REACTION OF ACETOACETIC ESTER WITH o-AMINOTHIOPHENOLS

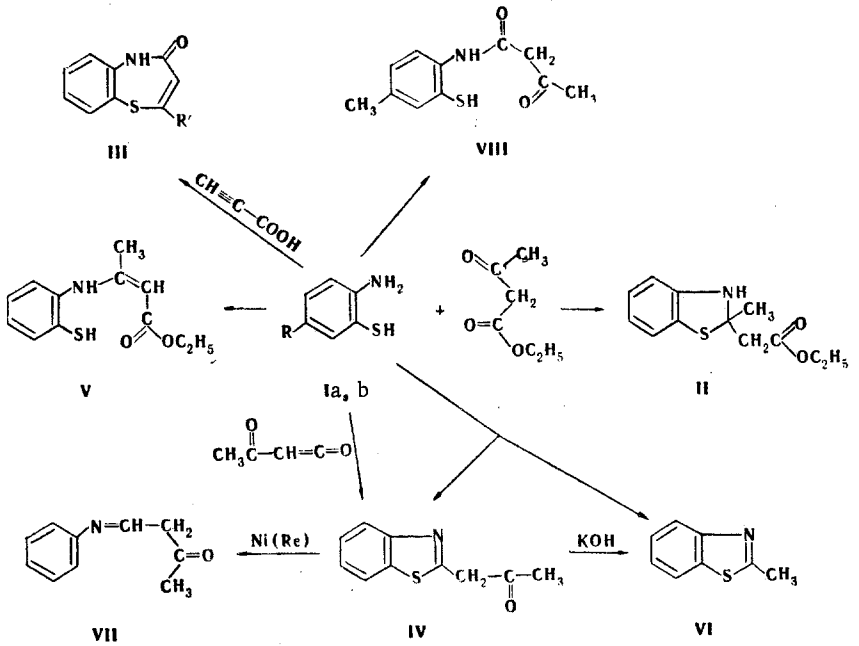
V. I. Avramenko, V. S. Fedenko,
Z. F. Solomko, and N. Ya. Bozhanova

UDC 547.789.6

Benzothiazole derivatives were obtained by condensation of o-aminothiophenol with acetoacetic ester in xylene. 4-Methyl-2-mercaptoacetoacetanilide was isolated in the case of 5-methyl-2-aminothiophenol, whereas ethyl 3-(5-methyl-2-aminophenylmercapto)crotonate was isolated without a solvent in the presence of hydrochloric acid.

The reaction of acetoacetic ester (AAE) with aminothiophenols (I) was first studied by A. I. Kiprianov and co-workers [1]. It was shown that 2-methyl-2-carbethoxymethylbenzothiazoline (II) is formed when these substances are heated in the absence of a solvent. The available data relative to this reaction in xylene are contradictory: according to the data in [2, 3], the principal product is 2-methyl-4,5-dihydro-1,5-benzothiazepin-4-one (III) or its isomer, whereas Buras and co-workers [4] assume that 2-acetonylbenzothiazole (IV) and II are formed under these conditions.

We have studied the reaction of AAE with o-aminothiophenols Ia, b. At room temperature in the presence of small amounts of hydrochloric acid amine Ia reacts with AAE and is converted quantitatively to benzothiazoline II, whereas thiophenol Ib forms ethyl 3-(5-methyl-2-aminophenylmercapto)crotonate (V) under these conditions.



Ia R=H; b R=CH$_3$, R'=H, CH$_3$

The IR spectrum of benzothiazoline II contains the absorption band of a secondary amino group (3360 cm^{-1}), the band of a C=O bond in an ester grouping (1725 cm^{-1}), a broad and intense absorption band of an ester group (1205 cm^{-1}), and two bands of stretching vibrations of CH_2 groups (2935 and 2985 cm^{-1}). A triplet of methyl protons (1.15 ppm) a quartet of methylene protons (4.03 ppm) of an ester group, singlets of methyl protons (1.68 ppm) and protons of an N–H bond (5.0 ppm), and a multiplet of aromatic protons (6.13-7.3 ppm) are

Dnepropetrovsk State University, Dnepropetrovsk 320010. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 8, pp. 1049-1052, August, 1978. Original article submitted January 3, 1978.

 0009-3122/78/1408-0840$07.50

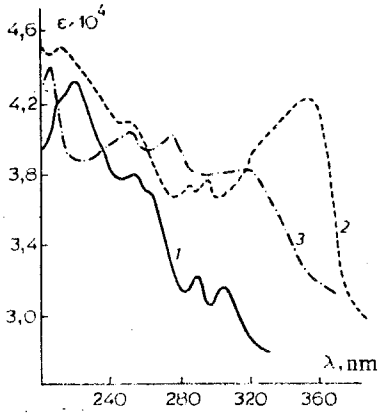


Fig. 1. UV spectra of 2-methylbenzothiazole (1), 2-acetonylbenzothiazole (2), and 4,5-dihydro-1,5-benzothiazepin-4-one (3).

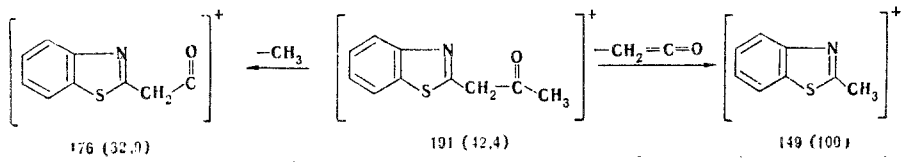
observed in the PMR spectrum of thiazoline II. The multiplicity of the signal of protons of the C—CH_2 group (2.88 ppm) is evidently associated with their diastereotopic character.

The IR spectrum of ester V contains absorption bands of a secondary NH group (3340 cm^{-1}) and a C=O group (1635 cm^{-1}), the shift of which to the low-frequency region is probably associated with the presence of conjugation. Intense absorption of an ester group at 1250-1300 cm^{-1} consisting of several bands is observed. The PMR spectrum of ester V contains a triplet of methyl protons (1.0 ppm) and a quartet of methylene protons (4.11 ppm) of an ester group with spin—spin coupling constant (SSCC) J = 7 Hz, singlets of a methylidyne proton (4.79 ppm) and of protons of two methyl groups (2.26 and 2.85 ppm), and signals of aromatic protons (6.97-7.55 ppm).

Three substances — 2-acetonylbenzothiazole (IV), benzothiazoline (II), and 2-methylbenzothiazole (VI) — can be isolated if the condensation of amine Ia and AAE is carried out by heating in xylene. The yield of IV reaches 40%, and the amount of thiazole VI increases as the heating time is increased.

2-Acetonylbenzothiazole IV was previously obtained [6] from 2,2'-diaminodiphenyl disulfide and AAE in chlorobenzene and also by condensation of 2-methylbenzothiazole with ethyl acetate in the presence of potassium ethoxide [7]. A dihydrobenzothiazepinone structure (III, R' = CH_3) was assigned to ketone IV; however, the UV spectra of ketone IV and 2-methylbenzothiazole VI in the short-wave region are similar (Fig. 1) and differ from the spectrum of benzothiazepinone III (R' = H) obtained by the method in [8] from o-aminothiophenol and propiolic acid.

We confirmed the structure of ketone IV by alternative synthesis from o-aminothiophenol and diketene and by desulfuration in the presence of Raney nickel. In this case we obtained the previously described [5] 1-phenyliminobutan-3-one (VII) rather than crotonanilide, which would have been formed from benzothiazepinone III (R' = CH_3). The character of the PMR and IR spectra provides a basis for the assumption that a tautomeric equilibrium exists for ketone IV:



In addition to signals of the protons of the methyl and methylene groups of tautomer A (2.43 and 4.76 ppm), the PMR spectrum contains signals of methyl and methylidyne protons of tautomer B (2.23 and 5.92 ppm). The signal of the aromatic protons is found at 7.15-8.22 ppm. The IR spectrum of ketone IV does not contain the absorption bands characteristic for a carbonyl group; the band at ∿1610 cm^{-1} can be assigned to the vibrations of a C=C bond. The broad absorption band of a hydroxyl group with a maximum at ∿2800 cm^{-1} confirms the

presence of an enol form in IV with a chelated hydrogen bond. A similar instance of an intramolecular hydrogen bond between a hydroxyl group and a heterocyclic nitrogen atom has been described [9].

The mass spectrum of ketone IV contains an intense molecular-ion peak (m/e 191). The principal fragmentation pathway involves ejection of a molecule of ketene and cleavage in the alkyl group, in agreement with the data in [8]:

A B

The condensation of amine Ib with AAE in xylene leads to the formation of 4-methyl-2-mercaptoacetanilide (VIII), the IR spectrum of which contains absorption bands of stretching vibrations of a secondary NH group at 3190 cm^{-1} and of an amide grouping at 1675 cm^{-1} and intense absorption at ∿1725 cm^{-1}, which attests to the presence of a second carbonyl group.

Signals of methyl (2.08 and 2.29 ppm), methylene (4.32 ppm), and aromatic (6.6-7.0 ppm) protons are observed in the PMR spectrum of acetoacetanilide VIII. The structure of anilide VIII was also confirmed by the mass spectrum, which contains a low-intensity molecular-ion peak at m/e 223 (5.9).*. The base peak of the spectrum at 221 (100) evidently arises as a result of splitting out of two hydrogen atoms from the molecular ion; the latter ejects a molecule of ketene to give an ion at 179 (99.6).

EXPERIMENTAL

The IR spectra of thin layers of KBr pellets of the compounds were recorded with a UR-20 spectrometer. The UV spectra of solutions of the compounds in ethanol were obtained with a Specord UV-vis spectrophotometer. The PMR spectra of solutions of the compounds in carbon tetrachloride (II) and trifluoroacetic acid (IV, V, and VIII) were recorded with a Tesla BS-487B spectrometer with hexamethyldisiloxane as the internal standard. The mass spectra were obtained with an MKh-1303 spectrometer with a system for volatilization of the substances in the immediate vicinity of the ionization region at an ionizing-electron energy of 50 eV, an emission current of 150 μA, and a temperature of 110-120°C. The course of the reactions and the purity of the products were monitored by thin-layer chromatography (TLC) on activity II aluminum oxide or on Silufol UV-254 plates.

2-Methyl-2-carbethoxymethylbenzothiazoline (II). An 8-g (0.061 mole) sample of AAE was added with stirring in the course of 30 min to 6.65 g (0.051 mole) of o-aminothiophenol Ia, and the mixture was acidified with a few drops of concentrated hydrochloric acid and stirred for 5 h. It was then vacuum distilled to give 10.8 g (90%) of a product with bp 172-173°C (10 mm), n_D^{20} 1.5750, and R_f 0.61 [ether–hexane (1:1)] (bp 190-192°C (15 mm) [1]).

2-Acetonylbenzothiazole (IV). A) An 11.5-g (0.089 mole) sample of AAE was added in the course of 30 min to a solution of 9.3 g (0.074 mole) of aminothiophenol Ia in 100 ml of absolute xylene, and the mixture was refluxed in a nitrogen atmosphere for 2.5 h. The solvent was removed by distillation, the residue was cooled, and the precipitated crystals were removed by filtration, washed with ether, and recrystallized from ethanol to give 5.35 g (38%) of a product with bp 122-123°C and R_f 0.68 [Silufol UV-254, chloroform–alcohol (20:1)]. The mother liquor was evaporated, and the residue was vacuum distilled. Repeated vacuum distillation gave 3.25 g (30%) of 2-methylbenzothiazole (VI), with bp 104°C (10 mm), and 0.5 g (3%) of 2-methyl-2-carbethoxymethylbenzothiazoline (II) with bp 172-173°C (10 mm).

B) A solution of 1.15 g (0.014 mole) of diketene in 3 ml of benzene was added with stirring in the course of 10-12 min in a nitrogen atmosphere to a solution of 1.8 g (0.014 mole) of amine Ia in 30 ml of hot benzene, after which the mixture was heated on a water bath for 2 h. The precipitate was separated and recrystallized from ethanol to give 0.46 g (25%) of a product with mp 118-120°C. The IR spectra of the compounds obtained by methods A and B were identical.

Ethyl 3-(5-Methyl-2-aminophenylmercapto)crotonate (V). A drop of concentrated hydrochloric acid was added to a mixture of 3 g (0.02 mole) of 5-methyl-2-aminothiophenol Ib and 8.4 g (0.06 mole) of AAE, and the mixture was stirred for 1 h and allowed to stand at room temperature for 10-12 h. The orange mass was diluted with ether, and the crystals were

*The m/e values are presented; the relative intensities in percent are given in parentheses.

separated to give 2.75 g (55%) of a product with mp 117-118°C and R_f 0.91 [Silufol UV-254, chloroform–ethanol (20:1)]. Found: N 5.6; S 12.6%. $C_{13}H_{17}NO_2S$. Calculated: N 5.6; S 12.7%.

1-Phenyliminobutan-3-one (VII). A mixture of 0.5 g (0.0025 mole) of thiazole IV, 5 g of Raney nickel, and 30 ml of absolute alcohol was refluxed for 6 h, after which it was filtered. The alcohol was removed from the filtrate, and the residue was distilled to give 0.11 g (30%) of a product with bp 123-125°C (2-3 mm) (bp 128-134°C (2-5 mm) [5]).

4-Methyl-2-mercaptoacetoacetanilide (VIII). A solution of 3.1 g (0.024 mole) of AAE in 5 ml of o-xylene was added in the course of 15 min to a refluxing solution of 3 g (0.02 mole) of 5-methyl-2-aminothiophenol in 30 ml of o-xylene, and the mixture was heated for 2 h. It was then cooled, and anilide VIII was separated to give 1.4 g (32%) of a product with mp 176-178°C (from ethanol) and R_f 0.70 [Silufol UV-254, chloroform–alcohol (20:1)]. Found: N 6.4; S 14.3%. $C_{11}H_{13}NO_2S$. Calculated: N 6.3; S 14.3%.

LITERATURE CITED

1. A. I. Kiprianov and V. A. Portnyagina, Zh. Obshch. Khim., 25, 2257 (1955).
2. W. Ried and W. Marx, Chem. Ber., 90, 2683 (1957).
3. E. B. Towne, W. H. Moore, and J. B. Dickey, US Patent No. 3125563 (1964); Chem. Abstr., 61, 3238 (1964).
4. A. Buras, F. Cossais, and J. P. Jacquet, Compt. Rend., C272, 403 (1971).
5. Thielepape, Ber., 55, 130 (1922); Beilstein, 12, II, 120.
6. M. A. T. Rogers and W. A. Sexton, J. Chem. Soc., 1619 (1947).
7. F. I. Stepanov and S. A. Danilova, Zh. Obshch. Khim., 28, 891 (1958).
8. G. Salmona, R. Gugtielmett, and E. C. Vincent, Compt. Rend., C271, 141 (1970).
9. P. F. Branch, Nature, 177, 671 (1956).

THERMAL ISOMERIZATION OF 5-METHOXY-3-ARYLISOXAZOLES TO METHYL 3-ARYL-2H-AZIRINE-2-CARBOXYLATES

M. I. Komendantov, R. R. Bekmukhametov, and R. R. Kostikov

UDC 547.717.786:542.952

The thermal isomerization of 5-methoxy-3-arylisoxazoles to methyl 3-aryl-2H-azirine-2-carboxylates was subjected to a kinetic study. A correlation between the isomerization rate constants and the σ^+ constants of the substituents in the aromatic ring is observed. The enthalpies of formation of a number of isoxazoles and 2H-azirines were calculated. The effect of the nature of the substituents on the mutual isomerization of isoxazoles and azirines is discussed. The results make it possible to refute the approved and previously proposed diradical mechanism for the isomeric transformations and are in agreement with a nitrene mechanism for the formation of azirines.

When isoxazoles containing alkoxy [1, 2], alkylthio [2], and amino [3, 4] groups in the 5 position are heated, they undergo isomerization to the corresponding derivatives of 2H-azirine-2-carboxylic acids.

In the present research we made a kinetic study of the thermal isomerization of 5-methoxy-3-arylisoxazoles (Ia-e) to methyl 3-aryl-2H-azirine-2-carboxylic acids (IIa-e). Isoxazoles Ia-e were synthesized by the method in [2] from the corresponding isoxazolones obtained by the method in [5]. Azirines IIa-e were obtained from isoxazoles Ia-e by the method in [2].

A. A. Zhdanov Leningrad State University, Leningrad 199004.

Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 8, pp. 1053-1056, August, 1978. Original article submitted August 1, 1977.