Volodymyr Mizyuk and Volodymyr Shibanov

STUDY OF THE INFLUENCE OF SUBSTITUENT R NATURE IN PHENYLSULFONES DERIVATIVES PhSO₂R ON THE CHEMICAL SHIFTS OF PHENYL RING PROTONS IN NMR ^{1}H SPECTRA

Ukrainian Academy of Printing, Lviv, Ukraine

Abstract. At the explanation of the spectra peculiarities of phenylsulfones of the general formula $C_6H_5SO_2R$ the arguments in favour of intramolecular influence through the space of functional groups situated in fragment R on the value of phenyl protons chemical shifts d_i^H have been adduced.

Keywords: NMR ^{1}H spectrum, phenylsulfone, basic spectral parameter, differential spectral parameters, "threshold", intramolecular influence, space.

Introduction

It has been shown [1-3] that in NMR ^{1}H spectra the basic spectral parameters (chemical shifts d^H) of all three types of hydrogen atoms nuclei (d_j^H) composing the aromatic fragment in monoalkylbenzenes and *para*-substituted alkylbenzenes depend upon the volume of the space occupied by alkyl substituent in a definite place of alkyl chain. Thus, if the changes of alkyl substitutent volume, which result from alkyl chain branching, take place near α-carbon atom, the above-mentioned changes in d values are called *a*-effect; if the branching takes place near *b*-atom – *b*-effect is observed.

In *para*-substituted alkylbenzenes [3] the changes in d_j^H values (where j is the type of hydrogen atoms in phenyl fragment – *ortho*- or *meta*-) observed at the volume increase (alkyl chain branching) near its α-carbon atom are called "proton volumetric α-effects". These effects are divided into *ortho*-α-effect and *meta*-α-effect. Proton *b*-effects are classified and called in the same way. To our mind, the mentioned classification may be universally applicable and used for NMR spectra of other aromatic compounds.

While studying the dependencies of the basic spectral parameters (d_j^H) in NMR ^{1}H spectra of mono-substituted benzenes upon substituent's σ constants [4, 5]

we paid attention to the anomalously large shift of d_n^H values of some $C_6H_5SO_2R$ sulfone derivatives to the low field[1]. Thus, the aim of the present paper is the study of peculiarities of NMR ^{1}H spectra of phenylsulfone derivatives **1–29** of the general formula $C_6H_5SO_2R$ [6]. Unsubstituted and substituted alkyl and aryl groups as well as other substituents containing heteroatoms in the point of addition to $C_6H_5SO_2$-, for example haloid atoms (Cl), alkylamino- (NR^IR^{II}) and alkoxygroups (OR^{III}), are marked by the "R" symbol. Thus, the general formula $C_6H_5SO_2R$ unites compounds which are different from the chemical point of view: sulfones ($C_6H_5SO_2Alk$ and $C_6H_5SO_2Ar$), benzene sulfonic acid ethers ($C_6H_5SO_2OAlk$ and $C_6H_5SO_2OAr)_2$, its amides, haloidanhydrides, and other similar compounds. However, for our purpose these structural differences are inessential, therefore spectra of all the above mentioned compounds are examined together, being divided into two types (main and auxiliary).

---

[1] The existence of linear dependence of *para*-protons chemical shift in monosubstituted benzenes PhX upon the X substituent constants, *e.g.* Hammet constants, was proved earlier [4]. According to the constant values, methylsulfonic group (X = –SO₂Me, σ = 0.72) together with nitrogroup (X = NO₂, σ = 0.79) are the most electron-withdrawing substituents X. The values of δ_p^H basic spectral parameters of Ph-SO₂-Me phenylmethylsulfone, taken from different literature sources ($\delta_p^{H,3[8]}$ = 7.650 ppm, $\delta_p^{H,3[9]}$ = 7.670 ppm, see below) and nitrobenzene ($\delta_p^{H[9]}$ = 7.710 ppm), were the most low-field parameters among all 26 monosubstituted benzenes PhX. However the careful analysis of the data given in [9] show that values of δ_p^H basic spectral parameters of some phenylalkylsulfones Ph-SO₂-R are even higher than 7.71 ppm for nitrobenzene. If we assume that electron-withdrawing ability of the substituent X (alkylsulfogroup –SO₂-R in our case) is the only factor affecting the δ_p^H value, then Hammet constant may achieve the value of 0.90 for the same substituents in Ph-SO₂-R. Such conclusion contradicts the common sense, because the exchange of methyl group for alkyl one during the transfer of phenylmethylsulfone to phenylalkylsulfones cannot cause such a significant shift of δ_p^H signal to the low field overlapping the effect of nitrogroup, which is more electron-withdrawing. To our mind, the presence of additional factor affecting the chemical shift of *para*-protons in Ph-SO₂-R is more probable. Therefore, we investigated this assumption.

2. Experimental

2.1. Objects

The main investigated objects were unsubstituted and substituted into alkyl fragment alkylsulfones **1–21** of the general formula $C_6H_5SO_2C(Y^I)(Y^{II})(Y^{III})$, which necessarily contain "sulfone" fragment C-S-C. The spectra of auxiliary compounds **22–29**, containing C-S-Het$(Y^I)(Y^{II})$ fragment (where "Het" denotes O, N, Cl and other heteroatoms) were used for comparison. The used literature sources contain sufficient amount of spectral data allowing to trace the structure/property regular dependencies (in our case the influence of substituent R structure on changes of phenyl fragment d_j^H values).

The second argument is peculiarities of spatial arrangement of R substituent relative to phenyl ring in compounds $C_6H_5SO_2R$ **1-21** with sufficiently long alkyl chain. Fig. 1 shows that if sulphur atom is situated in the centre of conditional tetrahedron, then 4 adjoined substituents (two oxygen atoms, pnehyl ring C-1 atom and X-atom (C-atom or Het of R group)) will be in its corners. Generally, such tetrahedron does not need to be a regular one because of the different lengths of atomic bonds and angles between corresponding atomic bonds differing from the required value (~109.5°). However, we assume the existence of $C_6H_5SO_2R$ molecule conformation, where phenyl group and alkyl chain of R fragment are situated in the space as a half-loop depicted in Fig. 1. The spatial approaching between H-2, H-3 and probably H-4 phenyl ring with outlying carbon atoms (C^γ, C^δ, C^ε, *etc.*) of the R fragment alkyl chain takes place. The interference of the mentioned atoms through the space becomes possible and we may expect the change of the studied spectral parameters.
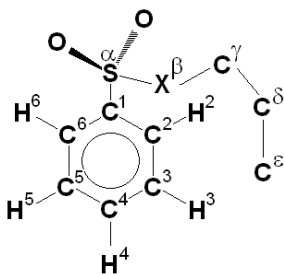

Fig. 1. Phenylsulfone derivatives **1-29**

2.2. Procedure

The previously accepted approach [1-3], based on the virtual division of investigated molecule into two fragments – "invariable" and "variable" one – is used for the comparison of spectral parameters of different compounds. The changes in differential spectral parameters (see below) which take place in the investigated part of the "invariable" fragment under the influence of the changing structure of the "variable" fragment (substituent R) are examined.

The fragment $C_6H_5-S^\alpha O_2-C^\beta$- in the main compounds **1–21** is chosen as the "invariable" one and three "variable" substituents at *b*-carbon atom are denoted as (-Y^I), (-Y^{II}) and (-Y^{III}). Similarly, the $C_6H_5-S^\alpha O_2$-Het$^\beta$- is an "invariable" fragment and "variable" substituents at heteroatom (Het) are denoted as (-Y^I) and (-Y^{II}) for the comparative auxiliary compounds **22–29**. Their amount depends on heteroatom valency.

3. Results and Discussion

3.1. Basic Spectral Parameters

3.1.1. Introduced symbols and information sources

Basic spectral parameters in NMR ^{1}H spectra of $C_6H_5SO_2R$ phenylsulfone derivatives are denoted as $\delta_j^{H,N(i)}$. The superscript symbols mean: (i) type of NMR spectrum (H); (ii) number of compounds (*N*); (iii) type of *R* substituent (i). In some cases references number is indicated as well. Subscript symbol (*j*) was discussed above.

The sources of spectral data were chosen on the assumption of their reliability and compatibility, whose criteria were discussed earlier [7]. We used $\delta_j^{H,N(i)}$ values obtained in deuterochloroform and given in Refs. [8, 9]. Spectra obtained in other solvents (*e.g.* DMSO-d$_6$) were used only in separate cases, which were specified. CDCl$_3$ use as a solvent is dictated by considerable dependence of δ^H values upon the solvent nature. When comparing relatively small changes in δ^H basic spectral parameters resulting from probable spatial interaction between molecule fragments, it is impossible to take into account greater changes, which may be caused by the use of solvents different by their nature.

3.1.2. Signals attribution in the spectra

The author's signals attribution of NMR ^{1}H spectra to the corresponding values $\delta_j^{H,N(i)}$ for two *ortho*-, two *meta*- and one *para*-protons is given in [8] in all cases. Since in [9] the signals attribution is absent, it was made by us. Usually values of $\delta_j^{H,N(i)[8]}$ parameters given in [8] and $\delta_j^{H,N(i)[9]}$ parameters attributed by us using spectra presented in [9] are in a good agreement and the difference between them rarely exceeds 0.020 ppm. The latter is assumed as an average possible experimental error, *i.e.* $\delta_j^{H,N(i)}$ parameters determination.

In some cases simple attribution of the mentioned signals is difficult due to the closeness of $\delta_m^{H,N(i)}$ and

$\delta_p^{H,N(i)}$ parameters differing by 0.1 ppm. The authors of such signals attribution [8] assume that the mentioned ones may trade places. For those cases (compounds **23–27**) we did not calculate differential parameters and put dashes in the Table.

Basic spectral parameters $\delta_j^{H,N(i)}$ given in [8] were obtained using instruments with different working frequency: 90 and 400 MHz. In order to calculate the differential parameters, in the cases when both values of $\delta_j^{H,N(i)}$ are given in [8] and they are different, we used $\delta_j^{H,N(i)[8]}$ parameter obtained by the high-frequency instrument. "Low-frequency" parameter was forcedly used only in the absence of "high-frequency" parameter.

3.2. Differential Spectral Parameters $\Delta\delta_o^{H,N(i)}$

Since the differential parameters indicate the quantitative estimation of *a*- and *b*-effects in NMR¹H and ¹³C spectra of alkylbenzenes mentioned in [1-3], in this work we carefully analyze just $\Delta\delta_j^H$ differential parameters.

Differential parameters $\Delta\delta_j^{H,N(i)}$ were calculated in accordance with the formula (1) given in [2]:
$$\Delta\delta_j^{H,N(i)} = \delta_j^{H,N(i)} - \delta_j^{H,N(0)} \qquad (1)$$
where $\delta_j^{H,N(i)}$ is studied basic parameter in $C_6H_5SO_2R$ compounds with the substituent R (R ≠ Me), and "zero" parameters $\delta_j^{H,N(0)}$ are chemical shifts of nuclei of hydrogen aryl atoms in the "standard" compound $C_6H_5SO_2CH_3$, containing methyl group as *R* fragment.

3.2.1. Introduced symbols

Values of $\Delta\delta_j^{H,N(i)}$ differential spectral parameters are represented in the Table. Every cell of the Table has two values of $\Delta\delta_j^{H,N(i)}$ differential parameter given as a fraction: numerator is the value calculated by formula (1) using $\delta_j^{H,N(i)[9]}$ basic parameters taken from [9] and denominator is the same parameter but calculated using parameter $\delta_j^{H,N(i)[8]}$. The numerator is presented in common type and denominator – in bold type; both numerals are given without parentheses.

In the cases when values of $\delta_j^{H,N(i)}$ basic parameter are absent in [8] or [9] it is impossible to calculate the value of corresponding differential parameter. To increase the statistic amount of data we calculated so-called "crosseded" differential parameter. It is calculated with simultaneous use of different sources ([8] and [9]) and placed in the cell instead of lacking value. "Crosseded" differential parameters are presented in bold type in parentheses. For example, "crosseded" parameter may be calculated by formula: $\Delta\delta_o^{H,N(i)} = \delta_o^{H,N(i)[9]} - \delta_o^{H,N(0)[8]}$ or *vice versa*: $\Delta\delta_o^{H,N(i)} = \delta_o^{H,N(i)[8]} - \delta_o^{H,N(0)[9]}$.

Discussing the results we preferred $\Delta\delta_o^{H,N(i)[9]}$ parameters compared with those of $\Delta\delta_j^{H,N(i)[8]}$. Such preference is determined by the possibility to control the

author's attribution of $\delta_j^{H,N(i)}$ signals by scale enlargement of that part of the spectrum we are interested in. Thus, we decrease the risk of errors possibly committed by the authors [8].

Whereas we assume that accuracy and reliability of both differential parameters $\Delta\delta_j^{H,N(i)[9]}$ and $\Delta\delta_j^{H,N(i)[8]}$ are considerably higher than those of corresponding "crossed" parameters $\Delta\delta_j^{H,N(i)}$, as well as taking into account that "crossed" parameters are given because of calculation impossibility of corresponding differential parameters, their own worth is low. If the value of "crossed" differential parameter does not practically differ from the second parameter in the cell (*i.e.* $\Delta\delta_j^{H,N(i)[9]}$ or $\Delta\delta_j^{H,N(i)[8]}$), the "crossed" parameter serves only for the confirmation of the latter value. If not, we do not take them into consideration.

3.2.2. Classification of *R* substituents. Meaning of "*i*" Symbol

Let us accept the following classification of *R* substituents for all **1–29** compounds. The type of substituent we denote by symbol "*i*" (see above), consisting of two parts. The first part is a Greek letter indicating the position of the functional group in the alkyl chain. For compounds **1–21** such position is determined by the number of carbon atom in the chain which functional group is attached to (Fig. 1). In the case when multiple bond (C–C) is a functional group, the nearest to the sulfonic fragment carbon atom is denoted by this letter. All auxiliary compounds **22–29** relate to *a*-type, since carbon chain in *R* fragment is absent in them and functional group (which is, in fact, the *R* fragment) is attached to the sulfur atom in $-S^\alpha O_2-$ group.

The second part of "*i*" symbol is a numeral denoting the type of functional group. Let us introduce the following numbers of functional groups types for **1–29** compounds. The number depends upon the position of the functional group atom attached to the alkyl chain in the substituent *R* (or to the sulfonic fragment $-S^\alpha O_2-$ for **22–29** compounds) in the periodic table. The first five numbers are assigned to "carbon" functional groups, the next five – to corresponding heteroatoms.

1 – double bond C=C

2 – triple bond C≡C

3 – aryl group (phenyl group or phenyl groups substituted into nucleus)

4 – triple bond C≡N (nitrile group)

5 – double bond C=O (in our case it is carboxyl group and its derivatives: COOH, COOR, including ortho-etheric functional group $(OR)_3$)

6 – alkylamine group (NR^IR^{II})

7 – alkoxyl group OR (OH and cyclic tetrahydropyranyl fragment – THP)

8 – alkylthiol group (SR^I)
9 – alkylsulfonic group (SO_2R^I)
10 – haloid atom

Number "0" denotes the hydrogen atom at the most outlaying carbon atom in the alkyl chain of *R* substituent, because functional group is absent in such compounds.

3.3. Table of Spectral Parameters

In the Table there are only values of three differential spectral parameters $\Delta\delta_j^{H,N(i)}$ for compounds **1–29**; they were calculated by the formula (1). The values of basic spectral parameters $\delta_j^{H,N(i)}$ (except $\delta_j^{H,\mathbf{3}(\beta0)}$) are minuends in formula (1) and are not presented in the Table. They may be calculated by addition of corresponding differential parameter (given in the Table) and subtrahend – parameter $\delta_j^{H,\mathbf{3}(\beta0)}$.

The values of both parameter types ($\delta_o^{H,N(i)}$ and $\Delta\delta_o^{H,N(i)}$) are given with the accuracy of 0.001 ppm. Below are the parameters $\delta_j^{H,\mathbf{3}(\beta0)}$, used as the subtrahends in the formula (1) and taken from [8] and [9]: $\delta_o^{H,\mathbf{3}(\beta0)[8]} = \mathbf{7.943}$ ppm; $\delta_o^{H,\mathbf{3}(\beta0)[9]} = \mathbf{7.950}$ ppm; $\delta_m^{H,\mathbf{3}(\beta0)[8]} = \mathbf{7.610}$ ppm;

$\delta_m^{H,\mathbf{3}(\beta0)[9]} = \mathbf{7.580}$ ppm; $\delta_p^{H,\mathbf{3}(\beta0)[8]} = \mathbf{7.650}$ ppm and $\delta_p^{H,\mathbf{3}(\beta0)[9]} = \mathbf{7.670}$ ppm. The parameters $\delta_J^{H,\mathbf{3}(\beta0)[8]}$ were obtained using low-frequency instrument. Therefore, as was mentioned above, parameters $\delta_J^{H,\mathbf{3}(\beta0)[9]}$ obtained using high-frequency instrument of 300 MHz seem to be more reliable. The greatest difference between the similar parameters is equal to 0.030 ppm for *meta*-protons. This value is half as much again as our estimated value of the experimental error, which makes "crossed" differential parameters ($\Delta\delta_m^{H,N(i)}$) doubtful. The same, just to a lesser degree, refers to *para*-protons. The difference between $\delta_p^{H,\mathbf{3}(\beta0)[8]}$ and $\delta_p^{H,\mathbf{3}(\beta0)[9]}$ is equal to the value of the experimental error. Only for *ortho*-protons ($\Delta\delta_o^{H,N(i)}$) the "crossed" differential parameters may be considered as reliable values, because the difference between $\delta_o^{H,\mathbf{3}(\beta0)[8]}$ and $\delta_o^{H,\mathbf{3}(\beta0)[9]}$ is equal to 0.007 ppm, which is three times less than the experimental error.

After every three columns with the values of $\Delta\delta_o^{H,N(i)}$ there are columns with the estimation of relative value of differential parameters, which will be discussed in detail below.

Table

**Values of basic ($\delta_j^{H,N(i)}$) and differential ($\Delta\delta_o^{H,N(i)}$)
spectral parameters for 1–29 compounds**

No. of compounds	Compound formula	Substituent symbol "i"	$\Delta\delta_o^{H,N(i)} = \delta_o^{H,N(i)} - \delta_o^{H,N(0)}$	Relative value of $\Delta\delta_o^{H,N(i)}$ parameter	$\Delta\delta_m^{H,N(i)} = \delta_m^{H,N(i)} - \delta_m^{H,N(0)}$	Relative value of $\Delta\delta_m^{H,N(i)}$ parameter	$\Delta\delta_p^{H,N(i)} = \delta_p^{H,N(i)} - \delta_p^{H,N(0)}$	Relative value of $\Delta\delta_p^{H,N(i)}$ parameter
1	2	3	4	5	6	7	8	9
1	$C_6H_5–SO_2–C_6H_5$	α3	0.000 (+**0.007**)		−0.090 (−**0.120**)	– – – – – –	−0.120 (−**0.100**)	– – – – – –
2	$C_6H_5–SO_2–C_6H_4$ (o–NH_2)	α3	−0.040 (−**0.033**)		−0.140 (−**0.170**)	– – – – – –	−0.150 (−**0.130**)	– – – – – –
3	$C_6H_5–SO_2–CH_3$	β0	0.000 **0.000**		0.000 **0.000**		0.000 **0.000**	
4	$C_6H_5–SO_2–CH=CH_2$	β1	−0.055 (−**0.048**)	−	−0.030 (−**0.060**)		−0.030 (−**0.010**)	
5	$C_6H_5–SO_2–CH_2–$ C_6H_4(o–CH_3)	β3	−0.310 (−**0.303**)	– – – – – – – –	−0.140 (−**0.170**)	– – –	−0.060 (−**0.040**)	−
6	$C_6H_5–SO_2–CH_2–$ C_6H_4(o–CH_2Br)	β3	−0.235 (−**0.228**)	– – – – – – – –	−0.090 (−**0.120**)	– – – –	−0.030 (−**0.010**)	
7	$C_6H_5–SO_2–THP–2*$	β7	−0.030 (−**0.023**)		−0.030 (−**0.060**)		0.000 (+**0.020**)	
8	$C_6H_5–SO_2–CH_2–S–CH_3$	β8	+0.015 (+**0.022**)		0.000 (−**0.030**)		+0.010 (+**0.030**)	
9	$C_6H_5–SO_2–CH_2–SO_2–$ C_6H_5	β9	−0.010 (−**0.003**)		−0.020 (−**0.050**)		+0.020 (+**0.040**)	
10	$C_6H_5–SO_2–CH_2Cl$	β10	+0.030 +**0.040**		+0.040 +**0.012**		+0.070 +**0.084**	+ + + +

1	2	3	4	5	6	7	8	9
11	C$_6$H$_5$–SO$_2$–CH$_2$Br	β10	+0.035 (**+0.042**)		+0.040 (**+0.012**)		+0.060 (**+0.080**)	+ + +
12	C$_6$H$_5$–SO$_2$–CH$_2$–CH$_3$	γ0	(**–0.033**) **–0.026**		(**+0.005**) **–0.025**		(**–0.003**) **+0.017**	
13	C$_6$H$_5$–SO$_2$–CH$_2$– CH=CH$_2$	γ1	–0.075 **–0.065**	– – – –	–0.025 **–0.050**		–0.020 **0.000**	
14	C$_6$H$_5$–SO$_2$–CH$_2$–C≡CH	γ2	–0.010 (**–0.003**)		–0.010 (**–0.040**)		+0.010 (**+0.030**)	
15	C$_6$H$_5$–SO$_2$–CH$_2$C≡N	γ4	+0.080 **+0.096**	+ + + +	+0.070 **+0.056**	+ + +	+0.110 **+0.135**	+ + + + + +
16	C$_6$H$_5$–SO$_2$–CH$_2$– COOCH$_3$	γ5	0.000 (**+0.007**)		+0.010 **–0.020**		+0.030 (**+0.050**)	
17	C$_6$H$_5$– SO$_2$–CH$_2$–CH$_2$– OH	γ7	–0.025 (**–0.018**)		0.000 (**–0.030**)		+0.010 (**+0.030**)	
18	Z–C$_6$H$_5$–SO$_2$–CH=CH– SO$_2$–C$_6$H$_5$	γ9,β1	+0.075 (**+0.082**)	+ + + +	–0.010 (**–0.040**)		+0.020 (**+0.040**)	
19	C$_6$H$_5$–SO$_2$–CH$_2$–CH$_2$– C≡N	δ4	+0.005 (**+0.012**)		+0.120 (**+0.090**)	+ + + + +	+0.130 (**+0.150**)	+ + + + + +
20	C$_6$H$_5$–SO$_2$–CH$_2$–CH$_2$– C(OCH$_3$)$_3$	δ5	–0.020 (**–0.013**)		0.000 (**–0.030**)		0.000 (**+0.020**)	
21	C$_6$H$_5$–SO$_2$–CH$_2$–CH$_2$– COOH	δ5	–0.045 (**–0.038**)		+0.050 (**+0.020**)	+	+0.050 (**+0.070**)	+ +
22	C$_6$H$_5$–SO$_2$–NH$_2$	α6	(**–0.099**) **–0.092**	– – – –	(**0.000**) **–0.030**		(**–0.090**) **–0.070**	– –
23	C$_6$H$_5$–SO$_2$–NHCH$_3$	α6	(**–0.088**) **–0.081**	– – – –	–		–	
24	C$_6$H$_5$–SO$_2$–NHC$_4$H$_9$^{n}	α6	(**–0.060**) **–0.053**	– –	–		–	
25	C$_6$H$_5$–SO$_2$–OCH$_3$	α7	–		–		–	
26	C$_6$H$_5$–SO$_2$–O–CH$_2$– CH$_3$	α7	(**–0.050**) **–0.043**		–		–	
27	C$_6$H$_5$–SO$_2$–O–C$_4$H$_9$^{n}	α7	(**–0.030**) **–0.023**		–		–	
28	C$_6$H$_5$–SO$_2$–O–CH$_2$– C(CH$_3$)$_3$	α7	(**–0.037**) **–0.030**		(**–0.021**) **–0.051**		(**–0.024**) **–0.004**	
29	C$_6$H$_5$–SO$_2$–Cl	α10	+0.095 **+0.090**	++ ++	+0.050 (**+0.020**)	+	–0.040 (**–0.020**)	

2-THP – 2-Tetrahydropyranyl fragment

3.4. Classification of Differential Spectral Parameters for Compounds 1-29

The main compounds **1–21** are listed in the Table in the order of functional group in the substituent *R* moving away from sulfonic fragment in the alkyl chain (*i.e.* from α- to *d*-) and substituent type number increase. The auxiliary compounds **22–29** with the values "*i*" from α6 to α10 are situated below.

3.4.1. Introduction of the notion of "threshold" values of differential parameters

Taking into account the postulated value of the experimental error (0.020 ppm) we accepted a definite "threshold" value for absolute magnitudes of differential parameter. The notion of "threshold" value is introduced with the aim to determine those compounds for which the differential parameters difference value we consider "significant", *i.e.* stipulated not by the experimental errors but by the influence of the differences in the substituent R structure.

For "protonic" parameters $\Delta\delta_j^{H,N(i)}$ the value of 0.050 ppm is chosen as a "threshold" one. This value is 2.5 times higher than the accepted experimental error. At the determination of "threshold value exceeding" the value of $\Delta\delta_j^{H,N(i)}$ parameters are rounded to the nearest values which are divisible by 0.005 ppm. Such cases of exceeding (or equality) of "threshold values" are presented in the Table in the columns next to the column of $\Delta\delta_j^{H,N(i)}$ parameter. In other cases (when there is no exceeding) there are not denotations in the Table.

Let us introduce a semi-quantitative scale of exceeding (or equality) of $\Delta\delta_j^{H,N(i)}$ parameters "threshold" values and corresponding symbols for each of the 4 types of "exceeding".

1. Relatively small "threshold exceeding". The absolute value of $\Delta\delta_j^{H,N(i)}$ parameters is within the range from |0.050 ppm| to |0.065 ppm|. Depending upon the sign of $\Delta\delta_j^{H,N(i)}$ parameter symbols "+" (for the positive values) and "–" (for the negative values) are introduced by bold type.

2. Medium "threshold exceeding". The range of parameters is from |0.065 ppm| to |0.100 ppm|. Symbols "++" or "– –".

3. Large "threshold exceeding". The range of $\Delta\delta_j^{H,N(i)}$ parameters is from |0.100 ppm| to |0.200 ppm|. Symbols "+++" or "– – –".

4. Huge "threshold exceeding". The value of $\Delta\delta_j^{H,N(i)}$ parameters is above |0.200 ppm|. Symbols "++++" or "– – – –".

3.5. Possible Relationship between "Threshold Exceeding" of 1−29 Compounds and *R* Fragment Structure

Let us observe the tendency of "threshold exceeding" by the absolute values of $\Delta\delta_j^{H,N(i)}$ differential parameters in the set of the main compounds **1-21** depending upon the type of functional group in the *R* fragment. One can see from the Table that different types of functional groups "*i*" lead to the different changes by sign and magnitude in $\Delta\delta_j^{H,N(i)}$ parameters for protons in different "*j*" positions of phenyl ring.

3.5.1. Functional groups in a-position (compounds 1 and 2)

In compounds **1** and **2** the alkyl chain in the *R* substituent is absent. Functional group (in our case aryl group) is the *R* substituent. It is directly connected with the $C_6H_5SO_2$ fragment. That is why phenylarylsulfones **1** and **2** are compounds of α-type by definition.

In both compounds **1** and **2** the "threshold exceeding" by $\Delta\delta_o^{H,N(i)}$ parameters of *ortho*-protons is absent. At the same time for *meta*- and *para*-protons there is a large negative "threshold exceeding" by $\Delta\delta_m^{H,N(i)}$ and $\Delta\delta_p^{H,N(i)}$ parameters ("– – –").

3.5.2. Functional groups in *b*-position (compounds 3−11)

A different situation is observed for the compounds with *b*-position of functional groups in the alkyl chain (**3–11**). Let us divide them into 2 parts depending on the nature of functional groups contained in the *R* substituent.

For the compounds where double bond C=C (compound **4**) and the system of 6 *p*-electrons of aryl ring (compounds **5** and **6**) are functional groups, there is small negative ("–") "threshold exceeding" by $\Delta\delta_o^{H,\mathbf{4}(\beta1)}$ parameter for vinylsulfone **4** and huge ("– – – –") "threshold exceeding" for *b*-arylsulfones (benzylsulfones) **5** and **6**. The absolute values of the latter parameters are the maximum ones among all investigated values.

For *meta*-protons in the compounds **5** and **6** the negative values of $\Delta\delta_m^{H,\mathbf{5}(\beta3)}$ and $\Delta\delta_m^{H,\mathbf{6}(\beta3)}$ parameters are less, though they are large according to our classification. For *para*-protons the mentioned parameters are even less, because only one parameter $\Delta\delta_p^{H,\mathbf{5}(\beta3)}$ demonstrates "low" negative "threshold exceeding" for the compound **5**.

In case when the functional group is connected with *b*-carbon atom of the alkyl chain in the compounds **7–11** and the group begins with a heteroatom (the types of functional groups are denoted as *b*7, *b*8, *b*9 and *b*10), none of the functional groups affects *ortho*- and *meta*-protons sufficiently strong to initiate exceeding of the

"threshold". Therefore we may suppose that the effect of heteroatom in *b*-position of the *R* fragment on *ortho-* and *meta*-protons of phenyl ring in the compounds **7–11** is weaker than the effect of C=C double bond and especially the system of C=C double bonds in aryl group bound with β-carbon atom of the alkyl chain.

At the same time for *para*-protons the "threshold exceeding" was discovered for two compounds – **10** and **11** containing haloid atoms (type *b*10) as functional groups. The values of "threshold exceeding" for $\Delta\delta_p^{H,\mathbf{10}(\beta10)}$ and $\Delta\delta_p^{H,\mathbf{11}(\beta10)}$ parameters are positive and medium (approximately +0.070 ppm). A similar difference is also observed between the compounds **4–6** on the one part and **7–11** – on the other part.

3.5.3. Functional groups in *g*-position (compounds 13–18)

As it was mentioned above, *cis*-di(phenylsulfono)ethylene **18** contains two functional groups at the same time and therefore it will not be examined. The rest 5 compounds (**13–17**) have 5 different types of functional groups in *g*-position (or attached to *g*-carbon atom of the chain, see Fig. 1). One can see from the Table that those functional groups are: C=C double bond in **13** (*g*1), C≡C triple bond in **14** (*g*2), C≡N triple bond in **15** (*g*4), COOMe carbmethoxyl group in **16** (*g*5) and OH (*g*7) hydroxyl group in **17**.

The "threshold exceeding" is observed only in two cases. For allylphenylsulfone **13** the medium negative value of $\Delta\delta_o^{H,\mathbf{13}}$ parameter is observed. For nitrile **15** the "threshold exceeding" was found for all three types of protons. All of them have positive values from medium to large.

For *ortho*-protons "exceeding" by its absolute value is greater than that for *b* vinylsulfone **4,** but three times less than huge values for *b*-arylsulfones **5** and **6**.

g-Nitrile finctional group in the compound **15** (*g*4 type) together with *b*-aryl group in benzyl sulfone **5** (*b*3) are only two functional groups in the *R* fragment for all studied 29 compounds, for which the "threshold exceeding" by all three differential parameters (*ortho-*, *meta-* and *para-*) is observed.

3.5.4. Functional groups in *d*-position (compounds 19–21)

In three compounds (**19–21**) there are three different functional groups. All of them are in *d*-position of the alkyl chain: C≡N triple bond in **19** (*d*4), C(OMe)₃ orthoetheric group in **20** (*d*5) and COOH carboxy group in **21** (*d*5).

It should be noted that NMR ^{1}H spectrum of the compound **19** was obtained in hexadeuteriodi-methylsulfoxide (DMSO-d₆) and the spectrum of the compound **21** – in the mixture of CDCl₃ + DMSO-d₆ [6]. As it was mentioned above, this fact calls in question all conclusions concerning differential spectral parameters of the compounds **19** and **21**. Therefore, large positive values of "threshold exceeding" for *meta-* and *para*-protons in nitrile-containing sulfone **19** have no independent value. However, it is advisable to examine them together with the others, keeping in mind their defect. All the mentioned above for the compound **19** is valid for the small positive "threshold exceeding" of *meta-* and *para*-protons of sulfone-containing acid **21**.

3.5.5. Auxiliary compounds 22–29 with functional groups in a-position

One can see from the Table that "threshold exceeding" is observed only for *ortho*-protons for the compounds **22–29**, because values of two parameters $\Delta\delta_m^{H,\mathbf{28}} = 0.051$ ppm and $\Delta\delta_m^{H,\mathbf{29}} = 0.050$ ppm among *meta-* and *para*-protons are on the verge of such "exceeding". Therefore they will not be discussed here. The negative values of "threshold exceeding" ($\Delta\delta_o^{H,N(i)}$ parameter) for *ortho*-protons in all three phenylarylsulfamides **22–24**, as well as the positive value in sulfochloride **29** are "low" (compound **24**) or "medium" by our classification. As it was mentioned above, benzene sulfamide spectrum was obtained in DMSO-d₆. It is the reason why "threshold exceeding" by its *ortho*-parameter $\Delta\delta_o^{H,\mathbf{22}}$ will not be discussed, though parameters $\Delta\delta_o^{H,\mathbf{22}}$ on the one part, and $\Delta\delta_o^{H,\mathbf{23}}$ together with $\Delta\delta_o^{H,\mathbf{24}}$ on the other part are comparable. It may indicate only insignificant effect of differences in the nature of solvents used for NMR ^{1}H spectra.

The possible determinative of the observed "threshold exceeding" by $\Delta\delta_o^{H,N(i)}$ parameters in sulfamides **22–24** (*a*6) is the influence of nitrogen amide atom on *ortho*-protons, because there is no "threshold exceeding" for sulfoesters. Perhaps, *ortho*-protons of phenyl fragment are "inert" to the oxygen atom of sulfoesteric group.

3.6. Effect of Functional Group Position on the Magnitude and Sign of $\mathbf{\Delta\delta_j^{H,N(i)}}$ Differential Parameters

The double bond C=C (type 1), aryl group (type 3) and triple bond C≡N in the nitrile group (type 4) are among functional groups generating "threshold exceeding" in the main compounds **1–21**. Carboxyl group (type 5, *meta-* and *para*-protons in the compound **21,** though NMR ^{1}H spectrum was obtained in CDCl₃+DMSO-d₆ [6]) and haloid atoms (type 10, *para*-protons in the compounds **10** and **11**) are noted

episodically. The parameters of *ortho*-protons (type 1 and 9) in bifunctionally substituted *R* fragment (compound **18**) are not discussed. No "threshold exceeding" is observed for the following functional groups: triple bond C≡C (type 2); alkoxyl group OR (OH and cyclic tetrahydropyranyl fragment – THP, type 7) and alkylthiol group (SR[1], type 8).

Let us group $\Delta\delta_j^{H,N(i)}$ differential parameters which overcome the "threshold" on the basis of functional groups (C=C, Ar, C≡N) numbers (types) and consider the signs of these parameters.

1. The double bond C=C in the compounds **4** (*b*1) and **13** (*g*1). *b*- and *g*-Atoms of the alkyl chain are bound by C=C bond in the compound **4**; in the compound **13** the bond is in *g-d* position of the *R* fragment. For the compounds of type 1 only two cases of "threshold exceeding" were observed. Both of them are for *ortho*-protons and both of them have negative values. Parameter $\delta_o^{H,4(1)}$ has a small value ("–") and parameter $\delta_o^{H,13(1)}$ – a medium one ("– –"). "Threshold exceeding" for *meta*- and *para*-protons in the compounds with double bond C=C was not observed.

Thus, for the both compounds – vinylsulfone **4** and allylsulfone **13** – small or medium shift to the high field of $\delta_o^{H,N(1)}$ basic spectral parameters is typical only of *ortho*-protons. The value of shift increases as C=C bond moves off from sulfonic group.

2. Aryl groups found in the compounds **1** (α3), **2** (α3), **5** (β3) and **6** (β3). In the compounds **1** and **2** the aryl group is in α-position and in the compounds **5** and **6** – in *b*-position of the *R* fragment. There is no "threshold exceeding" by *ortho*-protons in the compounds **1** and **2**; and negative "exceeding" by *meta*- and *para*-protons are large ("– – –"). The compounds **5** and **6** have huge negative "exceeding" ("– – – –") by *ortho*-protons, which diminishes to large ("– – –") and medium ("– –") values for *meta*-protons and small ("–") value for *para*-proton $\Delta\delta_p^{H,5(\beta3)[9]}$ = –0.060 ppm. It should be noted that two other *para*-parameters ($\Delta\delta_p^{H,6(\beta3)[9]}$ and $\Delta\delta_p^{H,6(\beta3)[8]}$ which do not "exceed threshold") also have negative sign and do not "exceed threshold" as well. Hence, they are not discussed.

Thus, for both types of compounds – α-compounds **1** and **2** and *b*-compounds **5** and **6** the large (sometimes huge) shift to the high field of $\delta_j^{H,N(3)}$ basic spectral parameters is typical of all three types of protons, especially for *ortho*-protons in **6**.

3. The functional group containing triple bond C≡N (nitrile) is observed only in the compounds **15** (*g*4) and **19** (*d*4). In the compound **15** *g*-C and *d*-N atoms of the alkyl chain is bound by C≡N bond; in the compound **19** it is in *d-e* position. Due to the use of hexadeuteriodimethyl-sulfoxide as a solvent instead of deuterochloroform in the

compound **19** [6], the results of its differential parameters comparison cannot be accepted as absolutely corrected. However, as it was mentioned above for the compounds **22–25**, it is possible that the change of differential parameters connected with the solvent exchange is not large and does not distort the principal results. Therefore the nitrile compound **19** still should be discussed.

"Threshold exceeding" is observed for all three parameters $\Delta\delta_j^{H,15(\gamma4)}$ in the compound **15**, as well as two parameters $\Delta\delta_m^{H,19(\delta4)}$ and $\Delta\delta_p^{H,19(\gamma4)}$ in the compound **19**. All the mentioned parameters are positive and have values "++" for *ortho*- and *meta*-protons in the compound **15** and "+++" for *meta*-protons in **19** and *para*-protons in both compounds.

Thus, medium or large shift to the low field of all three basic spectral parameters $\Delta\delta_j^{H,N(4)}$ (except *ortho*-protons in **19**) is typical of both nitrilesulfones **15** and **19.**

4. Conclusions

1. The double bond C=C or aryl group (which may be considered as the system consisting of three conjugate double bonds C=C) situated correspondingly in the fragment *R* of arylsulfones of the general formula $C_6H_5SO_2R$ <u>causes the shift</u> of the basic spectral parameters δ^H_j of all three types of phenyl ring protons <u>to the high field,</u> compared with the value of corresponding parameters $\delta_j^{H,3(\beta0)}$ of etalon phenylmethylsulfone **3** without functional groups.

2. The triple bond C≡N in nitrile group situated correspondingly in the fragment *R* of arylsulfones of the general formula $C_6H_5SO_2R$ <u>causes the shift</u> of the basic spectral parameters δ^H_j of all three types of phenyl ring protons <u>to the low field,</u> compared with the value of corresponding parameters $\delta_j^{H,3(\beta0)}$ of etalon phenyl-methylsulfone **3**.

3. The presence of other studied functional groups in the fragment *R* of arylsulfones of the general formula $C_6H_5SO_2R$ does not lead to uniquely interpretive results.

4. It is interesting to compare the absolute values of differential parameters $\Delta\delta_m^{H,N(i)}$ and $\Delta\delta_p^{H,N(i)}$ in the compounds **1** and **2** with α-position of aryl groups in the fragment *R* and those in the compounds **5** and **6**, where aryl rings (as functional groups in the fragment *R*) are bound with β-carbon atom of the chain. The values of *meta*-parameters in all 4 compounds are practically the same and the values of *para*-parameters are greater in the case of the compounds **1** and **2**. If we take into consideration that in the case of *ortho*-parameters the opposite situation is observed (*i.e.* the absolute values are greater for the parameters in the compounds **5** and **6**), we may assume the following: aryl ring of the benzyl group in the compounds **5** and **6** is situated one methylene group further from the phenyl ring of phenylsulfonic fragment

(spectra of which we study). It has a stronger influence on the nuclei of hydrogen atoms situated closer, *i.e.* mainly on *ortho-* and *meta-*prtons. Its influence on *para-*protons is weaker. On the contrary, if aryl rings in the fragment *R* in phenylarylsulfones **1** and **2** are directly connected with sulfonic fragment (without additional methylene group, the same as in **5** and **6**), then they may spatially affect only outlying nuclei of hydrogen atoms in the phenyl ring, *i.e. meta-* and *para-*protons.

In that case *ortho-*protons are apparently too close to the main direction of the substituent influence (system of 6 π-electrons of aryl ring), therefore they are "beyond reach".

5. The same results can be observed in the cases when multiple bonds C=C or C≡N are functional groups in the fragment *R*. However, there is an opposite dependence upon functional group position in the fragment *R*. Multiple bonds (C=C in *b-g* position for **4** and C≡N in *g-d* position for **15**) which are closer to the $C_6H_5SO_2R$ fragment, affect the closer situated nuclei of *ortho-* and *meta-*hydrogen atoms in the phenyl ring in a greater degree, while more outlaying bonds (C=C in *g-d* position for **13** and C≡N in *d-e* position for **15**) in a greater degree affect more outlaying nuclei of *meta-* and *para-*protons. Thus, the elongation of alkyl chain by one methylene group shifts the "focus" of the greatest influence of multiple bonds to more outlaying hydrogen atoms in *para-* (or *meta-*positions) of phenyl ring in the $C_6H_5SO_2R$ fragment.

6. The absence of large and huge (according to the accepted classification) values of differential parameters $\Delta\delta_j^{H,N(i)}$ for the auxiliary compounds **22–29**, *i.e.* benzene sulfonic acid derivatives, indirectly confirms our assumption that it is spatial intramolecular interactions between phenyl and functional groups (in the *R* fragment) and not the nature of heteroatom in α-position of this fragment that play the main role in changing of chemical shifts of phenyl protons in the compounds **1–29**.

Acknowledgements

References

[1] Mizyuk V. and Shibanov V.: Proceed. 12th Int. Electronic Conf. on Synthetic Organic Chemistry (ECSOC-12), 2008, A-35.
[2] Mizyuk V. and Shibanov V.: Proceed. 13th Int. Electronic Conf. on Synthetic Organic Chemistry (ECSOC-13), 2011, E-3.
[3] Mizyuk V. and Shibanov V.: XXII Ukrain. Conf. Organicheskoi Khimii , Ukraine, Uzhgorod 2010, 308.
[4] Mizyuk V. and Shibanov V.:// Proceed. 13th Int. Electronic Conf. on Synthetic Organic Chemistry (ECSOC-13), 2009, G-22.
[5] Shibanov V.: Proceed. 14th Int. Electronic Conf. on Synthetic Organic Chemistry (ECSOC-14), 2010.
[6] Mizyuk V.: Proceed. 14th Int. Electronic Conf. on Synthetic Organic Chemistry (ECSOC-14) 2010.
[7] Mizyuk V. and Shybanov V.: Chem. & Chem. Techn., 2011, **5**, 259.
[8] www.aist.go.jp
[9] Aldrich/ACD Library of FT NMR Spectra (Pro) Data Base Window.

ВИВЧЕННЯ ВПЛИВУ ПРИРОДИ ЗАМІСНИКА R В ПОХІДНИХ ФЕНІЛСУЛЬФОНІВ PhSO₂R НА ХІМІЧНІ ЗСУВИ ПРОТОНІВ ФЕНІЛЬНОГО КІЛЬЦЯ В ЯМР ¹Н СПЕКТРАХ

Анотація. При поясненні особливостей ЯМР ¹Н спектрів фенілсульфонів загальної формули $C_6H_5SO_2R$ приведено аргументи на користь внутрішньо молекулярної дії через простір функційних груп, розташованих у фрагменті R, на величину хімічних зсувів d_i^H фенільних протонів.

Ключові слова: ЯМР ¹Н спектр, фенілсульфон, базовий спектральний параметр, диференційний спектральний параметр, «поріг», внутрішньо молекулярна взаємодія, простір.