

Thermal Behaviour of Some 2-(3-R-Thioureido)benzonnitriles

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The behaviour of some 2-(3-R-thioureido)benzonnitriles under heating without solvent at the temperature higher than their melting point or boiling in aqueous dimethylformamide was followed. It was found that primary and secondary alkyl or aryl derivatives afford by the cyclization reaction followed by a rearrangement 4-(R-amino)-2-thioxo-1,2-dihydroquinazolines.

3-*tert*-Butyl derivative eliminates methylpropene and in the following cyclization 4-amino-2-thioxo-1,2-dihydroquinazoline is formed. 2-(3-Adamantylthioureido)benzonnitrile under similar conditions decomposes to aminoadamantane and 2-isothiocyanatobenzonnitrile.

2-(3-R,3-R'-Thioureido)benzonnitriles under similar conditions eliminate alkene and the following cyclization and rearrangement gives 4-(R-amino)-2-thioxo-1,2-dihydroquinazolines. Heating of 2-(3,3-dimethylthioureido)benzonnitrile ends in the formation of carbene that in the dependence on conditions of the reaction either dimerizes or polymerizes.

A thermally initiated isomerization of 2-(3-R-thioureido)benzonnitriles to 3-R-4-imino-2-thioxo-1,2,3,4-tetrahydroquinazolines has already been studied [1–4].

It was found that the reactivity of substituted thioureidobenzonnitriles decreases with branching of the alkyl substituent bound to the thioureido group. 2-(3-*tert*-Butylthioureido)benzonnitrile does not cyclize. The isomerization is based on the attack of the thioureido group nitrogen atom N-3 upon the cyano group carbon atom with the simultaneous transfer of the hydrogen atom. In case the hydrogen atom is substituted with alkyl group the alkyl does not migrate and the starting 2-(3-R,3-R'-thioureido)benzonnitrile does not undergo the mentioned isomerization [5].

During melting point measurements of the synthesized 2-(3-alkyl- [2] and 2-(3,3-dialkylthioureido)benzonnitriles [6] we have already observed that further heating of the melt in most cases leads to its rapid solidification.

The aim of the presented work was the study of 2-(3-R- and 2-(3-R,3-R'-thioureido)benzonnitriles thermal behaviour by methods of the thermal analysis.

EXPERIMENTAL

Melting points were measured on Boetius Rapido PHMK 79/2106 (Wägetechnik) instrument. The purity of compounds was tested by elemental analysis on an instrument 1102 (Erba) and the found values correspond to the calculated ones.

The thermal behaviour of compounds was followed with Derivatograph OD-102 (MOM, Budapest). The analyses were provided in about 100 mg samples in a platinum crucible without lid in a stationary atmosphere of the furnace, as a standard material preglowed α -Al₂O₃ was used. The measurements were carried out at 600 °C, TG 100 mg, DTG 1/10 and DTA 1/5. The heating rate was 6 °C min⁻¹.

IR spectra were taken on a spectrometer SP 1000 (Unicam) in KBr pellets, ¹H NMR spectra on BS 567 (Tesla, 100 MHz) or WH-90 (Bruker, 90 MHz) apparatus either in saturated deuteriochloroform (2-(3-R,3-R'-thioureido)benzonnitriles) or in saturated hexadeuterodimethyl sulfoxide (substituted quinazolines), internal standard TMS.

TLC was carried out on Silufol UV 254 (Kavalier, Votice) and the detection with Fluotest Universal (Quartzlampen, Hanau). As an eluent chloroform, diethyl ether, and acetonitrile in a container saturated with the vapours of the used solvent was used.

Dibromoalkanes were identified by GC on Chrom 5 instrument (Laboratorní přístroje, Prague) using glass capillary column with Silicon OV 61 OH (Fluka) comparing them with the standards.

2-(3-R-Thioureido)benzonnitriles (cyclohexyl *Ia*, benzyl *Ib*, phenyl *Ic*, and *tert*-butyl *Id*), 3-cyclohexyl-*IIIa*, 3-benzyl-*IIIb*, 3-ethyl-*IIIc*, 3-butyl-*IIId*, 3-methyl-*IIIe*, 3-(2-hydroxyethyl)-*IIIf*, and 3-phenyl-4-imino-2-thioxo-1,2,3,4-tetrahydroquinazoline (*IIIg*), 4-amino-2-thioxo-1,2-dihydroquinazoline (*IV*) were prepared following papers [2, 3]. 2-(3-R,3-R'-Thio-

ureido)benzonitriles *IIa–IIg* were prepared according to the patent [6]. Their characteristics are presented in Tables 1 and 2.

2-(3-Adamantylthioureido)benzonitrile (*IIe*)

Adamantylammonium chloride (18.8 g; 0.1 mol) was suspended in aqueous solution of sodium hydroxide (100 cm³; 20 %) and the suspension covered with diethyl ether (50 cm³). The mixture was shaken in a separating funnel till the starting compound dissolved (about 3 min). Then the ethereal layer was separated and the water layer twice extracted with 25 cm³ of diethyl ether. Ethereal extracts were combined and dried with potassium hydroxide. So prepared ethereal extract was then added to 2-isothiocyanatobenzonitrile solution in dichloromethane (16 g; 0.1 mol; 50 cm³). Solvents from the reaction mixture were removed on a vacuum rotating evaporator and the crude product crystallized from ethanol as a white crystalline compound with m.p. = 203–205 °C, yield 28.3 g (90 %).

IR spectrum, $\tilde{\nu}/\text{cm}^{-1}$: 3310 $\nu(\text{NH})$, 3050, 2930, 2860 $\nu(\text{CH})$, 2230 $\nu(\text{C}\equiv\text{N})$, 1645 $\delta(\text{NH})$, 1560 $\nu(\text{NHCS})$. ¹H NMR spectrum, δ : 1.42–2.50 (m, 15H, CH), 6.58 (s, 1H, NH), 7.25–8.25 (m, 5H, NH + H_{arom}).

4-Amino-2-thioxo-1,2-dihydroquinazoline (*IV*)

2-(3-*tert*-Butylthioureido)benzonitrile (*Id*) (11.7 g; 50 mmol) was heated in an Erlenmeyer flask

(100 cm³) on an oil bath at the temperature (175 ± 5) °C till the primarily formed melt solidified (2–3 min). The gaseous products formed during the reaction were absorbed in bromine water. 1,2-Dibromo-2-methylpropane formed was then extracted with dichloromethane and isolated by a fractional distillation of the extract (boiling point 150–151 °C).

The solid after reaction was ground and the unreacted adduct *Id* was extracted boiling the reaction mixture in chloroform (200 cm³) for 10 min. Yield 3.5 g (29.9 %). The part insoluble in chloroform crystallized from aqueous dimethylformamide gave 5.6 g (63.3 %) of the product. Melting point, mixed melting point, IR and ¹H NMR spectra were identical with those reported in [2].

4-(R-Amino)-2-thioxo-1,2-dihydroquinazolines *Va–Vj*

Procedure A. Compound *IIa–IIg* (50 mmol) was heated in an Erlenmeyer flask (100 cm³) in an oil bath at the temperature ($\theta_{\text{DTA}}^{\text{R}} \pm 5$) °C given in Table 6 till the primarily formed melt got solid (2–5 min). Gaseous products formed during the reaction of *IIa–IIc* were absorbed in bromine water and so prepared dibromo derivatives were worked up by the procedure mentioned above and identified by GC comparing them with standards. Acetaldehyde formed by the decomposition of *IIg* was absorbed in the saturated solution of 2,4-dinitrophenylhydrazine in 2 M-HCl and identified as hydrazone.

Table 1. Characterization and IR Spectral Data ($\tilde{\nu}/\text{cm}^{-1}$) of Compounds *IIa–IIg*

Compound	R	R'	Yield %	M.p. °C	$\nu(\text{NH})$	$\nu(\text{C}\equiv\text{N})$	$\nu(\text{NHCS})$
<i>IIa</i>	CH ₃	CH ₃	82	178–180	3200	2230	1540
<i>IIb</i>	C ₂ H ₅	C ₂ H ₅	74	103–104	3180	2230	1535
<i>IIc</i>	n-C ₄ H ₉	n-C ₄ H ₉	93	101–103	3300	2230	1530
<i>IId</i>	(CH ₂) ₂ OH	(CH ₂) ₂ OH	70	96–98	3200	2210	1550
<i>IIe</i>	—(CH ₂) ₄ —		92	182–184	3300, 3180	2230	1540
<i>IIf</i>	—(CH ₂) ₅ —		85	135–137	3220	2230	1530
<i>IIg</i>	—(CH ₂) ₂ O(CH ₂) ₂ —		82	134–135	3260	2230	1535

Table 2. ¹H NMR Spectral Data of Compounds *IIa–IIg*

Compound	δ
<i>IIa</i>	2.96 (s, 6H, 2 x CH ₃), 7.28–7.75 (m, 4H, H _{arom}), 9.24 (s, 1H, NH)
<i>IIb</i>	1.30 (t, 6H, 2 x CH ₃ , $J = 7.5$ Hz), 3.80 (q, 4H, 2 x CH ₂ , $J = 7.5$ Hz), 7.39–7.96 (m, 4H, H _{arom}), 9.40 (s, 1H, NH)
<i>IIc</i>	0.96 (t, 6H, 2 x CH ₃ , $J = 6.5$ Hz), 1.12–1.92 (m, 8H, 4 x CH ₂), 3.88 (t, 4H, 2 x N—CH ₂ , $J = 7.5$ Hz), 7.30–7.80 (m, 4H, H _{arom}), 8.75 (s, 1H, NH)
<i>IId</i>	3.75–4.00 (m, 8H, 4 x CH ₂), 3.40 (s, 1H, OH), 7.12–7.75 (m, 4H, H _{arom}), 8.80 (s, 1H, NH)
<i>IIe</i>	1.59–1.92 (m, 4H, 2 x CH ₂), 3.87–4.09 (m, 4H, 2 x CH ₂), 7.23–7.75 (m, 4H, H _{arom}), 8.75 (s, 1H, NH)
<i>IIf</i>	1.50–1.88 (m, 6H, 3 x CH ₂), 3.90–4.15 (m, 4H, 2 x CH ₂), 7.25–7.80 (m, 4H, H _{arom}), 8.70 (s, 1H, NH)
<i>IIg</i>	3.70–3.80 (m, 4H, 2 x CH ₂), 3.90–4.15 (m, 4H, 2 x CH ₂), 7.30–7.80 (m, 4H, H _{arom}), 8.90 (s, 1H, NH)

Table 3. Characterization of Compounds Va–Vj Obtained by the Procedure A–C

Compound	R	M.p.	Yield/%		
		°C	A	B	C
Va	cyclo C ₆ H ₁₁	282–284	–	75–87	–
Vb	CH ₂ C ₆ H ₅	215–217	–	76–90	–
Vc*	C ₆ H ₅	239–240	–	90	–
Vd	n-C ₄ H ₉	249–251	75	82	–
Ve	CH ₃	223–225	79	87	85
Vf	C ₂ H ₅	228–230	78	88	–
Vg	(CH ₂) ₂ OH	203–205	63	79	–
Vh	(CH ₂) ₂ CH=CH ₂	294–296	81	89	–
Vi	(CH ₂) ₃ CH=CH ₂	217–218	80	86	–
Vj	(CH ₂) ₂ OCH=CH ₂	252–254	85	88	–

*According to Ref. [1] m.p. = 239–240 °C (methanol) and yield 91 %.

The solid rest after reaction was worked up by the procedure mentioned above. Products were crystallized from aqueous dimethylformamide.

Procedure B. Compounds Ia–Ic, IIa–IIg, IIIa–IIIg (10 mmol) were refluxed in the mixture dimethylformamide–water ($\varphi_r = 2 : 1$; 50 cm³) for 15–20 h. The reaction was followed by TLC. After the starting product disappeared charcoal was added and the hot reaction mixture was filtered. The equivalent

Table 4. IR Spectral Data ($\tilde{\nu}/\text{cm}^{-1}$) of Compounds Va–Vj

Compound	$\nu(\text{NH})$	$\nu(\text{NHCS})$	$\nu(\text{C}=\text{N})$	$\nu(\text{CH})$	Others
Va	3180	1550	1625	2950, 2890	
Vb	3180, 3250	1545	1620	2920	
Vc	3150	1535	1625		
Vd	3160, 3220	1545	1625	2960, 2870	
Ve	3180, 3340	1550	1620	2960, 2880	
Vf	3150, 3320	1540	1620	2970, 2860	
Vg	3180, 3270	1545	1620	2960, 2870	1050 $\nu(\text{C}=\text{O})$
Vh	3150, 3320	1550	1620	3090, 3030, 2960, 2870	1640 $\nu(\text{C}=\text{C})$, 970 $\delta(\text{CH})$
Vi	3180	1545	1625	3090, 3040, 2970, 2870	1645 $\nu(\text{C}=\text{C})$, 975 $\delta(\text{CH})$
Vj	3160	1540	1620	3090, 3030, 2970, 2920 2860	1645 $\nu(\text{C}=\text{C})$, 965 $\delta(\text{CH})$ 1265, 1030 $\nu(\text{C}=\text{O}-\text{C})$

Table 5. ¹H NMR Spectral Data of Compounds Va–Vj

Compound	δ
Va	7.09–8.00 (m, 4H, H _{arom}), 10.00 (s, 1H, NH), 6.82 (d, 1H, NH, $J = 6.3$ Hz), 1.06–2.48 (m, 11H, cyclo C ₆ H ₁₁)
Vb	6.89–7.93 (m, 9H, H _{arom}), 9.12 (s, 1H, NH), 6.75 (t, 1H, NH, $J = 6.3$ Hz), 5.50 (d, 2H, CH ₂ , $J = 6.3$ Hz)
Vc	6.98–7.97 (m, 9H, H _{arom}), 8.08 (s, 2H, 2 x NH)
Vd	7.12–8.02 (m, 4H, H _{arom}), 9.28 (s, 1H, NH), 6.60 (t, 1H, NH, $J = 6.3$ Hz), 3.94–4.12 (m, 2H, N–CH ₂), 1.00–2.01 (m, 7H, 2 x CH ₂ and CH ₃)
Ve	7.00–8.06 (m, 4H, H _{arom}), 8.48 (s, 1H, NH), 6.78 (q, 1H, NH, $J = 6.3$ Hz), 2.75 (d, 3H, CH ₃ , $J = 6.3$ Hz)
Vf	7.02–8.00 (m, 4H, H _{arom}), 8.35 (s, 1H, NH), 6.80 (t, 1H, NH, $J = 6.3$ Hz), 4.28–4.54 (m, 2H, CH ₂), 1.33 (t, 3H, CH ₃ , $J = 7.5$ Hz)
Vg	7.10–8.06 (m, 4H, H _{arom}), 9.34 (s, 1H, NH), 6.65 (t, 1H, NH, $J = 6.3$ Hz), 3.92–4.12 (m, 5H, 2 x CH ₂ and OH)
Vh	7.08–8.02 (m, 4H, H _{arom}), 9.12 (s, 1H, NH), 6.72 (t, 1H, NH, $J = 6.3$ Hz), 5.66–5.96 (m, 1H, =CH), 4.35–5.00 (m, 4H, N–CH ₂ and =CH ₂), 1.91–2.20 (m, 2H, CH ₂)
Vi	7.10–8.02 (m, 4H, H _{arom}), 9.08 (s, 1H, NH), 6.68 (t, 1H, NH, $J = 6.3$ Hz), 5.53–5.80 (m, 1H, =CH), 4.31–4.98 (m, 4H, N–CH ₂ and =CH ₂), 1.26–1.54 (m, 2H, CH ₂)
Vj	7.08–8.00 (m, 4H, H _{arom}), 9.18 (s, 1H, NH), 6.70 (t, 1H, NH, $J = 6.3$ Hz), 6.33–6.59 (m, 1H, =CH), 3.92–4.60 (m, 4H, N–CH ₂ and =CH ₂)

amount of water was added to the filtrate and the suspension so formed was heated to dissolve and then left to crystallize. The crystalline product was filtered, washed with ethanol and dried under reduced pressure.

Procedure C. Compound IIa (6.3 g; 30 mmol) was refluxed for 20 h in the mixture dimethylformamide–water ($\varphi_r = 2 : 1$; 50 cm³). After the starting product disappeared (reaction followed by TLC) aqueous solution of sodium hydroxide (50 cm³; 15 %) was added and the hot mixture filtered.

The solid remain (polyethylene) was washed with aqueous solution of sodium hydroxide (20 cm³; 15 %) and then by water, ethanol and dried in vacuum. Yield 0.23 g, m.p. = 92–115 °C. IR spectrum, $\tilde{\nu}/\text{cm}^{-1}$: 2930, 2850 $\nu(\text{CH})$, 1465, 720 $\delta(\text{CH})$.

The alkaline filtrate was acidified with acetic acid to pH 6–8, the precipitate Ve was filtered off and crystallized from aqueous dimethylformamide.

Characteristics of compounds Va–Vj are presented in Tables 3–5.

Thermal Decomposition of Ie

Compound Ie (3.1 g; 10 mmol) was melted and the melt kept for 90 min at the temperature 215–

220 °C with nitrogen bubbling through. The leaving gaseous products of decomposition were condensed at a condenser and after reaction extracted with chloroform (50 cm³).

The chloroform extract was filtered with silica gel and the filtrate was mixed with diethylamine (1 cm³). So formed mixture was evaporated to dryness and the remainder crystallized from ethanol. The melting point, IR and ¹H NMR spectra of the product were identical with those of 2-(3,3-diethylthioureido)-benzonitrile (*IIb*). Yield 0.95 g (40.7 %).

The solid remainder after decomposition was ground and boiled with chloroform (100 cm³) and then filtered with silica gel. Extract was washed twice with hydrochloric acid (20 cm³; 15 %). The chloroform layer was dried over anhydrous sodium sulfate, the solvent evaporated and the solid crystallized from ethanol. Thus we obtained the starting compound *Ie* (1.26 g; 40.6 %).

Aqueous acidic extract was heated with charcoal, filtered and evaporated. The remainder was crystallized from aqueous ethanol. The melting point and IR spectrum were identical with those of adamantylammonium chloride. Yield 0.75 g (39.9 %).

DISCUSSION

The thermal analyses of compounds *Ia–Ie* and *IIa–IIg* showed that during the temperature raising

in all the cases a change was observed accompanied with an endothermic peak at the DTA curve. (The characteristic records of DTA, DTG, and TG curves are presented in Figs. 1a–1c.)

Because the temperature corresponding to the endothermic peak maximum θ_{DTA}^E is equal to the temperature of melting point we consider the change to be the melting of the measured compound. Further temperature increase leads to an exothermic action (exothermic peak on DTA curve) which is in case of compounds *Ia*, *IIa*, *IIb*, *IIe*, and *IIf* so pronounced that the heat evolved is registered also by the thermocouple sensor (the curve T in Figs. 1b and 1c).

One can observe on the curves that the exothermic process in case of compounds *Id*, *IIa–IId* is accompanied with a defined and reproducible mass loss of the measured sample. Relative mass loss Δm_r of the samples and the temperatures corresponding to the peak maxima on DTA or DTG curves, respectively, are presented in Table 6.

Further heating of the products leads to melting and decomposition (an endothermic peak of the changeable intensity on DTA curve, a mass decrease on TG curve and a peak on DTG curve, respectively).

Compound *Ie* showed a different behaviour. Its decomposition has been observed already during temperature increase over the temperature cor-

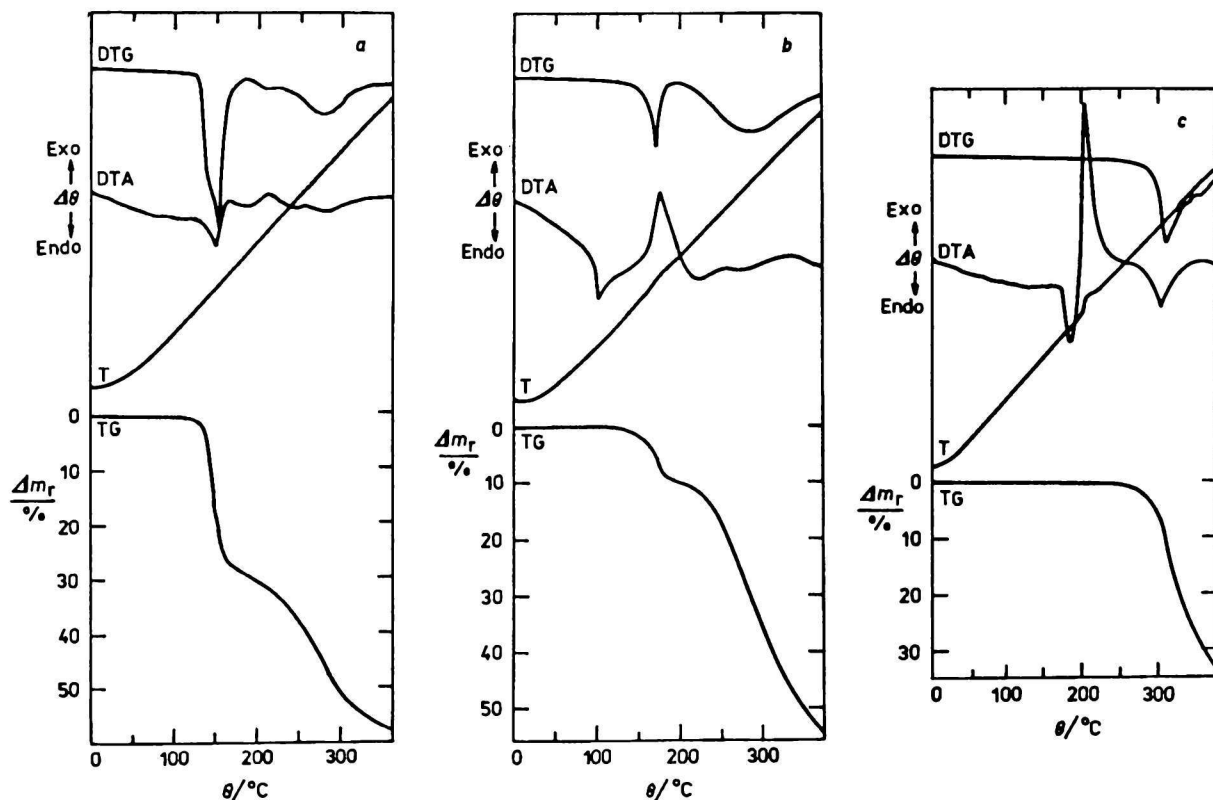


Fig. 1. TG, DTG, and DTA curves of compounds *Id* (a), *IIb* (b), and *IIe* (c).

Table 6. Thermal Analysis of Compounds *Ia–Id* and *Ila–Ilg*

Compound	θ_{DTA}^E	θ_{DTA}^R	θ_{DTG}^R	Eliminated product	$\Delta m_r(\text{exp.})/\Delta m_r(\text{calc.})$	
	°C	°C	°C		%	%
<i>Ia</i>	171	172	—	—	—	—
<i>Ib</i>	196	198	—	—	—	—
<i>Ic</i>	185	188	—	—	—	—
<i>Id</i>	163	175	163	Methylpropene	26.5	24.1
<i>Ila</i>	179	194	192	Ethene	6.7	12.8
<i>Ilb</i>	102	182	180	Ethene	11.8	12.0
<i>Ilc</i>	101	179	175	1-Butene	18.9	19.5
<i>Ild</i>	98	168	165	Ethanal	18.0	16.6
<i>Ile</i>	182	218	—	—	—	—
<i>Ilf</i>	135	178	—	—	—	—
<i>Ilg</i>	140	180	—	—	—	—

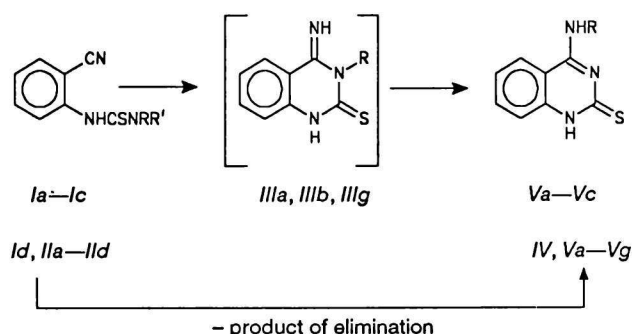
$\theta_{DTA}^E, \theta_{DTA}^R$ — the temperatures corresponding to an endothermic and exothermic peak maximum on the DTA curve, respectively, θ_{DTG}^R — the temperature corresponding to the peak maximum on the DTG curve.

responding to the endothermic peak maximum on DTA curve ($\theta_{DTA}^E = 204$ °C). The decomposition was manifested by an endothermic peak on DTA curve, by peak on DTG curve (both with maximum at 263 °C) and by a mass decrease on TG curve.

In order to identify products of the exothermic processes we heated all the compounds of the studied series (with the exception of *Ie*) at the temperature of the exothermic peak maximum on DTA curve till the reaction mixture solidified (Scheme 1). TLC of the melt showed that beside an unreacted starting compound the only one polar product *IV* or *Va–Vj*, respectively, was observed (TLC, acetonitrile). The unreacted compound was removed by extraction with hot chloroform and the remainder containing product was crystallized from aqueous dimethylformamide (identity of *Va–Vj* before and after crystallization was proved by TLC).

TLC, elemental analysis, IR and ^1H NMR spectra showed product *IV* to be identical with 4-amino-2-thioxo-1,2-dihydroquinazoline [2]. It means that heating of compound *Id* leads to the fragment C_4H_6 , which is supported also by the mass loss calculated from TG curve of compound *Id*.

The same values of elemental analysis were ob-

**Scheme 1**

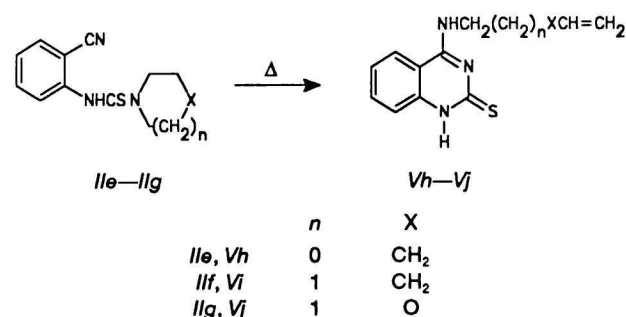
served with products *Va–Vc*, *Vh–Vj* as well as the corresponding starting compounds *Ia–Ic* and *Ile–Ilg*. But neither melting points, TLC nor IR and ^1H NMR spectral characteristics (Tables 4 and 5) corresponded to that. In their IR spectrum the band of stretching vibration of a cyano group was missing. On the other hand, one could find bands corresponding to the groups NHCS, $\text{C}=\text{N}$, and alkyl group vibrations. In the case of compounds *Vh–Vj* C–H and $\text{C}=\text{C}$ vibration bands of vinyl group were observed. This could be formed by the ring opening of the pyrrolidine, piperidine, and morpholine ring, respectively (Scheme 2).

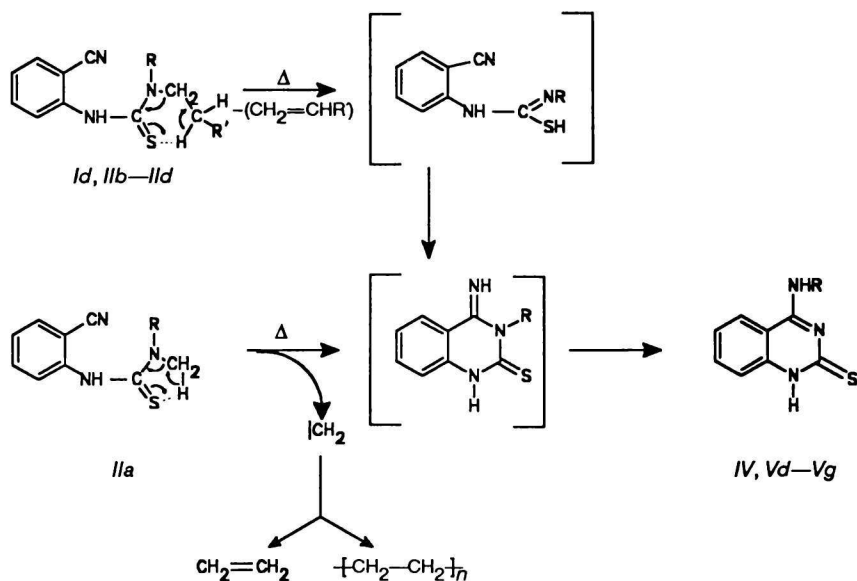
^1H NMR spectra of solid products *Va–Vg* being formed during the thermal transformation of 2-(3-R,3-R'-thioureido)benzonitriles *Ila–Ild* showed the presence of one of the formerly two present alkyls only. The relative loss of the mass deducted from the corresponding TG curves (for compound *Ila* fragmentation of CH_3 , for *Ilb* C_2H_5 , for *Ilc* C_4H_8 and for *Ild* $\text{C}_2\text{H}_4\text{O}$) corresponds to the observed fact.

At first we expected during the heating of compounds *Ia–Ic* and *Ila–Ilg* the formation of 3-R-4-imino-2-thioxo-1,2,3,4-tetrahydroquinazolines similarly as we observed after cyclization of *Ia–Ic* boiling in ethanol [2]. But comparison of chromatograms, melting points, IR and ^1H NMR spectra of the products with the standards *IIIa*, *IIIb*, and *IIIg* did not support our expectations.

^1H NMR spectra showed that alkyl group in the product of the thermal transformation is bound to the NH group as indicates the fact that the signal of the hydrogen atom of the N–H alkylamino group is split by the protons of the CH , CH_2 , or CH_3 groups. Simultaneously one can observe splitting of the signals of the neighbouring hydrogen atoms of alkyl groups by the hydrogen atom of the NH group (coupling constant $J = 6.3$ Hz). Signal of the NH group disappears after deuterium oxide addition to the measured sample.

The fact that compounds *Va–Vj* are not 4-imino derivatives of quinazoline is supported by the position of the doublet in the multiplet of aromatic

**Scheme 2**



Scheme 3

protons. The doublet corresponds to the hydrogen in position 5 of the quinazoline ring. Its upper limit position lies at the value of the chemical shift lower than 8.10. 4-Oxo- and 4-imino-2-thioxo-1,2,3,4-tetrahydroquinazolines [2–5, 7, 8] have this value in comparison with 4-amino analogues shifted higher than 8.10 due to anisotropic effect of C=O or C=N bond.

Signals of the protons in ^1H NMR spectrum of *Ile*–*Ilg* showed the presence of the “end” vinyl group.

All the mentioned facts led us to the conclusion that the products *Va*–*Vj* are 4-(R-amino)-2-thioxo-1,2-dihydroquinazolines. These compounds are accessible by the thermally initiated Dimroth rearrangement as we already showed at isomerization of 3-phenyl-4-imino-2-thioxo-1,2,3,4-tetrahydroquinazoline to 4-phenylamino-2-thioxo-1,2-dihydroquinazoline boiling the starting compound in aqueous dimethylformamide [1].

In order to prove our conclusion we carried out Dimroth rearrangement of 3-R-4-imino-2-thioxo-1,2,3,4-tetrahydroquinazolines *IIla*–*IIlg* boiling them in the mixture dimethylformamide–water ($\varphi_r = 2 : 1$). The most rapid isomerization was observed with 3-phenyl derivative (reaction time about 3 h), the slowest reaction was observed with 3-cyclohexyl-4-imino-2-thioxo-1,2,3,4-tetrahydroquinazoline (reaction time about 10 h). The rearranged products of compounds *IIla*–*IIlg* were identical with the products *Va*–*Vg* isolated after thermal treatment of compounds *Ila*–*Ic* or *Ila*–*Ild* (the proof was carried out by TLC, melting points, mixed melting points, IR and ^1H NMR spectroscopy).

During the isomerization of *IIla*–*IIlg* in the melt (compounds were heated to the temperature by

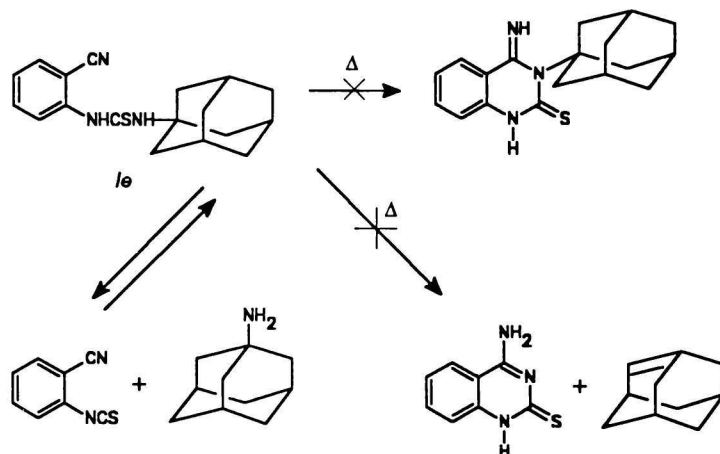
5–10 °C higher than their melting points) the products *Va*–*Vg* were formed but in a low yield only. The melt after reaction contained besides unreacted starting compound polar compounds of decomposition. Those impurities complicated the isolation of compounds *Va*–*Vg* and their amount increased with the reaction time.

We tried to catch the corresponding 3-R-4-imino-2-thioxo-1,2,3,4-tetrahydroquinazolines heating compounds *Ia*–*Ic*, resp. *Ila*–*Ilg* in the mixture dimethylformamide–water. TLC proved that during the reaction both *IIla*, *IIlb*, *IIlg* and products of their rearrangement *Va*–*Vc* were formed (Scheme 1). Reaction time prolongation caused that compounds *Va*–*Vc* were isolated only. Under the same conditions compounds *Ila*–*Ilg* gave only rearranged products *Vd*–*Vj*. The composition of 3-R-4-imino-2-thioxo-1,2,3,4-tetrahydroquinazolines in the reaction mixture we did not succeed to prove by TLC.

Compound *Id* at the same conditions gave 4-amino-2-thioxo-1,2-dihydroquinazoline (*IV*) and compound *Ie* was stable against any change.

Gaseous products formed during the reaction of compounds *Id*, *Ila*–*Ilc* under melting were absorbed in bromine water (we expected them to be unsaturated hydrocarbons). After separation we identified them by GC as the corresponding dibromoalkanes. We identified methylpropene after the reaction of *Id* as 1,2-dibromomethylpropane, ethylene after reaction of *Ila* and *Ilb* as 1,2-dibromoethane and 1-butene eliminated from compound *Ilc* as 1,2-dibromobutane. Acetaldehyde (tautomeric form of expected split vinyl alcohol) eliminated from *Ild* was identified as its 2,4-dinitrophenylhydrazone.

We consider a mechanism of pyrolytic *cis* elimina-



Scheme 4

tion (Chugaev or Cope elimination [9]) for explanation of alkene elimination from *1d* and *11a–11g*. It means that β -hydrogen atom enters into interaction with the sulfur atom in a six-membered ring intermediate which disintegrates and liberates the corresponding alkene (Scheme 3).

Such a mechanism would not fulfil requirements for the reaction of compound *11a*. There we suppose an α -elimination process through five-membered ring intermediate to methylene. That in the melt dimerizes to ethylene which was proved as 1,2-dibromoethane. Therefore the mass loss $\Delta m_r(\text{exp.})$ presented in Table 6 is only the half of the value calculated for the formation of ethylene. During the reaction of *11a* in a solvent a polymerization of methylene to polyethylene was observed (the identity proved by IR spectrum and elemental analysis).

Similar eliminations under formation of methylene and their following reactions were observed during heating tetramethylammonium salts in the presence of strong bases [10].

By the elimination process formed 2-(3-R-isothioureido)benzothioamide behaves like *1a–1c*, *i.e.* it can enter into cyclization reaction to 3-R-4-imino-2-thioxo-1,2,3,4-tetrahydroquinazoline. The fact that this immediately enters into Dimroth rearrangement to compound *11d–11h* we explain by the value of energy barrier comparable with that of the elimination reaction. A heat release during all the process which is manifested by the exothermic peak on the DTA curve is probably caused by the release of the delocalization energy during formation of 4-(R-amino)-2-thioxo-1,2-dihydroquinazoline.

Compound *1e* probably neither cyclized to 3-adamantyl-4-imino-2-thioxo-1,2,3,4-tetrahydroquinazoline nor rearranged to 4-adamantylamino-2-thioxo-1,2-dihydroquinazoline because of steric

hindrance similarly as *tert*-butyl derivative *1d*. Compound *1e* in the melt is probably in an equilibrium with products of its thermal dissociation, *i.e.* aminoadamantane and 2-isothiocyanatobenzonitrile (*cf.* [11]). This was isolated from the melt by a stream of nitrogen and after reaction with diethylamine identified as 2-(3,3-diethylthioureido)benzothioamide (*11b*). Aminoadamantane was separated by the treatment of hydrochloric acid and isolated as chloride (Scheme 4).

Elimination to 1-adamantene was not observed, which is in a good agreement with Bredt's rule [12, 13].

REFERENCES

1. Taylor, E. C. and Ravindranathan, R. V., *J. Org. Chem.* **27**, 2622 (1962).
2. Pazdera, P., Ondráček, D., and Nováček, E., *Chem. Papers* **43**, 771 (1989).
3. Pazdera, P., Nováček, E., and Ondráček, D., *Chem. Papers* **43**, 465 (1989).
4. Pazdera, P. and Pichler, J., *Chem. Papers* **45**, 517 (1991).
5. Pazdera, P. and Pichler, J., in *Proceedings of the 17th Conference Progress in Organic Chemistry*, p. 51. Stará Lesná, 1990. Faculty of Natural Sciences, Comenius University, Bratislava, 1990.
6. Pazdera, P. and Ondráček, D., *Czechoslov. Appl.* **264942** (1990).
7. Pazdera, P., Potůček, V., Nováček, E., Kalviňš, I., Trapencieris, P., and Pugovics, O., *Chem. Papers* **45**, 527 (1991).
8. Pazdera, P. and Potůček, V., *Chem. Papers* **45**, 677 (1991).
9. De Puy, C. H. and King, R. W., *Chem. Rev.* **60**, 431 (1960).
10. Musker, K. W., *J. Chem. Educ.* **45**, 200 (1968).
11. Bogemann, M., Petersen, S., Schultz, O.-E., and Soll, H., in *Methoden der organischen Chemie* (Houben-Weyl), Vol. IX, p. 899. G. Thieme Verlag, Stuttgart, 1955.
12. Fawcett, F. S., *Chem. Rev.* **47**, 219 (1950).
13. Bredt, J., *Justus Liebigs Ann. Chem.* **437**, 1 (1924).

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