

STUDY OF POLAR EFFECTS IN N-ARYLMETHANESULFONYLAMIDES

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IR spectra (in CS₂ and CH₃CN), PMR spectra (in (CD₃)₂SO) and mass spectra of 14 N-arylmethanesulfonylamides have been measured. The PMR signals and IR absorption bands have been ascribed and a fragmentation scheme suggested. The proton chemical shifts of NH and CH₃ groups, frequencies of stretching vibrations of N—H and S—O bonds and the fragmentation rate of molecular ion were correlated with the Hammett substituent constants and HMO electron densities.

In recent papers we described substituent effects in some aromatic systems having hydrogen bond¹⁻³. From the study of the dependence of PMR chemical shifts, frequencies of valence out-of-plane and deformation vibrations of the OH and NH groups bound by hydrogen bond on substituent constants of ring substituents we found that slope of these dependences was influenced by hydrogen bond, the direction of this influence being predictable.

The present study has been carried out with the aim of evaluation of the polar effects of substituents in N-arylmethanesulfonylamides, namely the influence on PMR chemical shifts of NH and CH₃ groups, on stretching vibrations of N—H and S—O bonds, and on the rate of fragmentation of molecular ion.

IR spectra of sulfonylamides were dealt with in a number of papers⁴⁻¹⁹; the substituent effects on $\nu(\text{NH})$ in sulfonylamides of the type $\text{X}^1\text{C}_6\text{H}_4\text{SO}_2\text{NHC}_6\text{H}_4\text{X}^2$ are described in paper⁷. IR spectra of sulfonylamides exhibit a number of characteristic bands due to valence and deformation vibrations of N—H, S—O, N—S, C—N and C—S bonds; for our study the absorption bands due to stretching vibrations of N—H and S—O bonds were significant being well observable in acetonitrile solutions.

In the branch of mass spectra, studies of pharmacologically active sulfonamides were published²⁰⁻²⁴. Whereas the substituent polar effects on PMR and IR spectral parameters were dealt with in a number of works, there are only few publications relating to mass spectrometry; the systems described therein are simple, e.g. benzophenones²⁵⁻²⁷, phenyl-*p*-toluenesulphonates²⁸, phenyl-*p*-toluylates²⁹, toluidines³⁰, acetophenones³¹, aryl esters³¹, and acetanilides³². With substituent constants they usually correlate the relative intensities of the peaks of mass spectra corresponding to individual fragments and molecular ion, i.e. the rate of decomposition of the molecular or other ions formed during the fragmentation process.

EXPERIMENTAL

The N-arylmethanesulfonylamides were prepared by known methods from the respective amines and methanesulfonyl chloride. Purity of the compounds was checked by melting points and PMR spectra. IR spectra were measured with the use of a UR-20 spectrophotometer (Zeiss, Jena) in acetonitrile and carbon disulphide solutions. PMR spectra were measured with the use of a 60 MHz spectrometer Varian A60 in hexadeuteriodimethyl sulphoxide using tetramethylsilane as internal standard. Mass spectra were measured with the use of an A.E.I. MS 902 spectrometer with direct inlet. Temperature of ionic source was 140°C and electron energy was 70 eV.

RESULTS AND DISCUSSION

PMR spectra of the compounds studied exhibited three groups of signals corresponding to the protons of CH₃ and NH groups and to the aromatic ring protons. The polar effects could be studied best with NH and CH₃ signals (Table I). High value of chemical shift of the NH protons indicates that the proton of this group is bound to dimethyl sulphoxide molecules by strong intermolecular hydrogen bond. Dependences of chemical shift of the NH and CH₃ protons on the substituents constants (Table I) have the following form:

$$\delta(\text{NH}) = 9.58 + 0.83\sigma^-, \quad r = 0.994, \quad s = 0.02 \text{ p.p.m.},$$

$$\delta(\text{CH}_3) = 2.93 + 0.19\sigma^-, \quad r = 0.988, \quad s = 0.02 \text{ p.p.m.},$$

$$\delta(\text{CH}_3) = 2.93 + 0.27\sigma, \quad r = 0.991, \quad s = 0.02 \text{ p.p.m.}$$

Cf. the dependence $\delta(\text{NH}_2) = 4.84 + 1.32\sigma^-$ for substituted anilines³³. The effect of substituents on $\delta(\text{NH})$ is about one third that of anilines. Similarly lower, compared to arylamines³³, is the influence of aryl group on chemical shift of the protons of NH group in the series phenyl, 2-naphthyl, 2-anthryl derivative, 1-naphthyl being out of this series. Surprisingly marked is the influence of substituents on chemical shift of the protons of CH₃ group. In the case of substituted toluenes³⁴ measured in non-aromatic solvents (tetrachloromethane, dioxane) the slope is $d\delta(\text{CH}_3)/d\sigma = 0.24 \text{ p.p.m.}$ A certain complication is caused here by interaction of toluene methyl group with the *para* position of another molecule, which leads to formation of weak associates in solution and, hence, to a dependence of chemical shifts of the CH₃-protons on solvent and concentration^{35,36}. Therefore, we have measured also the chemical shifts of the CH₃-protons of toluene and its 4-amino and 4-nitroderivatives in dimethyl sulphoxide for comparison. The respective $\delta(\text{CH}_3)$ values are 2.28, 2.44 and 2.10 p.p.m., the graphically estimated reaction constant being $d\delta(\text{CH}_3)/d\sigma = 0.24 \text{ p.p.m.}$ The reaction constant values 0.19 and 0.27 indicate that, in the case of N-arylmethanesulfonylamides, the transmission of inductive effect through NHSO₂ grouping is not the only factor. This high value of the reaction constant can be explained either by a marked primary or secondary substituent effect through

the field or by conjugation of the whole NHSO_2CH_3 chain with π -electron system of the aromatic ring. The former possibility is supported by the correlation $\delta(\text{CH}_3)$ vs σ being better than that of $\delta(\text{CH}_3)$ vs σ^- , the latter one is supported by the dependence of $\delta(\text{CH}_3)$ and $\delta(\text{NH})$ on the calculated electron density (q) at nitrogen resp. methyl carbon in the series phenyl, 2-naphthyl, 2-anthryl derivative and by relation between $\delta(\text{NH})$, q and σ^- in the case of our N-arylmethanesulfonylamides and arylamines³³.

IR spectra were most useful in the region of absorption bands of valence vibrations of N—H bonds ($\nu(\text{NH})$) which reflected the polar effects of substituents in contrast to frequency of symmetrical stretching vibration of SO_2 group which did not reflect the substituent effects. The dependences of $\nu(\text{NH})$ on substituent constants have the form given:

$$\nu(\text{NH}) = 3382 + 7.2\sigma^- \text{ (graphically; in CS}_2\text{)},$$

$$\nu(\text{NH}) = 3271 - 12.3\sigma^-, \quad r = 0.967, \quad s = 1.7 \text{ (in CH}_3\text{CN)}.$$

In the series phenyl, 2-naphthyl and 2-anthryl derivatives (in CH_3CN) the $\nu(\text{NH})$

TABLE I

Frequencies of Valence Vibrations of S—O and N—H Bonds, Chemical Shifts of Protons of NH and CH_3 Groups, and Relative Intensities Z of Substituted N-Arylmethanesulfonylamides

Substituent	$\nu(\text{SO}_2)_{\text{sym}}$	$\nu(\text{NH})_{\text{v}}$		$\delta(\text{CH}_3)$	$\delta(\text{NH})$	$\log Z^a$	$\sigma^- (\sigma)$
		CS_2^b	CH_3CN				
4-OCH ₃	1 160	<i>b</i>	3 270	2.85	9.28	0.858	-0.268
4-CH ₃	1 161	3 380	3 275	2.89	9.44	0.660	-0.170
3-CH ₃	1 159	3 381	3 273	2.92	9.56	0.500	-0.07
H	1 160	3 382	3 272	2.93	9.64	0.533	0.00 ^c
4-Cl	1 163	3 384	3 265	2.97	9.79	0.602	0.23
3-Cl	1 161	3 383	3 265	3.02	9.86	0.520	0.37
4-COCH ₃	1 159	—	3 262	3.08	10.23	—	0.83
4-CN	1 161	—	3 259	3.11	10.41	—	1.00
3-NO ₂	1 162	—	3 260	3.10	10.25	0.252	0.71
4-SO ₂ CH ₃	1 162	—	3 258	3.12	10.44	—	1.05
4-NO ₂	1 160	—	3 257	3.17	10.66	0.00	1.27
β -C ₁₀ H ₇	1 158	—	3 266	3.02	9.84	0.430	— ^d
α -C ₁₀ H ₇	1 159	—	3 269	2.98	9.54	0.540	— ^e
β -C ₁₄ H ₉	1 159	—	3 259	3.12	10.05	—	— ^f

^a $Z = (a + (a + 1))/M^+$; ^b value is missing in the cases where the derivative was not sufficiently soluble in CS_2 ; ^c electron density 1.360; ^d electron density 1.345; ^e electron density 1.310; ^f electron density 1.320.

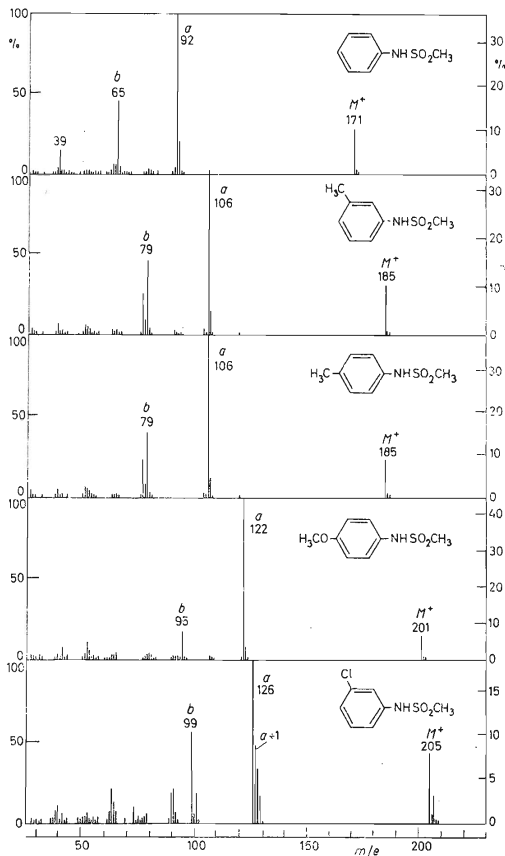


FIG. 1 a

Mass Spectra of the N-Arylmethanesulfonylamides Studied

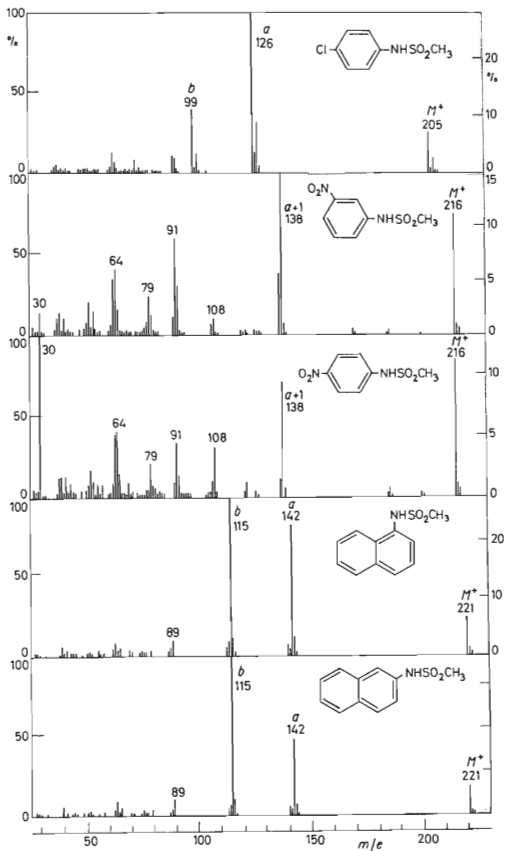


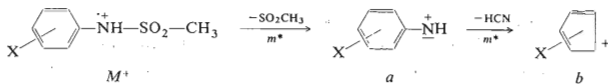
FIG. 1 b

Mass Spectra of the N-Arylmethanesulfonylamides Studied

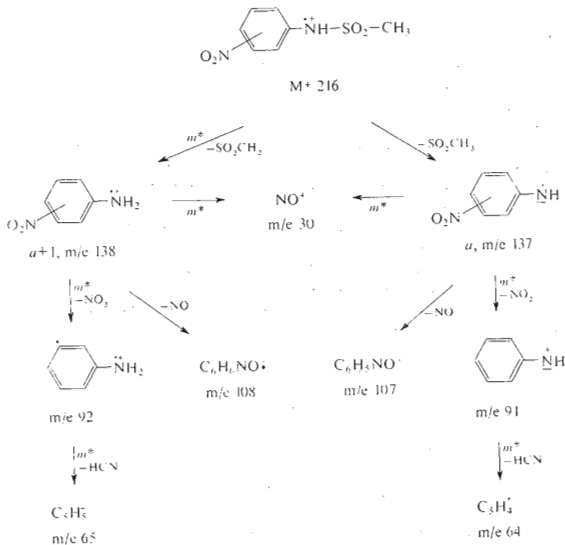
value decreases with decreasing electron density at nitrogen atom in the expected way, 1-naphthyl derivative being again out of the series. It can be seen from the both dependences of $\nu(\text{NH})$ vs σ^- , that the reaction constant $d\nu(\text{NH})/d\sigma^-$ changes its sign from positive to negative when going from CS_2 to CH_3CN solutions. This change is due to the intermolecular hydrogen bond formed between NH group and CH_3CN molecules. Formation of this hydrogen bond causes lowering of $\nu(\text{NH})$, this lowering being proportional to the strength of the hydrogen bond formed. Substituents influence the strength of this hydrogen bond and, hence, also $\nu(\text{NH})$ value according to their effect on the electron density at nitrogen, as it was the case with anilines and phenols³. It was surprising to find that $\nu(\text{SO}_2)_{\text{sym}}$ was independent of the nature of substituents; in the case of the sulfonylamides $\text{XC}_6\text{H}_4\text{SO}_2\text{NH}_2$ measured under the same conditions⁸ the slope was $d\nu(\text{SO}_2)_{\text{sym}}/d\sigma = 8.6 \text{ cm}^{-1}$. If the conjugation of the whole chain NHSO_2CH_3 with the aromatic π -electron system is adopted for interpretation of the results obtained, then the independence of $\nu(\text{SO}_2)_{\text{sym}}$ with respect to substituent and nature of aryl group confirms that the sulphur atom in the system aryl-N-S-C represents an inactive position quite in accordance with the model aryl-C-C-C used for calculation.

Mass spectra of the compounds studied are given in Fig. 1, the course of fragmentation is represented in Schemes 1 and 2. According to the Scheme 1 the molecular ion eliminates a neutral fragment SO_2CH_3 giving the ion which decomposes into HCN and ion *b*, as it is the case with anilines. Further fragmentation is rather inexpressive. Splitting off of a methyl from the molecular ion was not observed. In the case of 1- and 2-naphthyl derivatives the ion *b* eliminates $\text{CH}\equiv\text{CH}$, which is characteristic for condensed aromatic systems. In the spectra of the both methyl derivatives metastable ions were identified confirming splitting off of two hydrogen atoms from ions *m/e* 79 to give ions *m/e* 77. Chloro substituent at *meta* position causes a transfer of hydrogen from methyl to amino nitrogen, so that spectrum of this compound shows a slight peak *a* + 1 (*m/e* 127).

The fragmentation is most influenced by nitro group, see Scheme 2. Nitro group affects the transfer of hydrogen from methyl group to amino nitrogen so strongly that the peaks of ions *a* + 1 are substantially greater than those of ions *a*, the former being the base peak of the spectrum of 3-nitro derivative. Ions *a* + 1 resp. *a* eliminate neutral fragments NO and NO_2 from the substituent, and first then the splitting off of HCN occurs. Besides the fragmentation described in Scheme 2 the both nitro compounds eliminate O, NO and NO_2 from molecular ion. The ion having *m/e* 30, which forms the base peak in spectrum of 4-nitro derivative and 15% of the base peak in that of 3-nitro derivative, has the formula NO^+ (according to precise mass measurements) and is formed from ions *a* or *a* + 1 or the both. This statement cannot be described more explicitly, as the metastable ion *m* 6.5 found in the spectra can belong to both the ions. It is noteworthy that nitro group in *para* position gives a several times greater amount of the ions NO^+ than the same group in *meta* position.



SCHEME 1



SCHEME 2

This fact has not yet been mentioned in literature; we observed this phenomenon also with nitro derivatives of ethyl arylhydrazonocynoacetylcarbamates³⁷. We presume that the easier formation of NO^+ ion from *p*-nitro derivatives is due to stable quinone-imine structure of the neutral fragment being splitt off. This is confirmed also by an easier elimination of neutral fragment NO from molecular ion of *p*-nitro compound, where the ion formed will have a similar structure. As it can be seen from the analysis given, the fragmentation according to basic scheme is accompanied by further ones the nature and intensity of which is different for different substituted compounds, which complicates the study of substituent effects on the fragmentation

according to the basic scheme. The dependence of the ratio of peak intensities $Z = [a + (a + 1)]/M^+$ on the substituent constants has the following form: $\log Z = 0.63 - 0.53\sigma^-$. Thus electron-withdrawing substituents slow down the fragmentation of the molecular ion. In the series of aryl derivatives the fragmentation rate is similar to the dependences found in PMR and IR spectral data.

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