Chemistry of Heterocyclic Compounds Vol. 30, No. 7, 1994

SYNTHESIS AND MASS SPECTRAL STUDY OF N,N′-BIS(2-R-5-PHENYL)THIAZOLYLUREAS

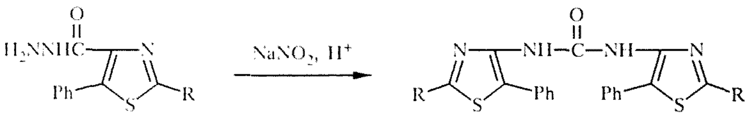
V. A. Mamedov, I. Kh. Rizvanov, I. A. Nuretdinov,
and Yu. Ya. Efremov

The action of nitrous acid on hydrazides of 2-substituted 5-phenylthiazolecarboxylic acids gives N,N′-bis(2-R-5-phenyl)thiazolylureas, whose structure was established by mass spectrometry and IR and PMR spectroscopy.

In previous work on the preparation of new thiazole-containing bicyclic systems [1-3], we showed that the reaction of hydrazides of 2-substituted 5-phenylthiazolecarboxylic with KSCN and PhNCS [1] leads to various thiosemicarbazide derivatives, which give bisthiazoles and thiazolylthiazolidones upon reaction with esters of 3-phenyl-3-chloro-2-oxopropionic acid [2] and chloroacetyl chloride. Our study of the cyclodehydration of thiosemicarbazides of thiazolecarboxylic acids showed that thiazolotriazoles or thiadiazoles are obtained depending on the condensing agent [3].

In the present work, we studied the reaction of hydrazides of 2-substituted 5-phenylthiazolecarboxylic acids Ia and Ib with nitrous acid obtained *in situ* by the reaction of $NaNO_2$ with acetic and trifluoroacetic acid. N,N′-Bis(2-R-5-phenyl)thiazolylureas IIa and IIb are formed in the reaction of thiazolecarboxylic acid hydrazides Ia and Ib with nitrous acid instead of the expected thiazolecarboxylic acid azides.

The presence of water does not affect the final result.



Ia,b IIa,b

Ia, IIa R = Me; Ib IIb R = Ph

The formation of bisthiazolylureas IIa and IIb probably results from the action of nitrous acid on starting hydrazides Ia and Ib to give thiazolecarboxylic acid azides, which undergo the Curtius rearrangement [4] under the reaction conditions leading to the corresponding isocyanates. Upon reaction with acetic or trifluoroacetic acid, these isocyanates readily give a mixture of substituted anhydrides of carbamic and/or carboxylic acids, which decompose to give disubstituted ureas IIa and IIb, acid anhydrides, and CO_2. In the presence of water, the isocyanate and the resultant amine react also probably to give ureas IIa and IIb.

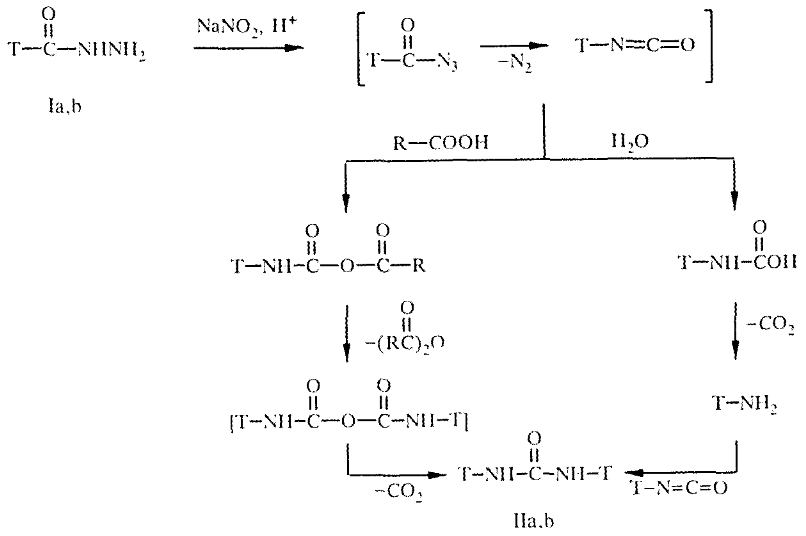
The mass spectra of IIa and IIb* show molecular ion peaks ($M^{+\cdot}$): 406.093 (calculated: 406.092 for $[C_{21}H_{18}N_4OS_2]$, absolute error $\Delta m = 0.001$) and 530.122 (calculated: 530.123 for $[C_{31}H_{22}N_4OS_2]$, $\Delta m = 0.001$) (the *m/z* values will not be given below but only the elemental compositions of the ions, see Experimental). The fragmentation of these compounds is determined by cleavage of the β- and γ-bonds relative to the thiazole ring. The radical-cations formed then dissociate with loss of a neutral N≡C—R molecule (where R = CH_3, Ph). When the dissociative ionization of the molecular ion proceeds at the β-bond, a hydrogen atom migrates with the formation of radical-cations 190 (IIa) and 252 (IIb). The probability of such

---

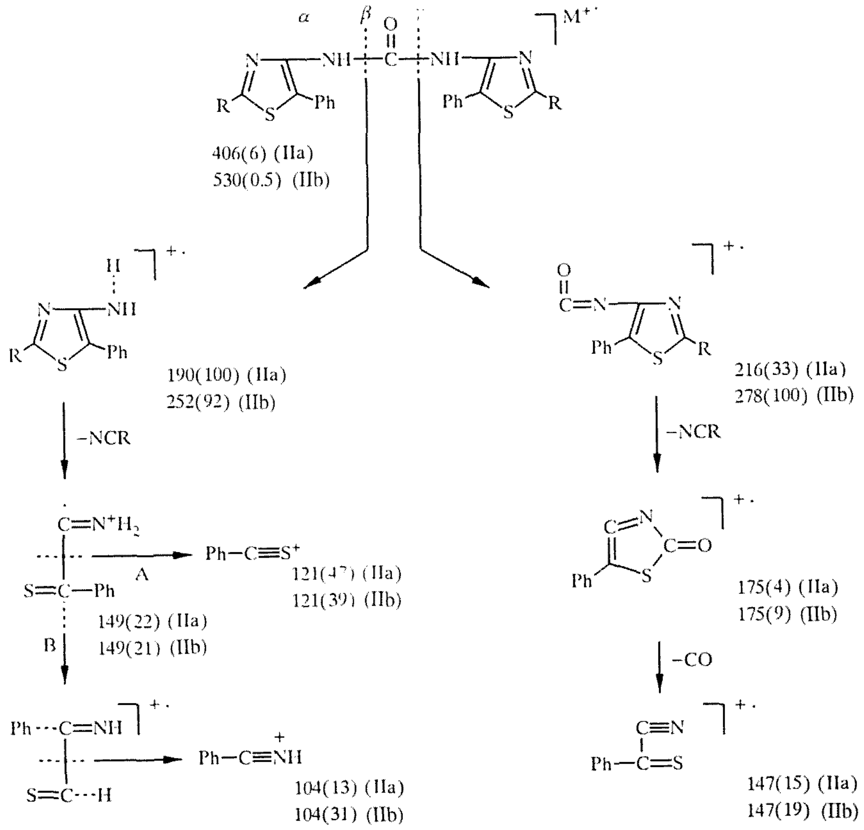
*Here and subsequently, the *m/z* (*I*, %) values are given for the ion peaks.

A. E. Arbuzov Institute of Organic and Physical Chemistry, Kazan Science Center, Russian Academy of Sciences, 420083 Kazan. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 7, pp. 987-990, July, 1994. Original article submitted May 5, 1994.

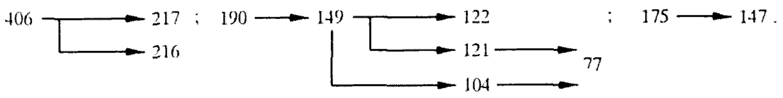
bond cleavage is very high since formation of this ion is possible through four independent pathways: 1 and 2) cleavage at the β- and γ-bonds with charge localization on the light fragment and 3 and 4) direct formation of $M^{+\cdot}$ through loss of CO with charge localization on either fragment since both fragments are identical.



Ia and IIa T = 2-methyl-5-phenylthiazolyl, Ib and IIb T = 5,5-diphenythiazolyl



Since the dissociative ionization of ureas is characterized by the appearance of strong radical-cation peaks in the mass spectrum, the determination of metastable ion peaks was carried out for IIa. The following channels for ion decomposition were established:



These data clearly show that the decomposition of ion 149 proceeds in two directions (see Scheme 2). Pathway A proceeds with retention of the original bonds in the ions formed (stronger ion peaks), while pathway B proceeds with rearrangement of the ion and formation of a new bond with the phenyl group (weaker ion peaks).

The IR spectra of ureas IIa and IIb show N—H stretching bands at 3250 and 3275 cm^{-1}, while the PMR spectra show broad singlets for the protons bound to nitrogen at 8.05 and 8.94 ppm, respectively, which indicates formation of disubstituted ureas.

EXPERIMENTAL

The melting points were determined on a Boetius block. The PMR spectra were taken on an MW-250 spectrometer in DMSO-d_6. The IR spectra were taken on a UR-20 spectrometer in Vaseline mull. The electron impact mass spectra of IIa and IIb with precise determination of the molecular and fragmentation ions (the average absolute error was 1×10^3) were obtained on an MKh-1310 mass spectrometric unit at 70 eV. The electron collector current was 30 μA. The ion source temperature was 140°C. An SVP-5 direct inlet system was used; R (m/Δm) = 1×10^4.

N,N'-Bis(2-methyl-5-phenyl)thiazolylurea (IIa). A. A solution of 1.4 g (0.016 mole) $NaNO_2$ in 3 ml water was added to a solution of 2.3 g (0.01 mole) hydrazide (Ia) in 20 ml acetic acid at 0°C. The reaction mixture was maintained at 0°C for 5 min and poured into 100 ml ice water. The mixture was extracted with three 50-ml chloroform portions and dried over $MgSO_4$. After evaporation, the residue was recrystallized from methanol to give 1.8 g (78%) IIa, mp 236-237.5°C. IR spectrum: 700, 760, 1180, 1380, 1465, 1580, 1630, 3200-3350 cm^{-1}. PMR spectrum in DMSO-d_6: 2.11 (3H, s, CH_3), 6.80-7.04 (5H, m, C_6H_5), 8.05 ppm (1H, s, NH). Mass spectrum (elemental composition): 406(6) ($C_{21}H_{18}N_4OS_2$) ($M^{+\cdot}$), 217(20) ($C_{11}H_9N_2OS$), 216(33) ($C_{11}H_8N_2OS$), 191(13), 190(100) ($C_{10}H_{10}N_2S$), 175(4) (C_9H_5NOS), 149(22) (C_8H_7NS), 148(7) (C_8H_6NS), 147(15) (C_8H_5NS), 146(6) (C_8H_4NS), 122(20) (C_7H_6S), 121(47) (C_7H_5S), 120(6) (C_7H_4S), 105(6) (C_7H_7N), 104(13) (C_7H_6N), 103(8) (C_7H_5N), 89(3) (C_7H_5), 77(21) (C_6H_5).

N,N'-Bis(2,5-diphenyl)thiazolylurea (IIb) was obtained similarly to IIa but 1:1 $CH_3CO_2H—CF_3CO_2H$ was used instead of acetic acid. A crystalline precipitate formed upon treatment with water, which was dried and recrystallized. The yield of IIb was 86%, mp 252-253.5°C (from DMSO). IR spectrum: 695, 765, 1030, 1380, 1465, 1570, 1650, 3150-3250 cm^{-1}. PMR spectrum (DMSO-d_6): 7.47-8.05 (10H, m, $2C_6H_5$), 8.94 ppm (1H, s, NH). Mass spectrum (elemental composition): 530(0.5) ($C_{31}H_{22}N_4OS_2$) ($M^{+\cdot}$), 280(6), 279(22), 278(100) ($C_{16}H_{10}N_2OS$), 253(18), 252(92) ($C_{15}H_{12}N_2S$), 175(9) (C_9H_5NOS), 149(21) (C_8H_7NS), 148(6) (C_8H_6NS), 147(19) (C_8H_5NS), 146(9) (C_8H_4NS), 139(5) (*m/e* $^+$278), 126(3) (*m/e* $^+$252), 122(18) (C_7H_6S), 121(39) (C_7H_5S), 120(8) (C_7H_4S), 105(11) (C_7H_7N), 104(31) (C_7H_6N), 103(15) (C_7H_5N), 89(3) (C_7H_5), 77(23) (C_6H_5).

B. A sample of 1.4 g (0.016 mole) $NaNO_2$ was added to a solution of 2.3 g (0.01 mole) hydrazide Ia in 20 ml glacial acetic acid at 0°C. The reaction mixture was maintained at 0°C for 30 min, brought to 20°C, stirred for an additional 1 h, and poured into 100 ml cold water. The further work-up was as in procedure A. The yield of urea IIa was 1.8 g (85%). A 1:1 mixture of CH_3CO_2H and CF_3CO_2H was used in the case of Ib. The yield of IIb was 91%.

REFERENCES

1. V. A. Mamedov, I. A. Nuretdinov, and F. G. Sibgatullina, Izv. Akad. Nauk SSSR, Ser. Khim., No. 12, 2832 (1991).
2. V. A. Mamedov and I. A. Nuretdinov, Izv. Akad. Nauk SSSR, Ser. Khim., No. 9, 2159 (1992).
3. V. A. Mamedov, I. A. Nuretdinov, and F. G. Sibgatullina, Izv. Akad. Nauk SSSR, Ser. Khim., No. 3, 679 (1992).
4. E. Lieber, R. L. Minnis, and C. N. R. Rao, Chem. Rev., 65, 381 (1965).