# STRUCTURE AND SOME PROPERTIES OF TETRAZOLE 5-METHYLPYRIMIDO[4,5-e]-[1,2,4]TRIAZINE-6,8-DIONE AND ITS AZIDE IN DIFFERENT PHASE STATES

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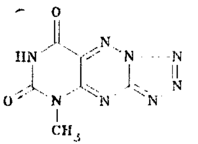
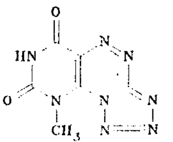
The structure of the tetrazole, 5-methylpyrimido[4,5-e][1,2,4]triazine-6,8-dione was established by x-ray structural analysis. The tautomeric equilibrium with its azide isomer in solution was examined. The effect of bases on this equilibrium was discovered. Analytical criteria were proposed which permit identification of the tetrazole and the azide forms in the gas phase.

The present study is a continuation of our previous work [1-3] on the physicochemical properties of pyrimido-as-triazine antibiotics including rheumacine, fervenuline, and xanthotricine and their structural analogs [4-6] having antiviral activity [7].

In the present work, we established the nature of the ring fusion in the tetrazole, pyrimido[4,5-e][1,2,4]triazine-6,8-dione (Ia or Ib) in the crystalline state and elucidated the differences between the cyclic form (Ia or Ib) and its isomer (Ic) in the aizde form relate to dissociative ionization upon electron impact. The structural results were compared for isomers Ia-c (taking account of possible tautomerism) for different aggregate states.


Ia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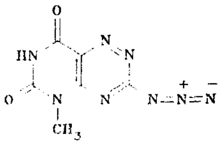
I c

In our previous work, by analogy to the studies of Messmer [8] and Bogatskii [9] for the cyclic form, we adopted the angular structure (Ib) for both the crystalline and gaseous states of this molecule. There is no common opinion presently in the literature concerning the nature of the cyclization of the 3-azido group in 1,2,4-triazine derivatives. Thus, x-ray diffraction structural analysis has shown that the tetrazole isomer of 3-azido-5-p-chlorophenyl-1,2,4-triazine exists in crystals as the linear analog, 5-p-chlorophenyltetrazolo[1,5-b]-1,2,4-triazine [10]. On the other hand, Messmer et al. [8] have shown that 3-azido derivitives of benzotriazine cyclize in solution mainly to give the angular tetrazolo[5,1-c]benzo-as-triazine and only a small amount of linear tetrazolo[1,5,-b]benzo-as-triazine is observed in highly polar aprotic solutions. Recently, Nishigaki et al. [11] studied the UV spectra of model azolopyrimidopyridazines and found that 3-azido-6,8-dimethylpyrimido[5,4-3][1,2,4]triazine-5,7-dione cyclizes to linear 1,3-dimethyltetrazolo[4,5-b]pyrimido[5,4-e]-as-triazine-2,4-dione but they did not present melting point or elemental analysis data for this compound. In addition, no data were given on the state of the azido—tetrazole equilibrium for this isomer pair or for the PMR and UV spectra of the azido derivative.

Thus, the lack of reliable data on the nature of the ring fusion of the tetrazole ring in 1,2,4-triazines requires a special study in each specific case.

In order to determine the nature of the condensation of the tetrazole system in pyrimido-[4,5-e][1,2,4]triazine-6,8-dione, we studied the molecular and crystal structure of this compound by x-ray diffraction structural analysis and established that the tetrazole ring is fused with the as-triazine ring at the $C_{(4)}$—$N_{(4)}$ bond (structure Ia) and not at the $C_{(4)}$—$N_{(8)}$ bond (structure Ib, Fig. 1). Dione Ia consists of three planar condensed heterocyclic rings, namely, a uracil ring (A), as-triazine ring (B) and tetrazole ring (C, Table 1), and has a

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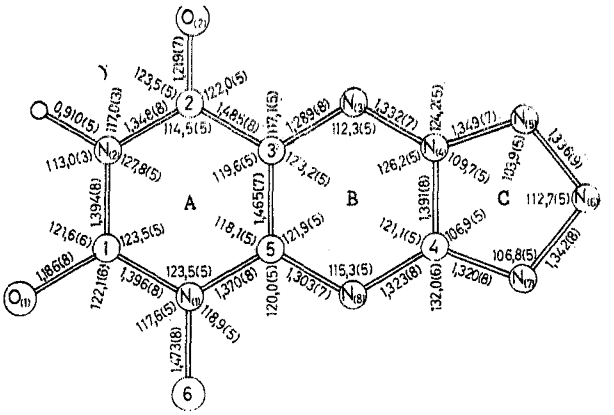

Fig. 1. Bond lengths and angles in Ia.

TABLE 1. Coefficients of the Plane Equations Az + By + Cz − D = 0 of Several Planar Fragments of Ia and Deviation of the Atoms from These Planes, Å

| Plane | Atoms | *A* | *B* | *C* | *D* |
|---|---|---|---|---|---|
| A | $N_{(1)}$ $C_{(1)}$ $N_{(2)}$ $C_{(2)}$ $C_{(3)}$<br>−0,002 −0,010 0,021 −0,035 0,020<br>$C_{(5)}$ $O^*_{(1)}$ $O^*_{(2)}$ $C^*_{(6)}$<br>−0,005 −0,021 −0,109 −0,043 | 0,9088 | −0,0324 | −0,4160 | 2,0077 |
| B | $C_{(3)}$ $N_{(3)}$ $N_{(4)}$ $C_{(4)}$ $N_{(8)}$ $C_{(5)}$<br>−0,010 0,001 0,006 −0,010 0,000 0,009 | 0,9109 | −0,0017 | −0,4126 | 2,2999 |
| C | $N_{(4)}$ $N_{(5)}$ $N_{(6)}$ $N_{(7)}$ $C_{(4)}$<br>−0,008 0,007 0,000 −0,006 0,013 | 0,9075 | 0,0228 | −0,4193 | 2,4839 |
| D | $N_{(1)}$ $C_{(1)}$ $N_{(2)}$ $C_{(2)}$ $C_{(3)}$ $N_{(3)}$<br>0,028 0,001 −0,001 −0,071 0,007 0,070<br>$N_{(4)}$ $N_{(5)}$ $N_{(6)}$ $N_{(7)}$ $C_{(4)}$ $N_{(8)}$<br>0,011 0,038 −0,007 −0,047 −0,014 −0,004<br>$C_{(5)}$ $O^*_{(1)}$ $O^*_{(2)}$ $C^*_{(6)}$<br>0,016 0,000 −0,170 0,020 | 0,9093 | −0,0092 | −0,4161 | 2,2103 |

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*Atoms not included in the calculation of the corresponding plane. Planes A, B, and C form the dihedral angles: A/B = 1.8; A/C = 3.2; B/C = 1.5°.

highly compressed boat conformation. The plane of the central ring B forms dihedral angles of 1.8 and 1.5° with rings A and C, respectively.

The bond length distribution in Ia (Fig. 1) indicates the electron delocalization usual for such conjugated nitrogen-containing heterocycles: All the formal single C—N and N—N bonds are shortened while the double bonds are extended relative to the standard values: C—N, 1.474; N—N, 1.451; N=N, 1.25; C=N, 1.29 Å [12].

Each molecule of Ia in the crystal participates in the formation of two intermolecular hydrogen bonds: $N_{(2)}$—H...$O_{(2)}$ ($^1/_2 - x$, $1 - y$, $^1/_2 + z$) and $O_{(2)}$...H—N $_2$ ($^1/_2 - x$, $1 - y$, $^1/_2 + z$) [N—H 0.91(5); N...O, 2.819(7), H...O, 1.91(5) Å, < [N—H...O, 168(2)°], which leads to the formation of spirals of Ia molecules about $2_1$ axes parallel to the c-axis. The somewhat greater $C_{(2)}$—$O_{(2)}$ bond length [1.219(7) Å] relative to $C_{(1)}$—$O_{(1)}$ [1.186(8) Å] is a consequence of the participation of $O_{(2)}$ in hydrogen bonding.

Crystalline azide and tetrazole isomers are sometimes capable of interconversion. Thus, Messmer et al. [13] noted that solid 3-azidopyrido[2,3-3]-as-triazine spontaneously converts to solid pyrido[2,3-3]tetrazole[5,1-e]-as-triazine. Equilibrium between these isomers is established in dimethylsulfoxide solution. Irreversible conversion to the tetrazole isomer occurs upon heating crystals of 3,3'-diazido-5,5'-bis-as-triazine [14]. The reverse process of the conversion of solid tetrazole derivatives of quinazoline to azide derivatives has also been noted [15]. A unique case of the conversion of the tetrazole isomer of naphthothiazole upon heating to the aizde isomer and the reverse process upon cooling were noted by Postovskii et al. [16].

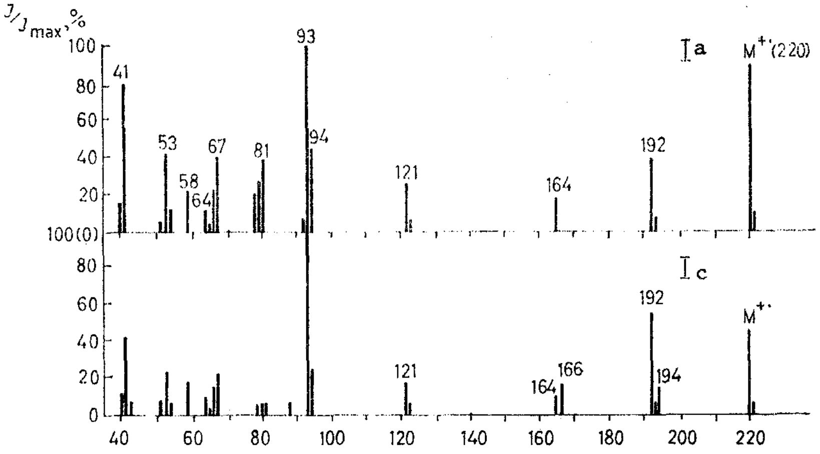

Fig. 2. Mass spectra of isomers Ia and Ic.

TABLE 2. Elemental Composition of Ions Indicated by the High-Resolution Mass Spectra of Tetrazole (Ia) and Azide (Ic) of Pyrimido[4,5-e][1,2,4]triazine-6,8-dione and Their Metastable Ion Mass Spectra

| Ions | Measured | | Ion composition | Calculated | Mass spectra of metastable ions [deflecting voltage of the electrostatic sector ($E_0$ and $E_i$, V)] |
|---|---|---|---|---|---|
| | Ia | Ic | | | |
| $M^{+\cdot}$ | 220,0449 | 220,0462 | $C_6H_4N_8O_2$ | 220,0457 | |
| $[(M-N_2)+2H]^{+\cdot}$ | | 194,0538 | $C_6H_6N_6O_2$ | 194,0552 | |
| $[M-N_2]^{+\cdot}$ $(\Phi_1)$ | 192,0388 | 192,0399 | $C_6H_4N_6O_2$ | 192,0395 | 506 (220)* ⟶ 441 (191,7)† |
| $[(\Phi_1-N_2)+2H]^{+\cdot}$ | | 166,0455 | $C_6H_6N_4O_2$ | 166,0491 | 506 (192) ⟶ 433 (164,3) |
| $[\Phi_1-N_2]^{+\cdot}$ $(\Phi_2)$ | 164,0364 | 164,0351 | $C_6H_4N_4O_2$ | 164,0351 | ⟶ 320 (121,4) |
| $[\Phi_2-HNCO]^{+\cdot}$ $(\Phi_3)$ | 121,0290 | 121,0292 | $C_5H_3N_3O$ | 121,0276 | ⟶ 248 (94,1) |
| $[\Phi_3-HCN]^{+\cdot}$ | 94,0174 | 94,0143 | $C_4H_2N_2O$ | 94,0167 | 505(164) ⟶ 373 (121,1) |
| $[\Phi_3-CO]^{+\cdot}$ | 93,0340 | 93,0333 | $C_4H_3N_3$ | 93,0326 | 504 (121) ⟶ 392 (94,1) |
| | 81,0308 | | $C_3H_3N_3$ | 81,0326 | ⟶ 387 (92,9) |

*Parent peak (m/z).

†Calculated mass of the daughter ion (m/z).

Hence, prior to examining the analytical aspects of the mass spectrometric fragmentation of isomers Ia and Ic, we must study the possible interconversion of these compounds in the gas phase. Precedents exist for such isomerization [17, 18].

However, there are no isomerizational processes for azide Ic and tetrazole Ia under the conditions of direct inlet to the ion source (150-170°C injector temperature) as indicated by the different values of the IE and PE of the $[M - N_2]^+$ ions upon photoionization [3].* This finding indicates definite differences in the nature of the fragmentation of isomers Ia and Ic and requires detailed examination of their mass spectra (Fig. 2).

The fragmentation sequence of the molecular ($M^+$) and major fragment ions for Ia and Ic was established relative to the mass spectra of the metastable ions obtained in the secondary fieldless space on a "reverse geometry" spectrometer (DADI/MIKES technique [19]). The ion composition was found by high-resolution mass spectrometry (Table 2).

Figure 2 indicates that the major difference in the nature of the fragmentation of azide Ic relative to tetrazole isomer Ia lies in the detection of ions with m/a 194 and 166 (the difference in the ratio of the intensities of the peaks of ions $M^+/[M - N_2]^+$ was discussed in our previous work [3]). The appearance of these ions is probably not dictated by ion—molecule reactions ($1 \cdot 10^{-7}$ torr vacuum) although some workers have made such conclusions [20]. In our opinion, it is more realistic to assume the addition of a hydrogen atom to the nitrene

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*The lack of interconversions upon heating crystals of I and Ic was indicated in a thermogravimetric study. The DTA curves for each compound differ and there are no peaks for thermal isomerization effects which should be observed in temperature ranges excluding change in the sample mass (TG and DTG curves).

TABLE 3. Atomic Coordinates ($\times 10^4$, $\times 10^3$ for H) and Their Anisotropic Temperature Factors $T = \exp[-1/4(B_{11}h^2a^{*2}+\ldots+2B_{23}klb^*c^*)]$

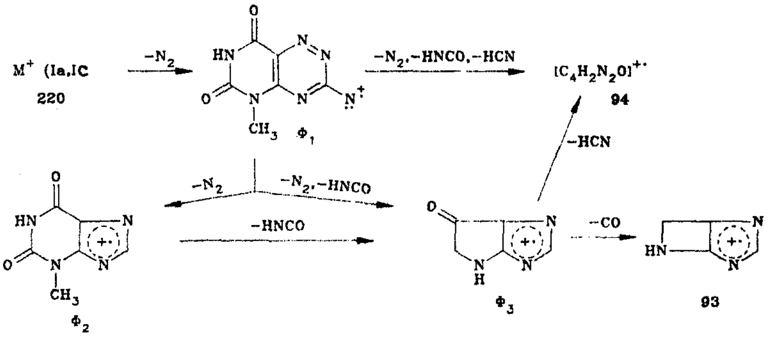
| Atom | $x$ | $y$ | $z$ | $B_{11}$ | $B_{22}$ | $B_{33}$ | $B_{12}$ | $B_{13}$ | $B_{23}$ |
|---|---|---|---|---|---|---|---|---|---|
| $O_{(1)}$ | 1902 (5) | 7724 (3) | −2219 (6) | 5,2 (2) | 3,8 (2) | 3,8 (2) | 0,2 (2) | −1,1 (2) | 0,8 (2) |
| $O_{(2)}$ | 2980 (5) | 4871 (3) | 1365 (6) | 6,4 (2) | 2,5 (2) | 3,9 (2) | −0,1 (2) | −0,2 (2) | 0,2 (2) |
| $N_{(1)}$ | 2924 (5) | 8139 (4) | 448 (6) | 4,0 (2) | 2,6 (2) | 3,2 (2) | 0,2 (2) | 0,1 (2) | 0,4 (2) |
| $N_{(2)}$ | 2534 (5) | 6309 (4) | −454 (7) | 3,6 (2) | 2,9 (2) | 3,1 (2) | −0,0 (2) | −0,3 (2) | −0,5 (2) |
| $N_{(3)}$ | 4137 (5) | 6237 (4) | 3856 (6) | 3,4 (2) | 3,7 (2) | 3,4 (2) | 0,4 (2) | −0,0 (2) | 0,0 (2) |
| $N_{(4)}$ | 4558 (5) | 7010 (5) | 4995 (6) | 3,1 (2) | 4,6 (3) | 3,1 (2) | 0,4 (2) | −0,3 (2) | 0,2 (2) |
| $N_{(5)}$ | 5177 (6) | 6811 (5) | 6599 (7) | 4,5 (3) | 6,3 (3) | 3,8 (3) | 0,0 (2) | −0,6 (3) | 0,7 (3) |
| $N_{(6)}$ | 5391 (6) | 7804 (5) | 7290 (8) | 4,0 (3) | 6,8 (3) | 4,4 (3) | −0,3 (3) | −0,3 (2) | −1,9 (3) |
| $N_{(7)}$ | 4951 (6) | 8605 (4) | 6190 (4) | 5,3 (3) | 4,7 (3) | 3,7 (3) | −0,3 (3) | 0,8 (2) | −0,8 (3) |
| $N_{(8)}$ | 3911 (5) | 8533 (4) | 3225 (7) | 4,0 (2) | 3,2 (2) | 3,5 (3) | −0,1 (2) | −0,2 (2) | −0,3 (2) |
| $C_{(1)}$ | 2404 (6) | 7417 (5) | −847 (8) | 3,3 (3) | 3,3 (3) | 3,5 (3) | 0,3 (2) | 0,0 (2) | 0,0 (2) |
| $C_{(2)}$ | 3008 (7) | 5850 (5) | 1079 (8) | 3,9 (3) | 3,3 (3) | 3,2 (3) | 0,3 (2) | 0,7 (3) | 0,0 (2) |
| $C_{(3)}$ | 3598 (6) | 6637 (4) | 2405 (8) | 3,0 (3) | 3,0 (3) | 3,0 (3) | 0,2 (2) | 0,3 (2) | 0,2 (2) |
| $C_{(4)}$ | 4447 (7) | 8131 (5) | 4730 (8) | 4,1 (3) | 3,6 (3) | 3,7 (3) | 0,4 (3) | 0,4 (3) | −0,3 (3) |
| $C_{(5)}$ | 3495 (6) | 7810 (4) | 2054 (8) | 3,6 (3) | 2,7 (2) | 3,1 (3) | 0,2 (2) | 0,3 (2) | −0,2 (2) |
| $C_{(6)}$ | 2794 (8) | 9316 (5) | 78 (9) | 6,9 (4) | 2,8 (3) | 5,0 (3) | 0,6 (3) | −0,8 (4) | 0,3 (3) |
| $HN_{(2)}$ | 241 (5) | 586 (4) | −142 (7) | 5* | | | | | |
| $H_{(62)}$ | 227 (5) | 971 (4) | 107 (7) | 5* | | | | | |
| $H_{(61)}$ | 223 (5) | 946 (5) | −107 (7) | 5* | | | | | |
| $H_{(63)}$ | 377 (5) | 962 (4) | −5 (7) | 5* | | | | | |

*Value of B.

[17, 18, 21] formed exclusively from the azide form upon the loss of an $N_2$ molecule as a result of thermolysis. This hypothesis is supported by the increase of the peak intensities of the ions with m/z 192 and 194 over time and the lack of metastable transition from $M^+$ for the ion with m/z (Table 2). The addition of hydrogen to the nitrene in this specific case is apparently accomplished by migration of hydrogen atoms upon the thermal decomposition of the dimeric or trimeric aggregate of Ic existing in the gas phase. The possible existence of such aggregates was noted previously for derivatives of tetrazole [22] and pyrazole [23].

Thus, in azide Ic, the $[M - N_2]^+$ ($\Phi_1$) arises both due to dissociative ionization and thermolysis leading finally to ionization of the nitrene and its amine addition product $[(M - N_2) + 2H]^+$. The formation of amines was observed in the thermolysis of tetrazoles [17].

The appearance of the other fragment ions is related to the decomposition of the $\Phi_1$ ion. The $\Phi_3$ ion and ions with m/z 94 and 93 (Table 2) arise as the result of one-, or two- and three-step reactions. The metastable ion mass spectra obtained for isomers Ia and Ic coincide fully, which proves the identity in structure and energy parameters (release of the same kinetic energy) for ions $\Phi_1$, $\Phi_2$, and $\Phi_3$. The following decomposition scheme illustrates the formation of the major ions:



These results indicate that Ia and Ic in the gas phase have structures analogous to those in the crystalline state (Ic is apparently associated in pairs).

Information on the azide–tetrazole equilibrium in solution was obtained by PMR spectroscopy. Thus, the PMR spectrum of Ia in DMSO-$d_6$ has two singlets with δ 3.37 and 3.57 ppm and a broad signal with δ 14.00 ppm. Upon the addition of a few drops of $CF_3CO_2H$, the intensity of the signal at 3.37 ppm increases and that of signal at 3.57 ppm decreases (the signal at 14.00 ppm disappears). The downfield signal apparently is related to the NH group proton in the uracil fragment, while the interconversion of the intensities of the signals at 3.37 and 3.57 ppm upon acidification reflects the conversion of the tetrazole isomer to the azide isomer. Upon increasing the temperature of the solution of Ia, there is a shift in the tautomeric equilibrium toward the azide. Thus, at 35°C, we find 91% Ia and 9% Ic. At 60°C, we find 89% Ia and 11% Ic. At 100°C, we find 77% Ia and 23% Ic, while at 140°C, we find 67% Ia and 33% Ic. In aqueous solution, the equilibrium is shifted toward the azide; at 35°C, we find 32% Ia and 68% Ic. The tetrazole isomer predominantes in pyridine; at 35°C, we find 65% Ia and 35% Ic. It is interesting that in the case of 3-azido-5,7-dimethylpyrimido-[4,5-e][1,2,4]triazine-6,8-dione, the fraction of the tetrazole isomer [4] in pyridine is 15% less than for the monomethyl derivative Ia. A significant shift in the Ic $\rightleftarrows$ Ia equilibrium toward tetrazole Ia ($\Delta$ = 15%) is also observed in aqeuous solution upon the addition of an equimolar amount of sodium azide.

The azide—tetrazole equilibrium is established most slowly in dimethylsulfoxide solution (4-5 h). PMR spectroscopy may be used to observe the formation of azide form Ic from an authentic sample of linear tetrazole Ia. Since only signals for Ia and Ic are seen in the PMR spectrum, we may conclude that angular tetrazole Ib does not exist in solution.

## EXPERIMENTAL

The electron impact mass spectra were taken on a Varian MAT-311A mass spectrometer under standard conditions with 70 eV ionization energy and 1.0 mA cathode emission current. The accelerating voltage was 3 kV and the injector temperature was 150-170°C. The high-resolution mass spectra and the mass spectra of the metastable ions were measured on the same instrument. The M/ΔM resolution was 15,000, PFC standard and 0.01 V error in the measurement of the peaks on a digital voltmeter.

The x-ray diffraction structural analysis was carried out on a Syntex P1 four-circle diffractometer using $\lambda CuK_\alpha$ radiation, graphite monochromator, $\theta/2\theta$ scanning ($2° \leq 2\theta \leq 120°$). A total of 614 reflections with $F^2 \geq 2\sigma$ were recorded. The unit cell parameters of orthorhombic crystals of Ia are $a = 9.288(2)$, $b = 12.254(3)$, $c = 7.456(2)$ Å, $d_{calc} = 1.72$ g/cm³, $z = 4$, space group $P2_12_12_1$. The structure was solved by the direct method and refined by the method of least squares in the anisotropic full-matrix approximation* to $R = 0.049$, $R_w = 0.056$. The atomic coordinates and temperature factors are given in Table 3.

The thermal analysis was carried out on an MOM derivatograph under the conditions described in our previous work [18].

The PMR spectra were taken on a Perkin—Elmer R-12B spectrometer at 60 MHz with TMS as the internal standard using the $\delta$ scale.

## LITERATURE CITED

1. V. M. Adanin, S. E. Esipov, A. M. Zyakun, N. A. Klyuev, L. A. Saburova, and V. A. Bondar', Khim. Geterotsikl. Soedin., No. 9, 1270 (1979).
2. V. M. Kazakova, S. E. Esipov, I. G. Makarov, N. E. Minina, and A. I. Chernyshev, in: Abstracts of the All-Union Symposium on Magnetic Resonance in Biology and Medicine [in Russian], Moscow (1981), p. 16.
3. N. A. Klyuev, V. M. Adanin, I. Ya. Postovskii, and Yu. A. Azev, Khim. Geterotsikl. Soedin., No. 4, 547 (1983).
4. Yu. A. Azev, I. Ya. Postovskii, E. L. Pidémskii, and A. F. Goleneva, Khim.-farm. Zh., 14, 39 (1980).
5. Yu. A. Azev, N. N. Verreshchagin, I. Ya. Postovskii, E. L. Pidémskii, and A. F. Goleneva, Khim.-farm. Zh., 15, 50 (1981).
6. Yu. A. Azev, N. N. Verreshchagina, E. L. Pidémskii, A. F. Goleneva, and G. A. Aleksandrova, Khim.-farm. Zh., 18, 573 (1984).
7. C. Kuechler, W. Kuechler, and L. Heinisch, Arzneimit. Forsch., 16, 1122 (1966).
8. A. Messmer, G. Hajos, J. Tamas, and A. Nessmelyi, J. Org. Chem., 44, 1823 (1979).
9. A. V. Bogatskii, S. A. Andronati, Z. I. Zhilina, and N. I. Danilina, Zh. Org. Khim., 13, 1773 (1977).
10. M. M. Goodman, J. L. Atwood, R. Carlin, W. Hunter, and W. Paudler, J. Org. Chem., 41, 2860 (1976).

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*Only the positional parameters were refined for the hydrogen atoms found in the difference map with fixed $B_{iso} = 5.0$ Å².

11. S. Nishigaki, M. Ichiba, and K. Senga, J. Org. Chem., 48, 1628 (1983).
12. Tables of Interatomic Distances and Configuration in Molecules and Ions, Special Publication No. 18, London (1965).
13. A. Messmer, G. Hajos, P. Benko, and L. Benko, J. Heterocycl. Chem., 10, 575 (1973).
14. Yu. A. Azev and N. P. Lobanova, in: Abstracts of the All-Union Conference on Aromatic Nucleophilic Substitution [in Russian], Novosibirsk (1982), p. 85.
15. I. Ya. Postovskii and I. N. Goncharova, Zh. Obshch. Khim., 33, 2334 (1963).
16. I. Ya. Postovskii, G. N. Tyurenkova, and L. F. Lipatova, Dokl. Akad. Nauk SSSR, 179, 111 (1968).
17. C. Wentrup, Tetradedron, 26, 4969 (1970).
18. Yu. V. Shurukhin, N. A. Klyuev, I. I. Gradnberg, and V. A. Konchits, Khim. Geterotsikl. Soedin., No. 10, 1422 (1984).
19. N. A. Klyuev, É. N. Istratov, R. A. Khmel'nitskii, V. A. Zyrayanov, V. L. Rusinov, and I. Ya. Postovskii, Zh. Org. Khim., 13, 2218 (1977).
20. D. M. Forkey and W. R. Carpenter, Org. Mass Spectrom., 2, 433 (1969).
21. C. Wentrup, A. Maquestiau, and R. Flammang, Org. Mass Spectrom., 16, 115 (1981).
22. R. R. Fraser and G. K. E. Maque, J. Org. Chem., 34, 4118 (1969).
23. A. N. Kost and I. I. Grandberg, Advances in Heterocyclic Chemistry, Vol. 6, New York (1966), p. 347.

# 10-ALKENYLPHENOTHIAZINES.

## 1. SYNTHESIS AND CIS,TRANS-ISOMERIZATION OF 10-PROPENYLPHENOTHIAZINES

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541.634

A study was carried out on the isomerization of 10-allylphenothiazine (I) in DMSO by the action of t-BuOK, KOH and NaOH. The isomerization proceeds stereospecifically at room temperature by the action of t-BuOK at an elevated temperature by the action of KOH and NaOH to give cis-10-propenylphenothiazine (II). The effect of the t-BuOK concentration, temperature and reaction time on the isomeric composition of the 10-propenylphenothiazines formed was studied. Under conditions of kinetic control, I gives II, which isomerizes under the reaction conditions to give an equilibrium mixture of cis- and trans-10-propenylphenothiazine with 44-45% trans isomer III. The isomerization temperature has virtually no effect on the II/III isomer ratio.

Of the N-akenylphenothiazines, only N-vinylphenothiazine has been studied in considerable detail [1-3], while the homologs of this compound have not been described in the literature. There has only been mention of 10-propenylphenothiazine obtained by the multistep procedure in the proof of the structure of the product of the alkylation of phenothiazine by 1-chloro-2-dimethylaminopropane [4].

The base-catalyzed isomerization of N-allylamines is commonly employed in preparative organic chemistry to obtain N-allylamines [5] but this reaction has not been studied for thiazines.

In order to obtain 10-propenylphenothiazine, we studied the isomerization of 10-allylphenothiazine (I) in DMSO by the action of t-BuOK, KOH and NaOH.

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