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SYNTHESIS AND ISOMERISM OF AZINES BASED ON 3-METHYL-2-BENZOTHIAZOLINONE HYDRAZONE

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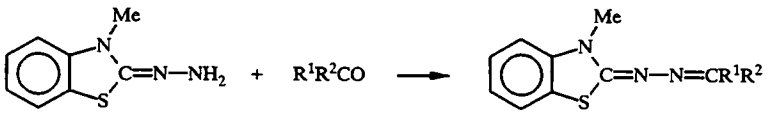
It was found by ESR spectroscopy that asymmetric azines obtained from 3-methyl-2-benzothiazolinone hydrazone can exist in solutions in the form of a mixture of syn and anti isomers, depending on the structure of the carbonyl compound introduced into the condensation reaction.

E,Z-Geometric syn and anti isomerism of azines of aliphataic and aromatic carbonyl compounds has been treated in several papers [1-4]. Asymmetric azines based on 3-methyl-2-benzothiazolinone hydrazone were prepared for the purpose of further synthesis of cyanine dyes [5], but the literature lacks any data on their structure. In order to fill the existing gap in this area, we expanded the number of asymmetric azines based on 3-methyl-3-benzothiazolinone hydrazone and studied the structure of the azines obtained.

Azines I-XIII were isolated in the reaction of condensation of 3-methyl-2-benzothiazolinone hydrazone with aldehydes and ketones containing different functional groups.

Scheme 1

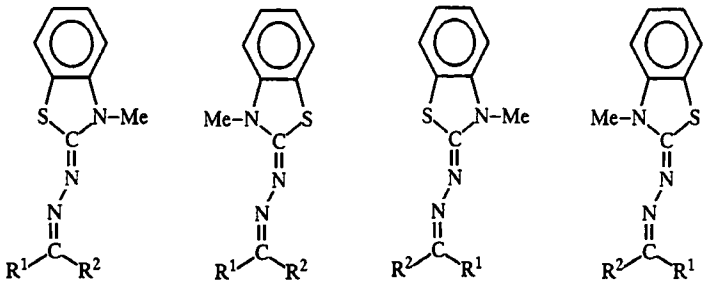


I–XIII

I—IX R^1 = H; X—XII R^1 = CH_3; I R^2 = 2,3-$(CH_3O)_2C_6H_3$; II R^2 = 4-HOC_6H_4; III R^2 = 2-HOC_6H_4; IV R^2 = 3,4-(OCH_2O)-C_6H_3; V R^2 = 3,4-$(HO)_2C_6H_3$; VI R^2 = 4-$CH_3OC_6H_4$; VII R^2 = 3-$NO_2C_6H_4$; VIII R^2 = 4-ClC_6H_4; IX R^2 = 2-BrC_6H_4; X R^2 = CH_3; XI R^2 = C_6H_5; XII R^2 = 3,4-$(OCH_2O)C_6H_3CH_2$; XIII R^1 = R^2 = C_3H_7

For asymmetric azines, the existence of 12 stereoisomeric forms is theoretically possible [6], but the presence of a large dipole moment in azines [1, 2] and the data of ESR spectra [3] attest to the real existence of only the s-trans-isomeric forms.

Scheme 2



syn-anti anti-anti syn-syn anti-syn

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TABLE 1. ESR Spectra of Azines I-XIII

Compound	Solvent	Chemical shifts, δ, ppm			syn-Isomer, %
		CH_3N, s	=CH, s	other signals	
I	(DMF)-D_7	3,49 (syn)	8,40	3,73 (d, CH_3O, 64)	100
	(DMSO)-D_6	3,47 (syn)	8,42	3,73 (d, CH_3O, 64)	100
II	(DMF)-D_7	3,51 (syn)	8,24	—	100
	(DMSO)-D_6	3,47 (syn)	8,18	—	100
III	(DMF)-D_7	3,44 (syn) 3,54 (anti)	8,42	11,01 (s, OH, 1H)	50
	CD_3COCD_3	3,44 (syn) 3,51 (anti)	8,29	10,93 (s, OH, 1H)	50
	CD_3COCD_3*	3,60 (syn)	8,40	—	100
IV	(DMF)-D_7	3,51 (syn)	8,22	4,93 (s, OCH_2O, 2H)	100
	C_6D_6	2,64 (syn)	8,16	6,01 (s, OCH_2O, 2H)	100
V	(DMF)-D_7	3,53 (syn)	8,15	—	100
	CD_3COCD_3	3,47 (syn)	7,93	—	100
VI	(DMF)-D_7	3,44 (syn), 3,53 (anti)	8,11	3,53 (s, CH_3O, 3H)	80
	(DMSO)-D_6	3,42 (syn) 3,51 (anti)	8,20	3,71 (s, CH_3O, 3H)	76
	C_6D_6	2,87 (syn) 2,93 (anti)	8,44	3,21 (d, J = 6 Hz, CH_3O, 3H)	25
	CD_3COCD_3	3,51 (syn), 3,62 (anti)	8,29	3,80 (s, CH_3O, 3H)	72
	CD_3COCD_3*	3,64 (syn)	8,31	3,82 (s, CH_3O, 3H)	100
VII	(DMSO)-D_6	3,47 (syn) 3,56 (anti)	8,31	—	46
	(DMF)-D_7	3,51 (syn) 3,62 (anti)	8,24	—	47
	(DMF)-D_7*	3,51 (syn)	8,33	—	100
VIII	(DMF)-D_7	3,56 (syn) 3,64 (anti)	8,34	—	70
	C_6D_6	2,78 (syn) 2,89 (anti)	8,16	—	28
	CD_3COCD_3	3,42 (syn) 3,51 (anti)	8,16	—	71
	CD_3COCD_3*	3,91 (syn)	8,47	—	100
IX	(DMF)-D_7	3,58 (syn)	8,36	—	100
	C_6D_6	2,60 (syn)	8,82	—	100
	CCl_4	3,40 (syn) 3,49 (anti)		—	17
X	(DMF)-D_7	3,47 (syn)	—	1.89 (s, CH_3C, 3H, syn), 1.95 (s, CH_3C, 3H, anti)	100
	C_6D_6	2,91 (syn)	—	1,80 (s, CH_3C, 3H, syn), 1,91 (s, CH_3C, 3H, CH_3, anti)	100
XI	(DMF)-D_7	3,49 (syn)	—	2,58 (s, CH_3C, 3H)	100
	CD_3COCD_3	3,47 (syn)	—	2,33 (s, CH_3C, 3H)	100
	CCl_4	3,33 (syn)	—	2,22 (s, CH_3C, 3H)	100
XII	(DMF)-D_7	3,40 (syn)		1,84 (s, CH_3C, 3H), 5,78 (s, OCH_2O, 2H)	100
XIII	(DMSO)-D_6	3,56 (syn)		0,78 (m CH_3C, 6H, syn, anti)	100

*The ESR spectrum was recorded after addition of trifluoroacetic acid to the solution.

We established with ESR spectra that the azines I, II, IV, V, X-XIII in the solutions exist in a single isomeric form, and the remaining azines exist in a mixture of two isomeric forms, since the proton signals of the methyl of the benzothiazole ring are doubled. Thus, the signal of the NCH_3 group of azine II is expressed as a singlet with a chemical shift of 3.51 ppm, and the corresponding signal of azine VI is expressed as a doublet, 3.44 ppm and 3.53 ppm. The chemical shift of the protons of the methyl group found in the syn isomers is smaller than in the anti isomers [4].

It is evident from Table 1 that the azines III, VI-IX exist in a mixture of isomeric forms. The ratio of the syn and anti isomers depends on the solvent polarity: in the polar solvents (DMF, DMSO, acetone), the syn isomer predominates, and in the nonpolar ones (C_6H_6, CCl_4), the anti isomer.

TABLE 2. Properties of Azines I-XII

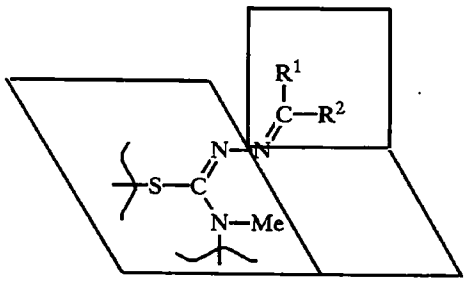
Compound	Found, %			Empirical formula	Calculated, %			mp, °C	Yield, %
	C	H	S		C	H	S		
I	62,22	5,31	9,52	$C_{17}H_{17}N_3O_2S$	62,38	5,22	9,77	130...132	73,5
II	63,68	4,78	11,19	$C_{15}H_{13}N_3OS$	63,79	4,64	11,33	231...232	72,1
III	63,61	4,70	11,15	$C_{15}H_{13}N_3OS$	63,79	4,64	11,33	87...88	87,4
IV	61,89	4,35	10,11	$C_{16}H_{13}N_3O_2S$	61,70	4,21	10,27	150...152	92,5
V	60,31	4,49	10,39	$C_{15}H_{13}N_3O_2S$	60,19	4,37	10,69	220...221	93,3
VI	64,23	5,20	10,59	$C_{16}H_{15}N_3OS$	64,64	5,07	10,76	102...104	86,5
VII	57,51	3,74	10,40	$C_{15}H_{12}N_4O_2S$	57,68	3,84	10,24	185...186	60,2
VIII	61,42	4,29	10,70	$C_{15}H_{12}ClN_3S$	61,53	4,13	10,93	146...148	85,6
IX	52,15	3,61	9,06	$C_{15}H_{12}BrN_3S$	52,00	3,49	9,24	145...146	51,9
X	57,80	6,42	15,25	$C_{10}H_{13}N_3S$	57,96	6,32	15,44	92...93	82,2
XI	68,22	5,27	11,11	$C_{16}H_{15}N_3S$	68,31	5,36	11,37	99...101	47,6
XII	63,62	5,10	9,25	$C_{18}H_{17}N_3O_2S$	63,71	5,03	9,43	116...118	65,7
XIII	63,99	8,16	11,97	$C_{14}H_{21}N_3S$	63,84	8,05	12,15	39...41	64,1

Substitution of a nonpolar solvent (C_6H_6) for a polar one (DMF) results in an appreciable displacement of the proton signal of NCH_3 groups of both the syn and anti isomers to a stronger field ($\Delta\delta$ ~0.7-0.8 ppm).

Quantum-chemical calculations for symmetric azines indicate the unfolding of the azomethine fragments about the N—N axis in azines whose molecules become noncoplanar. Such unfolding breaks down the conditions of $\pi-\pi$ conjugation, and at a given unfolding angle, the interaction of the π-orbitals of one azomethine bond with the p-orbital of the unshared pair of the nitrogen atom of the other bond becomes possible. On the basis of the above, and also considering the presence of a large dipole moment, Kitaev et al. [2] favored a configuration with a syn-syn arrangement of the smaller substituents.

Similarly, it can be assumed that the azines I, II, IV, V, X-XIII which we obtained, and which exist in a single isomeric form in the solutions, correspond to a syn-syn arrangement (Scheme 3).

Scheme 3



Introducing electron-acceptor groups into the composition of the azine reinforces the conjugation of the azine system and promotes displacement of electrons from the benzothiazole ring to the radical with electron-acceptor groups. In this case, $\pi-\pi$- $\pi-\pi$ conjugation takes place, and N—N becomes a double bond; as a result, the energy barrier of rotation increases in comparison with azines existing in a single isomeric form. This assumption is confirmed by data obtained by studying the ESR spectra of azine III. The methyl group is expressed in the form of two signals with δ 3.44 ppm and 3.54 ppm, although by analogy with other azines, a singlet could be expected (o-hydroxy-phenyl is not an electron-acceptor one), and the molecule could be noncoplanar.

Symmetric azines of o-hydroxybenzaldehyde have a planar system thanks to the strong intramolecular bond of the electron doublet of the azine nitrogen to the hydroxide proton [2]. The coplanarity of the molecule provides for $\pi-\pi$- $\pi-\pi$ conjugation and the presence of a mixture of isomeric forms. The weak luminescence of azine III confirms a strong intramolecular bond, as we established for hydrazones of such structure [7].

Addition of trifluoroacetic acid to the solution of azines III, VI-VIII, which exist in a mixture of syn and anti isomers, gives rise to only one isomeric form (Table 1). Apparently, these cases involve protonation of the electronegative nitrogens of the azine bond, as a result of which $\pi-\pi-\pi$-π conjugation breaks down, and the energy barrier of rotation about the N—N bond decreases. However, referring the signal to the syn form is debatable.

In the ESR spectra of azines X and XIII, the splitting of the signals of the methyl protons indicates a nonequivalency of the methyl groups in the syn and anti positions relative to the C=N bond. Thus, in the DMF solution, the signal of the methyl protons of $(CH_3)_2C=$ is expressed as two signals, with δ_1 1.89 ppm and δ_2 1.95 ppm. A similar effect was established for symmetric dimethylketazine, for which the chemical shift of the methyl group in the syn position is smaller than in the anti position [1].

EXPERIMENTAL

The ESR spectra were recorded on a Hitachi R-22 spectrometer (90 MHz), with HMDS as the internal standard. The quantitative determinations were carried out on the basis of the ESR spectra by quintuple integration of the signal of the CH_3N group.

The ultimate analysis data for compounds I-XIII for C, H, and S agree with the calculated data.

Asymmetric Azine of 3-Methylbenzothiazolinone-2 and 2,3-Dimethoxybenzaldehyde (I). A mixture of 5.37 g (30 mmole) of 3-methyl-2-benzothiazolinone hydrazone (hydrazone), 4.98 g (30 mmole) of 2,3-dimethoxybenzaldehyde, and 80 ml of dioxane is agitated for 3 h at 80°C, the dioxane is partially driven off, the solution is diluted with water, and the crystals are recrystallized from isopropanol.

Asymmetric Azine of 3-Methylbenzothiazolinone-2 and 4-Hydroxybenzaldehyde (II) is obtained from 5.37 g (30 mmole) of hydrazone, 3.66 g (30 mmole) of 4-hydroxybenzaldehyde and 80 ml of dioxane by use of the method described for azine I.

Asymmetric Azine of 3-Methylbenzothiazolinone-2 and 2-Hydroxybenzaldehyde (III). A mixture of 5.37 g (30 mmole) of hydrazone, 3.66 g (30 mmole) of 2-hydroxybenzaldehyde, and 70 ml of dioxane is agitated for 2 h at 60°C, the dioxane is partially driven off, the solution is diluted with water, and the crystals are filtered off and washed with isopropanol.

Asymmetric Azine of 3-Methylbenzothiazolinone-2 and 3,4-Methylenedioxabenzaldehyde (IV) is obtained from 5.37 g (30 mmole) of hydrazone and 4.5 g (30 mmole) of 3,4-methylenedioxabenzaldehyde by use of the method described for azine III.

Asymmetric Azine of 3-Methylbenzothiazolinone-2 and 3,4-Dihydroxybenzaldehyde (V) is obtained from 5.37 g (30 mmole) of hydrazone and 4.14 g (30 mmole) of 3,4-dihydroxybenzaldehyde by use of the method described for azine III.

Asymmetric Azine of 3-Methylbenzothiazothiazolinone-2 and 4-Methoxybenzaldehyde (VI). A mixture of 5.37 g (30 mmole) of hydrazone, 4.08 g (30 mmole) of 4-methoxybenzaldehyde, and 70 ml of dioxane is agitated for 3 h at 70°C, the dioxane is partially driven off, the mixture is diluted with petroleum ether, and the crystals are filtered off and washed with isopropanol.

Asymmetric Azine of 3-Methylbenzothiazolinone-2 and 3-Nitrobenzaldehyde (VII). A mixture of 3.58 g (20 mmole) of hydrazone, 3.02 g (20 mmole) of 3-nitrobenzaldehyde, and 60 ml of dioxane is agitated for 2 h at 65°C, and the abundant precipitated amorphous crystals are filtered off and washed with isopropanol.

Asymmetric Azine of 3-Methylbenzothiazolinone-2 and 4-Chlorobenzaldehyde (VIII) is obtained from 5.37 g (30 mmole) of hydrazone and 4.2 g (30 mmole) of 4-chlorobenzaldehyde by use of the method described for azine III.

Asymmetric Azine of 3-Methylbenzothiazolinone-2 and 2-Bromobenzaldehyde (IX). A mixture of 5.37 g (30 mmole) of hydrazone, 5.55 g (30 mmole) of 2-bromobenzaldehyde, and 70 ml of dioxane is agitated for 1 h at 40°C and diluted with petroleum ether, and the precipitate is filtered off and washed with petroleum ether.

Asymmetric Azine of 3-Methylbenzothiazolinone-2 and Acetone (X) is obtained from 5.37 g (30 mmole) of hydrazone and 1.74 g (30 mmole) of acetone by use of the method described for azine III.

Asymmetric Azine of 3-Methylbenzothiazolinone-2 and Acetophenone (XI) is obtained from 5.37 g (30 mmole) of hydrazone and 3.6 g (30 mmole) of acetophenone by use of the method described for azine VI.

Asymmetric Azine of 3-Methylbenzothiazolinone-2 and (3,4-Methylenedioxaphenyl)acetone (XII). A mixture of 5.37 g (30 mmole) of hydrazone, 5.34 (30 mmole) of (3,4-methylenedioxaphenyl)acetone and 70 ml of dioxane is agitated for 3 h at 70°C, the dioxane is partially driven off and diluted with petroleum ether, and the crystals are filtered off and recrystallized from a 3:10 dioxane–isopropanol mixture.

Asymmetric Azine of 3-Methylbenzothiazolinone-2 and Heptan-4-one (XIII). A mixture of 5.37 g (30 mmole) of hydrazone, 3.32 g (30 mmole) of heptan-4-one, and 70 ml of dioxane is agitated for 2 h at 70°C, the dioxane is partially driven

off, the mixture is diluted with petroleum ether, the solution is separated from the oily residue and evaporated off, and the precipitated crystals are ground up with water, filtered off, and washed with water.

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