A NEW EXAMPLE OF THE DIMROTH REARRANGEMENT IN THE 1,2,4-TRIAZOLO[4,3-c]PYRIMIDINE SERIES

G. G. Danagulyan, L. G. Saakyan, and M. G. Zalinyan

The Dimroth rearrangement of 7-benzyl-5-methyl-1,2,4-triazolo[4,3-c]pyrimidine to 7-benzyl-5-methyl-1,2,4-triazolo[2,3-c]pyrimidine was realized by the action of sodium ethoxide and other nucleophilic agents. The rearrangement was investigated by the dynamic PMR spectroscopic method.

The Dimroth rearrangement has been studied in considerable detail for the series of condensed pyrimidines including triazolopyrimidines [1,2]. Articles on the recyclization of substituted 1,2,4-triazolo[4,3-c]pyrimidines to the isomeric 1,2,4-triazolo[2,3-c]pyrimidines have been published [3-5]; under certain conditions the transformation can even take place during the synthesis of triazolo[4,3-c]pyrimidine [6,7].

We rearranged the previously uninvestigated model 7-benzyl-5-methyl-1,2,4-triazolo[4,3-c]pyrimidine (I) to 7-benzyl-5-methyl-1,2,4-triazolo[2,3-c]pyrimidine (II) with an almost quantitative yield by boiling compound (I) in an alcohol solution containing a catalytic amount of sodium ethoxide for 30 min.

The rearrangement process was also observed in the dynamic variation of the PMR spectra of compound (I), recorded in CD_3OD with the addition of a small amount of CD_3ONa. Here the signal at 4.40 ppm, corresponding to the CH_2 fragment of the benzyl group, first disappeared with a simultaneous change in the signals for the protons of the phenyl group (conversion of the singlet of the aromatic protons into a multiplet). A singlet for an aromatic proton, corresponding to the proton of the pyrimidine ring in the recyclization product, then appeared in the downfield region (8.08 ppm).

At the end of the process the PMR spectrum corresponded to the spectrum of an authentic sample of the transformation product. The recyclization observed in the tube was also monitored by chromatography.

The initial disappearance of the signal for the protons of the methylene group was probably due to their high CH acidity, which leads to basic isotopic exchange. Thus, it can be concluded on the basis of the PMR spectra that initial attack by the nucleophilic agent takes place in two alternative directions: First, the reversible removal of a proton from the benzyl group with the production of an anionic adduct, not capable of rearrangement but also not preventing it on account of the reversibility of the process; second, nucleophilic attack by the alkoxyl group at position 7 with subsequent ring opening and recyclization at another nitrogen atom of the triazole ring.

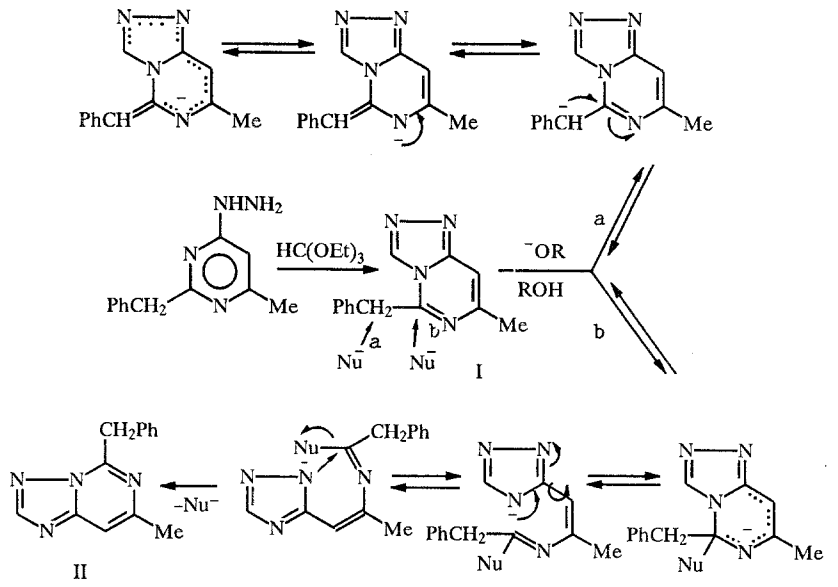
All stages of both processes are basically reversible, but the thermodynamic stability of 1,2,4-triazolo[2,3-c]pyrimidines compared with 1,2,4-triazolo[4,3-c]pyrimidines predetermines the unambiguous transformation of compound (I) into compound (II).

Compound (I) is very mobile; its rearrangement to the isomer (II) is also observed under the influence of other nucleophilic agents, e.g., during boiling in an alcohol solution of triethylamine (12 h) and even during prolonged boiling in ethanol. (See scheme at the top of the next page.)

In an alcohol solution of potassium hydroxide, containing a small amount of water, quantitative conversion is observed even after 3-5 min in the cold, but further boiling leads to destruction of the molecule. Compounds (I) and (II) differ greatly in their chromatographic mobility, and this makes it possible to monitor the rearrangement by TLC.

Erevan Institute of National Economy, Erevan. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 2, pp. 225-227, February, 1992. Original article submitted September 27, 1990.

0009-3122/92/2802-0186$12.50



The PMR spectra of the initial compound (I) and of the final recyclization product (II) only differ in the downfield region. In particular, in the spectrum of compound (I) the signals for the protons of the benzene, pyrimidine (4-H), and triazole (1-H) rings are superimposed and appear as a single singlet in the region of 7.23 ppm, whereas the signal of the pyrimidine proton in the spectrum of compound (II) is shifted downfield (8.08 ppm), and the protons of the benzene ring appear as a multiplet (7.20 ppm). The change in the form in which the C_6H_5 protons appear in the spectrum of compound (II) compared with compound (I) is due to the electronic effect of the nitrogen atom at position 1, which leads to some restricted rotation of the phenyl group.

EXPERIMENTAL

The PMR spectra were recorded on a Varian T-60 instrument with HMDS as standard. The mass spectra were recorded on an MX-1303 instrument with injection of the substance into the ionization zone at 50 eV.

The elemental analyses of compounds (I) and (II) for C, H, and N agree with the calculated data.

7-Benzyl-5-methyl-1,2,4-triazolo[4,3-c]pyrimidine (I) ($C_{13}H_{12}N_4$). A solution of 4.28 g (0.02 mole) of 2-benzyl-4-hydrazino-6-methyl pyrimidine in 10 ml of triethyl orthoformate was boiled for 4 h. The orthoformic ester residue and the released alcohol were distilled to dryness under vacuum. Hexane was added to the residue, and the precipitate was filtered off and recrystallised from an 11:2 mixture of ethanol and hexane; mp 186-187°C, R_f 0.44 (ethyl acetate). PMR spectrum (carbon tetrachloride): 2.48 (3H, s, CH_3); 4.40 (2H, s, CH_2); 7.23 ppm (7H, s, C_6H_5, 1-H and 4-H). Mass spectrum:* 224 (100), 223 (53), 197 (7), 196 (20), 195 (46), 183 (4), 181 (7.3), 171 (5.2), 117 (16), 108 (62.5), 91 (27.1). The yield was 3.9 g (88%)

7-Benzyl-5-methyl-1,2,4-triazolo[2,3-c]pyrimidine (II) ($C_{13}H_{12}N_4$). A. To a solution of sodium ethoxide, prepared from 0.18 g (0.008 mole) of sodium and 20 ml of absolute ethanol, we added a solution of 2.5 g (0.011 mole) of compound (I) in 30 ml of absolute ethanol. The mixture was boiled for 30 min, and the reaction was monitored by chromatography on silica gel with ethyl acetate as eluant. After 30 min the solution was cooled and neutralized with an ethanol solution of hydrochloric acid. The alcohol was distilled to dryness, and the residue was extracted with hot hexane. On cooling a white needle-type precipitate separated from the hexane extract. We obtained 2.3 g (92%) of compound (II); mp 86-87°C, R_f 0.74 (ethyl acetate). PMR spectrum (carbon tetrachloride): 2.83 (3H, s, CH_3); 4.45 (2H, s, CH_2); 7.18 (6H, m, C_6H_5 and 2-H); 8.08 ppm (1H, s, 4-H). Mass spectrum: 224 (100), 223 (29.8), 197 (2.7), 183 (1.3), 171 (1.9), 117 (4.5), 112 (3.6), 108 (26), 91 (4.2).

*Here and subsequently the m/z values are given, and the relative intensities in relation to the maximum ion peak are given in parentheses.

B. A mixture of 0.224 g (1 mmole) of compound (I) and 1 ml (10 mmole) of triethylamine was boiled in 10 ml of absolute ethanol until the spot of compound (I) on the chromatogram had disappeared (about 12 h). The mixture was evaporated to dryness under vacuum, and the residue was extracted with hot hexane and filtered. On cooling the chromatographically pure compound (II) separated from the hexane solution; mp 86-88°C. The yield was 0.19 g (85%).

LITERATURE CITED

1. A. N. Kost, R. S. Sagitullin, and G. G. Danagulyan, *Khim. Geterotsikl. Soedin.*, No. 5, 706 (1976).
2. F. S. Babichev and V. A. Kovtunenko, *Khim. Geterotsikl. Soedin.*, No. 2, 147 (1977).
3. O. Nagase, M. Hirata, and M. Inaoka, *Yakugaku Zasshi*, **82**, 528 (1962); Chem. Abs., **58**, 3430 (1963).
4. G. W. Miller and E. P. Rose, *J. Chem. Soc.*, No. 12, 5642 (1963).
5. C. T. Shisdo, M. B. Devani, G. B. Ullas, S. Anathan, and V. S. Bhadti, *J. Heterocycl. Chem.*, **22**, No. 3, 831 (1985).
6. G. W. Miller and F. L. Rose, British Patent No. 897870; Chem. Abs., **58**, 10211 (1963).
7. G. W. Miller and F. L. Rose, British Patent No. 859287; Chem. Abs., **55**, 17665 (1961).

SYNTHESIS AND THERMAL DECOMPOSITION OF HALOGENOALKOXY-, HALOGENOALKYLTHIO-, AND HALOGENOALKOXYAMINO-SYM-TRIAZINES

13.* SYNTHESIS AND THERMOLYSIS OF 4,6-DISUBSTITUTED 2-(2-CHLOROETHOXY)- AND 2-(2-CHLOROETHYLAMINO)-SYM-TRIAZINES

K. A. Éliazyan, A. M. Akopyan, V. A. Pivazyan, A. G. Akopyan, and V. V. Dovlatyan

4-Amino-, 4-methoxy-, 4-methylthio-, 4-alkylamino-, and 4-dialkylamino-6-alkyl(dialkyl)amino-2-(2-chloroethoxy)-sym-triazines and the corresponding 2-(2-chloroethylamino)-sym-triazines were obtained. Their cyclization led to the sym-triazinium chlorides or imidazo-sym-triazines.

In the development of the applications of the rearrangement—cyclization of chloroalkoxy- and chloroalkylthio-sym-triazines [1-5] it seemed of interest to study the reactions of 4-amino-6-dialkylamino-2-(2-chloroethoxy)-sym-triazines, which could lead to tetrahydroimidazo-sym-triazines-. (See scheme at the top of the next page.)

The initial chlorides (Ia, b) were obtained earlier [2] from the corresponding quaternary ammonium salts and ethylene chlorohydrin. However, instead of the expected hydrochlorides (IIa, b), thermolysis of compounds (Ia, b) gave the isomeric quaternary salts (IVa, b) (oxazolo-sym-triazinium chlorides), which did not change even under more drastic thermolysis conditions.

*For Communication 12, see [1].

Armenian Agricultural Institute, Erevan. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 2, pp. 228-230, February, 1992. Original article submitted October 2, 1989.

0009-3122/92/2802-0188$12.50