The character of the conjugation of the phenyl ring with the amidine system of bonds changes in this sort of solvated molecule, and this may lead to a decrease in the intensities in the maxima in the UV spectra [8, 9]. The formation of the indicated hydrogen bonds can be considered to be a process that precedes complete protonation.

EXPERIMENTAL

The IR spectra of mineral oil pastes and solutions ($CHCl_3$, CCl_4, dioxane, and C_2H_5OD) of the compounds were recorded with a Perkin–Elmer recording spectrometer. The UV spectra of solutions of the compounds in dioxane, hexane, 95% hexane + 5% dioxane, alcohol, aqueous alcohol mixtures, and aqueous and alcoholic 0.1 N HCl and 0.1 N NaOH were obtained with an EPS-3 spectrophotometer. The PMR spectra of CD_3OD solutions were recorded with a JNM-C-60HL spectrometer with tetramethylsilane as the internal standard.

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BENZOXAZINES AND RELATED COMPOUNDS

V.* SYNTHESIS OF 2,4,4-TRISUBSTITUTED 4H-1,3-BENZOTHIAZINES

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The reaction of 2-mercapto(and benzylthio)-α,α-dialkylbenzyl alcohols with nitriles under the influence of acids serves as a method for the synthesis of 2,4,4-trisubstituted 4H-1,3-benzothiazines.

It has been shown that the reaction of 2-hydroxy-α,α-dialkylbenzyl alcohols with nitriles in the presence of acids leads to substituted 4H-1,3-benzoxazines [1, 2].

We have found that replacement of the 2-hydroxy group by a 2-mercapto(and benzylthio) grouping (alcohols IIa-d) leads to the previously unknown 2-substituted 4,4-dialkyl-4H-1,3-benzothiazines (IIIa-e) under similar conditions.

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*See [11] for communication IV.

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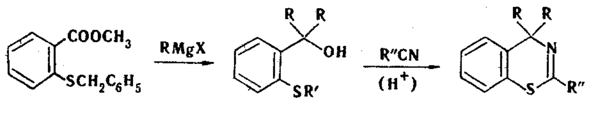
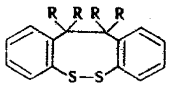
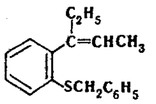


I IIa–d IIIa–e



IV



V

II a $R{=}C_2H_5$, $R'{=}H$, b $R{=}C_2H_5$, $R'{=}CH_2C_6H_5$, c $R{=}n\text{-}C_3H_7$, $R'{=}CH_2C_6H_5$, d $R{=}CH_3$, $R'{=}CH_2C_6H_5$; III a $R{=}C_2H_5$, $R''{=}CH_3$, b $R{=}n\text{-}C_3H_7$, $R''{=}CH_3$, c $R{=}C_2H_5$, $R''{=}C_6H_5$, d $R{=}R''{=}CH_3$, e $R{=}C_2H_5$, $R''{=}CH_2C_6H_5$; IV $R{=}C_2H_5$

Spontaneous splitting out of a benzyl radical, as was also observed in the cyclization of substituted 3-benzyl-1-thiopropanols, occurs in alcohols IIb–d with a protective mercapto group.

Benzothiazines III have basic character and give salts with acids (picrates and dihydrochlorides were obtained).

The IR spectra of III contain only ν_{CH} bands at 2400-3650 cm^{-1}. Intense $\nu_{C=N}$ bands are found at 1645-1660 cm^{-1} in the spectra of IIIa, b, d; these frequencies differ from the anomalously high (1700 cm^{-1}) frequencies in the spectra of the oxygen analogs – 2-alkyl-4,4-diethyl-4H-1,3-benzoxazines [1, 2] – and are found in the region of $\nu_{C=N}$ vibrations of thioimino ethers [4]. The mass spectrum of III is characterized by intense peaks corresponding to processes involving the formation of M^+, $(M-C_2H_5)^+$, $(M-N{\equiv}C{-}CH_3)^+$, $(M-2C_2H_5)^+$, $(M-C_2H_5, -N{\equiv}C{-}CH_3)^+$, and $(M-2C_2H_5, -HCN)^+$ions with masses of 219, 190, 178, 161, 149, and 134, respectively. The UV spectrum of benzothiazine IIIa contains absorption maxima at 214-216 and 270 nm, and their intensities are considerably higher than in the spectrum of thiophenol [5].

The formation of benzothiazine IIIa is accompanied by conversion of IIa to 7,7,8,8-tetraethyl-7,8-dihydrodibenzo[c,g]thiathiocine (IV), probably as a result of a redox process. The structure of IV is confirmed by its IR spectrum: ν_{OH} and ν_{SH} vibrations are absent, and there is intense absorption at 485 cm^{-1}, which can, with a certain amount of caution [6], be assigned to ν_{S-S}. The molecular ion (m/e 356) of IV formed under the influence of electron impact undergoes symmetrical fragmentation to a fragment ion with m/e 178, and this is accompanied by a metastable transition (m*/e 89). Nonequivalence of the CH_2 (and CH_3) groups is observed in the PMR spectrum, and this is interesting in connection with the conformational analysis of eight-membered rings with two sulfur atoms.

Alcohols IIb–d do not form IV; olefin V was isolated in the case of the reaction with IIb. According to the PMR spectral data, olefin V consists of two geometrical isomers with predominance (70%) of the trans isomer (Va). The configuration of the isomers can be established on the basis of an evaluation of the allyl and homoallyl constants. In the trans isomer, $^4J_{cis\text{-}all} = 1.5$ Hz and $^5J_{trans\text{-}homoall} = 1.5$ Hz; in the cis isomer, these constants are less than 0.8 Hz. There are data [7, 8] that indicate that trans-homoallyl constants are higher (1.59 Hz [7]) than the cis-homoallyl (1.12 Hz [7]) constants. The cis-allyl constants are usually higher than the trans constants (for example, see [9, 10]). Spin–spin coupling between the $\rangle C{=}CH{-}CH_3$ vicinal protons was established for both isomers by the double-resonance method.

EXPERIMENTAL

The IR spectra of the pure compounds or mineral oil suspensions of the compounds (in the case of the picrates and hydrochlorides) were recorded with DS-301 and UR-10 spectrometers. The UV spectra of ethanol solutions of the compounds were recorded with an SF-4 spectrophotometer. The PMR spectra of CCl_4 solutions were obtained with Varian T-60 or Bruker WN-90 spectrometers. The mass spectra were recorded with an MKh-1303 spectrometer with a system for direct introduction of samples into the ion source at an ionizing voltage of 30 V. The course of the reactions and the purity of the compounds were monitored by means of thin-layer chromatography (TLC) on the alkaline form of activity II aluminum oxide in an ether–petroleum ether system (1 : 2). Compound IIIa was also characterized by gas–liquid chromatography (GLC) (with a Khrom-2 chromatograph remodeled with a glass column 2 m by 3 mm; the stationary phases were Chromaton-N-AW-HMDS treated with 2% KOH and 10% Apiezon L).

Methyl 2-(Benzylthio)benzoate (I). An 8.4-g (50 mmole) sample of methyl thiosalicylate and 5.7 g (45 mmole) of benzyl chloride were added with stirring and cooling to a solution of sodium methoxide (from 1.15 g

TABLE 1. Benzothiazines (IIIa-e)

Compound	bp, °C (mm) or mp	n_D^{20}	IR spectrum, cm^{-1}	R_f	Empirical formula	Found, %					Calc. %					Yield, % (method)
						C	H	Cl	N	S	C	H	Cl	N	S	
IIIa	94—95 (2)	1,5652	1650	0,70	$C_{13}H_{17}NS$	71,2	7,8	—	6,2	14,7	71,2	7,8	—	6,4	14,6	87 (a), 32 (b)
IIIa*	176—177	—	—	—	$C_{13}H_{17}NS \cdot HCl$	61,1	7,2	13,9	5,7	12,6	61,0	7,1	13,9	5,5	12,5	—
IIIa†	162—163	—	1630	—	$C_{13}H_{17}NS \cdot C_6H_3N_3O_7$	51,0	4,4	—	12,5	7,5	50,9	4,5	—	12,5	7,2	—
IIIb	—	—	1660	0,66	$C_{15}H_{21}NS$	73,1	8,5	—	5,8	13,2	72,8	8,5	—	5,7	13,0	41 (a)
IIIb*	158,0—159,5	—	—	—	$C_{15}H_{21}NS \cdot HCl$	63,6	7,8	12,4	5,0	11,4	63,5	7,8	12,5	4,9	11,3	—
IIIc	—	—	—	0,63	—	—	—	—	—	—	—	—	—	—	—	19 (b)
IIIc†	176,5—177,0	—	1630	—	$C_{18}H_{19}NS \cdot C_6H_3N_3O_7$	56,3	4,4	—	11,1	6,2	56,4	4,3	—	11,0	6,2	—
IIId	82—83 (4)	1,5791	1645	0,68	$C_{11}H_{13}NS$	69,2	6,9	—	7,0	16,9	69,1	6,9	—	7,3	16,7	74 (a)
IIId*	~200 (dec.)	—	1653	—	$C_{11}H_{13}NS \cdot HCl$	—	—	15,5	—	—	—	—	15,6	—	—	—
IIIe*	169—171	—	—	0,76	$C_{19}H_{21}NS \cdot HCl$	68,4	6,8	10,7	4,2	10,3	68,7	6,7	10,7	4,2	9,7	50 (a)

*These are the hydrochlorides (crystallized from benzene).

†These are the picrates (crystallized from alcohol).

of sodium and 23 ml of methanol), after which the mixture was stirred at 40° for 30 min. The methanol was then removed by distillation, 200 ml of water was added, and the mixture was extracted with benzene. The benzene extracts were washed with water and vacuum evaporated, and the residue was washed on the filter with petroleum ether and recrystallized from ethanol to give 11.8 g (92%) of ester I with mp 63-63.5° and R_f 0.49. Found %: C 69.6; H 5.5; S 12.3. $C_{16}H_{14}O_2S$. Calculated %: C 69.7; H 5.5; S 12.4. PMR spectrum, δ, ppm: 4.2 (2H, s, CH_2) and 4.0 (3H, s, CH_3).

2-Mercapto-α,α-diethylbenzyl Alcohol (IIa). A solution of 60 g (0.31 mole) of methyl thiosalicylate in 400 ml of dibutyl ether was added dropwise at 20° to a solution of ethyl magnesium bromide (from 44 g of magnesium and 198 g of bromoethane) in 600 ml of absolute dibutyl ether at 20°, after which the mixture was heated at 80° for 12 h. It was then cooled and decomposed with 800 ml of saturated NH_4Cl solution. The dibutyl ether was decanted, and the residue was extracted with dibutyl ether. The organic solutions were combined and dried with $MgSO_4$, and the solvent was removed by distillation. The residue was dissolved in 200 ml of NaOH, and the alkaline solution was extracted with heptane (extract 1). Extract 1 was cooled with ice water, acidified to pH ~7 with HCl (1 : 1), and extracted with heptane. The heptane was removed thoroughly by distillation to give 34.7 g (60%) of quite pure oily alcohol IIa with R_f 0.10. Found %: C 66.8; H 8.2; S 16.3. $C_{11}H_{16}OS$. Calculated %: C 67.3; H 8.2; S 16.3. PMR spectrum, δ, ppm: 0.7 (6H, t, two CH_3 groups), 1.5-2.4 (5H, group of signals: OH and two CH_2 groups of the AB portion of the ABX_3 system), 3.7 (1H, s, SH). A small amount of bis[o-(3-hydroxy-3-pentyl)]phenyl sulfide with mp 71-72° (from heptane) and R_f 0.10 was isolated from extract 1 by evaporation. Found %: C 67.9; H 7.9; S 16.2. $C_{22}H_{30}O_2S_2$. Calculated %: C 67.7; H 7.8; S 16.4. IR spectrum (in oil), cm^{-1}: 3200-3500 (broad ν_{OH}) and 482 (possibly ν_{S-S}). The PMR spectrum was similar to the spectrum of IIa with respect to the chemical shifts and the form of the signals of the ethyl group.

2-Methyl-4,4-diethyl-4H-1,3-benzothiazine (IIIa). A) A solution of 7.6 g (30 mmole) of I in 30 ml of absolute toluene was added dropwise at 20° to a solution of ethylmagnesium bromide (from 2.2 g of magnesium and 9.8 g of bromoethane) in 90 ml of absolute dibutyl ether, after which the mixture was heated at 70-80° for 7 h. It was then cooled and decomposed with 60 ml of saturated NH_4Cl solution, and the organic layer was decanted. The residue was extracted with dibutyl ether. All of the organic solutions were combined, and the solvent was removed by distillation. The residual crude IIb was dissolved in 12 ml of acetonitrile, the solution was heated to 70°, and 13 ml of 85% H_2SO_4 was added dropwise at such a rate that the temperature of the reaction mixture remained at 85-90°. After 24 h, the mixture was poured over ice, and the aqueous mixture was extracted with ether (extract 2). The acidic aqueous solution was cooled with ice, made alkaline to pH ~ 10 with 40% NaOH solution, and extracted with ether. The ether was removed by distillation to give (without distillation) 5.6 g of IIIa. PMR spectrum, δ, ppm: 0.7 (6H, t, two 4-CH_3 groups), 1.95 (4H, q, two 4-CH_2 groups with almost equivalent protons of the AB portion of an ABX_3 system), 2.3 (3H, s, 2-CH_3), and 6.9-7.3 (4H, group of C_6H_4 signals). UV spectrum, λ_{max}, nm (log ε): 216 (4.31) and 270 (3.60). Evaporation of extract 2 yielded 1.3 g of V with mp 61-62° (from alcohol) and R_f 0.73. Found %: C 80.8; H 7.6; S 11.7. $C_{18}H_{20}S$. Calculated %: C 80.6; H 7.5; S 11.9. IR spectrum: 1660 cm^{-1} (very weak, $\nu_{C=C}$). PMR spectrum of Va, b, δ, ppm: 0.78 (CH_3CH_2 in Vb, t, ^3J = 7.5 Hz), 0.88 (CH_3CH_2 in Va, t, ^3J = 7.5 Hz), 1.32 ($CH_3CH{=}C$ in Va, ^3J = 6.5 Hz, ^5J = 1.5 Hz), 1.64 ($CH_3CH{=}C$ in Vb, ^3J = 6.5 Hz), 2.0-2.6 (CH_2CH_3 in Va, b, six lines of two overlapped quartets with ^3J = 7.5 Hz;

the components of Va with a more expressed fine structure are found at relatively stronger fields), 4.0 and 3.97 (SCH_2 singlet of Va, b, respectively), 5.22 ($C{=}CHCH_3$ in Vb, $^3J = 6.5$ Hz), 5.48 ($C{=}CHCH_3$ in Va, $^3J = 6.5$ Hz, $^4J = 1.5$ Hz), and 6.7-7.4 (9H, aromatic protons). In an attempt to subject Va, b to fractional crystallization it was found that the mixture did become somewhat enriched in Vb but melted over a rather narrow temperature range.

B) A 4-ml sample of 70% $HClO_4$ was added with stirring and cooling to a mixture of 3.6 g (18 mmole) of IIa and 5 ml of acetonitrile at such a rate that the temperature remained at 20-30°. After 24 h, the mixture was poured over ice, and the aqueous mixture was made alkaline with ammonium hydroxide and extracted with ether. The ether was removed by distillation, and the residue was fractionated to give 1.25 g of IIIa. According to its IR spectrum and R_f value, the product was identical to a sample obtained by method A. The picrate had mp 162-162.5° (from alcohol), and its IR spectrum was identical to a sample obtained by method A; no melting-point depression was observed for a mixture with it. The pot residue from the distillation was triturated with petroleum ether, and the resulting solid was recrystallized from heptane to give 1.45 g of IV with mp 88-89° and R_f 0.83. Found %: C 74.1; H 8.0; S 17.7. $C_{22}H_{22}S_2$. Calculated %: C 74.1; H 7.9; S 18.0.

2-Methyl-4,4-dipropyl-4H-1,3-benzothiazine (IIIb). A solution of 6.4 g (25 mmole) of I in 50 ml of absolute toluene was added gradually to a solution of propylmagnesium bromide (from 1.8 g of magnesium and 9.3 g of 1-bromopropane) in 50 ml of absolute dibutyl ether, after which the mixture was worked up by method A and subjected to reaction with 10 ml of acetonitrile in 11 ml of 85% H_2SO_4 at 80-90° to give IIIb (oil); the product was purified with a column filled with activity IV Al_2O_3 with elution by ether-petroleum ether (1 : 1) to give 2.5 g of product. PMR spectrum, δ, ppm: 0.6-1.4 (10H, group of signals of two $4\text{-}CH_2CH_3$ groups), 1.4-2.0 (4H, group of two methylene signals of $4\text{-}CH_2C_2H_5$), 2.2 (3H, s, $2\text{-}CH_3$), and 6.8-7.3 (4H, group of C_6H_4 signals).

2-Phenyl-4,4-diethyl-4H-1,3-benzothiazine (IIIc). A total of 6 ml of 70% $HClO_4$ was added with stirring and cooling (to 20-30°) to a mixture of 7.0 g (35 mmole) of IIa and 7.3 g (70 mmole) of benzonitrile, after which the mixture was worked up by method B, and the oily IIIc was converted to the hydrochloride. The hydrochloride was converted to the base with sodium bicarbonate solution, and the base was extracted with ether. The ether was removed by distillation to give 1.9 g of IIIc. PMR spectrum, δ, ppm: 0.8 (6H, t, two $4\text{-}CH_3$ groups), 2.0 (4H, q, two $4\text{-}CH_2$ groups), and 7.0-8.1 (9H, C_6H_4 and C_6H_5; the multiplet at 8 ppm is probably related to the two ortho protons of the C_6H_5 group).

2,4,4-Trimethyl-4H-1,3-benzothiazine (IIId). A solution of 6.4 g (25 mmole) of I in 30 ml of absolute toluene was added gradually to a solution of a Grignard reagent obtained from 1.8 g of magnesium and 10.6 of methyl iodide in 40 ml of absolute dibutyl ether, after which the mixture was worked up by method A and subjected to reaction with 10 ml of acetonitrile in 12 ml of 85% H_2SO_4 (80-85°). The mixture was then poured over ice, and the aqueous mixture was made alkaline with ammonium hydroxide and extracted with benzene. The benzene was removed by distillation, and the residue was fractionated to give 3.6 g of IIId. PMR spectrum, δ, ppm: 1.4 [6H, s, $4\text{-}(CH_3)_2$], 2.2 [3H, s, $2\text{-}CH_3$), and 6.9-7.4 (4H, group of C_6H_4 signals).

2-Benzyl-4,4-diethyl-4H-1,3-benzothiazine (IIIe). A solution of 5.2 g (20 mmole) of I in 50 ml of absolute toluene was added gradually to a solution of ethylmagnesium bromide (from 1.5 g of magnesium and 6.5 g of bromoethane) in 50 ml of absolute dibutyl ether, after which the mixture was worked up method A, and the oil was dissolved in 8 g of benzyl cyanide. The solution was treated with 8 ml of 85% H_2SO_4 (90-100°). After 24 h, the mixture was poured over ice, and the aqueous mixture was made alkaline with 40% NaOH and extracted with chloroform. The chloroform was removed by distillation, and the residue was treated with heptane. The heptane was evaporated, and the residue was converted to 3.3 g of the hydrochloride in absolute ether.

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