isolated in 81% yield from the reaction mixture in a similar experiment by the action of HNO_3 that did not contain nitrogen oxides on 0.1 g of $III^+ClO_4^-$ in 42% perchloric acid.

3-Nitrophenothiazine (IV). A 0.70-g (10.1 mmole) sample of sodium nitrite was added to a solution of 0.15 g (0.5 mmole) of phenazthionium perchlorate in 12 ml of acetonitrile, and the reaction mixture was stirred for 30 min. The excess sodium nitrite was removed by filtration, and the filtrate was diluted with water (30 ml). The precipitate was removed by filtration, washed with 20 ml of water, dried, and treated with boiling benzene (three 10-ml portions). The insoluble material was identified as 3,7-dinitrophenothiazine. The yield of the dinitro derivative was 0.02 g (13%). The IR spectrum of a genuine sample of 3,7-dinitrophenothiazine prepared by the method in [10]. Evaporation of the benzene filtrate gave 0.05 g (42%) of 3-nitrophenothiazine with mp 209-210°C (from benzene) (mp 210-211°C [11]).

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RING-CHAIN TAUTOMERISM OF SUBSTITUTED HYDRAZONES.

17.* ALKYL-SUBSTITUTED PERHYDRO-1,3,4-THIADIAZINES

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It was demonstrated by PMR spectroscopy that alkylidene derivatives of vic-(N-alkylhydrazino)thiols in solutions exist exclusively in the cyclic form, i.e., as perhydro-1,3,4-thiadiazines. Only pinacolone derivatives undergo reversible isomerization to the corresponding hydrazones. The thermodynamic parameters of the ring-chain equilibria were determined. The static stereochemistry and the dynamics of the conformational transitions of perhydro-1,3,4-thiadiazines are discussed.

To ascertain the general principles that govern reversible additive isomerization processes it is important to evaluate both the role of the heteroatom in the added grouping and the common character of the effect of substituents in different but similar series. Up until now, one of the most extensively studied systems has been the perhydro-1,3,4-oxadiazine—(β-hydroxyalkyl)hydrazone tautomeric system [4]; however, virtually no study has been devoted to similar transformations in series of analogs of hydroxyalkylhydrazones.

*See [1] for Communication 16; see [2, 3] for preliminary communications.

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TABLE 1. Vicinal Hydrazinothiols and Their Alkylidene Derivatives

Compound	bp, °C (mm)	d_4^{20}	n_D^{20}	Found				Empirical formula	Calculated				Yield, %
				C, %	H, %	S, %	MR_D		C, %	H, %	S, %	MR_D	
Ia	54—55 (8)	1,0167	1,5065			29,6	31,05	$C_3H_{10}N_2S$			30,2	31,09	58
Ib[a]	55—58 (10)	0,9738	1,4921				35,81	$C_4H_{12}N_2S$				35,74	44
Ic[b]	57—58 (8)	0,9490	1,4849				40,53	$C_5H_{14}N_2S$				40,38	48
Ie	81—84 (8)	0,9595	1,4895	44,7	10,5		40,41	$C_5H_{14}N_2S$	44,7	10,5		40,38	80
If	93—95 (14)	0,9233	1,4763	51,7	11,1	20,4	49,61	$C_7H_{18}N_2S$	51,8	11,2	19,7	49,68	67
IIIa	55—56 (8)	1,0033	1,5055	49,5	9,4		43,31	$C_6H_{14}N_2S$	49,3	9,6		43,33	42
IIb⇄IIIb[c]	81—83 (8)	0,9641	1,4957	57,6	10,6	17,1	57,01	$C_9H_{20}N_2S$	57,4	10,7	17,0	57,27[d,e]	48
IIc⇄IIIc	85—88 (8)[f]			59,6	11,0	16,1		$C_{10}H_{22}N_2S$	59,4	11,0	15,8		54
IIId	84—85 (11)	0,9628	1,4902	57,5	10,8		57,24	$C_9H_{20}N_2S$	57,4	10,7		57,27	67
IIe⇄IIIe[c]	79—81 (8)	0,9342	1,4892			14,6	66,54	$C_{11}H_{24}N_2S$			14,8	66,57[d,g]	53
IIIf	77—78 (12)	0,9746	1,4950			19,8	47,96	$C_7H_{16}N_2S$			20,0	47,98	73
IIIg	109—111 (32)	0,9848	1,4986			20,0	47,75	$C_7H_{16}N_2S$			20,0	47,98	61
IIh⇄IIIh	101—102 (6)	0,9558	1,4920			14,7	65,68	$C_{11}H_{24}N_2S$			14,8	66,57[d,g]	53
IIIi	104—105 (25)	0,9453	1,4829			16,5	57,34	$C_9H_{20}N_2S$			17,0	57,27	48
IIIj	82—85 (8)	0,9303	1,4825	59,4	11,1	15,8	62,06	$C_{10}H_{22}N_2S$	59,4	11,0	15,8	61,92	73
IIIk	70—71 (9)	1,0259	1,5123			21,4	42,80	$C_6H_{14}N_2S$			21,9	43,33	53
IIIl	80—83 (10)	0,9678	1,4910	54,7	10,5	18,5	52,16	$C_8H_{18}N_2S$	55,1	10,4	18,4	52,63	54

[a]According to [7], this compound had bp 76-81°C (20 mm). [b]According to [8], this compound had bp 70-75°C (13 mm). [c]The refractometric characteristics are presented for equilibrium mixtures. [d]For the cyclic form of II. [e]For the open form of III the calculated MR_D value is 57.92. [f]This compound had mp 16-18°C. [g]The calculated MR_D value for the open form of III is 67.22.

TABLE 2. Spectral Characteristics of the Vicinal Hydrazinothiols[a]

Compound	δ, ppm[b]				νS—H, cm^{-1}	νN—H, cm^{-1}	δNH_2, cm^{-1}
	R^1	R^2	R^3	CH_2			
Ia	2,49 s	2,60 m			2550	3215, 3320	1600
Ib	2,49 s	1,29 d	3,20 sex	2,38 d	2560	3210, 3350	1600
Ic	2,43 s	1,35 s		2,40 s	2560	3210, 3345	1600
Ie	0,90 t; 1,56 sex; 2,44 t	2,56 m			2575	3200, 3365	1595
If	0,90 t; 1,56 sex 2,51 t	1,41 s		2,52 s	2560	3200, 3350	1605

[a]The IR spectrum of Ia was obtained in a thin layer, whereas solutions in $CHCl_3$ were used in the case of Ib, c, f, and a solution in CCl_4 was used in the case of Ie. [b]Solutions in CCl_4; the vicinal spin—spin coupling constants in all cases were 7.5 Hz.

In this connection, in the present research we set out to establish the structures of alkylidene derivatives of (β-mercaptoalkyl)hydrazines, to detect tautomeric systems in this series, and to determine the factors that influence the position of the tautomeric equilibria. Considering the contributions of the C—X and X—H bonds to the heats and entropies of formation [5] of both tautomeric forms, one should have expected that the stability of the cyclic tautomeric form would be higher in the case of sulfur compounds than in the case of oxygen-containing analogs. This was confirmed to a certain degree in the case of tautomeric (mercaptoalkyl)imines [6] and (β-mercaptoalkyl)hydrazones of aromatic carbonyl compounds [1]. Since the three-dimensional structure of the cyclic tautomer has an appreciable effect on the position of the equilibrium, a study of the stereochemistry of perhydro-1,3,4-thaidiazones also seemed essential. In addition, this task, particularly the study of the dynamics of the conformational transformations in the perhydrothiadiazine series, also is of completely independent importance.

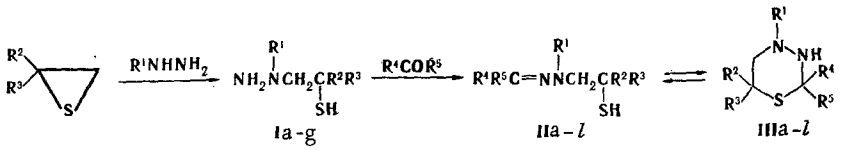
Starting hydrazinothiols Ia-g (Tables 1 and 2) were obtained in the reaction of alkylhydrazines with thiiranes by the method previously used for the synthesis of Ib, c [7, 8]. We have shown [9] that these reactions proceed with a high degree of regioselectivity and that hydrazinothiols Ia-g, which were isolated as a result of distillation, did not contain admixed structural isomers. The physical constants and the data from PMR spectroscopy of the products of condensation of hydrazinothiols Ia-g with aliphatic carbonyl compounds obtained by the usual methods are presented in Tables 1 and 3.

TABLE 3. PMR Spectra of Alkylidene Derivatives of Vicinal Hydrazinothiols[a]

Compound	δ, ppm (J, Hz)						
	R^1	R^2[b]	R^3[c]	CCHN[b]	CCHN[c]	R^4[b]	R^5[c]
IIIa	2,33 s	2,47 t (6,0)		2,87 t (6,0)		1,33 s	
IIb	2,29 s					1,09 s	1,95 s
IIIb	2,34 s	2,59	3,29	1,90	3,02	1,05 s	1,57 s
		($J_{5a5e}=-11,8$, $J_{6a6e}=-13,0$, $J_{5a6a}=11,8$, $J_{5a6e}=2,8$, $J_{5e6a}=J_{5e6e}=3,4$)					
IIc	2,27 s	1,22 d (7,0)				1,07 s	1,95 s
↓↑							
IIIc	2,33 s	1,09 d (7,0)	3,22	1,36	3,02	0,97 s	1,50 s
			($J_{5a5e}=-11,5$, $J_{5a6a}=11,5$, $J_{5e6a}=3,0$)				
IIId	2,40 s	1,14 s	1,40 s	1,70 d	2,64 d	0,97 and 1,00[d] (7,2), 1,80 m	4,06 d (6,5)
				($-11,2$)			
IIe	2,34 s	1,21 s		2,88 s		1,07 s	1,95 s
↓↑							
IIIe	2,42 s	1,12 s	1,63 s	1,60 d	2,70 d	1,03 s	1,52 s
				($-12,0$)			
cis IIIf	1,06 t, 2,51 q (7,0)	1,10 d (6,7)	3,15	1,56	3,01	1,27 d (6,8)	4,31 q (6,8)
			($J_{5a5e}=-11,7$, $J_{6a6a}=10,5$, $J_{5e6a}=3,1$)				
↓↑							
trans IIIf		1,08 d (6,7)				1,41 d (6,5)	4,39 q[e] (6,5)
IIIg	0,86 t, 1,54 m, 2,36 m (7,0)	2,61	3,30	2,08	2,98	1,26 d (6,7)	4,26 m[e]
		($J_{5a5e}=-11,8$, $J_{6a6e}=-12,5$, $J_{5a6a}=11,8$, $J_{5a6e}=2,5$, $J_{5e6a}=3,0$, $J_{5e6e}=2,5$—$3,0$)					
IIh[f]						1,09 s	1,92 s
↓↑							
IIIh[f]	0,81 t, 1,50 m, 2,24 t (7,5)	2,53	3,28	1,94	2,86	1,04 s	1,62 s
		($J_{5a5e}=-11,9$, $J_{6a6e}=-13,0$, $J_{5a6a}=11,9$, $J_{5a6e}=2,7$, $J_{5e6a}=3,4$, $J_{5e6e}=2,7$—$3,4$)					
IIIi	0,89 t (7,5), 1,48 m, 2,40 and 2,43 m[g]	1,14 s	1,43 s	1,80 d	2,61 d	1,25 d (6,8)	4,28 q[e] (6,8)
				($-11,9$)			
IIIj	0,91 t, 1,50 m, 2,48 t (7,5)	1,29 s		2,25 s[e]		1,42 s	
IIIk	0,99 d (6,5)	2,60—3,10 m				4,13 s	
IIIl	0,98 d (6,5)	2,50—3,00 m				1,43 s	

[a]Solutions in CCl_4. [b]The equatorial group in cyclic tautomer III. [c]The axial group in cyclic tautomer III. [d]Diastereotopic groups. [e]The signal is broadened. [f]Spectrum in d_5-pyridine. [g]Diastereotopic protons.

Most of the alkylidene derivatives of hydrazinothiols that we obtained exist exclusively in cyclic tautomeric form III. The presence of appreciable amounts of a second tautomer (IIb, c, e, h) is observed only in the case of the products of condensation with pinacolone. Signals of both the ring (III) and chain (II) forms are present in the PMR spectra of these compounds; the spectra undergo a reversible change as the temperature is changed. Bands of



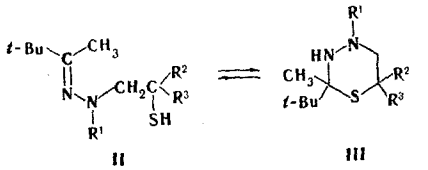
I* a R^1=Me; b R^1=R^2=Me; c R^1=R^2=R^3=Me; d R^1=Et, R^2=Me; e R^1=Pr; f R^1=Pr, R^2=R^3=Me; g R^1=*i*-Pr; II, III a R^1=R^4=R^5=Me; b R^1=R^5=Me, R^4=*t*-Bu; c R^1=R^2=R^5=Me, R^4=*t*-Bu; d R^1=R^2=R^3=Me, R^4=*i*-Pr; e R^1=R^2=R^3=R^5=Me, R^4=*t*-Bu; f R^1=Et, R^2=R^4=Me; g R^1=Pr, R^4=Me: h R^1=Pr, R^4=*t*-Bu, R^5=Me; i R^1=Pr, R^2=R^3=R^4=Me; j R^1=Pr, R^2=R^3=R^4=R^5=Me; k R^1=*i*-Pr, *l* R^1=*i*-Pr, R^4=R^5=Me

*Here and subsequently, the fact that R = H is not indicated.

TABLE 4. IR Spectra of Alkylidene Derivatives of Vicinal Hydrazinothiols

Compound	Medium	ν, cm⁻¹		
		C=N	S–H	N–H
IIIa	Thin layer	—	—	3150
IIb⇄IIIb	Thin layer	1630	2575	3200
IIc⇄IIIc	$CHCl_3$	1620	2570	3205
IIId	$CHCl_3$	—	—	3160
IIe⇄IIIe	$CHCl_3$	1620	2560	3210
IIIf	CCl_4	—	—	3155
IIIg	CCl_4	—	—	3145
IIh⇄IIIh	CCl_4	1640	—	3210
IIIi	$CHCl_3$	—	—	3130
IIIj	$CHCl_3$	—	—	3160
IIIk	Thin layer	—	—	3195
IIIl	CCl_4	—	—	3180

TABLE 5. Thermodynamic Parameters of the Tautomeric Equilibrium



II III

Compound	R¹	R²	R³	K_T=[II]/[III]				$-\Delta H^0$, kJ/mole	$-\Delta S^0$, J/mole·°K
				35°	50°	69°	90°		
IIb⇄IIIb	Me	H	H	0,47	0,92	1,63	3,12	31,5±1,2	96±4
IIc⇄IIIc	Me	Me	H	0,24	0,38	0,80	1,23	28,5±2,0	81±6
IIe⇄IIIe	Me	Me	Me	0,70	0,92	1,85	2,65	23,8±2,5	74±8
IIh⇄IIIh	Pr	H	H	0,27	0,45	0,78	1,24	25,8±0,9	73±3

stretching vibrations of C=N, S–H, and N–H bonds are observed in the IR spectra of such derivatives (Table 4). Their refractive indexes increase from the moment at which distillation is complete up to establishment of the equilibrium value; according to the PMR spectroscopic data obtained for the IIh ⇄ IIIh tautomeric system, the freshly distilled preparation is enriched in the chain form.

The PMR spectra of the remaining alkylidene derivatives of hydrazinothiols correspond exclusively to the perhydro-1,3,4-thiadiazine structure (see below) and remain virtually unchanged as the temperature is raised. Their IR spectra do not contain the bands of C=N and S–H stretching vibrations that are characteristic for the open tautomer (Table 4), and the refractive indexes are constant with time.

Regardless of the position of the tautomeric equilibria in solutions at room temperature, the fragmentation of all of the alkylidene derivatives of hydrazinothiols under the influence of electron impact is governed by the principles that are known for the corresponding alkylhydrazones that do not contain a thiol group [10]. We have already noted this previously in series of keto derivatives of hydrazinothiols that do not contain an alkyl substituent attached to the nitrogen atom [11].

We used PMR apectroscopy to determine the thermodynamic equilibrium parameters for the tautomeric preparations (Table 5). We selected the series of compounds in such a way as to be able to follow the effect of alkyl substituents in the 4 and 6 positions of the cyclic tautomer on the position of the tautomeric equilibrium. With respect to the equilibrium constants determined at 35°C, one may note that an increase in the size of the group in the 4 position, like the introduction of a substituent in the 6 position, shifts the equilibrium to favor the ring form, while the introduction of a second substituent in the 6 position is accompanied by the opposite effect. The same principles are also known for the oxygen analogs of the systems under consideration here [4]. It is apparent from Table 5 that an increase in the volume of the substituent in the 4 position leads to a

decrease in the difference in both the enthalpies and the entropies of the two tautomers. The first effect is due to intensification of the destabilization nonvalent interaction between the substituent and the hydrogen atom in the ring form (this interaction is absent in the chain form). Let us note that in the case of hydrocarbons a substituted chain has a more favorable enthalpy of cyclization than an unsubstituted chain [12]. The second effect is associated with a decrease in the entropy of rotation of the chain form as the volume of the substituent increases (the entropy of the ring form, which has less freedom of rotation, changes only slightly [12]). The relative stabilization of the cyclic tautomer when one methyl group is introduced in the 6 position of the ring is due precisely to this entropy factor, as is apparent from a comparison of the pair of IIb $\rightleftarrows$ IIIb and IIc $\rightleftarrows$ IIIc tautomeric systems (Table 5); the change in the ΔH° value in this case is within the limits of the experimental error. However, the introduction of a second methyl group in the same position has little effect on the ΔS° value, while the difference in the enthalpies decreases substantially (the pair of IIc $\rightleftarrows$ IIIc and IIe $\rightleftarrows$ IIIe systems in Table 5). In our opinion, this is due to the destabilizing interaction between the synaxial 2- and 6-CH_3 groups in the chairlike conformation of the cyclic tautomer (the three-dimensional structure of the perhydrothiadiazines is discussed below).

The thermodynamic equilibrium parameters found in the present research are higher than the analogous values that we previously determined for 2,2-dimethyl- and 2,2,6-trimethylperhydro-1,3,4-thiadiazines that do not have an alkyl substituent in the 4 position [11]. In all likelihood, this is associated with both the substitution effect described in [12] and, to a greater degree, with the relative stabilization of N-unsubstituted N-(β-mercaptoalkyl)hydrazones by an intramolecular NH...S hydrogen bond. A rigorous comparison of the thermodynamic equilibrium parameters cannot be made here because of the difference in the substituents in the 2 position. A qualitative comparison with the results obtained in [11] indicates a pronounced shift in the equilibrium to favor the cyclic tautomer when an alkyl substituent is introduced in the 4 position or the ring. The same effect was also observed in the case of the oxygen analogs [4].

The effect of alkyl substituents attached to the carbon atoms in series of tautomeric N-(β-mercaptoalkyl)hydrazones and their oxygen analogs also proved to be similar. However, the equilibrium position itself is shifted markedly to favor the ring form in the case of the sulfur compounds. Thus N-unsubstituted N-(β-hydroxyalkyl)hydrazones do not undergo cyclization at all, and the equilibrium concentrations of the ring forms of N-alkyl-N-(β-hydroxyalkyl)hydrazones of pinacolone at room temperature do not exceed 10%, whereas more significant amounts of these forms are observed for the derivatives of sterically less hindered ketones and aldehydes [4]. In the case of N-(β-mercaptoalkyl)hydrazones tautomerism is particularly characteristic precisely for the N-unsubstituted compounds [11]. As we have demonstrated in the present research, most of the N-substituted compounds exist exclusively in the cyclic form, which dominates at room temperature even in the case of the tautomeric derivatives of pinacolone. If a tert-butyl group is not present in the 2 position, even prolonged heating of, for example, perhydrothiadiazine IIIa at 150°C in diphenyl ether did not lead to the development of appreciable amounts of the hydrazone. This made it impossible to make a direct comparison of the thermodynamic equilibrium parameters for the oxygen- and sulfur-containing compounds. However, it must be noted that the ΔH° and ΔS° values that we obtained for the tautomeric perhydro-1,3,4-thiadiazines are two to three times higher than those for the perhydro-1,3,4-oxadiazines. (It must be noted, however, that only scanty quantitative data are available for the latter [13, 14.) The increase in the ΔH° value is in agreement with that predicted on the basis of an additive computational scheme [5]; however, according to the additive scheme, one should have expected that the ΔS° value would be approximately the same for both series of tautomeric systems. It seems to us that, first, weakening of the intramolecular hydrogen bond in the chain form (SH...N as compared with OH...N [15]) and, second, weakening of the steric strain in the cyclic form when the oxygen atom is replaced by a sulfur atom make substantial contributions to the relative stabilization of the ring tautomer in the series of sulfur compounds.

TABLE 6. Barriers to Conformational Interconversion of Perhydro-1,3,4-thiadiazines

Compound	Solvent	δ, ppm (J, Hz)[a]			T_c[b], °C	$\Delta G^{\neq}$[c], kJ/mole
		group	*a*	*e*		
IIIa	$CDCl_3$	2-CH_3	1,66 s	1,43 s	−31	51,0
IIIj	$CDCl_3$	6-CH_3	1,55 s	1,17 s	−21	52,1
		5-H	1,91 d (−12,0)	2,80 d (−12,0)	−16	51,3
IIIk	$CDCl_3$	2-H	4,45 dd (−12,7, 12,7)	4,07 d[d] (−12,7)	−21	51,5
	CD_3OD	2-H	4,35 d (−13,3)	3,97 d[d] (−13,3)	−25	50,6
IIIl	$CDCl_3$	2-CH_3	1,61 s	1,39 s	−19	53,7
IIIm	$CDCl_3$	2-CH_3	1,69 s	1,38 s	−20	52,7
IIIn	$CDCl_3$	2-CH_3	1,65 s	1,39 s	−14	54,4
IVa [23]	$CDCl_3$	2-H	4,90 d (−11,5)[e]	3,86 d (−11,5)[e]	−5	53,1
IVb [23]	$CDCl_3$	2-CH_3	1,84 s[e]	1,30 s[e]	−2	55,2

[a]At −60°C. [b]The coalescence temperature. [c]At the coalescence temperature; the accuracy in the determination of the barrier was 1.5 kJ/mole. [d]The signal is broadened. [e]At −51°C.

The weakening of the steric strain in the sulfur heterocycle is manifested particularly in the fact that 2,6-dimethyl-4-ethylperhydro-1,3,4-thiadiazine (IIIf), in contrast to the oxygen analogs [16, 17], exists in solutions in the form of a mixture of cis and trans isomers that undergo interconversion through chain tautomer IIf. This is indicated by the presence in the PMR spectrum (Table 3) of two sets of 2-CH_3, 6-CH_3, and 2-H signals. An analysis of the portion of the spectrum corresponding to the 5- and 6-H protons of the principal component (Table 3) provides evidence for an axial orientation of the 6-H proton in the chairlike conformation of the ring and, consequently, for an equatorial orientation of the 6-CH_3 group. The 6-CH_3 group in 2-tert-butyl-2,4,6-trimethylperhydro-1,3,4-thiadiazine (IIIc) (Table 3), which is present in the tautomeric mixture in the form of a single stereoisomer, is similarly oriented. Considering the large effective volume of the tert-butyl substituent, a cis configuration with an axial 2-CH_3 group should be assigned to IIIc. A comparison of the chemical shifts of the 2-CH_3 groups in perhydrothiadiazines IIIc and IIIf (the principal component) makes it possible to assume that it has an equatorial orientation in the latter case [this follows rigorously from an examination of the J_{23} values (see below)], i.e., that the principal stereoisomer of IIIf has a cis configuration. The ratio of the stereoisomers of IIIf changes only slightly as a function of the solvent and the temperature, and for solutions in d_4-methanol at 30°C, for example, $K_{cis/trans} = 3.3$. Let us note here that the intensities of the minor signals in the PMR spectra of IIIf are too high to allow one to assign them to the admixed structural rather than geometrical isomer.*

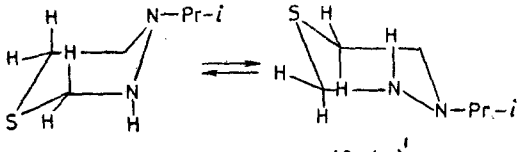
The PMR spectroscopic data (Table 3) indicate a chairlike conformation for the heteroring also for the other perhydrothiadiazines III. An analysis of the PMR spectra obtained for solutions in CCl_4 or C_2Cl_4 has usually been employed as a first approximation in estimating the J_{56} vicinal constants. In some cases it has proved to be expedient to use an aromatic solvent (d_5-pyridine); for a number of experimental subjects we have specially demonstrated that this change in solvents does not affect the spin–spin coupling constants (SSCC). The R factors calculated on the basis of the J_{56} vicinal constants [18, 19] range from 2.45 to 2.70, which correspond to N–C–C–S torsion angles of 60 to 61° in perhydrooxadiazines IIIb, g, h. These values of the torsion angles constitute evidence for a chairlike conformation of the ring; the perhydrothiadiazine ring is characterized by a high degree of puckering as compared with the perhydrooxadiazine ring, in which the N–C–C–O torsion angle ranges from 53 to 56° [20]. This sort of "bending" of the chair when a sulfur atom is introduced is known for saturated six-membered heterorings and is associated with an ∿15° increase in the CXC bond angle on passing from X = O to X = S [21]. The appearance of an axial methyl group in the 2 position (IIIb, h) has virtually no effect on the N–C–C–S torsion angle. This should have been expected, since, according to the

*The formation of the structural isomer, viz., 2,5-dimethyl-4-ethylperhydro-1,3,4-thiadiazine, is a consequence of alternative opening of the methylthiirane by ethylhydrazine. However, according to the data from chromatographic mass spectrometry, IIIf contains 4% of this isomer.

results of calculations [22], the torsion angles in the axial conformer of methylcyclohexane are virtually the same as the angles in the equatorial conformer.

The signal of the 2-H proton in the PMR spectra of 2-monosubstituted perhydrothiadiazines is usually broadened as a consequence of coupling with the NH proton. This broadening vanishes in the case of deuteration. Spin–spin coupling of the 2- and 3-H protons is always observed in the spectra obtained at low temperatures in aprotic solvents. The high value of the J_{23} constant (12-13 Hz) constitutes evidence for a diaxial orientation of these protons, and this constitutes additional evidence in favor of the chairlike conformation of the ring. The axial orientation of the NH proton is due to both the gauche effect of the hydrazine fragment and the anomeric effect of the sulfur atom. It was recently shown that an axial orientation is preferable even for the 3-methyl group in 3,4-dimethylperhydro-1,3,4-thiadiazines [23]. The available data on the gauche effect in hydrazines [24] make it possible to conclude that when the 3-H proton is axially oriented, the alkyl group attached to the N_4 atom is equatorially oriented.

The PMR spectra of IIIa, j-l obtained at 30°C indicate rapid (on the PMR time scale) conformational transitions that lead to averaging of the signals of the geminal methyl groups and the ring methylene protons.

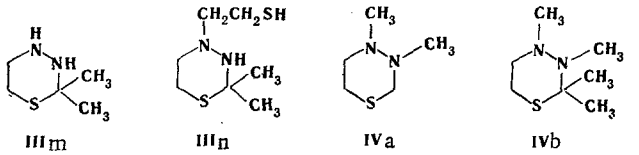


(3a4e) (3a4e)'

Sets of signals corresponding to the axial and equatorial orientations of the groups indicated above are observed as the temperature is lowered as a consequence of "freezing out" of the conversion processes in the PMR spectra (Table 6). Thus in the spectrum of 4-isopropylperhydro-1,3,4-thiadiazine (IIIk) the 2- and 3-H protons form an ABX (in $CDCl_3$, see Fig. 1) or AB (in CD_3OD) system. The signal of the equatorial 2-H proton remains broadened even in the latter case; this is due to long-range coupling with the equatorial 6-H proton, which is manifested in the case of a W orientation of the coupling protons in the chairlike conformation of the heteroring.

The spectral characteristics of 2,2,6,6-tetramethyl-4-propylperhydro-1,3,4-thiadiazine (IIIj) at −60°C (Table 6) are extremely similar to those of IIIi, l, for which there is no doubt that the chairlike conformation is preferred. In exactly the same way, the chemical shifts of the methyl and methylene protons of 2-tert-butyl-2,4,6,6-tetramethyl-substituted IIIe (Table 3) differ only slightly from the corresponding parameters for other perhydrothiadiazines that exist in a chairlike conformation. These data serve as evidence in favor of the fact that IIIe and IIIj also exist preferably in the chair conformation, although destabilizing interactions between the syn-axial 2- and 6-CH_3 groups should be manifested in this conformation. In the series of oxygen-containing analogs of compounds of the III type such interactions lead to the development of twist forms [17]. It is possible that this is a peculiarity of oxygen-containing heterocycles, since, according to the calculated [25] and experimental [26] data, 1,1,3,3-tetramethyl-substituted cyclohexanes exist in the chair conformation.

We determined the barriers to conversion of the chair conformations [(3a4e) ⇄ (3a4e)'] by dynamic PMR spectroscopy [27] from the coalescence temperatures of the signals. In calculations by means of the Eyring formula the transmission coefficient was assumed to be unity. For comparison, the barriers that we previously obtained [11] for perhydrothiadiazines IIIm, n and recently published data for 3,4-dimethylperhydrothiadiazines IVa, b [23] are presented in the same table:



IIIm IIIn IVa IVb

The following three types of conformational transformations are distinguished for six-membered saturated heterorings with an endocyclic N–N bond [23, 24, 28]: inversion of

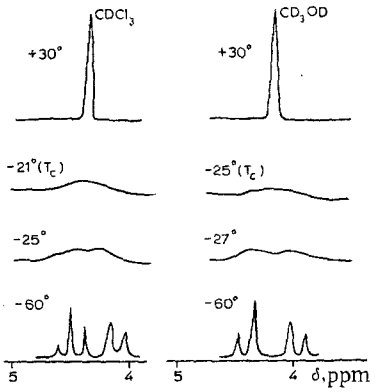
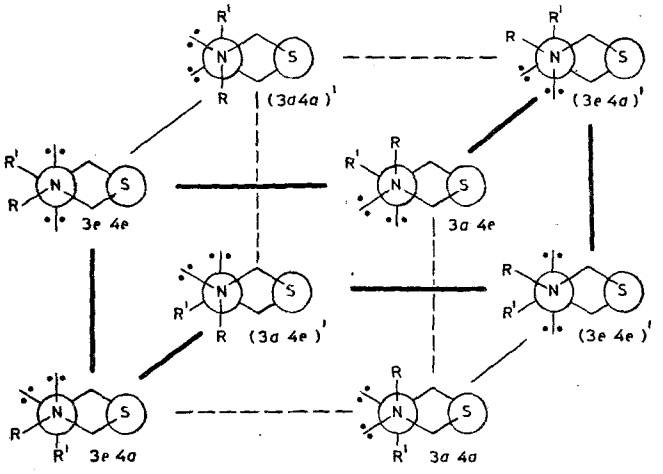


Fig. 1. Portion of the PMR spectrum of perhydrothiadiazine IIIk corresponding to the resonance of the methylene group in the 2 position.

the ring or the nitrogen atoms with eclipsing involving passage through a high barrier (>50 kJ/mole), low-barrier (<35 kJ/mole) inversion of the nitrogen atoms without eclipsing, and intermediate [with respect to the size of the barrier (40-45 kJ/mole)] inversion of the ring without eclipsing of the substituents attached to the nitrogen atoms in the transition state. The scheme of the conformational transformations for perhydrothiadiazines is presented below:



The "high" barriers to conformational interconversion have proved to be close to one another for all of the perhydrothiadiazines thus far investigated (Table 6). These barriers have made it possible to assume that in the case of 3,4-dimethyl-substituted IVa, b the "frozen out" 3a4e $\rightleftarrows$ (3a4e)' interconversion proceeds through a transition state that includes eclipsing of the substituents attached to the nitrogen atoms [23]. However, it is noteworthy that the replacement of one (in the 3 position) or two (in the 3 and 4 positions) methyl groups by hydrogen atoms and an increase in the volume of the alkyl group in the 4 position do not affect the height of the barrier.

The insensitivity of the size of the barrier to the development of 2,6-syn-axial methyl groups (IIIj) is in poor agreement with the assumption that this value corresponds to the barrier to ring inversion. It is known [29, 30] that similar changes in the structure in cyclohexane derivatives lead to a lowering of the barrier by no less than 5 kJ/mole. The fact that the size of the barrier does not change for perhydrothiadiazines as compared with perhydrooxadiazines [31], while the barrier undergoes a decrease of 3.8 kJ/mole on passing from tetrahydropyran to its sulfur analog [30], is also in poor agreement with this assumption. All of this, together with the material in question, makes it possible to assume that the sizes of the barriers obtained most likely correspond to inversion of the nitrogen atom in the 3 position.

The barriers to interconversion of perhydrothiadiazines are appreciably higher than those for perhydropyridazines [28]; this is evidently associated with the additional stabilization of the ground state (3a4e) due to the anomeric effect of the sulfur atom.

Let us note that replacement of an aprotic solvent ($CDCl_3$) by a proton-donor solvent (CD_3OD) has virtually no effect on the size of the barrier. The effect of such substitution is usually due to the formation of intermolecular hydrogen bonds; however, it is not always manifested in conformational transformations with the participation of the nitrogen atom [32, 33].

From the set of literature data and the data that we obtained one may conclude that processes involving inversion with eclipsing are not very sensitive to alkyl substitution in the ring. The data presented in Table 6 can apparently be regarded as an experimental confirmation of the fact that the development of "high" barriers to interconversion of six-membered saturated heterocycles with an endocyclic nitrogen–nitrogen bond is due exclusively to interaction of the unshared electron pairs rather than to spatial eclipsing of the substituents in the transition state (see also [28]).

EXPERIMENTAL

The PMR spectra of 15% solutions of the compounds in carbon tetrachloride, tetrachloroethylene, d_4-methanol, and d_5-pyridine (at 25-30°C) and in deuterochloroform and d_4 methanol (at low temperatures) were obtained with a Varian HA-100D-15 spectrometer with hexamethyldisiloxane (HMDS) as the internal standard. The temperature dependence of the tautomeric equilibrium constants was determined from the PMR spectra of solutions in tetrachloroethylene (1 mole/liter) with HMDS as the external standard; the results were treated by the method of least squares. The temperature was determined (with an accuracy of ±1°C) by means of a Varian thermometric standard. The establishment of equilibrium was monitored by repeated recording of the spectra; equilibrium was reached in 3-6 h in all cases. The IR spectra of thin layer or 5% solutions of the compounds in chloroform or carbon tetrachloride were recorded with a UR-20 spectrometer. The purity of the compounds obtained was monitored by gas–liquid chromatography (GLC) with a Tsvet-101 chromatograph with a flame-ionization detector; the glass silanized column was 1 m by 2 mm and was filled with 5% SE-30 on Inerton AW (0.125-0.16 mm), the column temperature was 150°C, the vaporizer temperature was 200°C, and the carrier gas was argon. The conditions under which the mass spectra were recorded with an LKB-2091 chromatographic mass spectrometer were as follows: The ionizing electron energy was 70 eV, the ionization current was 25 μA, the accelerating voltage was 3.5 kV, the separator temperature was 180°C, and the ion-source temperature was 200°C; the mass spectra were recorded at the maxima of the chromatographic peaks, and the scanning time was 2-4 sec. The peaks of the fragment ions with m/z less than 41 or relative intensities lower than 3% are not presented.

Vicinal hydrazinothiols I were obtained by heating mixtures of the corresponding thiiranes and alkylhydrazines by the method previously used for the synthesis of Ib, c, g [7, 8, 11] (see Tables 1 and 2).

2,2,4-Trimethylperhydro-1,3,4-thiadiazine (IIIa). A 6.4-g (0.11 mole) sample of acetone was added with shaking in the course of 15 min to 10.6 g (0.10 mole) of hydrazinothiol Ia, and the mixture was heated in a nitrogen atmosphere on a boiling-water bath for 3 h. It was then cooled and treated with 10 ml of benzene, and the organic layer was separated, dried with sodium sulfate and distilled *in vacuo*.

Compounds IIId, j, *l* were similarly obtained (Tables 1 and 3).

2-tert-Butyl-2-methyl-4-propylperhydro-1,3,4-thiadiazine (IIIh). A mixture of 13.4 g (0.10 mole) of hydrazinothiol Ie, 12.0 g (0.12 mole) of pinacolone, 60 ml of benzene, and 0.1 g of p-toluenesulfonic acid was refluxed with a Dean–Stark adapter until water separation ceased (∿30 h), after which the p-toluenesulfonic acid was washed away with water, and the organic layer was dried with sodium sulfate, and distilled *in vacuo* (Tables 1 and 3). Mass spectrum, m/z (relative intensity, %): 216 (M^+, 8), 170 (7), 169 (48), 159 (5), 127 (8), 118 (3), 100 (7), 72 (10), 69 (3), 61 (7), 59 (3), 58 (10), 57 (100), 56 (3), 55 (4), 43 (12), 42 (20), 41 (28).

The other pinacolone derivatives (IIIb, c, e) were similarly obtained (Tables 1 and 3).

2,6-Dimethyl-4-ethylperhydro-1,3,4-thiadiazine (IIIf). A 4.8-g (0.11 mole) sample of acetaldehyde was added with stirring and ice cooling in the course of 15 min to a solution of 13.4 g (0.10 mole) of hydrazinothiol Id in 40 ml of benzene, and the mixture was maintained at room temperature for 1 h and at 60°C for 1 h. The organic layer was separated, dried with sodium sulfate, and distilled *in vacuo* (Tables 1 and 3). Mass spectrum, m/z

(relative intensity, %): 161 (6), 160 (M^+, 30), 100 (7), 99 (100), 73 (4), 71 (15), 61 (7), 60 (7), 59 (6), 58 (12), 57 (7), 56 (12), 45 (6), 44 (27), 43 (7), 42 (22), 41 (10); m* 61.3, 51.0. The preparation contained 4% (according to GLC data) of admixed isomer, the mass spectrum of which [160 (M^+, 45), 158 (55), 143 (50), 113 (64), 102 (36), 73 (32), 71 (36), 60 (32), 59 (55), 58 (36), 57 (23), 56 (59), 44 (32), 42 (100), 41 (45)] was in agreement with the 2,5-dimethyl-4-ethylperhydro-1,3,4-thiadiazine structure.

Compounds IIIg, i were similarly obtained.

4-Isopropylperhydro-1,3,4-thiadiazine (IIIk). A mixture of 5.4 g (0.04 mole) of hydrazinothiol Ih, 15 ml of benzene, and 1.2 g (0.013 mole) of paraformaldehyde was refluxed with a Dean–Stark adapter (~6 h) until water separation ceased, after which it was distilled *in vacuo* (Tables 1 and 3). Mass spectrum, m/z (relative intensity, %): 148 (5), 147 (9), 146 (M^+; 100), 131 (18), 129 (6), 103 (10), 99 (38), 74 (4), 72 (7), 71 (57), 70 (10), 69 (4), 61 (12), 60 (7), 59 (7), 58 (7), 57 (97), 56 (29), 47 (7), 46 (9), 45 (9), 44 (8), 43 (57), 42 (14), 41 (17); m* 117.5, 67.1, 38.5, 32.8.

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HETEROATOMIC DERIVATIVES OF AZIRIDINE.

13.* NEW MACROHETEROCYCLIC COMPOUNDS CONTAINING ARYLALKYL AND FUNCTIONAL GROUPS ATTACHED TO THE ENDOCYCLIC NITROGEN ATOMS

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M. K. Butin, and O. B. Bannikova

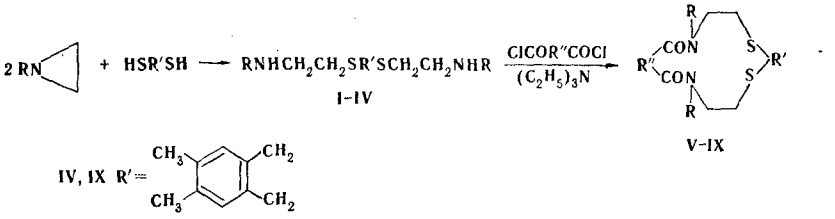
UDC 547.717'898

The reaction of N-substituted aziridines with 1,2-ethanedithiol and 1,2-bis(mercaptomethyl)-4,5-dimethylbenzene leads to N-substituted diamines. The reaction of the latter with adipic and phthalic acid dichlorides gives N-substituted macroheterocycles.

The introduction of alkyl and functional groups in the rings of macroheterocyclic compounds leads to an increase in their lipophilic and complexing properties [2-4]. Syntheses of cryptands and their polymacroheterocyclic analogs have been accomplished on the basis of functionally substituted macroheterocycles [5, 6]. Macroheterocycles with functional groups have been investigated as biologically active compounds [7, 8]. Immobilized on polymeric materials, they are used as new heterogeneous catalysts [9].

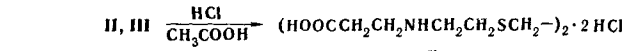
We have previously synthesized unsubstituted and functionally substituted macroheterocycles from primary and secondary diamines and dicarboxylic acid dichlorides. The diamines were obtained by the reaction of aziridine and 1-(2-carbomethoxyethyl)aziridine with dithiols [10-13].

In order to obtain arylalkyl- and functionally substituted macroheterocycles we synthesized diamines I-IV and studied their reaction with adipic and phthalic acid dichlorides.



I R=$C_6H_5CH_2CH_2$, R′=CH_2CH_2; II R=$CH_3OOCCH_2CH_2$, R′=CH_2CH_2; III R=$NCCH_2CH_2$, R′=CH_2CH_2; IV R=$CH_3OOCCH_2CH_2$; V R=$C_6H_5CH_2CH_2$, R′=CH_2CH_2, R″=—$(CH_2)_4$—; VI R=$CH_3OOCCH_2CH_2$, R′=CH_2CH_2, R″=—$(CH_2)_4$—; VII R=$NCCH_2CH_2$, R′=CH_2CH_2, R″=—$(CH_2)_4$—; VIII R=$C_6H_5CH_2CH_2$; R′=CH_2CH_2, R″=C_6H_4-*o*; IX R=$CH_3OOCCH_2CH_2$, R″=C_6H_4-*o*

Linear diamines I-IV were obtained in 70-80% yields by the reaction of N-substituted aziridines with 1,2-ethanedithiol and 1,2-bis(mercaptomethyl)-4,5-dimethylbenzene. The structure of diamines I-IV was proved by the preparation of their dihydrochlorides and by acid hydrolysis of 1,8-bis[2-(carbomethoxy)ethylamino]-3,6-dithiaoctane (II) and 1,8-bis(2-cyanoethylamino)-3,6-dithiaoctane (III) to the amino acid dihydrochloride (X).



Diamines I-IV react readily with adipic and phthalic acid dichlorides in a large volume of dry benzene in the presence of triethylamine to give macroheterocycles V-IX in 55-70% yields.

*See [1] for Communication 12.

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