Chemistry of Heterocyclic Compounds, Vol. 30, No. 2, 1994

SYNTHESIS AND PROPERTIES OF THIAZOLE HALOHYDRAZONES.

1. SYNTHESIS AND INTERACTION OF 2-α-CHLOROBENZYLIDENEHYDRAZINO-4-ETHOXYCARBONYL-THIAZOLE WITH TRIETHYLAMINE IN THE PRESENCE OF DIPOLAROPHILES

S. V. Usol'tseva and G. P. Andronnikova

In the interaction of 2-α-chlorobenzylidenehydrazino-4-ethoxycarbonylthiazole with triethylamine, a nitrilimine is formed as an intermediate that does not react with dipolarophiles, but rather undergoes intramolecular 1,5-dipolar cyclization to form 3-phenyl-5-ethoxycarbonylthiazolo[2,3-c]-1,2,4-triazole.

Halohydrazones containing a heterocyclic group in the hydrazone fragment have thus far received only limited attention, although they may be of practical interest for the synthesis of various derivatives. Continuing our studies of the properties of halohydrazones in the thiazole series [1-3], we have obtained 2-α-chlorobenzylidenehydrazino-4-ethoxycarbonylthiazole (I) and have studied its interaction with triethylamine in the presence of dipolarophiles.

The synthesis of the 2-α-chlorobenzylidenehydrazinothiazole I was accomplished by analogy with [4], by treatment of 2-benzoylhydrazino-4-ethoxycarbonylthiazole (II) with PCl_5 in PCl_3.

According to [5, 6], in the interaction of halohydrazones with tertiary amines, as a result of 1,3-elimination of a hydrogen halide molecule, highly reactive nitrilimines are formed. If a "trap," i.e., an active dipolarophile, is present in the reaction mass, the nitrilimines enter into the reaction of 1,3-dipolar cycloaddition, forming various five-membered heterocycles: pyrazolines, pyrazoles, 1,2,4-triazolines, 1,2,4-triazoles, etc. If there is a nucleophilic center in the molecule of the original hydrazone, intramolecular 1,5-dipolar cyclization is possible, forming 1,3,4-oxadiazoles, 1,3,4-thiadiazoles, or 1,2,4-triazoles, including annelated compounds.

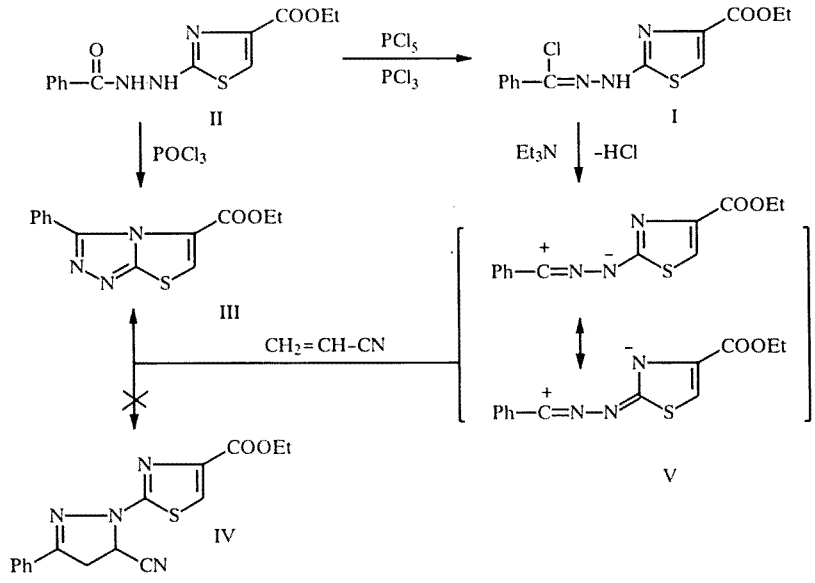
Upon interaction of the 2-α-chlorobenzylidenehydrazinothiazole I with triethanolamine in ethanol or chloroform, 3-phenyl-5-ethoxycarbonylthiazolo[2,3-c]-1,2,4-triazole (III) is formed. When such a dipolarophile as acrylonitrile is used as a "trap" for the nitrilimine, we would expect the formation of a derivative of 2-pyrazoline (IV) [5]. On the contrary, we found that under various conditions of reaction, regardless of the order and rate of triethylamine addition, reaction time and temperature, or the nature of the solvent (and also when using acrylonitrile as the solvent), we were unable to detect even traces of the product of 1,3-dipolar cycloaddition IV. In all cases, the sole product of the reaction was the thiazolotriazole III. Analogous results were obtained with other dipolarophiles such as malononitrile.

The structure of compound III was confirmed by spectroscopic data and by a counter-synthesis — cyclization of the 2-benzoylhydrazinothiazole II in phosphorus oxychloride [7].

From the data obtained in this work we can conclude that in the case of the 2-α-chlorobenzylidenehydrazinothiazole I, which contains a nucleophilic center in the molecule (i.e., the nitrogen atom of the thiazole ring), upon treatment with triethylamine in the presence of dipolarophiles, only one of the possible reaction paths is realized, specifically, intramolecular

Ural State Technical University, Ekaterinburg 620002. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 2, 253-255, February, 1994. Original article submitted November 30, 1993.

0009-3122/94/3002-0231$12.50 ©1994 Plenum Publishing Corporation



1,5-dipolar cyclization of the intermediate nitrilimine V, forming the stable thiazolotriazole III. The probable explanation for this behavior is that the rate of intramolecular cyclization is far higher than the rate of 1,3-dipolar cycloaddition with dipolarophiles [8, 9]. The intramolecular cyclization is favored by delocalization of negative charge with participation of the thiazole ring, and also by the presence of an electron-acceptor substituent that reduces the activity of the nitrilimine with respect to the dipolarophile.

EXPERIMENTAL

IR spectra were taken on a UR-20 spectrophotometer (KBr tablets); PMR spectra were taken on a Bruker WH-90 instrument (22.62 MHz), with DMSO-d_6 solvent and TMS internal standard. Mass spectra were obtained on a Varian MAT-311 A instrument with 70-eV ionizing radiation and with direct introduction of the sample into the source. The individuality of the substances was monitored by means of TLC on Silufol UV-254 plates in a 9:1 chloroform–ethanol system.

The elemental analyses of compounds II and III matched the calculated values.

2-α-Chlorobenzylidenehydrazino-4-ethoxycarbonylthiazole (I). To a suspension of 1.0 g (3.43 mmoles) of the hydrazide II in 5 ml of PCl_3, heated to 50°C, 1.43 g (6.86 mmoles) of PCl_5 was added in portions while stirring. The reaction mass was refluxed for 2 h and then cooled to −5° to −10°C, after which it was diluted with 60-70 ml of petroleum ether, and 10-15 ml of absolute ethanol was added in portions while stirring vigorously. The ether layer was decanted, and the remaining suspension was filtered. The solid residue was washed with a small amount of cold ethanol and recrystallized from absolute isopropyl alcohol. The product was stored in a vacuum desiccator over P_2O_5. R_f 0.93; mp 160-165°C [7], mp 150-152°C. IR spectrum, cm^{-1}: 1705 (C=O); 1605 (C=N). PMR spectrum, ppm: 8.0-7.7 (2H, m, Ph); 7.85 (1H, s, 5-H); 7.7-7.4 (2H, m, Ph); 4.3 (2H, q, CH_2); 1.3 (3H, t, CH_3). Mass spectrum: M^+ 309, 311 (5%); 273 $[M - HCl]^+$ (100%). Yield 57%.

2-Benzoylhydrazino-4-ethoxycarbonylthiazole (II). To a suspension of 1.0 g (5.34 mmoles) of 2-hydrazino-4-ethoxycarbonylthiazole [10] in 10 ml of dioxane, 0.63 ml (5.34 mmoles) of benzoyl chloride was added. The solid residue was filtered off, washed with dioxane, and recrystallized from a 1:1 mixture of isopropyl alcohol and water. R_f 0.43; mp 187-188°C. IR spectrum, cm^{-1}: 3290, 2995 (NH); 1720 (C=O); 1670 (C=O of amide I); 1580 (C=N); 1530 (amide II). PMR spectrum, ppm: 10.9 (1H, s, NH—C=O); 9.8 (1H, s, NH); 8.1-7.8 (2H, m, Ph); 7.69 (1H, s, 5-H); 7.75-7.3 (3H, m, Ph); 4.25 (2H, q, CH_2); 1.3 (3H, t, CH_3). Yield 64%.

3-Phenyl-5-ethoxycarbonylthiazolo[2,3-c]-1,2,4-triazole (III). To a solution of 0.2 g (0.65 mmole) of the chlorohydrazone in 5 ml of either ethanol, chloroform, or acrylonitrile, 1 ml of triethylamine was added. The solvent was removed under vacuum, and the residue was recrystallized from 50% aqueous ethanol. R_f 0.55; mp 158-160°C. IR spectrum, cm^{-1}: 1710 (C=O); 1555 (C=N). PMR spectrum, ppm: 8.29 (1H, s, 6H); 7.49 (5H, s, Ph); 3.95 (2H, q, CH_2); 0.92 (3H,

t, CH_3). Mass spectrum: M^+ 273 (100%). Yield 70%. A compound with identical characteristics was obtained with a 75% yield by a method given in [7].

REFERENCES

1. S. V. Usol'tseva, G. P. Andronnikova, S. L. Mertsalov, and S. L. Nikolaeva, Summaries of All-Union Conference on Organic Sulfur Compounds [in Russian], Tbilisi (1988), p. 194.
2. S. V. Usol'tseva and G. P. Andronnikova, All-Union Conference on the Chemistry of Heterocyclic Nitrogen Compounds (Summaries of Papers) [in Russian], Chernogolovka (1991), Vol. 2, p. 172.
3. S. V. Usol'tseva, G. P. Andronnikova, and V. A. Shevyrin, Khim. Geterotsikl. Soedin., No. 2, 257 (1993).
4. P. D. Callaghan and M. S. Gibson, J. Chem. Soc. C, p. 2106 (1970).
5. Yu. P. Kitaev and B. I. Buzykin, Hydrazones [in Russian], Nauka, Moscow (1974).
6. A. S. Shavali and C. Parkanyi, J. Heterocycl. Chem., **17**, 833 (1980).
7. Z. A. Bredikhina, B. I. Buzykin, and Yu. P. Kitaev, Khim. Geterotsikl. Soedin., No. 4, 537 (1991).
8. J. P. Ferris and R. W. Trimmer, J. Org. Chem., **41**, 13 (1976).
9. A. Padwa, E. Chen, and A. Ku, J. Am. Chem. Soc., **97**, No. 22, 6484.
10. A. L. Suslova, M. G. Bazhenova, G. I. Validuda, S. L. Nikolaeva, and G. P. Andronnikova, paper filed at VINITI, December 10, 1984, No. 825; Ref. Zh. Khim., No. 145 (1985).