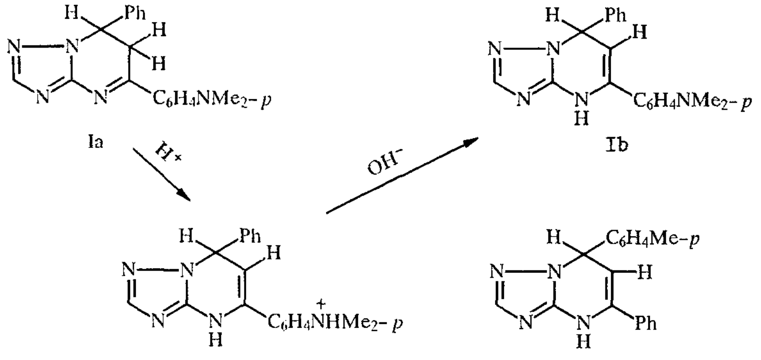
MOLECULAR STRUCTURE AND TAUTOMERIC CONVERSIONS OF 5-(4-DIMETHYLAMINOPHENYL)-7-PHENYL-6,7-DIHYDRO-1,2,4-TRIAZOLO[1,5-*a*]PYRIMIDINE

S. M. Desenko, V. D. Orlov,
O. V. Shishkin, V. V. Lipson,
S. V. Lindeman, and Yu. T. Struchkov

The x-ray structure is solved and the three-dimensional structure is analyzed for 5-(4-dimethylaminophenyl)-7-phenyl-6,7-dihydro-1,2,4-triazolo[1,5-a]pyrimidine. Its reverse isomerization into the 4,7-dihydro species is studied.

We previously demonstrated [1] that most 5,7-disubstituted dihydro-1,2,4-triazolo[1,5-*a*]pyrimidines exist in solutions and solids as the 4,7-dihydro enamine species. However, 5-(4-dimethylaminophenyl)-7-phenyl-6,7-dihydro-1,2,4-triazolo[1,5-*a*]pyrimidine (I) in DMSO-D$_6$ and CDCl$_3$ solutions forms mixtures of the 6,7- and 4,7-dihydro tautomers (Ia and Ib) [1, 2]. In order unambiguously to establish the tautomeric structure of this compound in the solid, we solved its x-ray structure. This demonstrated that it has the 6,7-dihydro structure Ia (Fig. 1 and Tables 1 and 2).



Ia

Ib

II

As in other dihydro-1,2,4-triazolopyrimidines [1], the triazole ring in Ia is practically planar (see the torsion angles in Table 1). The conformational parameters calculated according to the previous data [3] for the dihydropyrimidine ring are $S = 0.56$, $\theta = 49.1°$, and $\psi = 28.7°$. According to the literature [3], this is consistent with a chair conformation for this ring. The three-dimensional structures of the dihydropyrimidine ring in Ia and that in analogous 4,7-dihydro-1,2,4-triazolo[1,5-*a*]pyrimidines are substantially different (for example, the conformational parameters of the corresponding fragment of II are $S = 0.25$, $\theta = 108°$, and $\psi = 92°$ [1]). This difference probably also determines the previously noted [4] influence of steric factors on the position of the equilibrium between the dihydroazolopyrimidine tautomers. The phenyl substituent on $C_{(5)}$ occupies a pseudoaxial position; $H_{(5)}$, pseudoequatorial. The preference for such an orientation of the phenyl agrees with common conformational features of dihydroaromatic systems [5]. It should be related to the larger steric interaction with the triazole ring of the substituent in the pseudoequatorial position than of that in the pseudoaxial position [the $N_{(1)}N_{(2)}C_{(5)}H_{(5)}$ and $N_{(1)}N_{(2)}C_{(5)}C_{(6)}$ torsion angles are $-46.9(5)$ and $79.2(6)°$, respectively].

A. M. Gor'kii Khar'kov State University, Khar'kov 310077. A. N. Nesmeyanov Institute of Organometallic Compounds, Russian Academy of Sciences, Moscow 117813. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 7, pp. 933-936, July, 1992. Original article submitted January 29, 1991.

0009-3122/92/2807-0776$12.50

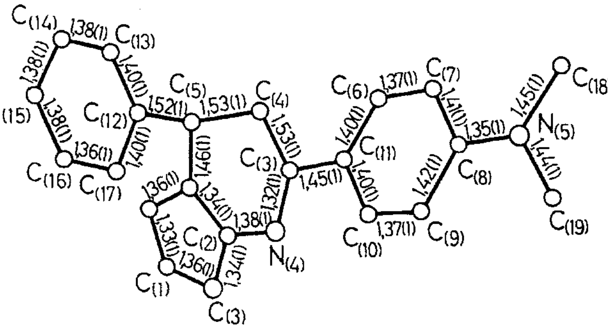


Fig. 1. Structure and bond lengths of Ia.

TABLE 1. Certain Bond (ω) and Torsion (τ) Angles in Ia

Angle	ω°	Angle	τ°
$N_{(2)}N_{(1)}C_{(1)}$	101,9 (6)	$C_{(1)}N_{(1)}N_{(2)}C_{(2)}$	-1,7 (5)
$N_{(2)}C_{(1)}N_{(3)}$	115,7 (8)	$N_{(2)}N_{(1)}C_{(1)}N_{(3)}$	1,6 (6)
$C_{(1)}N_{(3)}C_{(2)}$	102,0 (6)	$C_{(2)}N_{(3)}C_{(1)}N_{(1)}$	-1,0 (7)
$N_{(2)}C_{(2)}N_{(3)}$	110,2 (6)	$C_{(1)}N_{(3)}C_{(2)}N_{(2)}$	-0,2 (6)
$N_{(1)}N_{(2)}C_{(2)}$	110,1 (6)	$N_{(3)}C_{(2)}N_{(2)}N_{(1)}$	1,2 (6)
$C_{(2)}N_{(2)}C_{(5)}$	123,3 (6)	$N_{(4)}C_{(2)}N_{(2)}C_{(5)}$	-3,6 (7)
$N_{(2)}C_{(2)}N_{(4)}$	124,5 (6)	$C_{(2)}N_{(2)}C_{(5)}C_{(4)}$	32,0 (5)
$C_{(2)}N_{(4)}C_{(3)}$	115,8 (5)	$N_{(2)}C_{(5)}C_{(4)}C_{(3)}$	-43,7 (6)
$N_{(4)}C_{(3)}C_{(4)}$	121,8 (6)	$C_{(5)}C_{(4)}C_{(3)}N_{(4)}$	34,1 (7)
$C_{(3)}C_{(4)}C_{(5)}$	113,1 (5)	$C_{(4)}C_{(3)}N_{(4)}C_{(2)}$	-3,9 (6)
$N_{(2)}C_{(5)}C_{(4)}$	105,5 (5)	$C_{(3)}N_{(4)}C_{(2)}N_{(2)}$	-12,9 (5)
$N_{(4)}C_{(3)}C_{(11)}$	118,5 (6)	$C_{(2)}N_{(4)}C_{(3)}C_{(11)}$	179,3 (6)
$C_{(4)}C_{(3)}C_{(11)}$	119,6 (6)	$C_{(2)}N_{(2)}C_{(5)}H_{(5)}$	142,9 (7)
$N_{(2)}C_{(5)}C_{(12)}$	111,9 (5)	$C_{(2)}N_{(2)}C_{(5)}C_{(12)}$	-91,0 (6)
$C_{(4)}C_{(5)}C_{(12)}$	112,7 (6)	$N_{(4)}C_{(3)}C_{(11)}C_{(10)}$	-18,2 (5)
		$C_{(4)}C_{(3)}C_{(11)}C_{(10)}$	165,0 (5)

An analysis of the torsion angles of the *p*-dimethylaminobenzalaminotriazole fragment, which are less than 18.2(5)° (see Table 1), reveals that it is planar. This makes possible conjugation of the π-electron systems of the *p*-dimethylaminophenyl substituent, the azomethine group, and the triazole ring. These facts confirm the previous suggestion [2] that the relative stabilization of the imine tautomers of dihydroazolopyrimidines by electron-donating substituents (the dimethylamino group for Ia) is due to conjugation effects.

We have earlier found [1] that I in CF_3CO_2H solutions completely converts to the dihydro species Ib with a protonated dimethylamino group. By rapidly neutralizing a CF_3CO_2H solution of I at reduced temperature, we were able to prepare crystals of pure Ib. The reverse conversion is achieved by crystallization of Ib from CH_3OH or $CHCl_3$. The IR spectrum of Ib in KBr pellets contains a strong $\nu_{C=C}$ band at 1650 cm^{-1}. This is typical of spectra of 4,7-dihydro-1,2,4-triazolo[1,5-*a*]pyrimidines [1]. The electronic absorption spectra of freshly prepared solutions of Ib in CH_3OH (see Experimental) have much less long-wavelength absorption than that of Ia (λ_{max} 391 nm [1]). However, bands of Ia appear if Ib is stored. Simultaneously, the intensities of the bands with λ_{max} = 277 and 301 nm decrease. Equilibrium is established after 1.5-2 days at 20°C. This process is sharply accelerated after adding catalytic amounts of acids or on heating. An investigation of the kinetics of this conversion demonstrated that the change of concentration of Ib in CH_3OH at 20°C obeys a first-order law with a constant of $(2.3 \pm 0.1)\cdot 10^{-5}$ sec^{-1}.

EXPERIMENTAL

X-Ray Structure Study. Crystals of 5-(4-dimethylaminophenyl)-7-phenyl-6,7-dihydro-1,2,4-triazolo[1,5-*a*]pyrimidine (Ia) $C_{19}H_{19}N_5$ are monoclinic. At 20°C, a = 15.025(3), b = 6.457(1), c = 18.336(4) Å, β = 114.12(3)°, Z = 4, d_{calc} =

TABLE 2. Coordinates of Nonhydrogen ($\times 10^4$) and H Atoms ($\times 10^3$) in Ia

Atom	x	y	z	Atom	x	y	z
$N_{(1)}$	6164 (4)	-1763 (10)	2211 (3)	$C_{(18)}$	12380 (5)	-229 (12)	912 (5)
$N_{(2)}$	6939 (4)	-1753 (8)	2005 (3)	$C_{(19)}$	11737 (5)	3302 (12)	567 (5)
$N_{(3)}$	6821 (4)	1465 (9)	2350 (3)	$H_{(1)}$	561 (5)	57 (12)	259 (4)
$N_{(4)}$	8058 (4)	730 (8)	1864 (3)	$H_{(4A)}$	868 (5)	-352 (5)	242 (4)
$N_{(5)}$	11620 (4)	1257 (8)	831 (3)	$H_{(4B)}$	852 (5)	-399 (12)	147 (4)
$C_{(1)}$	6140 (4)	191 (12)	2424 (4)	$H_{(5)}$	726 (5)	-472 (12)	190 (4)
$C_{(2)}$	7312 (4)	166 (10)	2080 (3)	$H_{(6)}$	1007 (5)	-317 (12)	177 (4)
$C_{(3)}$	8536 (4)	-808 (10)	1715 (3)	$H_{(7)}$	1133 (5)	-229 (12)	145 (4)
$C_{(4)}$	8322 (4)	-3065 (9)	1830 (4)	$H_{(9)}$	1019 (5)	357 (12)	75 (4)
$C_{(5)}$	7243 (4)	-3463 (10)	1638 (4)	$H_{(10)}$	891 (5)	255 (11)	107 (4)
$C_{(6)}$	10051 (4)	-1746 (10)	1536 (3)	$H_{(13)}$	690 (5)	-666 (12)	68 (4)
$C_{(7)}$	10804 (4)	-1240 (10)	1326 (4)	$H_{(14)}$	596 (5)	-698 (12)	-64 (4)
$C_{(8)}$	10874 (5)	737 (10)	1027 (3)	$H_{(15)}$	511 (5)	-418 (12)	-142 (4)
$C_{(9)}$	10138 (4)	2196 (10)	966 (3)	$H_{(16)}$	523 (5)	-97 (12)	-82 (4)
$C_{(10)}$	9405 (4)	1653 (10)	1185 (4)	$H_{(17)}$	616 (5)	-43 (12)	57 (4)
$C_{(11)}$	9320 (4)	-317 (9)	1476 (3)	$H_{(18A)}$	1220 (6)	-84 (12)	147 (4)
$C_{(12)}$	6621 (4)	-3614 (9)	749 (3)	$H_{(18B)}$	1285 (5)	-134 (13)	61 (4)
$C_{(13)}$	6538 (4)	-5517 (10)	360 (4)	$H_{(18C)}$	1285 (5)	46 (12)	80 (5)
$C_{(14)}$	5972 (5)	-5700 (12)	-447 (4)	$H_{(19A)}$	1222 (5)	323 (10)	41 (4)
$C_{(15)}$	5477 (5)	-4016 (12)	-887 (4)	$H_{(19B)}$	1112 (5)	381 (10)	17 (4)
$C_{(16)}$	5566 (4)	-2124 (11)	-509 (4)	$H_{(19C)}$	1168 (5)	434 (10)	90 (4)
$C_{(17)}$	6137 (4)	-1891 (10)	293 (4)				

1.298 g/cm^3, space group $P2_1/c$. The cell constants and intensities of 1326 unique reflections with $|F| \geq 6\sigma(F)$ were measured on a Siemens P3/PC automated four-circle diffractometer with a graphite monochromator using Mo $K\alpha$-radiation.

The structure was solved by direct methods using the SHELXTL PLUS programs. All H atoms were found in a different synthesis. Anisotropic (isotropic for H atoms) refinement gave $R = 0.095$ ($R_w = 0.085$). Atomic coordinates are given in Table 2.

The IR spectrum of Ib was measured in KBr pellets on a Specord IR-75 spectrophotometer. UV spectra were taken on a Specord M-40 instrument in CH_3OH with (2-3)$\cdot 10^{-5}$ M concentrations.

5-(4-Dimethylaminophenyl)-7-phenyl-4,7-dihydro-1,2,4-triazolo[1,5-*a*]pyrimidine (Ib). A CF_3CO_2H solution (2 ml) of 5-(4-dimethylaminophenyl)-7-phenyl-6,7-dihydro-1,2,4-triazolo[1,5-*a*]pyrimidine (Ia, 0.1 g) was added with stirring and cooling to aqueous ammonia (10 ml, 15%) cooled to $-5°C$. The rate of addition was such that the temperature of the reaction mixture was less than 0°C. The precipitate was filtered off and washed with water. Yield 0.08 g (80%) of crystalline Ib, mp 227-229°C, λ_{max} ($\varepsilon \cdot 10^{-3}$) in CH_3OH: 277 (12.4), 301 nm (10.4); $\nu_{C=C}$ 1650 cm^{-1} (in KBr).

The synthesis of Ia has previously been described [1].

REFERENCES

1. V. D. Orlov, S. M. Desenko, K. A. Potekhin, and Yu. T. Struchkov, *Khim. Geterotsikl. Soedin.*, No. 2, 229 (1988).
2. S. M. Desenko, V. D. Orlov, and V. I. Beskorovainyi, *Khim. Geterotsikl. Soedin.*, No. 2, 245 (1991).
3. N. S. Zefirov, E. E. Dashevskaya, and V. A. Palyulin, *Dokl. Akad. Nauk SSSR*, **292**, 1380 (1987).
4. S. M. Desenko, V. D. Orlov, V. V. Lipson, and Kh. Éstrada, *Khim. Geterotsikl. Soedin.*, No. 9, 1215 (1991).
5. A. N. Vereshchagin, *Usp. Khim.*, **52**, No. 11, 1879 (1983).