SYNTHESIS AND INVESTIGATION OF ENAMINE–IMINE TAUTOMERISM OF 2,6-DISUBSTITUTED 4*H*-1,3-THIAZIN-4-ONES

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Substituted thioureas, obtained by reaction of 3-chloro-3-phenylpropenoyl isothiocyanate with primary aliphatic or aromatic amines, were cyclized to 2-N-alkyl(aryl)amino-6-phenyl-4*H*--1,3-thiazin-4-ones. The enamine–imine tautomerism was investigated by means of infrared and ultraviolet spectra and also by model substances prepared either by reacting the starting isothiocyanate with secondary amines, or by methylation of 2-N-alkyl(aryl)amino-6-phenyl-4*H*--1,3-thiazin-4-ones. The structure of the synthesized compounds was corroborated by ^{1}H NMR and electron impact mass spectra. 2-N-Arylamino derivatives dissolved in chloroform exist prevalently an imino form whereas 2-N-aikylamino derivatives is an amino form. Reaction of 3-chloro-3-phenylpropenoyl isothiocyanate with aliphatic thiols gave 2-alkylthio-6-phenyl--4*H*-1,3-thaizin-4-ones and with sodium hydrosulfide (hydroselenide) 6-phenyl-2-thioxo-2,3-dihydro-4*H*-1,3-thiazin(selenazin)-4-ones.

Of various methods dealing with the synthesis of unsaturated 1,3-thiazin-4-ones the most frequented is the reaction of dithiocarbamates, thioureas and thioamides with derivatives of propynoic[1–3] and ethynyldicarboxylic acids[4–6]. This reaction, however, can also be accompanied by formation of five-membered thiazolone rings[7] depending on the type of substituents. Our preceding papers concerned the synthesis of thiazine derivatives from α,β-unsaturated acyl isothiocyanates. 3-Phenylpropenoyl isothiocyanate and 3-(2-furyl)propenoyl isothiocyanate react with amines to give the corresponding thioureas, which could be cyclized to 2,6-disubstituted-5,6-dihydro-4*H*-1,3-thiazin-4-ones only with thioureas prepared from secondary amines[8]. Thioureas obtained by reaction with primary amines, dimethyl- and diethylamine did not cyclize nor upon a long-lasting boiling in organic solvents. To obtain 6-phenyl-2-thioxo-2,3-dihydro-4*H*-1,3-thiazin-4-one, 3-phenylpropynyl isothiocyanate was reacted with NaSH (ref.[9]). Derivatives of 1,3-thiazin-4-one can be prepared from acyl isothiocyanates having a β-chlorovinyl grouping able to undergo an addition-cyclization reaction with nucleophilic reagents. Reactions of 3-chloropropenoyl isothiocyanates with aryl or aralkylamines gave, depending on the reaction conditions, either derivatives of 2-amino-4*H*-1,3-thiazin-4-one, or 2-thiouracils[10].

This paper is aimed to examine the reactions of 3-chloro-3-phenylpropenoyl isothiocyanate with primary and secondary amines, thiols, sodium hydrosulfide and

hydroselenide for preparing 2-substituted 6-phenyl-4*H*-1,3-thiazin-4-ones. The possible enamine-imine tautomerism of the prepared 2-N-alkyl(aryl)amino-6-phenyl-4*H*-1,3-thiazin-4-ones was investigated. The starting material for the synthesis of 3-chloro-3-phenylpropenoyl isothiocyanate was the Z-isomer of 3-chloro-3-phenylpropenoic acid[11] which was transformed with thionyl chloride into 3-chloro-3-phenylpropenoyl chloride (*I*); the latter afforded with lead thiocyanate the corresponding isothiocyanate *II*. Due to its thermal instability this product was directly used in the next step.

Reaction of 3-chloro-3-phenylpropenoyl isothiocyanate (*II*) with aliphatic or aromatic amines in acetone furnished thioureas *IIIa*–*IIIg* even at room temperature (Tables I, II). With methylamine as starting material N-methyl-3-chloro-3-phenylpropenoylamide was isolated as a by-product in a 17% yield. Its structure was evidenced by comparison of IR and ^{1}H NMR spectra with the standard *IV* prepared from *I* and methylamine. Secondary amines yielded under similar conditions thioureas, which, in turn, cyclized to afford N,N-disubstituted 2-amino-6-phenyl-4*H*-1,3-thiazin-4-ones *VIIa*–*VIIc* (Table III). Thioureas *IIIa*–*IIIg*, obtained by reaction with primary aliphatic and aromatic amines cyclized to 1,3-thiazin-4-ones *Va*–*Vg* by a several-hour boiling in toluene (Table III). As evident, 3-chloro-3-phenylpropenoyl isothiocyanate enables, in contrast to propenoyl isothiocyanates[8], to obtain cyclic products also with primary amines.

Thiazines *Va*–*Vg* can exist either in an amino form *A*, or in an imino form *B*. Backed by IR and UV spectral evidence derivatives of thiazine *XII* and *XIII* were assigned[5,7] the amino form. The structure of thiazines *Va*–*Vg* was deduced from IR, UV, ^{1}H NMR and mass spectrometric data (Table IV).

The IR spectra of N-alkyl derivatives *Va*–*Vd* measured in chloroform revealed strong absorption bands ν(C=O) at 1 615–1 618 cm^{-1} with characteristic shoulders at 1 654–1 696 cm^{-1} and two absorption bands ν(N—H) at 3 377–3 408 cm^{-1} and 3 410–3 435 cm^{-1}. The appearance of the carbonyl group absorption bands at lower wave numbers can be rationalized by a very strong conjugation in the ring if tautomeric amino form *A* is involved. The shoulder ν(C=O) at 1 654–1 696 cm^{-1}, as well as the lower intensity of the absorption band ν(N—H) at 3 377–3 408 cm^{-1} indicates that in solution the N-alkyl derivatives *Va*–*Vd* appear also in the imino form *B* to some extent. The absorptions of carbonyl groups of N-aryl derivatives *Ve*–*Vg* are at considerable higher wave numbers ν(C=O) 1 670–1 672 cm^{-1} and their amino groups are seen as one band only at 3 363–3 366 cm^{-1}. This fact provided evidence that here the tautomeric imino form *B* with exocyclic C=N bond is substantially pronounced. Like differences in the position of absorption bands ν(C=O) were also observed[7] with amino derivative *XIII* and imino derivative *XIV*. The IR spectra measured in KBr discs showed noticeable changes in positions and intensities of ν(C=O) absorption bands, namely with N-arylsubstituted derivatives *Ve*–*Vg*. The strong absorption bands of carbonyl groups of tautomeric form *A*

appeared at 1 619 – 1 625 cm^{-1}, whereas the intensity of ν(C=O) bands of the imino form *B* dramatically dropped and the absorption occurred as a shoulder at 1 653 to 1 661 cm^{-1}. A similar change was also observed in the C=N bond absorption region. The spectra displayed intensive bands of an endocyclic C=N bond at 1 505 – 1 517 cm^{-1} and less intense ones of the exocyclic C=N bond at 1 632 – 1 636 cm^{-1}. As it follows, derivatives *Ve – Vg* have the equilibrium in solid state shifted in favour of the amino form *A*. N-Alkyl derivatives *Vb – Vd* lacked in KBr discs the shoulders of ν(C=O) absorption bands at 1 654 – 1 663 cm^{-1}, associated with the imino form, this being indicative of a further shift towards the amino form. The exception was found with the N-methyl derivative *Va*, showing both in chloroform and KBr discs ν(C=O) bands of both tautomeric forms.

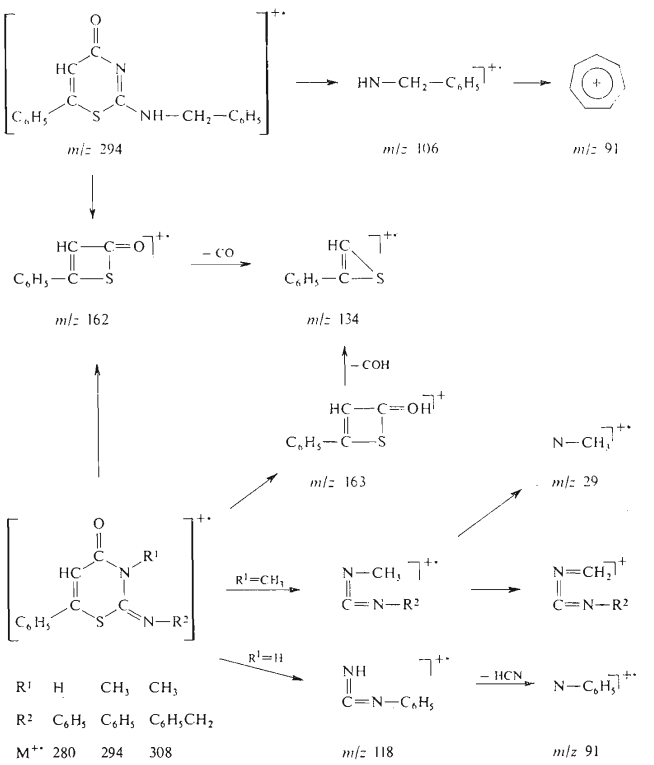
Aiming to verify the foregoing observations, model substances with a fixed endocyclic C=N bond were synthesized. Compounds *VIIa – VIIc* possessing the endocyclic C=N bond were prepared by reacting *II* with dimethylamine, N-methylaniline and diphenylamine (Table III), those having an exocyclic C=N bond (*VIa – VIc*) by methylation of *Va*, *Ve*, *Vc* with methyl iodide in dimethylformamide (Table III).

TABLE I

N-Substituted N'-(3-chloro-3-phenylpropenoyl)thioureas *IIIa – IIIg*

Compound Substituent	Formula (M_r)	M.p., °C (solvent)	Yield, %	Calculated/Found		
				% C	% H	% N
IIIa	$C_{11}H_{11}ClN_2OS$	134 – 136	43	51·86	4·35	11·00
CH_3	(254·7)	(CCl_4)		51·60	4·51	11·09
IIIb	$C_{14}H_{17}ClN_2OS$	161 – 163	48	56·65	5·77	9·44
C_4H_9	(296·8)	(ethanol)		56·45	5·58	9·43
IIIc	$C_{17}H_{15}ClN_2OS$	149 – 151	44	61·72	4·57	8·47
$C_6H_5CH_2$	(330·8)	(ethanol)		61·90	4·51	8·53
IIId	$C_{16}H_{19}ClN_2OS$	175 – 177	55	59·52	5·93	8·68
C_6H_{11}	(322·9)	(ethanol)		59·64	6·11	8·83
IIIe	$C_{16}H_{13}ClN_2OS$	177 – 179	51	60·66	4·13	8·84
C_6H_5	(316·8)	(ethanol)		60·89	4·01	9·00
IIIf	$C_{17}H_{15}ClN_2OS$	170 – 172	70	61·72	4·57	8·47
$CH_3C_6H_4$	(330·8)	(ethanol)		61·40	4·77	8·28
IIIg	$C_{17}H_{15}ClN_2O_2S$	165 – 166	67	58·87	4·36	9·08
$CH_3OC_6H_4$	(346·8)	(ethanol)		58·92	4·20	7·98

As reported[5], methylation of analogous compounds takes place at nitrogen in position 3 of the thiazine skeleton; this was evidenced by the synthesis of 2-methylimino--3-methyl-6-phenyl-2,3-dihydro-4*H*-1,3-thiazin-4-one (*VIa*) from ethyl 3-phenylpropynoate and N,N'-dimethylthiourea[2]. Other arguments proving the correctness of the structure were the electron impact mass spectra of methylated compounds (Scheme 1, Table IV), and, in the case of 2-phenylimino-3-methyl derivative *VIb*



SCHEME 1

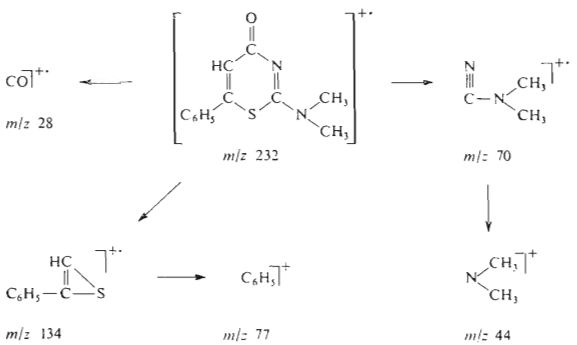
also the different physicochemical and spectral properties than those of analogous 2-N,N-phenylmethylamino derivative *VIIb* (Tables III, IV). The IR spectra of derivatives of secondary amines (N-methylaniline *VIIb*, diphenylamine *VIIc*), which could exist exclusively in amino form, showed in chloroform ν(C=O) absorption bands at 1 626 and 1 624 cm^{-1}, respectively and ν(C=N) bands at 1 531 and 1 504 cm^{-1}, respectively. Both bands are of high intensity and their position in KBr discs does not substantially alter when compared with that measured in chloroform (Table IV). The IR spectrum of 2-dimethylamino-6-phenyl-4*H*-1,3-thiazin-4-one (*VIIa*) displayed a noticeable difference: its intense band at 1 679 cm^{-1} can hardly be ascribed to vibrations of a carbonyl group. Since the mass spectra (Scheme 2, Table IV) and the elemental analysis unambiguously proved the structure of the above-mentioned compound, this strange behaviour can be rationalized by its zwitterionic structure *XV*. As a result we assume

TABLE II

Spectral data of N-substituted N'-(3-chloro-3-phenylpropenoyl)thioureas *IIIa*–*IIIg*

Compound	IR, cm^{-1} [a]				^{1}H NMR, ppm			
	ν(C=C)	ν(C=O)	ν(N—H) free	ν(N—H) assoc.	$\delta(CH_3)$ $\delta(CH_2)$	δ(—CH=)	δ(ArH)[f]	δ(NH)
IIIa[b]	1 605	1 661	3 404	3 194[d]	3·19	6·76	7·43	10·05
		1 675		3 255	—		7·74	10·64
IIIb[b]	1 606	1 659	3 404	3 198[d]	0·93	6·76	7·45	10·05
		1 678		3 257	1·13–1·88[e]		7·73	10·69
IIIc[b]	1 607	1 660	3 402	3 188[d]	—	6·69	7·46	9·92
		1 684		3 250	4·88		7·72	10·95
IIId[b]	1 604	1 654	3 402	3 190[d]	—	6·80	7·44	10·06
		1 671		3 244	0·91–2·23		7·74	10·69
IIIe[c]	1 606	1 659	3 398	3 173	—	7·13	7·45	11·08
		1 680		3 224[d]	—		7·72	12·61
IIIf[c]	1 605	1 659	3 397	3 170	2·34	—[g]	7·45	11·33
		1 678		3 227[d]	—		7·75	12·56
IIIg[c]	1 606	1 659	3 398	3 172	3·79	—[g]	7·46	11·08
		1 677		3 226[d]	—		7·74	12·46

[a] IR spectra measured in chloroform; [b] ^{1}H NMR spectra measured in deuteriochloroform; [c] in deuteriochloroform and hexadeuteriodimethyl sulfoxide; [d] shoulder; [e] δ(N—CH_2) 3·66; [f] aromate in C_6H_5CCl=CHCO—; [g] the —CH= signal is overlapped by the multiplet of aromates.



SCHEME 2

that the most intense band at 1 569 cm^{-1} of the three absorption bands in the 1 500 to 1 700 cm^{-1} region belongs to the extremely polarized carbonyl group, that at 1 679 cm^{-1} to the exocyclic $C{=}\overset{(+)}{N}$ bond. The UV and ^1H NMR measurements are in favour of this assumption. The absorption maximum λ_{max} 330 nm showed a bathochromic shift by 60 to 80 nm against all other thiazine derivatives (Table IV). The ^1H NMR spectrum showed a remarkable downfield shift of the methylidine proton resonance signal (δ_{CH} = 7·79), approximately 1 ppm when compared with other thiazine derivatives. Moreover, the non-equivalence of both methyl groups is seen by two distinct signals at δ 3·24 and 3·40 indicative of a restricted rotation of the dimethylamino group. The zwitterionic character was also assigned to 2-imino--5-phenyl-4-thiazolidinone[12] and 2-dimethylaminothiazolin-4-one[13] displaying two methyl group signals, as well. Methylated products *VIa – VIc* with a fixed exocyclic C=N bond exhibited either in chloroform or in KBr discs three discernible absorption bands associated with an exocyclic C=N bond at 1 620 cm^{-1}, an ethylenic C=C bond at ~1 585 cm^{-1} and a carbonyl group at ~1 655 cm^{-1}. Results of spectral measurements of model substances *VIa – VIc* and *VIIa – VIIc* were in favour of the assumption that N-substituted 2-amino-6-phenyl-4*H*-1,3-thiazin-4-ones *Va – Vg* exist in two tautomeric forms the abundance of which depends both on the character of the substituent on the amino group and conditions of measurement.

The differences in the long-wave maxima between amino and imino structures in the UV spectra are not substantial with the exception of the already mentioned dimethylamino derivative *VIIa*. The N-aryl derivatives *Ve – Vg* showed, when com-

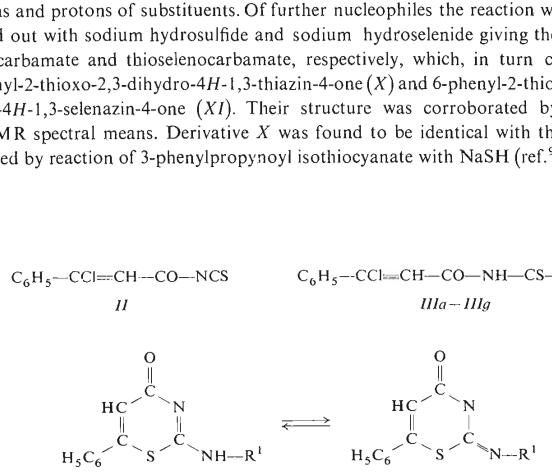
pared with N-alkyl derivatives *Va*–*Vd*, a bathochromic shift of the long-wave maximum by ~25 nm due to the presence of a further aromatic ring in the molecule (Table IV). The ^{1}H NMR spectra of the synthesized 1,3-thiazines are characteristic of a singlet of thiazine ring methylidine proton at δ 6·60–6·93. Signals of the

TABLE III
Compounds *V*–*VII*

Compound Substituent	Formula (M_r)	M.p., °C (solvent)	Yield, %	Calculated/Found		
				% C	% H	% N
Va	$C_{11}H_{10}N_2OS$	213–214	42	60·53	4·62	12·83
CH_3	(218·3)	(ethanol)		60·37	4·81	12·88
Vb	$C_{14}H_{16}N_2OS$	186–188	82	64·59	6·19	10·76
C_4H_9	(260·4)	(ethanol)		64·38	6·32	10·70
Vc	$C_{17}H_{14}N_2OS$	166–168	93	69·36	4·79	9·52
$C_6H_5CH_2$	(294·4)	(ethanol)		69·51	4·62	9·41
Vd	$C_{16}H_{18}N_2OS$	238–239·5	75	67·10	6·33	9·78
C_6H_{11}	(286·4)	(ethanol)		67·39	6·13	9·60
Ve	$C_{16}H_{12}N_2OS$	224–226	81	68·55	4·31	9·99
C_6H_5	(280·4)	(ethanol)		68·23	4·15	9·85
Vf	$C_{17}H_{14}N_2OS$	203–205	95	69·36	4·79	9·52
$CH_3C_6H_4$	(294·4)	(ethanol)		69·50	4·83	9·41
Vg	$C_{17}H_{14}N_2O_2S$	194–195·5	72	65·79	4·55	9·03
$CH_3OC_6H_4$	(310·4)	(ethanol)		65·93	4·66	9·13
VIa	$C_{12}H_{12}N_2OS$	123–125	55	62·04	5·21	12·06
CH_3	(232·3)	(C_6H_6–light petrol.)		61·89	5·10	12·11
VIb	$C_{17}H_{14}N_2OS$	110–112	67	69·36	4·79	9·52
C_6H_5	(294·4)	(C_6H_6–light petrol.)		69·50	4·83	9·41
VIc	$C_{18}H_{16}N_2OS$	96–98	62	70·10	5·23	9·08
$C_6H_5CH_2$	(308·4)	(C_6H_6–light petrol.)		70·28	5·37	9·15
VIIa	$C_{12}H_{12}N_2OS$	181–183	68	62·04	5·21	12·06
CH_3, CH_3	(232·3)	(ethanol)		61·84	5·20	12·08
VIIb	$C_{17}H_{14}N_2OS$	178·–180	42	69·36	4·79	9·52
CH_3, C_6H_5	(294·4)	(ethanol)		69·60	5·01	9·34
VIIc	$C_{22}H_{16}N_2OS$	226·5–228	49	74·13	4·52	7·86
C_6H_5, C_6H_5	(456·5)	(C_6H_6–light petrol.)		74·29	4·66	7·83

aromatic ring attached to position 6, forming with thioureas *IIIa*–*IIIg* one two-proton multiplet of *ortho* protons in lower field (δ ~7·74) and one three-proton multiplet of *meta* and *para* protons in higher field (δ ~7·44), collapsed after cyclization into one not discernible multiplet at δ 7·41–7·52. Signal of NH protons could not be observed in the ^{1}H NMR spectra of 1,3-thiazines *Va*–*Vg* due to a rapid chemical exchange. Structure of the thiazines under investigation was also backed by the mass spectra of the chosen substances *Vc*, *Ve*, *VIb*, *VIc*, and *VIIa* (Table IV). The high intensity of the molecular ion peaks indicates the stability of these species. The principal fragmentation pattern which is in agreement with the anticipated structure, is illustrated in Schemes 1 and 2.

The reaction of 3-chloro-3-phenylpropenoyl isothiocyanate (*II*) with ethyl, propyl and benzylthiol afforded the corresponding dithiourethanes *VIIIa*–*VIIIc*, which, when heated in toluene, cyclized to 2-alkylthio-6-phenyl-4*H*-1,3-thiazin-4-ones *IXa*–*IXc*. The IR spectra of dithiourethanes *VIIIa*–*VIIIc* displayed strong ν(C=O) absorption bands at 1 672–1 682 cm^{-1}, ν(C=C) bands at 1 598–1 601 cm^{-1} and ν(NH–C=S) bands at 1 456–1 463 cm^{-1}. The cyclization products *IXa*–*IXc* exhibited a mild decrease of the ν(C=O) and ν(C=C) absorption bands and an intense ν(C=N) band appeared at 1 490 cm^{-1}. The ^{1}H NMR spectra of dithiourethanes and their cyclic products displayed signals of phenyl and methylidene protons and protons of substituents. Of further nucleophiles the reaction with *II* was carried out with sodium hydrosulfide and sodium hydroselenide giving the unstable dithiocarbamate and thioselenocarbamate, respectively, which, in turn cyclized to 6-phenyl-2-thioxo-2,3-dihydro-4*H*-1,3-thiazin-4-one (*X*) and 6-phenyl-2-thioxo-2,3-dihydro-4*H*-1,3-selenazin-4-one (*XI*). Their structure was corroborated by IR and ^{1}H NMR spectral means. Derivative *X* was found to be identical with the product obtained by reaction of 3-phenylpropynoyl isothiocyanate with NaSH (ref.[9]).



R^1 = CH_3 (*a*), C_4H_9 (*b*), $C_6H_5CH_2$ (*c*), C_6H_{11} (*d*), C_6H_5 (*e*), $CH_3C_6H_4$ (*f*), $CH_3OC_6H_4$ (*g*).

TABLE IV

Spectral data of thiazines *Va*–*Vg*, *VIa*–*VIc*, *VIIa*–*VIIc*

Compound	IR, cm^{-1} ($CHCl_3$)				IR, cm^{-1} (KBr))			UV, λ_{max}, nm	^1H NMR, ppm[a]			
	ν(C=N)	ν(C=C)	ν(C=O)	ν(NH)	ν(C=N)	ν(C=C)	ν(C=O)	log ε, m mol^{-1}	$\delta(CH_3)$	$\delta(CH_2)$	$\delta(-CH=)$	δ(ArH)[c]
Va	1 523 1 628[b]	1 604	1 617 1 696	3 435 3 408	1 537 1 635[b]	1 602	1 621 1 693	247·5 3·01	3·18	—	6·78	7·50
Vb	1 515 1 633[b]	1 602	1 615 1 661[b]	3 426 3 392	1 540	1 600	1 617	248 3·29	0·91	1·28–1·69 3·55	6·72	7·46
Vc[d]	1 514 1 633	1 601	1 617 1 663	3 417 3 377	1 522	1 597	1 614	248 3·37	—	4·73	6·66	7·41
Vd	1 515 1 635[b]	1 606	1 618 1 654[b]	3 410 3 381	1 519	1 603	1 615	249 3·38	—	0·91–2·15	6·63	7·47
Ve[e]	1 627	1 587	1 672	3 363	1 633[b] 1 505	1 589 1 601	1 661[b] 1 625	269 3·44	—	—	6·61	7·46
Vf	1 628	1 584	1 670	3 365	1 632[b] 1 517	1 594 1 606	1 653[b] 1 622	271 3·40	2·32	—	6·60	7·43
Vg	1 628	1 585	1 671	3 366	1 636[b] 1 507	1 594 1 611	1 659[b] 1 619	276 3·40	3·78	—	6·61	7·43
VIa	1 622	1 585	1 652	—	1 616	1 579	1 650	252 3·12	3·23 3·45	—	6·61	7·52

VIb[f]	1 619	1 582	1 659	—	1 613	1 578	1 658	252 3·35	3·60	—	6·60	7·41
VIc[g]	1 620	1 586	1 652	—	1 609	1 577	1 643	251 3·33	3·54	4·59	6·63	7·41
VIIa[h]	1 679	1 614	1 569	—	1 675	1 612	1 577	330 3·42	3·24 3·40	—	7·79	7·46
VIIb	1 531	1 605	1 626	—	1 535	1 603	1 628	251·5 3·46	3·58	—	6·77	7·46
VIIc	1 504	1 603	1 624	—	1 506	1 600	1 632	257·5 3·46	—	—	6·76	7·43

[a] Solvent: $CDCl_3$ (*Va*–*Vc*, *VIa*–*VIc*, *VIIa*–*VIIb*); $CDCl_3$ + hexadeuteriodimethyl sulfoxide (*Vd*–*Vg*, *VIIc*); [b] shoulder; [c] aromate in position 6; [d] mass spectrum, *m*/*z* (% rel. int.): 294 (92), 162 (81), 134 (100), 106 (28), 91 (54), 28 (40); [e] mass spectrum, *m*/*z* (% rel. int.): 280 (95), 163 (100), 162 (42), 134 (91), 118 (44), 91 (20), 77 (23), 28 (15); [f] mass spectrum, *m*/*z* (% rel. int.): 294 (38), 163 (12), 162 (8), 134 (17), 132 (100), 131 (16), 29 (12), 28 (47); [g] mass spectrum, *m*/*z* (% rel. int.): 308 (80), 162 (71), 146 (37), 145 (44), 134 (100), 91 (72), 28 (20); [h] mass spectrum *m*/*z* (% rel. int.): 232 (42), 134 (100), 77 (6), 70 (13), 44 (83), 28 (99).

EXPERIMENTAL

3-Chloro-3-phenylpropenoyl Chloride (*I*)

3-Chloro-3-phenylpropenoic acid[11] (30 mmol) was refluxed with stirring with thionyl chloride (0·1 mol) in chloroform (15 ml) for 2 h. The solvent and the excess of thionyl chloride were evaporated under diminished pressure and the crude product dissolved in benzene. Benzene was evaporated and the product distilled *in vacuo*. Yield 84%, b.p. 104–106°C/470 Pa. IR spectrum, cm^{-1}: ν(C=O) 1 770, ν(C=C) 1 588. ^{1}H NMR spectrum ($CDCl_3$): 6·88 (s, —CH=), 7·47 and 7·74 (mm, C_6H_5).

3-Chloro-3-phenylpropenoyl Isothiocyanate (*II*)

The chloride *I* (25 mmol) and lead thiocyanate (30 mmol) in benzene (40 ml) were refluxed for 2 h. The hot mixture was filtered, the filtrate evaporated and the crude *II* directly used for the next reaction. IR spectrum, cm^{-1}: ν(C=C) 1 597, ν(C=O) 1 708, ν(NCS) 1 968. ^{1}H NMR spectrum ($CDCl_3$): 6·83 (s, —CH=), 7·46 and 7·72 (mm, C_6H_5).

N-Substituted N′-(3-chloro-3-phenylpropenoyl)thioureas *IIIa*–*IIIg*

To the respective amine (5 mmol) dissolved in acetone (10 ml) the isothiocyanate *II* prepared from the chloride *I* (5 mmol) in acetone (10 ml) was added with stirring. Methylamine, liberated from its hydrochloride with sodium hydroxide was introduced into the solution of isothiocyanate *II* in cyclohexane. Thioureas *IIIa*, *IIIe*–*IIIg* were directly precipitated from their solutions. Thioureas *IIIb*–*IIId* were obtained by evaporating the acetone solution to the half of its volume and cooling; the crystals were filtered off, washed with light petroleum and recrystallized from a proper solvent. The precipitate of the methylamine derivative was hot-extracted with tetrachloromethane; it precipitated after cooling. N-Methyl-N′-(3-chloro-3-phenylpropenoyl) thiourea *IIIa* thus prepared in a 43% yield was accompanied with an admixture (17%) of N-methyl-3-chloro-3-phenylpropenoylamide (*IV*). Recrystallization from tetrachloromethane gave the pure *IIIa* (Tables I, II).

N-Methyl-3-chloro-3-phenylpropenoylamide (*IV*)

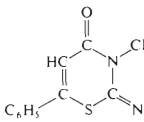
Methylamine (5 mmol) was added to a solution of chloride *I* (5 mmol) in hexane (15 ml) at 40°C. The precipitate was suction-filtered and crystallized from methanol. Yield 66%, m.p. 108 to 110°C. IR spectrum, cm^{-1}: νC=O) 1 654, ν(C=C) 1 613, δ(N–H) 1 524. ^{1}H NMR spectrum ($CDCl_3$): 2·94 (d, CH_3), 6·55 (s, C—CH=), 6·57 broad, (NH), 7·38 and 7·62 (mm, C_6H_5).

2-N-Substituted Amino-6-phenyl-4*H*-1,3-thiazin-4-ones *Va*–*Vg*

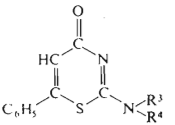
The respective thiourea *IIIa*–*IIIg* (5 mmol) in toluene (30 ml) was refluxed for 5 h. The separated product after cooling was filtered off, the filtrate evaporated to 10 ml from which an additional crop was obtained. Both were collected, washed with light petroleum and crystallized from a suitable solvent (Tables III, IV).

2-N-Substituted Imino-3-methyl-6-phenyl-2,3-dihydro-4*H*-1,3-thiazin-4-ones *VIa*–*VIc*

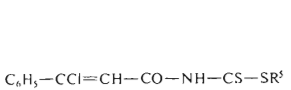
Thiazine *Va*, *Ve*, *Vc* (2 mmol) was added to the suspension of LiH (2 mmol) in dimethylformamide (20 ml) at room temperature, derivative *Va* at 40°C. The mixture was stirred until homogeneous



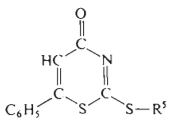
VIa – VIc



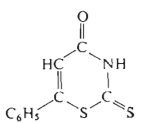
VIIa – VIIc



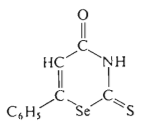
VIIIa – VIIIc



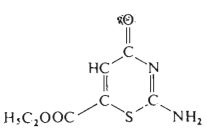
IXa – IXc



X



XI



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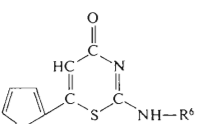

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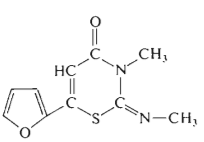

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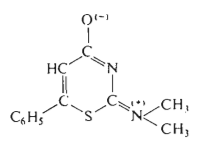

XV

R^2 = CH_3 (*a*), C_6H_5 (*b*), $C_6H_5CH_2$ (*c*)
R^3/R^4 = CH_3/CH_3 (*a*), CH_3/C_6H_5 (*b*), C_6H_5/C_6H_5 (*c*)
R^5 = C_2H_5 (*a*), C_3H_7 (*b*), $C_6H_5CH_2$ (*c*)
R^6 = H, CH_3

(40—90 min), then methyl iodide (2 mmol) was added and stirring was continued for 1 h. The mixture was poured into ice-cold water and the precipitated methylated product was filtered off. N-Benzyl derivative *VIc* separated after an overnight cooling. The products were washed with water and crystallized from a suitable solvent (Tables III, IV).

2-Methylimino-3-methyl-6-phenyl-2,3-dihydro-4*H*-1,3-thiazin-4-one (*VIa*)

Ethyl 3-phenylpropynoate (10 mmol) was refluxed with N,N'-dimethylthiourea (10 mmol) in methanol (20 ml) for 3 h. The solvent was evaporated, the cooled residue which crystallized during the night was washed with ether and recrystallized from benzene–light petroleum. Yield 42%, m.p. 123—125°C (ref.[2] 124°C). IR spectrum, cm^{-1}: ν(C=N) 1 585, ν(C=C) 1 622, ν(C=O) 1 652. ^1H NMR spectrum ($CDCl_3$): 3·23 and 3·45 (ss, CH_3), 6·61 (s, —CH=), 7·52 (m, C_6H_5).

2-N,N-Disubstituted Amino-6-phenyl-4*H*-1,3-thiazin-4-ones *VIIa—VIIc*

The respective secondary amine (5 mmol) in cyclohexane (10 ml) was added to the solution of isothiocyanate *II* obtained from 5 mmol of *I* in cyclohexane (10 ml). Dimethylamine, liberated by sodium hydroxide from dimethylammonium chloride was introduced into solution of *II* in cyclohexane (20 ml). The precipitate separated immediately; the mixture was stirred for 30 min, the precipitate was filtered off and crystallized from an appropriate solvent (Tables III, IV).

S-Alkyl-3-chloro-3-phenylpropenoyldithiourethanes *VIIIa—VIIIc*

Alkylthiol (10 mmol) in acetonitrile (10 ml) was added to isothiocyanate *II* prepared from *I* (10 mmol) dissolved in acetonitrile (10 ml) and the mixture was allowed to stand at an ambient temperature for 3 days. The solution was evaporated at an elevated temperature and the crystals separated after cooling; they were recrystallized from acetonitrile.

S-*Ethyl*-3-*chloro*-3-*phenylpropenoyldithiourethane* (VIIIa): yield 49%, m.p. 84—86°C. For $C_{12}H_{12}ClNOS_2$ (285·8) calculated: 50·43% C, 4·23% H, 4·90%N; found: 50·65% C, 4·10% H, 4·71% N. IR spectrum, cm^{-1}: ν(NH—C=S) 1 456, ν(C=C) 1 599, ν(C=O) 1 672, ν(NH) 3 368. ^1H NMR spectrum ($CDCl_3$): 1·36 (t, CH_3), 3·24 (q, CH_2), 6·69 (s, —CH=), 7·46 and 7·71 (mm, C_6H_5), 10·33 (broad, NH).

The separated dithiourethane was filtered off and the filtrate was slowly and with stirring poured into cold water (150 ml); a second crop which separated was filtered, washed with water and crystallized from ethanol.

S-*Propyl*-3-*chloro*-3-*phenylpropenoyldithiourethane* (VIIIb): yield 63%, m.p. 124—126°C. For $C_{13}H_{14}ClNOS_2$ (299·8) calculated: 52·07% C, 4·71% H, 4·67% N; found: 51·89% C, 4·80% H, 4·76% N. IR spectrum, cm^{-1}: ν(NH—C=S) 1 461, ν(C=C) 1 601, ν(C=O) 1 682, ν(NH) 3 371. ^1H NMR spectrum ($CDCl_3$): 1·03 (t, CH_3), 1·71 (m, CH_2), 3·21 (t, S—CH_2), 6·68 (s, —CH=), 7·46 and 7·70 (mm, C_6H_5), 10·31 (broad, NH).

S-*Benzyl*-3-*chloro*-3-*phenylpropenoyldithiourethane* (VIIIc): yield 65%, m.p. 152—153°C. For $C_{17}H_{14}ClNOS_2$ (347·9) calculated: 58·69% C, 4·06% H, 4·03% N; found: 58·90% C, 4·09% H, 4·29% N. IR spectrum, cm^{-1}: ν(NH—C=S) 1 463, ν(C=C) 1 598. ν(C=O) 1 675, ν (NH) 3 367. ^1H NMR spectrum ($CDCl_3$ + hexadeuteriodimethyl sulfoxide): 4·43 (s, CH_2), 7·18 (s, —CH=), 7·42 and 7·73 (mm, C_6H_5) in position 6, 12·30 (broad, NH).

2-Alkylthio-6-phenyl-4*H*-1,3-thiazin-4-ones *IXa—IXc*

Dithiourethane (*VIIIa—VIIIc*, 3 mmol) was refluxed in toluene (15 ml) for 5 h. The solution was filtered with charcoal and toluene was distilled off. The oily product was washed with light petroleum, allowed to crystallize overnight in cold and crystallized from a suitable solvent.

2-*Ethylthio*-6-*phenyl*-4H-1,3-*thiazin*-4-*one* (IXa): yield 46%, m.p. 75–77°C (benzene–light petroleum). For $C_{12}H_{11}NOS_2$ (249·4) calculated: 57·80% C, 4·45% H, 5·62% N; found: 57·98% C, 4·23% H, 5·79% N. IR spectrum, cm^{-1}: ν(C=N) 1 498, ν(C=C) 1 588, ν(C=O) 1 645. ^1H NMR spectrum ($CDCl_3$): 1·41 (t, CH_3), 3·37 (q, CH_2), 6·82 (s, —CH=), 7·51 (s, C_6H_5).

2-*Propylthio*-6-*phenyl*-4*H*-1,3-*thiazin*-4-*one* (IXb): yield 54%, m.p. 59–61°C (ether). For $C_{13}H_{13}NOS_2$ (263·4) calculated: 59·28% C, 4·97% H, 5·32% N; found: 59·22% C, 5·14% H, 5·13% N. IR spectrum, cm^{-1}: ν(C=N) 1 494, ν(C=C) 1 587, ν(C=O) 1 643. ^1H NMR spectrum ($CDCl_3$): 1·03 (t, CH_3), 1·78 (m, CH_2), 3·35 (t, S—CH_2), 6·81 (s, —CH=), 7·51 (s, C_6H_5).

2-*Benzylthio*-6-*phenyl*-4*H*-1,3-*thiazin*-4-*one* (IXc): Yield 57%, m.p. 103–105°C (ethanol). For $C_{17}H_{13}NOS_2$ (311·4) calculated: 65·56% C, 4·21% H, 4·50% N; found: 65·62% C, 4·42% H, 4·39% N. IR spectrum, cm^{-1}: ν(C=N) 1 498, ν(C=C) 1 588, ν(C=O) 1 645. ^1H NMR spectrum ($CDCl_3$): 4·60 (s, CH_2), 6·83 (s, —CH=), 7·33 (m, C_6H_5-benzylic), 7·49 (s, 6-C_6H_5).

6-Phenyl-2-thioxo-2,3-dihydro-4*H*-1,3-thiazin-4-one (*X*).

Isothiocyanate *II*, prepared from chloride *I* (10 mmol) was slowly added to a stirred solution obtained by introducing hydrogen sulfide (13·5 mmol) in an aqueous sodium hydroxide (13·5 mmol, 25 ml) solution. The immediately separated oil acidified with hydrochloric acid (1 : 1) solidified. The crude product was filtered off, washed with water, dried and crystallized from tetrachloromethane. Yield 49%, m.p. 186–188°C (ref.[9] 173–175°C). For $C_{10}H_7NOS_2$ (221·3) calculated: 54·27% C, 3·19% H, 6·33% N; found: 54·45% C, 2·98% H, 6·18% N. IR spectrum, cm^{-1}: ν(NH—C=S) 1 424, ν(C=C) 1 588, ν(C=O) 1 679, ν(NH) 3 332. ^1H NMR spectrum ($CDCl_3$ + hexadeuteriodimethyl sulfoxide): 6·76 (s, —CH=), 7·52 (s, C_6H_5).

6-Phenyl-2-thioxo-2,3-dihydro-4*H*-1,3-selenazin-4-one (*XI*)

Ethanol (5 ml) was slowly added under a nitrogen atmosphere to a mixture of powdered selenium (11·4 mmol) and $NaBH_4$ (13 mmol). After a 15-min stirring isothiocyanate *II* prepared from 5 mmol of chloride *I* was added, the mixture acidified with hydrochloric acid (1 : 1), the separated product filtered off, washed with light petroleum and crystallized from acetone–water. Yield 21%, m.p. 191–193°C. For $C_{10}H_7NOSSe$ (268·2) calculated: 44·78% C, 2·63% H, 5·22% N; found: 44·92% C, 2·48% H, 5·37% N. IR spectrum, cm^{-1}: ν(NH—C=S) 1 423, ν(C=C) 1 594: ν(C=O) 1 675, ν(NH) 3 319. ^1H NMR spectrum ($CDCl_3$ + hexadeuteriodimethyl sulfoxide), 6·93 (s, —CH=), 7·51 (s, C_6H_5).

Spectral Measurements

The IR absorption spectra of chloroform solutions (given in the experimental section) and KBr discs were recorded with a Specord 75 IR (Zeiss, Jena) apparatus in the 400–4 000 cm^{-1} spectral range, the UV spectra of ethanol solutions with a Superscan 3 (Varian) spectrophotometer in 1 cm-cells. The ^1H NMR spectra (ppm, δ scale) were taken with a Tesla BS 487 instrument operating at 80 MHz; internal reference tetramethylsilane. The electron impact mass spectra were run with an AEI MS 902 S (Manchester) spectrometer at an ionization energy 70 eV.

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