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RING – CHAIN ISOMERISM OF N-MONOSUBSTITUTED 2-CYANOBENZENESULFONAMIDES*

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A number of N-monosubstituted 2-cyanobenzenesulfonamides (A) and their chain isomers – 2-substituted 3-iminobenzothiazoline 1,1-dioxides (B), which are formed as a result of intramolecular nucleophilic addition of the sulfonamido group to the C≡N bond – were synthesized by acylation of primary amines with 2-cyanobenzenesulfonyl chloride. The interconversions of the isomers – A → B under alkaline-catalysis conditions and B → A under thermal conditions – were accomplished for the first time. The influence of the electronic and steric effects of the substituent attached to the nitrogen atom on the relative stabilities of the open and chain isomers was ascertained. The A ⇌ B equilibrium constants in solutions in a mixture of dioxane and triethylamine were determined by IR spectroscopy.

It is known [2-4] that 2-cyanobenzenesulfonyl chloride (I) reacts with ammonia and primary amines to give 2-cyanobenzenesulfonamides (II), which undergo isomerization to 3-iminobenzisothiazoline 1,1-dioxides (III) when excess amine is present.

Since little study has been devoted to intramolecular nucleophilic addition of a sulfonamido group to polar multiple bonds [5-7], the aim of the present research was to study the influence of the electronic and steric effects of substituents attached to the nitrogen atom on the relative stabilities of isomers II and III and on the possibility of realization of their interconversions.

3-Iminobenzisothiazoline 1,1-dioxides IIIa, b, e, g, h (Table 1) were obtained in the reactions of chloride I with excess primary amine carried out in dioxane with subsequent dilution of the reaction mixture with water. As has been demonstrated for N-methylamide IIa [3], the initially formed amides II undergo isomerization to III under the influence of excess amine.

N-tert-Butyl- and N-(1-adamantyl)amides IIc, d (Table 2) and anilide IIf, which do not undergo isomerization under the reaction conditions, constitute exceptions to the above. Special experiments designed to effect the isomerization of these compounds under the influence of alkaline agents [a refluxing ethanol solution of triethylamine, an aqueous dioxane solution of potassium hydroxide, and CH_3SOCH_2Na in dimethyl sulfoxide (DMSO)] were also unsuccessful.

TABLE 1. 3-Iminobenzisothiazoline 1,1-Dioxides III

Compound	mp, °C	IR spectra, ν, cm^{-1}		Found, %				Empirical formula	Calculated, %				Yield, %
		C=N	N–H	C	H	N	S		C	H	N	S	
IIIa	166—167*	1655 br	3313	48,7	3,8	13,9	16,4	$C_8H_8N_2O_2S$	49,0	4,1	14,3	16,4	74
IIIb	147—148	1648	3303	53,2	5,5	12,5	14,6	$C_{10}H_{12}N_2O_2S$	53,6	5,4	12,5	14,3	94
IIIe	127—128	1659, 1654 sh 1647 sh	3303	61,9	4,5	10,2	11,9	$C_{14}H_{12}N_2O_2S$	61,8	4,4	10,3	11,8	95
IIIg	165—166	1664	3284	61,7	4,6	10,3	11,9	$C_{14}H_{12}N_2O_2S$	61,8	4,4	10,3	11,8	72
IIIh	166—167	1668	3267	58,5	4,3	9,7	11,3	$C_{14}H_{12}N_2O_3S$	58,3	4,2	9,7	11,1	87

*According to the data in [3], this compound has mp 165-166°C.

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TABLE 2. 2-Cyanobenzenesulfonamides II

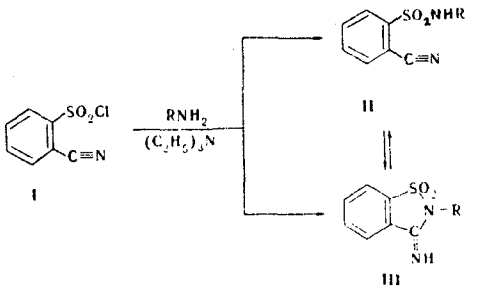
Compound	mp, °C	IR spectrum, ν, cm^{-1}		Found, %				Empirical formula	Calculated, %				Yield, %
		C≡N	N–H	C	H	N	S		C	H	N	S	
IIb	66—68	2258	3269	53,4	5,4	12,4	14,3	$C_{10}H_{12}N_2O_2S$	53,6	5,4	12,5	14,3	30*
IIc	141—143	2257	3275	55,1	5,8	11,7	13,8	$C_{11}H_{14}N_2O_2S$	55,4	5,9	11,8	13,5	76
IId	149—150	2231	3286	64,6	6,7	8,9	10,4	$C_{17}H_{20}N_2O_2S$	64,5	6,4	8,9	10,1	60
IIe	84—85	2231	3273	61,5	4,6	10,2	12.0	$C_{14}H_{12}N_2O_2S$	61,8	4.4	10,3	11,8	25*
IIf	152—154†	2245	3183	60,3	4,1	11,0	12,4	$C_{13}H_{10}N_2O_2S$	60,5	3,9	10,9	12,4	62
IIg	135—136	2258	3221	62,5	4,3	10,2	12,2	$C_{14}H_{12}N_2O_2S$	61,8	4,4	10,3	11,8	47*
IIh	131—133	2241	3213	58,8	4,1	9,5	11,2	$C_{14}H_{12}N_2O_3S$	58,3	4,2	9,7	11,1	62*

*This is the yield under thermal-isomerization conditions.
†According to the data in [3], this compound has mp 151-153°C.

TABLE 3. Constants for the II⇌Ring-Chain Equilibrium in Dioxane +10% Triethylamine

Compound	Analytical $\nu_{C\equiv N}$ band, cm^{-1}	K_T=[III]/[II]	Time required to establish equilibrium in solutions of II
IIa, IIIa	1660	>100	4 h
IIe IIIe	1656	2,1±0,2	36 h
IIf IIIf	1664	0,15±0,02	8 min
IIg IIIg	1662	0,29±0,03	25 min
IIh IIIh	1662	0,65±0,05	30 min

In the case of amides IIc, d the presence of a bulky tert-alkyl substituent in the sulfonamido group hinders cyclization. We have previously [1] observed a similar phenomenon in the case of N-monosubstituted 2-cyanobenzamides.



II, III a R = CH_3; b R = i-C_3H_7; c R = t-C_4H_9; d R = 1-adamantyl; e R = $C_6H_5CH_2$; f R = C_6H_5; g R = 4-$CH_3C_6H_4$; h R = 4-$CH_3OC_6H_4$

However, in contrast to 2-cyanobenzanilide, which is capable of undergoing isomerization to 2-phenyl-3-iminoisoindolinone in the presence of alkaline agents [1], 2-cyanobenzenesulfanilide does not undergo analogous isomerization. The introduction of a phenyl substituent in the sulfonamido group evidently reduces the nucleophilicity of the nitrogen atom to such an extent that isolation of the product of intramolecular nucleophilic addition to the C≡N group becomes impossible, although the IIf⇌IIIf equilibrium in dioxane solution in the presence of triethylamine (K_T = 0.15, Table 3) was detected by IR spectroscopy. This is confirmed by the fact that we were able to realize isomerization of II to III in the case of 4-methyl- and 4-methoxyphenylamides IIg, h, in the molecules of which the nucleophilicity of the nitrogen atom of the sulfonamido group is increased by the introduction of electron-donor substituents in the phenyl ring.

Brief heating of ring isomers IIIb, e, g, h to 220°C led to their thermal isomerization to the corresponding sulfonamides II. The low yields of amides II and the presence of the starting compound in the heat-treated mixture constitute evidence that the II⇌III equilibrium, which is shifted to favor the amide, especially when there is a bulkier substituent or an electron-acceptor substituent attached to the nitrogen atom, is reached when the compounds are heated. The presence of a small amount of open isomer IIa was detected in a heat-treated sample of N-methyl derivative IIIa by IR spectroscopy; however, we were not able to isolate it by crystallization.

In the case of the 4-methoxyanilide we demonstrated the possibility of the reverse isomerization IIh → IIIh by refluxing an ethanol solution of the amide with added triethylamine.

Both series of isomers are satisfactorily identified from their IR spectra. One observes $\nu_{C\equiv N}$ and ν_{N-H} bands in the spectra of open isomers II (Table 2). The latter bands appear at lower frequencies and are more broadened as compared with the ν_{N-H} bands in the spectra of ring isomers III. The spectra of the latter contain a $\nu_{C=N}$ band at 1648-1668 cm^{-1} in Nujol and at 1651-1664 cm^{-1} in dioxane (cf. [8]), which can be used as an analytical band in the quantitative determination of the composition of equilibrium mixtures, since amides II do not absorb in this spectral range.

It was established by IR spectroscopy that both series of isomers are stable in dioxane at room temperature and that the II⇌III tautomeric equilibrium is not observed. Mixtures, the compositions of which do not depend on which isomer was used to prepare the solution, are formed after the addition of triethylamine to dioxane solutions.

Within the limits of the sensitivity of IR spectroscopy, the equilibrium was shifted completely to favor ring isomer IIIa in a solution of N-methyl-2-cyanobenzenesulfonamide (IIa) obtained by the method in [3]. Both isomers of the N-isopropyl derivatives (IIb and IIIb) and N-tert-alkylamides IIc, d were found to be stable in dioxane in the presence of triethylamine; this is evidently due to the steric effect of the bulky substituent attached to the nitrogen atom. In the case of the N-benzylamide the IIe⇌IIIe equilibrium was shifted to favor the ring form, whereas the open form is favored in the case of N-arylamides IIf-h. It is apparent from Table 3 that the introduction of electron-donor substituents (CH_3 and CH_3O) in the aryl ring shifts the equilibrium to favor ring form III. The rate of the isomeric transformations is higher for the N-arylamides than for the N-alkylamides.

EXPERIMENTAL

The IR spectra of $5 \cdot 10^{-2}$ mole/liter solutions of the compounds were recorded with a Specord 75 IR spectrometer (the layer thickness was 0.01 cm). The tautomeric equilibrium constants were determined from the formula $K_T = [III]/[II] = D_S/(D_0 - D_S)$, where D_0 is the optical density at the maximum of the C=N band of a solution of ring isomer III in dioxane +10% triethylamine extrapolated to zero time after dissolving, and D_S is the optical density of a solution of the equilibrium mixture after establishment of equilibrium, which was reached on the basis of both the open and ring isomers (except for IIf).

2-Cyanobenzenesulfonamides (IIc, d, f, Table 2) and 3-Iminobenzisothiazoline 1,1-Dioxides (IIIa, b, e, g, h, Table 1). A solution of 2 g (0.01 mole) of chloride I in 10 ml of dioxane was added to a solution of 0.015 g of the amine and 2.1 ml (0.015 mole) of triethylamine in 10 ml of dioxane, and the mixture was maintained at room temperature for 24 h. It was then diluted with 150 ml of water, and the precipitate was separated after 2 h. In the synthesis of IIIa the reaction mixture was diluted with 100 ml of water, and 25 g of sodium chloride was added to the solution. The compounds were recrystallized from ethanol (IIId, e), benzene (IIc, f and IIIb, g, h), and benzene–hexane (IIIa).

Thermal Isomerization III→II. A 1-g sample of III was heated and maintained at 220°C for 10 min, after which it was cooled and recrystallized from benzene–hexane to give amides IIb, e, g, h (Table 2).

Alkaline Isomerization IIh→IIIh. A solution of 0.3 g of amide IIh and 1 ml of triethylamine in 5 ml of ethanol was refluxed for 2 h, after which it was vacuum evaporated, and the residue was recrystallized from benzene to give 0.1 g of IIIh.

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