

Reactions of amidinoyl isothiocyanates with *N*-sulfinylanilines

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Received 28 September 1982

Reactions of chosen amidinoyl isothiocyanates with some *N*-sulfinylanilines are described. The probable mechanism of formation of the final 4-anilinoquinazolines and their spectral characteristics are discussed.

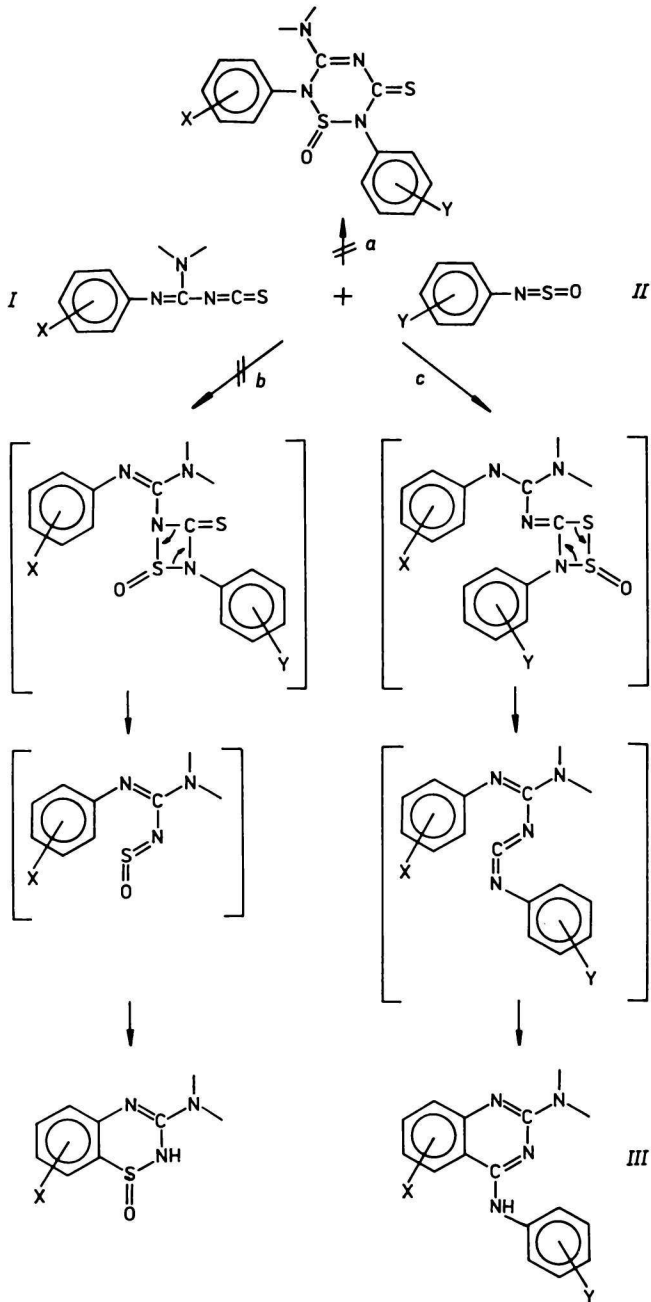
Описаны реакции избранных амидиноилизотиоцианатов с некоторыми *N*-сульфиниланилинами. Обсуждается вероятный механизм образования финальных 4-анилинохиназолинов и их спектральные характеристики.

It has been described in the previous paper [1] that amidinoyl isothiocyanates *I* enter the reaction with aromatic isothiocyanates to afford 4-anilinoquinazolines after decomposition of the intermediate formed by (2 + 2) π cycloaddition. Aromatic isocyanates, contrary to their sulfur analogues, react with amidinoyl isothiocyanates by means of a (4 + 2) π cycloaddition under the formation of triazine derivatives [2, 3].

In the present communication we have studied the reactions of amidinoyl isothiocyanates *I* with *N*-sulfinylanilines *II*, which have a similar heterocumulene grouping as isocyanates and their sulfur analogues, in purpose to use them for the preparation of heterocycles.

The *N*-sulfinyl group belongs to readily polarizable systems as to the N = S bond and is taken for a typical four-electron ("double") bond. It is a suitable dipole, with sulfur as positive and nitrogen as negative poles, for cycloaddition reactions [4]. Based on these facts, the following reactions of amidinoyl isothiocyanates could be expected (Scheme 1).

As the $\text{—N}=\overset{\text{I}}{\text{C}}\text{—N}=\text{C}=\text{S}$ grouping of amidinoyl isothiocyanates represents a heterodiene, it was reasonable to expect (4 + 2) π cycloaddition reactions (way *a*). Such reactions are characteristic of the NSO group which readily enters the reaction with butadiene and its derivatives giving thiazines [5] or with azoalkenes giving thiatriazines [6, 7]. In our experiments, carried out under similar conditions as in the reaction of butadiene with *N*-sulfinylanilines on heating or staying of the equimolar mixtures of components in benzene or chloroform, the expected products were not found. The only products formed under these

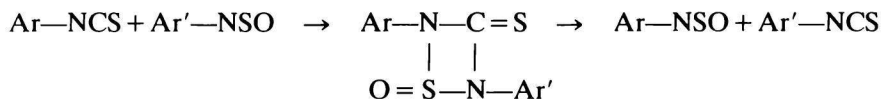


Scheme 1

The expected reactions of amidinoyl isothiocyanates with *N*-sulfinylanilines

conditions and identified by t.l.c. on Silufol (chloroform — acetone; volume ratio 95:5) on the basis of standards were the corresponding 3*H*-quinazoline-4-thiones and dimers of isothiocyanates.

Many reactions of *N*-sulfinylanilines proceed on the double X=Y bond (where X=C, N and Y=C, O, N, S, etc.) as a (2+2) π cycloaddition similar to the Wittig reaction [8] (way *b*). The formed four-membered heterocycles are either stable, and thus isolable, or they decompose. *Minami* and *Agawa* [9] heated aromatic isothiocyanates with sulfinylanilines at 180—200 °C without any solvent and found that a “transsulfinylation” took place



Therefore, in the reactions of amidinoyl isothiocyanates with sulfinylanilines it was reasonable to expect the formation of *N*-sulfinylbenzamidines which, similarly as other amidinoyl heterocumulenes, are unstable and on intramolecular cyclization give the corresponding benzothiazine-1-oxides [10]. In the experiments carried out in this work the formation of these compounds was not observed on heating the equimolar mixtures of the corresponding components in benzene, chloroform, chlorobenzene, or dimethylformamide.

From the reaction mixtures, obtained on heating the equimolar mixtures of *I* and *II* in dimethylformamide, 20—40 % yields of compounds identified as the corresponding 4-anilinoquinazolines were isolated (Table 1). The formation of these compounds can be explained as follows (way *c*).

Addition of the —NSO group to the C=S bond of the isothiocyanate gives rise to an unstable four-membered cycle which decomposes to a similarly unstable amidinoyl carbodiimide, sulfur, and SO₂ formed by disproportionation of sulfur(II) oxide. In further stage the known cyclization of amidinoyl carbodiimide to the corresponding 4-anilinoquinazoline took place at simultaneous 1,5+1',3' sigmatropic transfer of hydrogen [1]. This mechanism has been supported also by the results in [9] where in addition to the products of “transsulfinylation” also the formation of diaryl carbodiimide in low yields was proved by g.l.c. and by the fact that in some cases we have isolated sulfur from the reaction mixture. In all cases great amounts of not identified resinous compounds were obtained along with the final products, which reduced the total yield of the reaction. Probably SO₂ caused resinification both of the starting isothiocyanate and carbodiimide. It can be seen from Table 1 that [*N*¹,*N*¹-3-oxapentamethylene-*N*²-(4-chlorophenyl)]amidinoyl isothiocyanate was treated with *N*-sulfinylanilines having activation and/or deactivation substituents. The best yields were obtained with those having nitro substituents. This fact is evidently connected with the reactivity of the —NSO group which is more reactive in nitro than in phenyl or tolyl derivatives [11].

Table 1
 Characterization of the prepared 4-anilinoquinazolines

Compound	X	Y	N<	Formula	M _r	w, (calc.)/w, (found)			Yield %	M.p. °C
						% C	% H	% N		
IIIa	4-Cl	4-NO ₂	Mo	C ₁₈ H ₁₆ ClN ₅ O ₃	385.8	56.04	4.17	18.15	37	303—305
						55.90	4.05	18.20		
IIIb	4-Cl	2-NO ₂	Mo	C ₁₈ H ₁₆ ClN ₅ O ₃	385.8	56.04	4.17	18.15	31	224—228
						55.95	3.95	18.05		
IIIc	4-Cl	H	Mo	C ₁₈ H ₁₇ ClN ₄ O	340.8	63.43	5.02	16.43	25	260—262
						63.32	4.85	16.31		
III d	4-Cl	4-CH ₃	Mo	C ₁₉ H ₁₉ ClN ₄ O	354.8	64.31	5.39	15.79	21	236—239
						64.22	5.40	15.83		
IIIe	4-Cl	4-NO ₂	DE	C ₁₈ H ₁₈ ClN ₅ O ₂	371.3	58.23	4.88	18.86	32	262—266
						58.11	4.56	18.93		
III f	4-Br	4-NO ₂	Mo	C ₁₈ H ₁₆ BrN ₅ O ₃	430.2	50.25	3.74	16.27	41	303—306
						49.93	3.56	16.50		
III g	4-Br	4-NO ₂	DE	C ₁₈ H ₁₈ BrN ₅ O ₂	416.3	51.93	4.35	16.82	34	262—267
						51.80	4.27	16.93		
III h	4-Br	H	DE	C ₁₈ H ₁₉ BrN ₄	371.3	58.23	5.15	15.09	27	262—266
						58.14	5.03	15.15		
III i	H	4-NO ₂	PhPP	C ₂₄ H ₂₂ N ₆ O ₂	426.5	67.59	5.19	19.70	44	269—271
						67.43	5.02	20.03		
III j	4-Br	2-NO ₂	DE	C ₁₈ H ₁₈ BrN ₅ O ₂	416.3	51.93	4.35	16.82	30	279—283
						51.82	4.40	16.91		

Mo — morpholine, DE — diethylamine, PhPP — N-phenylpiperazine.

Therefore, in the reactions of amidinoyl isothiocyanates the nitro derivatives of sulfinylanilines were used because in the case of *N*-sulfinylaniline or toluidine side reactions of *I* occurred due to longer reaction time and consequently, the yield of the final product decreased significantly.

Table 2
Spectral characteristics of the prepared 4-anilinoquinazolines

Compound	IR			UV	
	$\tilde{\nu}(\text{C}=\text{N})/\text{cm}^{-1}$ $\tilde{\nu}(\text{C}=\text{C})/\text{cm}^{-1}$	$\tilde{\nu}(\text{CH})_{\text{ariph}}/\text{cm}^{-1}$	$\tilde{\nu}(\text{NH})/\text{cm}^{-1}$	$\lambda_{\text{max}}/\text{nm} (\log \{\epsilon\})$	
<i>IIIa</i>	1603	2830	3410	244 (3.45)	287 (3.32)
	1620			336 (3.14)	395 (3.15)
<i>IIIb</i>	1610	2830	3430	242 (3.53)	285 (3.44)
	1620			387 (2.77)	
<i>IIIc</i>	1605	2850	3350	239 (3.53)	286 (3.43)
	1625			370 (2.90)	
<i>III d</i>	1610	2850	3360	221 (3.28)	306 (3.26)
	1635			226 (3.23)	
<i>IIIe</i>	1610	2980	3420	247 (3.48)	284 (3.24)
				325 (3.00)	368 (3.34)
<i>III f</i>	1612	2950	3430	243 (3.45)	287 (3.27)
	1640			372 (2.26)	
<i>III g</i>	1630	2980	3420	243 (3.44)	288 (3.25)
	1660			335 (2.92)	396 (2.75)
<i>III h</i>	1609	2990	3430	231 (3.41)	287 (3.10)
	1670			250 (3.29)	322 (2.52)
<i>III i</i>	1625	2830	3380	257 (3.50)	277 (3.27)
	1640			342 (3.04)	384 (3.12)
<i>III j</i>	1660				
	1609	2950	3400	233 (3.54)	251 (3.49)
	1665			286 (3.24)	318 (2.56)

Spectral characteristics of the prepared 4-anilinoquinazolines (Table 2) unambiguously proved the structures of these compounds. The u.v. spectra of the compounds *IIIa—j* revealed three absorption maxima of similar intensities. The least intensive maximum appearing at $\lambda \approx 380$ nm pointed to the possibility of conjugation of the aniline group with the quinazoline skeleton.

Experimental

Preparation of the used amidinoyl isothiocyanates has been described in [12]. The appropriate *N*-sulfinylanilines were prepared after [13]. Physical constants of the starting compounds were in good agreement with the literature data.

Infrared absorption spectra of the prepared compounds were measured in the region of $\bar{\nu} = 700\text{--}3600\text{ cm}^{-1}$ by KBr technique on a Specord IR 71 apparatus (Zeiss, Jena) calibrated by polystyrene foil ($d = 0.25\text{ }\mu\text{m}$). The reading accuracy was $\pm 4\text{ cm}^{-1}$.

Electronic absorption spectra of compounds ($3 \times 10^{-5}\text{--}5 \times 10^{-5}\text{ mol dm}^{-3}$) in methanol were measured on a Specord UV VIS spectrophotometer (Zeiss, Jena) in the region of $\lambda = 200\text{--}800\text{ nm}$ in quartz cells of 10 mm thickness. Spectral characteristics of the prepared 4-anilinoquinazolines are presented in Table 2.

Preparation of 4-anilinoquinazolines IIIa—j

To the solution of amidinoyl isothiocyanate *I* (0.01 mol) in dry and purified dimethylformamide (10 cm³) the corresponding *N*-sulfinylaniline *II* (0.01 mol) was added. The reaction mixture was heated at 140—150 °C for 1—2 h and was allowed to stay overnight at room temperature. The products were obtained in two ways. When a precipitate was formed this was filtered through a sintered glass filter, washed with a small amount of ethanol, and purified by crystallization from benzene and ethanol, respectively.

When a solid product was not formed after staying, ethanol (5 cm³) was added and the reaction mixture was poured into cold water (150 cm³) with stirring. The formed resinous compound was filtered off and the supernatant was evaporated to dryness *in vacuo*. The residue was purified as in the previous case. The review of the prepared compounds and their physical constants are presented in Table 1.

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Translated by A. Kardošová