetic acid has the configuration R(+). The correctness of the spatial structures assigned to acids 10 and 12 is confirmed by the shifts of molar rotations

Tab. 4

Effect of solvent on optical rotation of dextrorotatory 1-naphthylsulfinylacetic, 4-bromo-1-naphthylsulfinylacetic, 4-nitro-and 5-nitro-1-naphthylsulfinylacetic acids

Solvent	1-Naphthylsulfinylacetic acid	4-Bromo-1-naphthylsulfinylacetic acid	4-Nitro-1-naphthylsulfinylacetic acid	5-Nitro-1-naphthylsulfinylacetic acid
Acetone	1092,6	1138,2	1016,5	1059,9
Methanol	1071,8	1112,5	988,6	1018,0
Ethanol	1056,1	1086,5	949,5	1006,0

caused by the solvent effect which are collected in Tab. 2.

On the basis of the data collected in Tab. 2 ($410 \leqslant \lambda \leqslant 600$ nm) we have determined functions $(M)(\lambda)$ for dextrorotatory acid 10 in four solvents. The functions have the character of three-term equations * which we give below:

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

a) In methanol

$$(M)^{20} = \frac{5,2991895 \times 10^9}{\lambda^2 - (229,00)^2} - \frac{6,3026504 \times 10^9}{\lambda^2 - (206,00)^2} + \frac{1,2920672 \times 10^9}{\lambda^2}$$

b) In ethanol

$$(M)^{20} = \frac{5,8842718 \times 10^9}{\lambda^2 - (229,00)^2} - \frac{7,0940030 \times 10^9}{\lambda^2 - (206,00)^2} + \frac{1,5014335 \times 10^9}{\lambda^2}$$

c) In acetone

$$(M)^{20} = \frac{7,8299668 \times 10^9}{\lambda^2 - (229,00)^2} - \frac{9,6753440 \times 10^9}{\lambda^2 - (206,00)^2} + \frac{2,1672992 \times 10^9}{\lambda^2}$$

d) In dioxane

$$(M)^{20} = \frac{9,9526519 \times 10^9}{\lambda^2 - (229,00)^2} - \frac{1,2510978 \times 10^9}{\lambda^2 - (206,00)^2} + \frac{2,8944908 \times 10^9}{\lambda^2}$$

The molar rotation values calculated by means of the above equations are given in Table 2 in brackets. The agreement between those values and the experimental data is fairly good.

The circular dichroism curve determined in acetonitrile for the dextrorotatory 5-nitro-1-naphthylsulfinylacetic acid (10) has two positive maxima at λ = 229 nm ([Q] = + 89091) and at λ = 308 nm ([Q] = + 7182) as well as one negative

maximum at λ = 206 nm ([Q] = - 120000). These extrema suggest that dextrorotatory 5-nitro-1-naphthylsulfinylacetic acid has two strong Cotton effects; one positive at 229 nm and one negative at 206 nm. These effects are localized in the regions corresponding to the dispersion constants of the three-term equations describing functions (M)(λ). It should be stressed that the signs of the rotational constants in these equations are in agreement with those of the Cotton effects.

The UV spectrum of acid 10 determined in acetonitrile has two gruops of bands. The first group in the 200-230 nm region has two strong maxima at λ = 222 nm (ε = 19525), and λ = 228 nm (ε = 20469) probably transition ($\pi - \pi^* {}^1B_b$) and one weak at λ = 204 nm (ε = 4316). The second group of bands at 240-280 nm has four weak maxima at λ = 252 nm (ε = 10237), λ = 256 nm (ε = 9952), λ = 263 nm (ε = 8408) and at 279 nm (ε = 3818). At the long wave end of the spectrum there is still one broad, weak band at λ = 330 nm (ε = 4506). The wavelengths λ = 204 and 228 nm (the optically active bands) in the UV spectrum of acid 10 are in a fairly good agreement with the values of dispersion constants of the three-term equations (M) (λ).

The clearest results concerning the problem of the optical effects caused by introduction of nitro group to the ana position of the aromatic ring of α-naphthylsulfinylacetic acid in the region of λ values, for which the optical rotatory dispersion is normal, we have obtained for free acid 10 and its p-bromophenacyl ester 16. In all the solvents used in the measurements these compounds had molar rotations much

lower than those of the corresponding unsubstituted compounds (for free acid 10 av. % ΔR_{mol} - - 5% for p-bromophenacyl ester 16 av. % ΔR_{mol} - - 18%).

Thus the introduction of nitro group to the ana position of 1-naphthylsulfinylacetic acid molecule causes a considerable decrease in rotation of the system. The recorder observations do not allow us in this stage of studies to draw conlusions of a general character. It may only be assummed that mesomeric (- M) and inductive (-I) effects induced by nitro group bonded with naphthalene ring exert a considerable effect on optical rotation of the compounds studied. This observation is in accord with the rotational regularities noted [2] previously in our laboratory. Unambiguous interpretation of the observed phenomena requires further systematic stereochemical studies.

EXPERIMENTAL

The melting points are uncorrected. The polarimetric measurements were carried out in Perkin-Elmer 241-MC spectropolarimeter in the solvents quoted in the text. IR and UV spectra were measured by means of SP-200 (IR) and SP-700 (UV) spectrophotometers. The CD measurements were carried out by means of Roussel Jouan III dichrograph. The spectra were obtained for suspension of the examined compounds in Nujol (IR) and for the solutions quoted in the text (UV, CD).

1. 5-Nitro-1-naphthylamine (1).

A sample of 100 g N-acetylnaphthionic acid sodium salt was converted into 5-nitro-N-acetylnaphthionic acid according to [5]. The nitro acid was suspended in 300 ccm 48% H_2SO_4 and hated to 80°C for 1,5 h. The solution was cooled, poured on crushed ice

and neutralized to pH = 8 with 20% ammonia. A fine, crystalline precipitate separated. It was filtered off, dried and crystalized from 50% ethanol (1 g subst. from 20 ccm of the solvent). Red plates (25 g), mp.115-116°C (Lit.[7]; mp. 119°C). The product was readily soluble in 96% ethanol, acetone, dioxane and benzene, sparingly soluble in carbon tetrachloride.

2. 5-Nitro-1-naphthythioglycolic acid (2).

5-Nitro-1-naphthylamine (18 g) was dissolved in 22 ccm of 36% HCl and 60 ccm of H_2O. The solution was cooled to - 5°C and diazotized with 8 g $NaNO_2$ dissolved in 15 ccm of H_2O. The solution of diazonium salt was added with small portions to 10 g of thioglycolic acid dissolved in 20 ccm of cooled H_2O. The reacting mass was stirred 2 h at room temperature. Then the mixture was poured in 200 ccm of H_2O. A fine crystalline precipitate which soon separated was filtered off and dissolved in 200 ccm of 5% $NaHCO_3$. The filtered solution was acidified to Congo with dilute (1:1 V/V) HCl and the resulting precipitate was filtered off. The nitro acid was suspended in 2 dcm^3 of hot (90°C) H_2O and neutralized with solid $BaCO_3$. The solution was filtered while hot and acidified (Kongo) with dilute (1:1 V/V) HCl. A crystalline precipitate which soon separated was filtered off, and after air drying crystallized from 50% ethanol (1 g subst. from 50 ccm of the solvent). Yellow plates (1 g), m.p. 157-158°C. The product is readily soluble in 96% ethanol, acetone and dioxane, fairly soluble in chloroform and ether and is sparingly soluble in carbon tetrachloride and benzene.

Analysis:

For $C_{12}H_9NO_4S$ (263,3) - calcd: 54,7% C, 3,4% H;
found: 54,8% C, 3,3% H.

IR (cm^{-1}): 650 ν C-S; 715, 745, 970, 1030, 1060, 1150 δ C_{Ar}-H subst.(1, 2, 3); 1460, 1590, 1618 ν $C_{Ar} = C_{Ar}$; 870 ν C-N; 1320 ν sNO_2; 1520 ν $asNO_2$; 900 δ OH (COOH); 1215, 1300, 1410 δ OH i ν C-O (COOH); 1695 ν C = O (COOH).

3. Methyl ester of 5-nitro-1-naphthylthioglycolic acid (3).

To a suspension of 7 g of powdered acid 2 in ether (50 ccm) was introduced dropwise with stirring a solution of diazomethane in ether (150 ccm) prepared from 11 g og N,N-nitrozomethylurea [8]. Then the mixture was refluxed 2 h ($CaCl_2$ tube) on a water bath. The cooled ether solution was washed first with 5% $NaCO_3$ (3 x 10 ccm) and then with water, and was dried with anhydrous $MgSO_4$. The solvent was evaporated under reduced pressure (12 mm Hg, water bath). The residue was crystallized from 96% ethanol (1 g subst. from 15 ccm of the solvent). Yellow needles (5,5 g), m.p. 69,5-70,5°C. The ester is readily soluble in acetone, chloroform, benzene and ether, fairly soluble in methanol.

Analysis:

For $C_{13}H_{11}NO_4S$ (277,3) - Calcd: 56,3% C, 4,0% H;
found: 56,3% C, 3,8% H.

4. Rac. 5-nitro-1-naphthylsulfinylacetic acid (4).

Powdered acid 2 (5 g) was suspended in 120 ccm of glacial acetic acid. The mixture was cooled to 12°C, 1 ccm of concentrated (d = 1,84) sulfuric acid was added, then 2 ccm of 30%

H_2O_2 and the mixture was shaken mechanically for 6 h at room temperature. During the reaction acid 2 was passing to the solution. Then the reaction mixture was left standing at room temperature for 10 h in order to complete the oxidation. The solvent was removed in a vacuum desiccator filled with solid KOH. The residue was washed with water (15 ccm), filtered and dried in the air. The crude product was crystallized from 50% methanol (1 g subst. from 70 ccm of the solvent). Light yellow plates (3 g) m.p. 184°C (decomp.). The sulfoxide is readily soluble in 96% ethanol and dioxane, fairly soluble in acetone and is sparingly soluble in chloroform, benzene and ether.

Analysis:

For $C_{12}H_9NO_5S$ (279,3) - Calcd: 51,6% C, 3,3% H;
found: 51,8% C, 3,3% H.

IR (cm^{-1}): 710, 790, 1040, 1145 δ C_{Ar}-H (subst. 1, 2, 3); 1465, 1590, 1620 ν C_{Ar}= C_{Ar}; 870 ν C-N; 1335 ν sNO_2; 1525 ν $asNO_2$; 1015 ν S-O; 915 δ OH(COOH); 1220, 1280, 1410 δ OH i C-O(COOH); 1715 ν C=O(COOH).

5. Methyl ester of rac. 5-nitro-1-naphthylsulfinyl-acetic acid (5).

Acid 4 (6 g) was converted into its methyl ester, as in section 3. The crude product was crystallized from methanol (1 g subst. from 20 ccm of the solvent). Pale yellow needles (4,5 g) m.p. 117-118°C. The racemic ester is readily soluble in acetone and chloroform, fairly soluble in 96% ethanol and benzene and is sparingly soluble in ether.

Analysis:

For $C_{13}H_{11}NO_5S$ (293,3) - Calcd: 53,2% C, 3,8% H;
found: 53,3%C, 3,7% H

6. Amide of rac. 5-nitro-1-naphthylsulfinylacetic acid (6).

A sample of 2,5 g of methyl ester 5 was suspended in 80 ccm of 14% ammonia and the suspension was mechanically shaken at room temperature for 2 h. The product was filtered off and after washing with water and drying in the air it was crystallized from methanol (1 g subst. from 200 ccm of the solvent). Pale yellow needles (1,5 g) m.p. 233-235°C. The product is readily soluble in dioxane, fairly soluble in 96% ethanol and acetone and is sparingly soluble in chloroform, ethyl acetate and benzene.

Analysis:

For $C_{12}H_{10}N_2O_4S$ (278,3) - Calcd: 10,1% N;
found: 10,2% N.

7. p-Nitrobenzyl ester of rac. 5-nitro-1-naphthylsulfinylacetic acid (7).

Racemic acid 4 (1,4 g) and p-nitrobenzyl bromide (1,08 g) were used in esterification which was carried out for 1 h in 43 ccm of 78% ethanol. The crude product was washed with 5% $NaHCO_3$, then with water, dried in the air and crystallized from methanol (1 g subst. from 110 ccm of the solvent). Yellow rods (0,8 g) m.p. 129-130°C. The racemic ester is readily soluble in acetone, chloroform and benzene, fairly soluble in ethyl acetate and sparingly soluble in 96% ethanol and ether.

Analysis:

For $C_{19}H_{14}N_2O_7S$ (414,4) - Calcd: 6,8% N;
found: 6,6 % N.

8. p-Bromophenacyl ester of rac. 5-nitro-1-naphthylsulfinylacetic acid (8).

Rac. acid 4 (1,4 g) and the bromphenacyl bromide (1,4 g) were used in esterification. The reaction was carried out for 1 h in 82% ethanol (58 ccm). The product was crystallized from methanol (1 g subst. from 200 ccm of the solvent). Light yellow needles (1 g), m.p. 159-160°C. The ester is readily soluble in acetone, chloroform and benzene, fairly soluble in ethyl acetate and sparingly soluble in carbon tetrachloride and ether.

Analysis:

For $C_{20}H_{14}BrNO_6S$ (476,3) - Calcd: 50,4% C, 3,0% H;
found: 50,3% C, 3,0% H.

9. Quinidine salt of dextrorotatory 5-nitro-1-naphthylsulfinylacetic acid (9).

A sample of 2,8 g (0,01 mole) of powdered acid 4 was mixed with 3,2 g (0,01 mole) of powdered quinidine and the mixture was dissolved in 100 ccm of boiling ethyl acetate. The hot solution was filtered and was left standing at room temperature for crystallization. After 24 h the first crop of crystals was filtered off. Yellow needles, m.p. 181°C $(\alpha)_D^{20} = + 292,0^\circ$ ($c = 0,5$, $d = 2$, $\alpha = + 2,92^\circ$) in chloroform. After two crystallizations of the first fraction from ethyl acetate the product had physical properties which remained unchanged by further crystallization. Yellow needles (0,9) m.p. 186-187°C (decomp.), $(\alpha)_D^{20} = + 315,0^\circ$ ($c = 0,5$, $d = 2$, $\alpha = + 3,15^\circ$) in chloroform. The quinidine salt of dextrorotatory antipode is readily soluble in 96% ethanol and

chloroform, fairly soluble in acetone and dioxane and sparingly soluble in carbon tetrachloride, benzene and ether.

Analysis:

For $C_{32}H_{33}N_3O_7S$ (603,7) - Calcd: 7,0% N;
found: 6,7% N.

Tab. 5

The course of fractional crystallization of quinidine salt of dextrorotatory 5-nitro-1-naphthylsulfinylacetic acid. Crystallization time 24 h

Fraction No	Volume of solvent ccm	Weight of the salt (g)	Specific rotation in chloroform $(\alpha)_D^{20}$	M.p. of the salt °C
1.	100	2,0	+ 292,0°	181
1.1.	600 (200*)	1,4	+ 314,0°	186-187
1.1.1.	450 (150*)	0,9	+ 315,0°	186-187

* evaporated to

10. Dextrorotatory 5-nitro-1-naphthylsulfinylacetic acid (10).

Powdered salt 9 (0,9 g) was added to 50 ccm of water. The mixture was stirred for several minutes and was carefully acidified to pH = 1 with 5% hydrochloric acid. Then of was stirred at room temperature for 30 min. The resulting 5-nitro-1-naphthylsulfinylacetic acid was filtered off suspended in 15 ccm of water and alkalized with 5% NaOH to pH = 8. The solution was filtered and the filtrate was extracted with chloroform (3 x 50 ccm). The alkaline liquid was freed from

dissolved chloroform by distillation under reduced pressure (12 mm Hg, water bath at 45°C) and after cooling to 10°C it was acidified to Kongo with 5% hydrochloric acid. The product was separated immediately. It was filtered off (0,4 g) and was crystallized from 50% methanol (0,1 g subst. from 5,5 ccm of the solvent). Light yellow plates (0,2 g) m.p. 183-184°C (decomp.) $(\alpha)_D^{20}$ = + 371,0° (c = 0,3, d = 2, α = + 2,3°) in methanol. The acid is readily soluble in methanol and dioxane, fairly soluble in acetone and ethyl acetate and sparingly soluble in chloroform, benzene and ether.

Analysis:

For $C_{12}H_9NO_5S$ (279,3) - Calcd: 51,6% C, 3,3% H;
found: 51,6% C, 3,0% H.

IR (cm^{-1}): 710, 800, 1030, 1090, 1155 δ C_{Ar}- H (subst. 1, 2, 3); 1465, 1538, 1590 ν $C_{Ar} = C_{Ar}$; 870 ν C-N; 1340 νsNO_2; 1520 $\nu asNO_2$; 1000 ν S-O; 890 δ OH(COOH); 1220, 1280, 1410 δ OH i C-O(COOH); 172^ ν C=O(COOH).

11. Hydroquinidine salt of laevorotatory 5-nitro-1-naphthylsulfinylacetic acid (11).

The mother liquors from the first fraction of quinidine salt of dextrorotatory 5-nitro-1-naphthylsulfinylacetic acid were evaporated under diminished pressure (12 mm Hg, water bath at 60°C) to dryness. The resulted quinidine salt (3,4 g) was converted into free acid as in section 10. Crude acid (1 g) was crystallized from 50% methanol. Light yellow needles m.p. 182-183°C $(\alpha)_D^{20}$ = - 76,0° (c = 0,1, d = 0,5, α = - 0,038°) in methanol. A sample of this acid (2,79 g, $(\alpha)_D^{20}$ = - 76,0) was mixed with 3,26 g of hydroquinidine and was dissolved in

140 ccm of boiling ethyl acetate. After 24 h the first fraction was of the salt was filtered off. Light yellow needles, m.p. 165-166°C (decomp.), $(\alpha)_D^{20}$ = + 72,0° (c = 0,1, d = 0,5, α = + 0,036°) in chloroform. After four crystallizations the physical properties of the salt remained unchanged by further purification. Light yellow needles (0,8 g), m.p. 175-176°C (decomp.), $(\alpha)_D^{20}$ = - 79,0° (c = 0,1, d = 0,5, α = - 0,0395° in chloroform. The salt is readily soluble in 96% ethanol and chloroform, fairly soluble in acetone and ethyl acetate and sparingly soluble in benzene and ether.

Analysis:

For $C_{32}H_{35}N_3O_7S$ (605,7) - Calcd: 6,9% N;
found: 7,1% N.

Tab. 6

The course of fractional crystallization of hydroquinidine salt of laevorotatory 5-nitro-1-naphthylsulfinylacetic acid. Crystallization time 24 h

Fraction No	Volume of the solvent ccm	Volume of the solvent evaporated ccm	Weight of the salt g	Specific rotation in chloroform $(\alpha)_D^{20}$	M.p. of the salt °C decomp.
1.	140	-	4,8	+ 72,0°	165-166
1.1.	590	460	1,9	- 46,0°	174-175
1.1.1.	260	215	1,5	- 74,0°	175-176
1.1.1.1.	200	170	1,0	- 79,0°	175-176
1.1.1.1.1.	200	170	0,8	- 79,0°	175-176

12. Laevorotatory 5-nitro-1-naphthylsulfinylacetic acid (12).

Powdered hydroquinidine salt 11 (0,8 g) was suspended in 100 ccm of water and converted into free acid as in section 10. Crude acid (0,3 g) was crystallized from 50% methanol (0,1 g subst. from 5,5 ccm of the solvent). Light yellow plates (0,2 g), m.p. 182-183°C (decomp.) $(\alpha)_D^{20} = -370,0°$ (c = 0,1, d = 0,5, $\alpha = -0,185°$) in methanol. The compound is readily soluble in 96% ethanol and dioxane, fairly soluble in acetone and ethyl acetate and sparingly soluble in benzene and ether.

Analysis:

For $C_{12}H_9NO_5S$ (279,3) - Calcd: 51,6% C, 3,3% H;
found: 51,5% C, 3,5% H.

13. Methyl ester of dextrorotatory 5-nitro-1-naphthylsulfinylacetic acid (13).

A sample (4,5 g) of dextrorotatory acid 10 was suspended in 40 ccm of ether and converted into methyl ester as in section 3, using 7 g N,N-nitrozomethylurea [6] in 120 ccm of ether. The crude product was crystallized from 50% ethanol (1 g subst. from 40 ccm of the solvent). Light yellow needles (3 g), m.p. 83-84°C, $(\alpha)_D^{20} = +373,0°$ (c = 0,3, d = 2, $\alpha = +2,24°$) in acetone. This ester is readily soluble in methanol, acetone and chloroform, fairly soluble in benzene and ethyl acetate, and sparingly soluble in carbon tetrachloride and ether.

Analysis:

For $C_{13}H_{11}NO_5S$ (293,3) - Calcd: 53,2% C, 3,8% H;
found: 53,1% C, 3,8% H.

14. Amide of dextrorotatory 5-nitro-1-naphthylsulfinylacetic acid (14).

Ester 13 (2 g) was converted into the corresponding amide as in section 6. The product was crystallized from methanol (1 g subst. from 540 ccm of the solvent). Light yellow needles (1,5 g), m.p. 245-246°C, $(\alpha)_D^{20}$ = + 360,0° (c = 0,005, d = 2, α = + 0,36°) in dioxane. The amide is fairly soluble in 96% ethanol and dioxane and sparingly soluble in acetone, benzene and ether.

Analysis:

For $C_{12}H_{10}N_2O_4S$ (278,3) - Calcd: 10,1% N;
found: 10,0% N.

15. p-Nitrobenzyl ester of dextrorotatory 5-nitro-1-naphthylsulfinylacetic acid (15).

Acid 10 (1,4 g) was converted in its p-nitrobenzyl ester as in section 7. The crude product was crystallized from methanol (1 g subst. from 150 ccm of the solvent). Light yellow needles (0,75 g), m.p. 141-142°C, $(\alpha)_D^{20}$ = + 316,0° (c = 0,3, d = 2, α = + 1,90°) in acetone. The ester is readily soluble in acetone, chloroform and dioxane, is fairly soluble in benzene and sparingly soluble in carbon tetrachloride and ether.

Analysis:

For $C_{19}H_{14}N_2O_7S$ (414,4) - Calcd: 6,8% N;
found: 6,9% N.

16. p-Bromophenacyl ester of dextrorotatory 5-nitro-1-naphthylsulfinylacetic acid (16).

Acid 10 (1,4 g) was converted into its p-bromophenacyl ester as in section 8. The crude product was crystallized from 96% ethanol (1 g subst. from 200 ccm of the solvent). Yellow needles (0,5 g), m.p. 168-169°C, $(\alpha)_D^{20} = +213,0°$ ($c = 0,3$, $d = 2$, $\alpha = +1,28°$) in acetone. The ester is readily soluble in chloroform, dioxane and benzene, fairly soluble in methanol and sparingly in carbon tetrachloride and ether.

Analysis:

For $C_{20}H_{14}BrNO_6S$ (476,0) - Calcd: 50,4% C, 3,0% H;
found: 50,6% C, 2,9% H.

17. 5-Nitro-1-naphthylsulfonylacetic acid (17).

A suspension of 4 g of acid 2 in 50 ccm of glacial acetic acid was treated with 4 ccm of 30% H_2O_2 and was refluxed for 1 h. Then 4 ccm of 30% H_2O_2 was added and the mixture was refluxed 1 h. The reaction mixture was evaporated under reduced pressure (12 mm Hg, water bath) to a small volume. The product (a fine crystalline precipitate) was filtered off and was crystallized from 70% methanol (1 g subst. from 20 ccm of the solvent). Light yellow plates (1,5 g), m.p. 200 - 201°C. The sulfone is readily soluble in acetone, ethyl acetate and dioxane, fairly soluble in methanol and sparingly soluble in benzene and ether.

Analysis:

For $C_{12}H_9NO_6S$ (295,3) - Calcd: 48,8% C, 3,1% H;
found: 48,9% C, 3,0% H.

IR (cm^{-1}): 715, 790, 985, 1030, 1065, 1160 $\delta C_{Ar} - H$ (subst. 1,2,3); 1460, 1510, 1595, 1620 νC_{Ar}; 870 ν C-N; 1335 νsNO_2; 1532 $\nu asNO_2$; 1120 νsSO_2; 1310 $\nu asSO_2$; 895 δ OH(COOH); 1220, 1250, 1410 δ OH i CO(COOH); 1720, 1748 ν C=O (COOH).

18. Racemization of dextrorotatory 5-nitro-1-naphthylsulfinylacetic acid.

Racemization of acid 10 was carried out according to [2]. The racemization process was investigated at 10, 14, 18, 22, 26 and 30°C. The compound recovered from control solutions in the mixture of hydrochloric acid and dioxane after the complete disappearance of optical activity (i.e. after a complete racemization of acid 10) was invariably identified as racemic acid 4. The calculations of the racemization parameters and of the experimental errors were carried out by means of digital calculating machine ODRA-1013.

REFERENCES

1. Janczewski M.: Roczniki Chem., 35, 585 (1961).
2. Janczewski M.; Kurys J., Polish J. Chem., 54, 2161 (1980).
3. Glastone S.: Laidler I., Eyring H., The Theory of Rate Processes, Mc Graw-Hill Book Co., New York 1941.
4. Janczewski M.: Roczniki Chem., 35, 601 (1961).
5. Bucherer H., Uhlmann A.: J. prakt. Chem., 80, 201 (1909).
6. Vogel A.: Preparatyka organiczna. WNT, Warszawa, 985 (1964).

STRESZCZENIE

Opisano syntezę i podstawowe własności kwasów 5-nitro-1-naftylosulfinylo- i sulfonylooctowych. Racemiczny sulfotlenek rozszczepiono w drodze krystalizacji frakcyjnej jego soli

z chinidyną i hydrochinidyną na enancjomery. Poszczególnym enencjomerom przypisano odpowiednie konfiguracje przestrzenne. Określono w rejonie $440 \leqslant \lambda \leqslant 600$ nm dyspersję rotacji optycznej prawoskrętnego enancjomeru oraz jego estrów p-nitrobenzylowego i p-bromofenacylowego. Wyznaczono trójczłonowe równania opisujące w kilku rozpuszczalnikach rotację optyczną prawoskrętnego antymeru w widzialnej i nadfioletowej części widma. Określono stałe racemizacji (K) oraz parametry aktywacji (Ea, $\Delta H^{\neq}$ i $\Delta S^{\neq}$) dla procesu racemizacji prawoskrętnego kwasu 5-nitro-1-naftylosulfinylooctowego w oparciu o metody kinetyki klasycznej.

РЕЗЮМЕ

Описано синтез и основные свойства кислот 5-нитро-1-нафтилсульфинил- и сульфонил- уксусных. Рацемическую сульфоокись расщеплено в ходе фракционной кристализации ее соли с хинидином и гидрохинидином на зеркальные изомеры. Отдельным зеркальным изомерам приписано соответствующие пространственные конфигурации. Определено в области $440 \leqslant \lambda \leqslant 600$ нм дисперсию оптического вращения правовращающего зеркального изомера и его сложных эфиров р-нитробензилового и р-бромфенацилового. Выделены трехчленовые уравнения, описывающие оптическое вращение правовращающего антимера в видимой и ультрафиолетовой части спектра в нескольких растворителях. Определенс постоянные рацемизации /K/, а также параметры активации /Ea,$\Delta H^{\neq}$ и $\Delta S^{\neq}$/ для процесса рацемизации правовращающей кислоты 5-нитро-1-нафтилсульфинилуксусной, опираясь на методы классической кинетики.