SYNTHESIS AND SOME CONVERSIONS OF THIOPHENE SERIES SULFIDES

XI. Synthesis Of 3,4-Dihydrothieno [3,2–e]-1,3-Thiazines*

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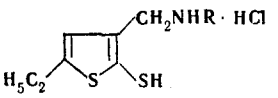
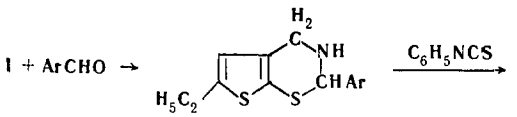
Condensation of 2-mercapto-5-ethyl-3-thenylamines with aromatic aldehydes and carbon disulfide gives some 2-substituted 3, 4-dihydro-6-ethylthieno [3, 2-e]-1, 3-thizines.

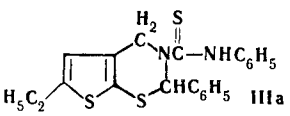
Previously we described [1] 2-mercapto-5-ethyl-3-thenylamines (I,II), prepared in high yields by reducing the corresponding mercaptoaldimines with lithium aluminum hydride. The present paper demonstrates some possibilities of using it to synthesize condensed heterocyclic systems, of potential interest from the point of view of checking their physiological activity [2,3].

The nature of the mercaptoamine I, as a compound with SH and CH_2NH_2 groups ortho to one another, is exhibited in its ability to react with aldehydes and carbon disulfide to give compounds related to the class of 3,4-dihydrothieno-1,3-thiazines. This kind of reaction with aldehydes [4,5] and carbon disulfide [6] is characteristic of aliphatic aminomercaptans and o-aminothiophenols. In the present case the latter are converted to benzothiazolines.

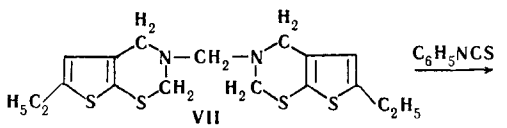


I R = H
II R = C_6H_{11}

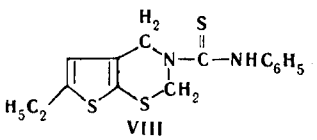




Ar = C_6H_5 (III), p-$C_6H_4NO_2$ (IV), o-C_6H_4OH (V), 2-C_4H_3S (VI)



VII

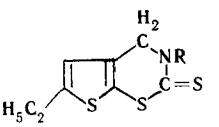


VIII

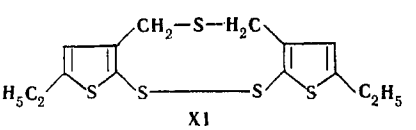
The literature [7,8] also describes closure of the 1,3-thiazine ring on the benzene ring, but there the starting compounds were different, and the yields negligible.

The IR spectra of the compounds prepared indicate that they are thienothiazine derivatives, and not tautomeric Schiff's bases. The absorption band characteristic of the NH group is found in the 3320–3340 cm^{-1} region, absorption bands for C—N and SH groups are absent. The thienothiazine III and phenylisothiocyanate give the derivative IIIa, which also serves to confirm the presence of a NH group. However with the reaction product from the mercaptoamine I and salicylaldehyde, it is impossible to exclude the second isomeric form as well. The presence of an intense band in the 1632^{-1} region, which can be assigned to C—N valence vibrations, and the absence of a well-defined NH band, which latter is plainly in evidence in the spectra of compounds III, IV, and VI, obviously indicates the existence of tautomeric equilibrium in this case (see figure).

Condensation of I with formaldehyde gives, instead of the unsubstituted thienothiazine, bis (3,4-dihydro-6-ethlhieno [3.2–e]-1,3-thiazine-3-yl) methane (VII), which reacts with phenylisothiocyanate to give derivative VIII.



IX R = H, X R = C_6H_{11}

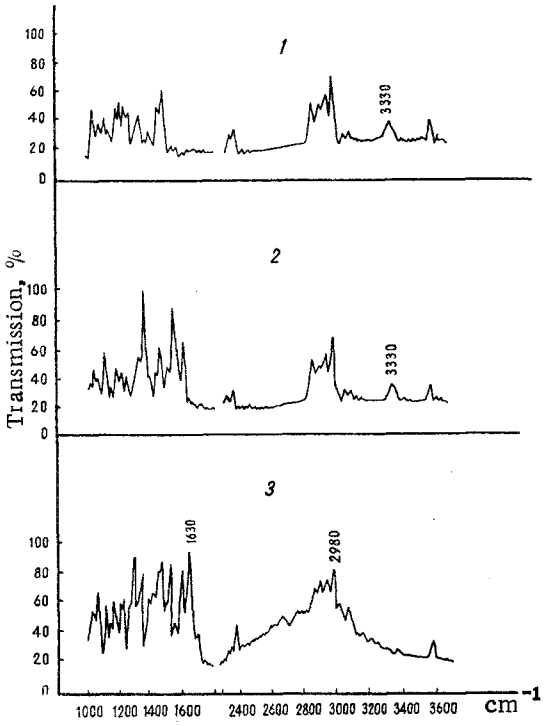


XI

Mercaptoamines I and II react with carbon disulfide at room temperature to give the thiones IX and X. If the reaction with carbon disulfide is carried out by refluxing for 30 min in the case of I, and by refluxing for 4 hr in the case of II, the yields of thiones are cut, and in both cases a crystalline substance is formed whose composition corresponds to the structure XI, but this has not yet been confirmed. When a prolonged refluxing (8 hr) was used with I, the only products isolated were XI and KCNS.

The IR spectra of products IX and X have bands at 1040 and 1042 cm^{-1}, which can be assigned to C—S vibrations [9]. The spectrum of compound IX has a marked NH group absorption band at 3160 cm^{-1}, though this band is lacking in the spectrum of X.

*For Part X see [1].



IR absorbtion spectra of thienothiazines in CCl_4. 1) VI; 2) IV; 3) V.

Compounds Synthesized

Compound number	Mp, °C	Formula	Found, %			Calculated, %			Yield %
			C	H	S	C	H	S	
III	82.5—83.5	$C_{14}H_{15}NS_2$	64.49; 64.21	5.97; 5.93	24.77; 24.59	64.32	5.90	24.53	80
IV	128—129 (decomp)	$C_{14}H_{14}N_2O_2S_2$	54.89; 54.83	4.72; 4.63	20.95; 21.16	54.88	4.60	20.93	68
V	93.5—95	$C_{14}H_{13}NOS_2$	61.21; 61.42	5.26; 5.45	22.79; 23.04	60.61	5.56	23.12	76
VI	71.5—72.5	$C_{12}H_{13}NS_3$	53.81; 53.64	4.94; 4.97	36.12; 36.21	53.89	4.90	35.97	82
VII[1]*	98.5—99.5	$C_{17}H_{22}N_2S_4$	53.47; 53.30	5.85; 5.72	33.29; 33.52	53.36	5.80	33.52	73.5
IIIa	148—148.5[2]*	$C_{21}H_{20}N_2S_3$	63.28; 63.20	5.14; 5.27	24.19; 24.34	63.60	5.08	24.26	94.6
VIII	132—133[3]*	$C_{15}H_{16}N_2S_3$	56.27; 56.44	4.89; 5.13	30.43; 30.20	56.21	5.05	30.02	86.5
IX	169—170	$C_8H_9NS_3$	44.29; 44.29	4.14; 4.19	44.55; 44.50	44.61	4.21	44.67	59
X	77—78	$C_{14}H_{19}NS_3$	56.45; 56.18	6.40; 6.43	32.29; 32.53	56.52	6.44	32.33	59
XI[4]*	154—154.5[5]*	$C_{14}H_{16}S_5$	48.67; 48.76	4.74; 4.73	46.31; 46.51	48.79	4.68	46.53	19 ex I 34 ex II

1* M, found (cryoscopic in benzene) 409; calculated 382.6. 2* Ex EtOAc. 3* Ex EtOH. 4* M, found (ex benzene) 351, calculated 344.6.
5* Ex heptane and EtOH.

EXPERIMENTAL

Condensation of 2-mercapto-5-ethyl-3-thenylamine (I) with aromatic aldehydes. 0.12 mole aldehyde, or an ethanol solution of it, was added to a solution of 0.1 mole I hydrochloride in 10 times the amount of ethanol, followed by a concentrated aqueous solution of 0.1 mole KOAc* at room temperature. The mixture was left overnight, but in the case of 2-thiophene aldehyde for 15 min only. The precipitate of thienothiazine was filtered off, washed with 50% ethanol, and recrystallized from heptane or ethanol (see table, compounds IV–VI). Under the above conditions the mercaptoamine II does not condense.

Bis(3, 4-dihydro-6-ethylthieno [3, 2-e]-1, 3-thiazine-3-yl) methane. (VII). 5 ml 30% formalin solution and 1.0 g KOAc in a small amount of distilled water were added to a solution of 2.0 g (about 0.1 mole) I hydrochloride in 20 ml EtOH, when a viscous yellow oil immediately came down. This was separated, washed with water and then with EtOH, and dissolved in ether. The ether solution was washed with water, dried over $MgSO_4$. The residue after evaporating off the ether was recrystallized from EtOH and EtOAc.

Condensation of mercaptoamines I and II with carbon disulfide. An ethanol solution of 0.2 mole KOH was added to a solution of 0.1 mole I or II hydrochloride in dry EtOH. After filtering the solution was mixed at 0° with 0.2 mole carbon disulfide, the mixture stirred for 4 hr at room temperature, then left overnight. The solvent was vacuum-evaporated, the residue washed with EtOH or benzene, and recrystallized from EtOH (see table, compounds IX, X).

* If the condensation was run without adding potassium acetate, no individual compounds could be isolated.

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