STUDIES ON ARYLHYDRAZONES OF ETHYL ARYLSULFONYLGLYOXYLATES

V. Substituted Arylsulfonylglyoxylic Acids with Heterocylic Residues

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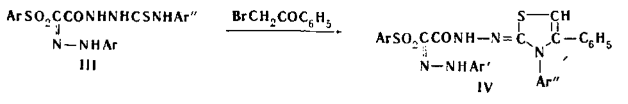
The reaction of arylhydrazones of 4-arylthiosemicarbazides of arylsulfonylglyoxylic acid with ω-bromoacetophenone has given arylhydrazones of N-(3-aryl-4-phenyl-2-thiazolinylidene)hydrazides of arylsulfonylglyoxylic acids. The reaction of ethyl p-toluenesulfonate with o-aminothiophenol and o-phenylenediamine in polyphosphoric acid has given 2-(p-tolylsulfonyl)methylbenzothiazole and 2-(p-tolylsulfonyl)methylbenzimidazole. From 2-(p-tolylsulfonyl)methylbenzothiazole, a styryl and the corresponding carbocyanine with a substituted indoline have been obtained. The considerable hypsochromic shift of the absorption maxima of the latter is explained by the influence of the voluminous electronegative group SO_2R in the position α to the heterocyclic nuclei.

In preceding papers [1,2] we have described the synthesis and properties of various derivatives of arylhydrazones of ethyl arylsulfonylglyoxylates (I) and arylhydrazones of arylsulfonylglyoxylic hydrazide (II) and its derivatives. The reaction of II with aryl isothiocyanates has given arylhydrazones of 4-arylthiosemicarbazides of arylsulfonylglyoxylic acids (III).

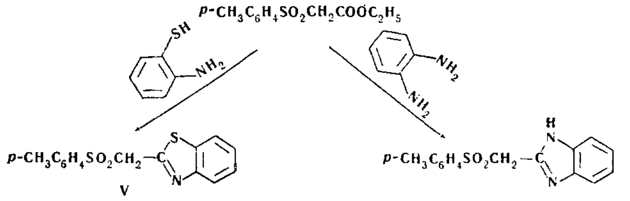
It was of interest to synthesize a series of heterocyclic compounds containing the arylsulfonyl group. For this purpose we have studied the compounds III synthesized previously [2], and also ethyl arylsulfonylacetates.

When III were boiled with ω-bromoacetophenone in ethanol, arylhydrazones of N-(3-aryl-4-phenyl-2-thiazolinylidene)hydrazides of arylsulfonylglyoxylic acids (IV) were obtained.



Compounds III and IV are given in Tables 1 and 2. They form yellow crystalline substances readily soluble in the majority of organic solvents and slightly soluble in ether and carbon tetrachloride. They are crystalized from ethanol.

When equimolar amounts of ethyl p-toluenesulfonate and o-aminothiophenol were heated in polyphosphoric acid, 2-(p-tolylsulfonyl)methylbenzothiazole (V) was obtained, and when the same ester was heated with o-phenylenediamine, 2-(p-tolylsulfonyl)methylbenzimidazole [3] was produced.



V

It is known that the mobility of the hydrogen atoms of the methyl group in nitrogen heterocycles leads to the situation that such heterocycles condense with aldehydes and ketones and undergo azo coupling and other condensations leading to cyanine dyes. The methyl group exhibits activity when it is in the α or γ position of the nucleus of the nitrogen heterocycle, i.e. when it is in σ-π conjugation with the —N=C group. The mobility of the hydrogen atoms of the methyl group rises considerably on passing from the base to a quaternary salt. The formation of the cationic charge increases the electrophilicity of the nitrogen atom and thereby favors the drawing off of electrons from the methyl group.

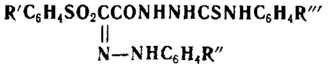
It appeared of interest to study the reaction of the methylene group in compound V, where it is in the position α to the benzothiazole nucleus and is adjacent to the sulfonyl group.

The reactions of a quaternary salt of V with p-dimethylaminobenzaldehyde (giving the corresponding styryl VII), with 2-formylmethylene-1,3,3-trimethylindolene (giving the carbocyanine IX) and with aryldiazonium chlorides were studied.

It is known that on passing from a styryl dye unsubstituted in the side chain to its α-methyl derivative, the long-wave absorption band is markedly displaced

Table 1

Arylhydrazones of 4-Arylthiosemicarbazides of Arylsulfonylglyoxylic Acids

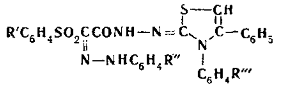


$$\underset{\displaystyle N{-}NHC_6H_4R''}{R'C_6H_4SO_2\overset{}{C}\!CONHNHCSNHC_6H_4R'''}$$

No.	R	R″	R	Mp, °C	Empirical formula	N, %		Yield, %
						found	calculated	
1	H	*p*-Cl	*p*-CH₃	193	$C_{22}H_{20}ClN_5O_3S_2$	14.08; 14.18	13.95	92
2	H	*p*-Cl	*p*-OC₂H₅	184	$C_{23}H_{22}ClN_5O_4S_2$	S 12.09; 12.13	12.04	77
3	H	*p*-Cl	*p*-Cl	192	$C_{21}H_{17}ClN_5O_3S_2$	13.39; 13.55	13.41	89
4	*p*-CH₃	H	H	178—179	$C_{22}H_{21}N_5O_4S_2$	15.68; 15.71	15.51	96

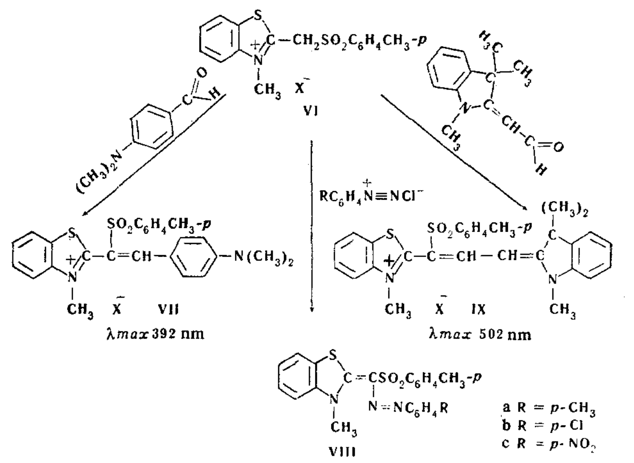
Table 2

Arylhydrazones of N-(3-Aryl-4-phenyl-2-thiazolinylidene)hydrazides of Arylsulfonylglyoxylic Acids



No.	R	R″	R	Mp, • C	Empirical formula	N, %		Yield, %
						found	calculated	
1	H	H	*p*-CH_3	195—196	$C_{30}H_{25}N_5O_3S_2$	12.39; 12.51	12.34	68
2	H	H	*p*-Br	189—190	$C_{29}H_{23}BrN_5O_3S_2$	10.76; 10.99	11.07	87
3	H	*p*-Cl	*p*-CH_3	223—225	$C_{30}H_{24}ClN_5O_3S_2$	11.25; 11.42	11.63	57
4	H	*p*-Cl	*p*-Cl	216	$C_{29}H_{21}Cl_2N_5O_3S_2$	11.34; 11.45	11.25	85
5	H	*p*-Cl	*p*-OC_2H_5	228—229	$C_{31}H_{26}ClN_5O_4S_2$	10.96; 11.07	11.08	94

in the direction of the violet part of the spectrum. As A. I. Kiprianova and F. A. Mikhailenko [4] have shown,



the hypsochromic shift is connected with a disturbance of the coplanarity of the molecule. The benzothiazole group rotates about the single (predominantly single) bond and consequently the conjugation and the color are weakened.

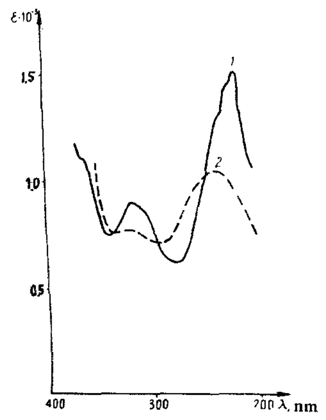


Fig. 1. Absorption curves of ethanolic solutions in UV, c 5 • 10^{-5} mole/*l*: 1) phenylhydrazones of the N-(p-bromo phenylamidocarbothio) hydrazide of phenylsulfonylglyoxylic acid; 2) phenylhydrazone of the N-[3′-(p-bromophenyl)-4′-phenyl-2-thiazolinylidene]hydrazide of phenylsulfonylglyoxylic acid.

In the styryl VII, there is an SO_2R group in the α position which has a greater volume than the CH_3 group and causes a greater disturbance to the coplanarity and a considerable displacement of the maximum to the short-wave region (by 133 nm) while giving a lower extinction than that of the styryl dye unsubstituted in the chain. In this case, in addition to what has been discussed above, the electronegative nature of the arylsulfonyl group has a strong influence on the hypsochromic shift.

On considering the absorption maximum of the carbocyanine IX, it can be seen that the large hypsochromic shift is connected with the presence in the α position of the benzothiazole nucleus of the voluminous and electronegative RSO_2 group.

Kiprianov and Pilyugin [5] in 1937, and Brooker later [6], established that a disturbance of the symmetry and equivalence of the structures in cyanine dyes led to a weakening of the color. The carbocyanine IX that we have synthesized has an absorption maximum at 502 nm (the corresponding unsubstituted, unsymmetrical carbocyanine has λ_{max} = 542 nm) [7]. This pronounced hypsochromic shift is caused not only by a disturbance in the symmetry and equivalence of the structures but also by the presence in the α position of the benzothiazole nucleus of the electronegative RSO_2 group.

The reaction of the quaternary salt VI with aryldiazonium chlorides has given arylazo derivatives of 2-(p-tolylsulfonylmethylene)-N-methylbenzothiazole (VIII).

The absorption curves of the compounds obtained are given in Figs. 1 and 2.

As can be seen from Fig. 2, compound VIIIc is more deeply colored than compound VIIIa. This is in agreement with literature data, since the nitro group is an auxochrome capable of giving rise to ionic charges [8].

EXPERIMENTAL

p-Chlorophenylhydrazone of the 4-(p-chlorophenyl)thiosemicarbazide of phenylsulfonylglyoxylic acid (preparation 3, Table 1). A mixture of 0.18 g (0.0005 mole) of the p-chlorophenylhydrazone of phenylsulfonylglyoxylic hydrazide, 0.08 g (0.0005 mole) of p-chlorophenylisothiocyanate, and 2 ml of benzene was boiled in the water bath under reflux for 30 min. After cooling, the precipitate was filtered off, washed with benzene and dried in the air. Yield 0.23 g (89%). It was crystallized from ethanol. Mp 192° C.

The compounds given in Table 1 were obtained under similar conditions.

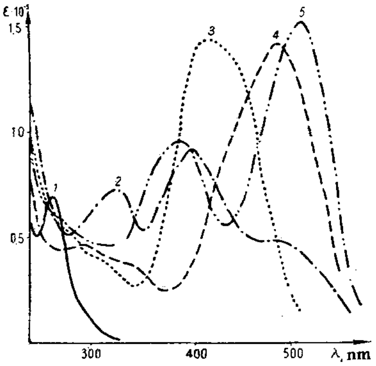


Fig. 2. Absorption curves of ethanolic solutions in the UV and visible region, c $5 \cdot 10^{-5}$ mole/l: 1) 2-(p-tolylsulfonyl)-methylbenzothiazole; 2) 2-[p-dimethylamino-β-(p-tolylsulfonyl)styryl]benzothiazole methiodide; 3) 2-[p-tolueneazo(p-tolylsulfonyl)methylene]-N-methylbenzothiazole; 4) 2-[p-nitrobenzeneazo(p-toluenesulfonyl)methylene]-N-methylbenzothiazole; 5) [3-methylbenzothiazolyl-(2)]-[1,3,3-trimethylindolene-(2)]-[8-(p-tolylsulfonyl)]trimethinecyanine iodide.

p-Chlorophenylhydrazone of the N-[3-(p-chlorophenyl)-4-phenyl-2-thiazolinylidene]hydrazide of phenylsulfonylglyoxylic acid (preparation 4, Table 2). To 0.1 g (0.00002 mole) of the p-chlorophenylhydrazone of the 4-(p-chlorophenyl)thiosemicarbazide of phenylsulfonylglyoxylic acid were added 0.04 g of ω-bromoacetophenone and 2 ml of ethanol, and the mixture was boiled under reflux for 1 hr. The slightly yellowish precipitate that deposited was crystallized from ethanol. Yield 0.1 g (85%), mp 216° C. The compounds given in Table 2 were obtained under similar conditions.

2-(p-Tolylsulfonyl)methylbenzothiazole (V). A mixture of 9.7 g (0.04 mole) of ethyl p-toluenesulfonylacetate, 5 g (0.04 mole) of o-aminophenol, and the polyphosphoric acid obtained from 21 g of orthophosphoric acid and 20 g of phosphorus pentoxide was stirred in a current of nitrogen at 160°-165° C for 2 1/2 hr and then at 210° C for 1 1/2 hr. It gradually darkened. After the end of the heating, it was cooled to 90° C and was then slowly poured into 500 ml of water with vigorous stirring. The solidifying oil was triturated, filtered off, washed, and suspended in 300 ml of 10% aqueous sodium carbonate. The brown precipitate was filtered off, washed carefully with water, and dried in the air. Yield 10 g (84%). The product was crystallized from ethanol with the addition of carbon. Faintly grayish crystals. Yield 7.3 g (60%), mp 173° C. Found, %: S 20.69; 20.96. Calculated for $C_{15}H_{13}NO_2S_2$, %: S 21.14.

2-(p-Tolylsulfonyl)methylbenzimidazole was obtained similarly. Mp 209°-210° C. Found, %: N 10.31; 10.41; S 11.40; 11.42. Calculated for $C_{14}H_{12}N_2O_2S$, %: N 10.29; S 11.77.

2-(p-Tolylsulfonyl)methylbenzothiazole methyl methosulfate (VI). 2.5 g of dimethyl sulfate was added to 5.7 g (0.02 mole) of 2-(p-toluenesulfonyl)methylbenzothiazole. The reaction mixture was heated in the oil bath. The mixture melted and darkened slightly at 130° C. It was heated at this temperature for 30 min. After cooling, the mixture solidified. The solid product was triturated with ether, filtered, and washed with benzene and then with ether. It was dried in the air. Yield 8.4 g. It was crystallized from ethanol. Yield 5.9 g (73%). Light gray crystals. Mp 188°-189° C (decomp.). Found, %: S 22.22, 22.32. Calculated for $C_{17}H_{19}NO_6S_3$, %: S 22.39.

2-[p-Dimethylamino-β-(p-toluenesulfonyl)styryl]benzothiazole methiodide (VII). A mixture of 0.2 g (0.0005 mole) of 2-(p-toluenesulfonyl)methylbenzothiazole methyl methosulfate and 0.07 g (0.0005 mole) of p-dimethylaminobenzaldehyde in 2 ml of acetic anhydride was heated in the boiling water bath for 1 hr. After cooling, the methyl methosulfate of 2-[p-dimethylamino-β-(p-toluenesulfonyl)-styryl]benzothiazole was precipitated with ether. Yield 0.21 g (81%).

The methyl methosulfate of 2-[p-dimethylamino-β-(p-toluenesulfonyl)styryl]benzothiazole was dissolved in ethanol and converted by the addition of potassium iodide into the corresponding methiodide. It was crystallized from ethanol. Mp 152°-153° C (decomp.). Found, %: S 11.10; 11.16. Calculated for $C_{25}H_{25}IN_2O_2S_2$, %: S 11.12.

2-[p-Tolylazo(p-tolylsulfonyl)methylene]-N-methylbenzothiazole (VIIIa). A solution of 0.2 g (0.0005 mole) of the methyl methosulfate of 2-(p-tolylsulfonyl)methylbenzothiazole in 20 ml of ethanol was treated with 5 ml of saturated aqueous sodium acetate, and then, with constant stirring, a solution of p-toluenediazonium chloride obtained from 0.06 g of p-toluidine, 0.035 g of sodium nitrite, and 2 ml of 15% hydrochloric acid was slowly added at 0°-2° C. The reaction mixture was kept in ice-water for 2 hr, and the yellow precipitate that had deposited was filtered off, washed with water, and dried in the air. Yield 0.2 g (95%). It was crystallized from a mixture of ethanol and nitromethane (2:1). Yellow elongated needles. Mp 198°-200° C. Found, %: S 14.81; 14.88. Calculated for $C_{23}H_{21}N_3O_2S_2$, %: S 14.72.

Compounds VIIIb and VIIIc were obtained under similar conditions. The yields of the products were quantitative. The melting point of VIIIb was 214°-215° C. Found, %: S 13.97; 14.03. Calculated for $C_{22}H_{18}ClN_3O_2S_2$, %: S 14.06.

The melting point of VIIIc was 233°-234° C. Found, %: S 13.60; 13.60. Calculated for $C_{22}H_{18}N_4O_4S_2$, %: S 13.75.

[3-Methylbenzothiazolyl-(2)]-[1,3,3-trimethylindolenin-(2)]-[8-(p-tolylsulfonyl)]trimethinecyanine iodide (IX). A mixture of 0.43 g (0.001 mole) of the methyl methosulfate of 2-(p-tolylsulfonyl) methylbenzothiazole, 0.2 g (0.001 mole) of 2-formylmethylene-1,3,3-trimethylindoline, and 4.5 ml of acetic anhydride was heated in the oil bath at 150° C for 20 min. After cooling, about half the acetic anhydride was distilled off in vacuum and the methosulfate was precipitated with ether. An oil deposited which solidified on trituration in ether. The resulting powdery product was dissolved in 10 ml of ethanol and a hot solution of 0.7 g of KI in 10 ml of aqueous ethanol was added. Red crystals deposited. Yield 0.58 g (92%). The substance was crystallized from ethanol. Mp 183° C (decomp.). Found, %: S 10.11; 10.17. Calculated for $C_{29}H_{29}IN_2O_2S_2$, %: S 10.20.

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