MESOIONIC COMPOUNDS WITH A BRIDGE NITROGEN ATOM.
19.* THIAZOLO[3,2-a]QUINOXALINIUM OXIDES

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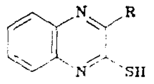
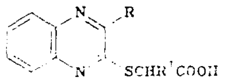
(2-Quinoxalylthio)acetic acids have been found to cyclize on treatment with acetic anhydride to give the mesoionic thiazolo[3,2-a]quinoxalinium oxides. Some reactions of these compounds have been studied, and the relationship of the color of the compounds to their chemical structure examined.

There has been ever-increasing interest in recent times in mesoionic heterocyclic compounds, which display high and frequently specific reactivities. For example, it has been found that (2-pyridylthio)- and (2-quinolylthio)acetic acids readily afford a variety of thiazolopyridinium and thiazoloquinolinium oxides, depending on the cyclization conditions [2, 3]. It is significant that mesoionic compounds can be used to obtain novel types of polymethine dyes [2, 4].

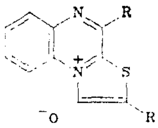
In order to examine the relationships between the colors and reactivities of mesoionic condensed heterocyclic compounds with a nodal nitrogen atom and their chemical structure, it was of interest to synthesize some new thiazoloazinium oxides and examine their reactions. With this in view, we used the 2-mercaptoquinoxalines (Ia-c) to obtain the (3-R-2-quinoxalylthio)acetic (II) and -phenylacetic (III) acids.



Ia-c



IIa-c,IIIa-c



IVa-c,Va-c,VI, VII

a $R=H$, b $R=CH_3$, c $R=C_6H_5$, II, IV $R^1=H$, III, V $R^1=C_6H_5$, VI $R^1=COCF_3$, VII $R^1=N=N-C_6H_4NO_2$

Acids (II) and (III) were found to behave differently toward acetic anhydride. For example, while the phenyl-substituted derivatives on heating with acetic anhydride gave, like (2-quinolylthio)acetic acid [5], colored, readily crystallizable new compounds, the acids (IIa-c) failed to give isolable pure reaction products. However, cyclization with a mixture of acetic anhydride and pyridine, as in [6], gave colored compounds, although these were of low stability. The structures of the products were established by PMR spectroscopy. Comparison of the spectra of the starting acids (II) and (III) (Table 1) with those of their cyclization products (Table 2) shows that the spectra of the latter no longer contain signals for the aliphatic protons of the hetarylthioacetic acids, but new signals are present which are characteristic of condensed thiazoloazinium oxides [5]. The signal appearing at lowest field is that for the proton in position 9. The shift of this signal to lower field is due to the influence of the lone pairs of electrons of the adjacent oxygen atom. In the cyclization products of the acids (IIa-c), the aromatic proton signals appearing at highest field are those for the 2-proton, as a result of the electron-donor effect of the oxide group. These observations enable the thiazolo[3,2-a]quinoxalinium 1-oxide structure to be assigned to the products isolated, (IVa-c) and (Va-c). It is obvious that on heating the acids (IIa-c) in acetic anhydride the initially formed oxides (IV), in consequence of their structure and the effects of the acetic acid liberated, undergo further deep-seated changes.

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*For Communication 18, see [1].

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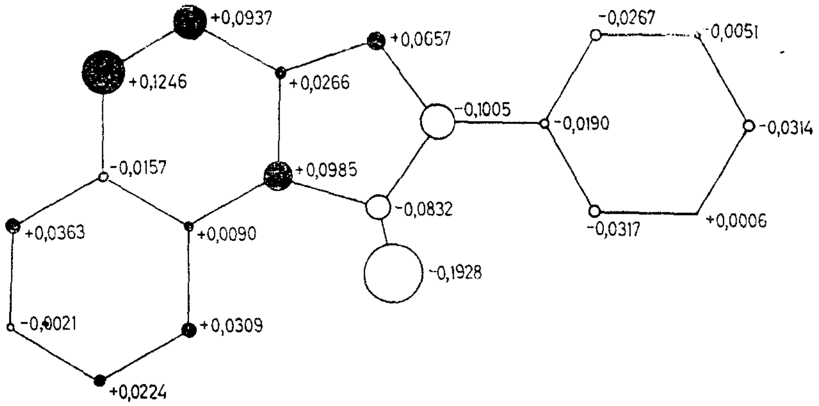

Fig. 1. Diagram of the redistribution of π-electron density at the atoms of the oxide (Va) molecule on passing to the first excited state.

TABLE 1. PMR Spectra of Acids (IIa-c) and (IIIa-c) in $CDCl_3$

Compound	Chemical shift, ppm		
	S—CHR^1	R	Ar—H
IIa	4,07	8,74	7,65 . . . 8,15
IIb	4,08	2,77	7,6 . . . 7,8; 7,8 . . . 8,15
IIc	3,98	*	7,2 . . . 8,5
IIIa	5,72	8,64	7,2 . . . 8,1
IIIb	5,64	2,68	7,3 . . . 8,1
IIIc	5,56	*	7,2 . . . 8,1

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*This signal coincides with the aromatic proton multiplet.

TABLE 2. PMR Spectra of Compounds (IVa-c), (Va-c), and VI

Compound	Solvent	Chemical shift, ppm			
		R	R^1	9-H*	Ar—H
IVa	C_5D_5N	9,09	6,29	10,53	7,65 (2H); 8,16 (1H)
IV	C_5D_5N	2,57	6,19	10,60	7,6 . . . 7,7 (2H); 8,13 (1H)
IV	C_5D_5N	**	6,35	10,66	7,62 (3H); 7,68 (2H); 8,12 (2H); 8,32 (1H)
Va	$CDCl_3$	8,83	**	10,25	7,2 . . . 8,2
V	$CDCl_3$	2,77	**	10,21	7,2 . . . 8,1
V	$CDCl_3$	**	**	10,35	7,2 . . . 8,2
VI	$CDCl_3$	9,11	—	9,99	7,92 (2H); 8,27 (1H)

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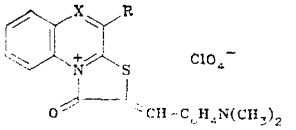
*Doublet, J = 9 Hz.

**This signal coincides with the aromatic proton multiplet.

It is important to note that until recently only a single example of a compound of this type (a mesoionic thiazolopyrimidinium oxide unsubstituted in the 2-position) has been reported, and its structure unambiguously proved [7].

The structures proposed for these compounds are supported by their chemical behavior. For example, the oxides (IV) readily react with electrophiles to give the 2-substituted derivatives (VI-VIII).



VIII, IX

VIII X=N; IX X=CH

TABLE 3. Properties of Compounds Obtained

Compound	Empirical formula	mp, °C	λ, nm (log ε)	Yield, %
IIa	$C_{10}H_8N_2O_2S$	218...219	—	95
IIb	$C_{11}H_{10}N_2O_2S$	167...168	—	98
IIc	$C_{16}H_{12}N_2O_2S$	152...153	—	98
IIIa	$C_{16}H_{12}N_2O_2S$	105...106	—	78
IIIb	$C_{17}H_{14}N_2O_2S$	176...177	—	87
IIIc	$C_{22}H_{16}N_2O_2S$	187...188	—	95
IVa	$C_{10}H_6N_2OS$	255...256	475 (4,14)	63
IVb	$C_{11}H_8N_2OS$	304...305	470 (4,09)	30
IVc	$C_{16}H_{10}N_2OS$	>300	477 (3,97)	62
Va	$C_{16}H_{10}N_2OS$	244...245	539 (4,39)	67
Vb	$C_{17}H_{12}N_2OS$	224...225	528 (4,32)	79
Vc	$C_{22}H_{14}N_2OS$	260...261	539 (4,42)	78
VI	$C_{12}H_5F_3N_2O_2S$	257...258	474 (4,55)	60
VII	$C_{16}H_9N_5O_3S$	282...283	546 (4,54)	29
VIII	$C_{19}H_{16}ClN_3O_5S$	>350	438 (4,27), 538 (4,18), 720 (4,73)	47

The thiazoloquinoxalinium oxides obtained were quite deeply colored compounds (Table 3). The long-wavelength absorption maxima lay in the same spectral region as with many polymethine dyes, the color being largely determined by the substituent in the 2-position, and introduction of electron-donor substituents resulting in a bathochromic shift of the absorption maximum.

Comparison of the spectral characteristics of the thiazoloquinoxalinium oxides with those of the corresponding thiazoloquinolinium oxides [3, 4, 8] shows that replacement of a methine group in the thiazoloquinoline nucleus by the more electronegative nitrogen atom results in a bathochromic shift in the absorption maximum. In the case of (IVa) and (Va) this shift amounts to 12 and 25 nm, respectively. This effect of aza-substitution is in qualitative agreement with the results of a quantum chemical analysis of the coloration of mesoionic compounds [8]. When the thiazoloquinolinium molecule is raised to its first excited state, transfer of electron density takes place from the oxygen atom predominantly to the 6-carbon atom. Naturally, replacement of this methine group by nitrogen will stabilize the excited state of the molecule and, consequently, give rise to a bathochromic shift. In the thiazoloquinoxalinium oxide molecule (IV) (Fig. 1), also, transfer of electron density is seen to take place from the oxygen atom and carbons $C_{(1)}$ and $C_{(2)}$ to the quinoxalinium moiety of the molecule. Consequently, electron-donor substituents in the 2-position, which facilitate this electron shift, will give rise to a deepening in color. Conversely, electron-acceptor substituents in this position will give rise to a hypsochromic effect, and this has been found experimentally. If, however, electron-donor substituents such as the methyl group are introduced into the azine moiety of the molecule, a bathochromic shift would be expected and is in fact observed.

In the case of the benzylidene derivative (VIII), the bathochromic shift is much greater (102 nm) than with the corresponding thiazoloquinolinium oxide (IX). The reason for such a large difference in the effects of aza-substitution in the original heterocycles and dyes therefrom is a different one. In fact, interaction between electronic transitions in the polymethine chain and the fundamental chromophore of the hetero-residue has been observed in dyes obtained from mesoionic thiazoloazinium oxides [9-11].

According to theory [12], the interaction of chromophores, manifested as a separation of the absorption maxima of the parent dyes, is greater, the closer are the energies of the electron transitions responsible for the long-wavelength absorption. It may therefore be assumed that the introduction of a nitrogen atom into (IX) to give the quinoxaline (VIII) will, in consequence of the stronger absorption of the hetero-residue, result in an increase in the degree of separation of the bands (cyanine and heterocyclic, respectively), i.e., a greater bathochromic shift of the maximum.

It has thus been found that thiazoloquinoxalinium oxides show promise for the development of novelly, highly colored dyes with a short polymethine chain.

EXPERIMENTAL

UV-visible spectra were obtained on an SF-8 spectrophotometer in acetonitrile. PMR spectra were recorded on WP-100SY (100 MHz) and WP-200 (200 MHz) spectrometers, internal standard TMS. Quantum chemical calculations were carried out in PPP approximation, the parameters used in the calculations being obtained from [8]. The elemental analyses of the compounds (II-VII) for N and S were in agreement with the calculated values.

(3-R-2-Quinoxalylthio)acetic Acids (IIa-c). To a solution of 4 mmoles of the 2-mercaptoquinoxaline (Ia-c) in 15 ml of 2% sodium hydroxide solution was added 0.38 g (4 mmoles) of monochloroacetic acid, and the mixture boiled for 1 h. The solution was filtered hot, cooled, and neutralized with acetic acid. The product was filtered off, washed with water, and crystallized from water. The properties of the compounds obtained are given in Table 3.

(3-R-2-Quinoxalylthio)phenylacetic Acids (IIIa-c). A solution of 10 mmoles of the 2-mercaptoquinoxaline and 2.15 g (10 mmoles) of bromophenylacetic acid in 16 ml of 5% sodium hydroxide solution was boiled for 1 h. The solution was filtered hot, cooled, and neutralized with acetic acid. The solid was filtered off, washed with water, and crystallized from aqueous alcohol.

4-R-Thiazolo[3,2-a]quinoxalinium 1-Oxides (IVa-c). To a solution of 1.5 mmoles of the acid (IIa-c) in 3 ml of pyridine was added 2 ml of acetic anhydride, and the mixture kept for 2 h at 0°C. The solid which separated was filtered off and washed with ether.

4-R-2-Phenylthiazolo[3,2-a]quinoxalinium 1-Oxides (Va-c). A solution of 5 mmoles of the phenylacetic acid (IIIa-c) in 5 ml of acetic anhydride was heated to the boil. The product which separated on cooling was filtered off, washed with ether, and crystallized from acetic anhydride.

2-Trifluoroacetylthiazolo[3,2-a]quinoxalinium 1-Oxide (VIa). To a suspension of 1.1. g (5 mmoles) of the acid (IIa) in 10 ml of acetonitrile was added 2 ml of trifluoroacetic anhydride, and the mixture kept in the refrigerator for 1 h. The solid was filtered off, washed with acetonitrile, and crystallized from acetic anhydride; yield 0.9 g.

2-(4-Nitrophenylazo)thiazolo[3,2-a]quinoxalinium 1-Oxide (VIIa). To a solution of 0.22 g (1 mmole) of the acid (IIa) in 3 ml of pyridine was added 2 ml of acetic anhydride, followed by 0.23 g (1 mmole) of 4-nitrophenyldiazonium tetrafluoroborate in small portions. The mixture was kept in the refrigerator for 3 h, and the dye then filtered off, washed with acetic anhydride and ether, and crystallized from acetic anhydride, yield 0.1 g.

2-(4-Dimethylaminobenzylidene)-1-oxo-1,2-dihydrothiazolo[3,2-a]quinoxalinium Perchlorate (VIII). To a hot solution of 0.3 g (2 mmoles) of p-dimethylaminobenzaldehyde in 10 ml of acetic anhydride was added in small portions a solution of 0.22 g (1 mmole) of the acid (IIa), and the mixture heated to the boil. After cooling, 0.2 ml (1 mmole) of 85% perchloric acid was added cautiously. The product was filtered off, washed with alcohol and ether, and crystallized from acetic anhydride, yield 0.2 g.

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