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# SYNTHESIS AND STRUCTURE OF 2'-SUBSTITUTED 1-(1,3-DIOXAN-5-YL)URACILS. POSITIVE ROLE OF THE $Eu(fod)_3$ NMR SHIFT REAGENT

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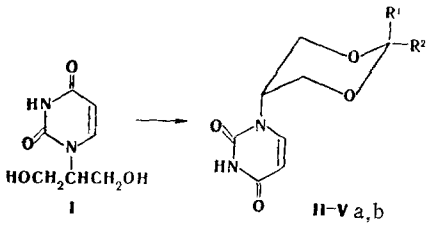
UDC 547.841'854.4.07:541.634:543.422.25

The configuration of 1-(2-R-1,3-dioxan-5-yl)uracils and the conformation of the dioxane ring in these compounds were investigated by $^1H$ NMR spectroscopy with the aid of the $Eu(fod)_3$ shift reagent. It is shown that the dioxane ring exists in the preferred chair conformation with an axial orientation of the pyrimidine ring; this is confirmed by the resonance of the 5'-$H_a$ proton in the form of a broad singlet with $\nu_{1/2} \sim 8.5$ Hz. An analysis of the spectral peculiarities of the synthesized compounds made it possible to establish the orientation of the substituents attached to the second $C_2$ steric center. The three-dimensional structure of 1-(2,2-dimethyl-1,3-dioxan-5-yl)uracil was determined by an x-ray diffraction study, and the axial orientation of the pyrimidine ring was confirmed. It is shown that significant flattening of the carbon part of the ring ($\psi$ = 46.6°) is observed in this molecule. An intramolecular ($C_6 \ldots O_{1'}$ = 3.05 Å) hydrogen bond was observed in the molecule of this compound.

By means of the reaction of 1-(1,3-dihydroxy-2-propyl)-uracil [1] with acetone, isobutyraldehyde, and orthoformic and orthoacetic esters with Dowex-50 ion-exchange resin in the $H^+$ form [2] as the catalyst we synthesized cyclic acetals and ketals, viz., 2'-substituted 1-(1,3-dioxan-5-yl)-uracils (II-V):




I II-V a,b

II $R^1=R^2=Me$; III $R^1=H$, $R^2=i$-Pr; IV a $R^1=OEt$, $R^2=H$; IV b $R^1=H$, $R^2=OEt$; Va $R^1=OEt$, $R^2=Me$; Vb $R^1=Me$, $R^2=OEt$

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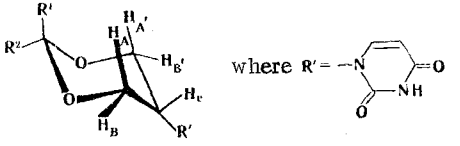
 0009-3122/81/1711-1112$07.50 

TABLE 1. 2'-Substituted 1-(1,3-Dioxan-5-yl)uracils

| Compound | Isomer | mp, °C | $R_f$ | Found, % | | | Empirical formula | Calc., % | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | C | H | N | | C | H | N |
| II | — | 204—205 | 0,63 | 53,5 | 6,4 | 12,3 | $C_{10}H_{14}N_2O_4$ | 53,1 | 6,2 | 12,4 |
| III | cis | 205—206 | 0,56 | 55,3 | 6,9 | 11,5 | $C_{11}H_{16}N_2O_4$ | 55,0 | 6,7 | 11,7 |
| IVa | trans | 177—180 | 0,87 | 50,2 | 6,0 | 11,6 | $C_{10}H_{14}N_2O_5$ | 50,4 | 5,9 | 11,8 |
| IVb | cis | 158—160 | 0,75 | 50,3 | 6,1 | 11,5 | $C_{10}H_{14}N_2O_5$ | 50,4 | 5,9 | 11,8 |
| Va | trans | 200—206 | 0,90 | 51,8 | 6,3 | 11,1 | $C_{11}H_{16}N_2O_5$ | 51,6 | 6,3 | 10,9 |
| Vb | cis | 116—117 | 0,68 | 51,7 | 6,3 | 10,8 | $C_{11}H_{16}N_2O_5$ | 51,6 | 6,3 | 10,9 |

TABLE 2. Parameters of the $^1H$ NMR Spectra of 2'-Substituted 1-(1,3-Dioxan-5-yl)uracils




| Compound, configuration | $R^1$ | $R^2$ | Solvent (concn., %), shift reagent in mole/liter, temp. | $\delta_H$, ppm | | | | | | | | | | $J$, Hz | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | 5-H | 6-H | 3-NH | 5'-H*$_e$ | $H_A$ | $H_B$ | 2'-H | 2'-Me | 2'-$OCH_2$ or 2'-H | β-Me | $^2J_{AB}$ | $^3J_{5e4a}$ | $^3J_{CH_2CH_3}$ |
| II | Me | Me | $CDCl_3$ (3), 29° | 5,76 | 8,25 | 9,56 | 4,41 | 4,34 | 3,93 | — | 1,43 (*a*)<br>1,50 (*e*) | — | — | −12,0 | | — |
| | | | $CDCl_3$ (3)+Eu(fod)$_3$, 0,005, 29° | 6,70 | 8,54 | —† | 5,08 (8) | 4,54 | 4,28 | — | 1,58 | — | — | −13,0 | 3,0 | — |
| III, cis | H | *i*-Pr | $CDCl_3$ (3), 29° | 5,72 | 8,28 | 9,91 | 4,42 | 4,16 | | 4,41 (*a*) | — | 1,88 | 0,94 | | 3,0 | 6,6 |
| | | | $CDCl_3$ (3)+Eu(fod)$_3$, 0,01, 29° | 7,26 | 8,79 | —† | 5,53 (8) | 4,47 | 4,84 | 4,63 (*a*) | — | 2,10 | 1,10 | −13,0 | ~2,5 | 6,4 |
| IVa, trans | OEt | H | $CDCl_3$ (3), 28° | 5,75 | 8,19 | 9,86 | 4,52 | 4,58 | 3,83 | 5,54 (*e*) | — | 3,63 | 1,26 | −12,6 | | 7,0 |
| | | | $CDCl_3$ (3)+Eu(fod)$_3$, 0,015, 28° | 8,36 | 9,03 | —† | 6,32 (8) | 5,10 | 4,86 | 5,96 (*e*) | — | 3,79 | 1,34 | −12,6 | ~2,5 | 7,0 |
| IVb, cis | H | OEt | $CDCl_3$ (5), 28° | 5,76 | 8,18 | 8,82 | 4,51 | 4,25 | | 5,34 (*a*) | — | 3,78 | 1,26 | −13,0 | 2,5 | 7,1 |
| | | | $CDCl_3$ (5)+Eu(fod)$_3$, 0,015, 28° | 8,63 | 9,15 | —† | 6,54 (8) | 4,83 | 5,34 | 5,76 (*a*) | — | 4,11 | 1,48 | −12,3 | ~2,5 | 7,0 |
| Va, trans | OEt | Me | $CDCl_3$ (4), 29° | 5,71 | 8,10 | 9,78 | 4,41 | 4,46 | 3,78 | — | 1,46 (*e*) | 3,53 | 1,22 | −12,1 | ~3 | 7,0 |
| Vb, cis | Me | OEt | $CDCl_3$+$CD_3OD$, 29° | 5,66 | 7,38 | 8,90 | 4,35 | 4,32 | 3,90 | — | 1,19 (*a*) | 4,66 | 1,21 | | — | 7,1 |

*The half width of the line of the 5'-H proton ($\Delta\nu_{1/2}$, Hz) is indicated in parentheses.

†Because of the pronounced broadening of the 3-NH band when Eu(fod)$_3$ is added, the position of the resonance in these cases was not determined.

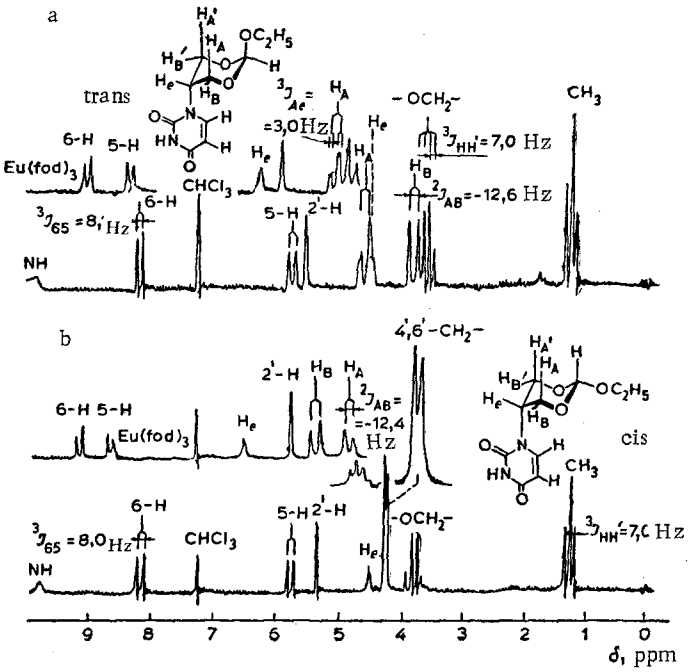



Fig. 1. $^1$H NMR spectra: a) trans-1-(2-ethoxy-1,3-dioxan-5-yl)uracil (IVa); b) cis-1-(2-ethoxy--3-dioxan-5-yl)uracil (IVb).

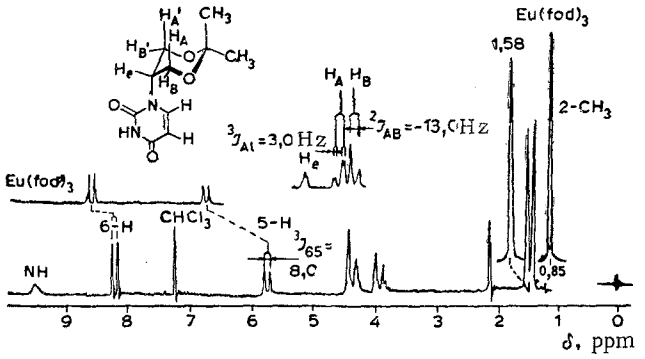



Fig. 2

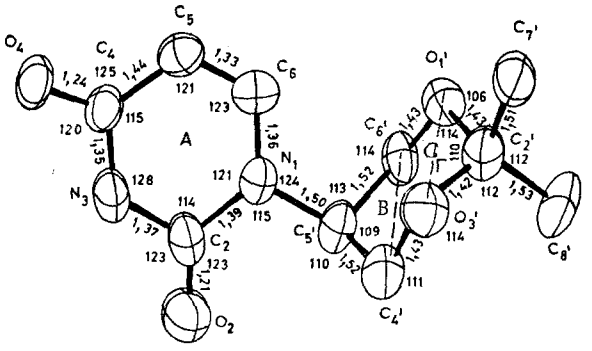


Fig. 3

Fig. 2. $^1$H NMR spectrum of 1-(2,2-dimethyl-1,3-dioxan-5-yl)uracil (II).

Fig. 3. Three-dimensional model and geometry of the uracil II molecule: The angles between A and B (B + C + D) = 87.5°, A and B = 73.3°, A and C = 83.7°, A and D = 71.7°, B and C = 43.9°, C and D = 50.7°, and B and D = 7.1°.

The separation of configurational isomers of IV-V was realized by means of preparative thin-layer chromatography (TLC) with monitoring of the degree of purity of the isomers on analytical plates (Table 1).

The configuration of III-V and the conformation of the 1,3-dioxane ring in pyrimidines II-V were established by an analysis of the $^1$H NMR spectra. The proton chemical shifts and the spin–spin coupling constants (SSCC) from the spectra of solutions of the compounds in $CDCl_3$ with and without the addition of the $Eu(fod)_3$ shift reagent are summarized in Table 2. The necessity for conducting the latter experiments was dictated by the peculiarities of the PMR spectra of the methylene protons of the dioxane ring of the cis isomers (III, IVb, and Vb), as well as by the superimposition of the band of the 5'-H methylidyne proton on the resonance lines of the other protons.

The preferred conformation of the 1,3-dioxane ring with substituents attached to the $C_5$' and $C_2$' atoms* [3, 4] and the spatial orientation of the pyrimidine ring can be judged from

*When other substituents are absent, the gem-dimethyl grouping attached to the $C_2$' atom in II usually promotes conformational mobility of the heteroring [5].

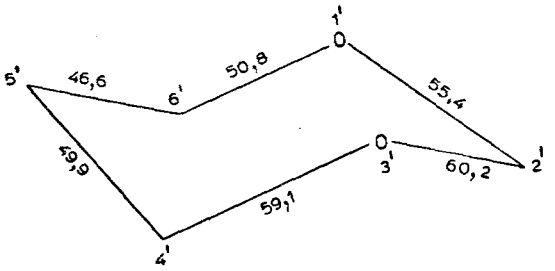



Fig. 4

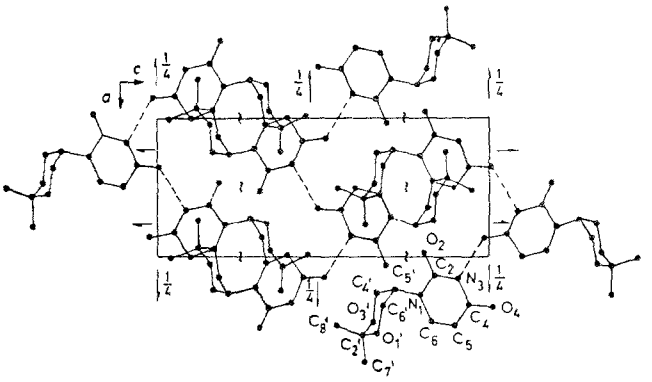



Fig. 5

Fig. 4. Torsion angles of the 1,3-dioxane fragment of the II molecule.

Fig. 5. Projection of the structure of the II molecule on the ac plane (the intermolecular hydrogen bonds are indicated by dash lines).

the character of the resonance of the methylene 4'- and 6'-H protons, as well as from the character of the methylidyne 5'-H proton. In the general case these protons form a strongly coupled spin system of the AA'BB'C type; however, in II, IVa, and Va, because of the small vicinal SSCC between the 5'-$H_e$ ($H_C$) and 4',6'-$H_a$ ($H_A$) protons, the 4',6'-$H_e$ ($H_B$) methylene protons to a first approximation display an AB quartet with geminal $^2J_{AB}$ constants from -11.5 to -13.0 Hz with relatively large nonequivalence, viz., $\Delta\delta_{AB}$ = 0.4-0.6 ppm (Fig. 1a). This peculiarity in the $^1$H NMR spectrum is typical for the 1,3-dioxane ring in the preferred chair conformation [6, 7].

In the cis isomers of III and IVb the 4',6'-$CH_2$ methylene protons resonate in the form of a doublet, while the 5'-H proton resonates in the form of a quintet with $^3J_{HH'}$ = 2.0-2.5 Hz (Fig. 1b); this is due to degenertion of the AA'BB'C system to an $A_4C$ system because of a change in the puckered character of the chair in the $C_{4'}$-$C_{5'}$-$C_{6'}$ region from a conformation with cyclic torsion angle $\psi$ = 54° (unsubstituted 1,3-dioxane) to a conformation with

TABLE 3. Coordinates of the Atoms
($\cdot 10^4$; $\cdot 10^3$ for the hydrogen atoms)

| Atom | x | y | z |
|---|---|---|---|
| $N_1$ | 2245 (6) | 4054 (5) | 7038 (2) |
| $C_2$ | 3750 (9) | 3477 (7) | 6632 (3) |
| $N_3$ | 3330 (6) | 3168 (5) | 5904 (2) |
| $C_4$ | 1631 (7) | 3299 (6) | 5560 (3) |
| $C_5$ | 0119 (7) | 3875 (6) | 6023 (3) |
| $C_6$ | 0491 (8) | 4206 (6) | 6730 (3) |
| $O_4$ | 1481 (5) | 2951 (4) | 4897 (2) |
| $O_2$ | 5317 (5) | 3273 (6) | 6894 (2) |
| $O_{1'}$ | −0457 (5) | 5170 (4) | 8313 (2) |
| $C_{2'}$ | −0597 (8) | 3811 (6) | 8747 (3) |
| $O_{3'}$ | 0420 (5) | 2613 (4) | 8393 (2) |
| $C_{4'}$ | 2392 (8) | 2932 (7) | 8299 (3) |
| $C_{5'}$ | 2669 (8) | 4368 (6) | 7837 (2) |
| $C_{6'}$ | 1438 (8) | 5639 (6) | 8156 (3) |
| $C_{7'}$ | −2657 (9) | 3342 (10) | 8717 (4) |
| $C_{8'}$ | 0076 (11) | 4083 (8) | 9545 (3) |
| $HN_1$ | 423 | 280 | 564 |
| $HC_4$ | −037 | 452 | 710 |
| $HC_5$ | −136 | 396 | 581 |
| $HC_{5'}$ | 433 | 464 | 782 |
| $H_1C_{4'}$ | 298 | 212 | 802 |
| $H_2C_{4'}$ | 304 | 315 | 887 |
| $H_1C_{6'}$ | 210 | 606 | 866 |
| $H_2C_{6'}$ | 091 | 652 | 775 |
| $H_1C_{7'}$ | −329 | 322 | 819 |
| $H_2C_{7'}$ | −331 | 418 | 905 |
| $H_3C_{7'}$ | −270 | 236 | 906 |
| $H_1C_{8'}$ | −010 | 321 | 980 |
| $H_2C_{8'}$ | −139 | 495 | 979 |
| $H_3C_{8'}$ | 189 | 437 | 964 |

$\psi < 54°$ (flattening) [3]. However, the degeneration of the spectra of the cis isomers is by no means a consequence of the conformational lability of the saturated heteroring, since when the Eu(fod)$_3$ shift reagent in concentrations of ∿0.005 to 0.015 mole/liter is added to deuterochloroform solutions of III and IVb, the $A_4C$ spin system is transformed to an AA'BB'X system. The spectra of samples of the cis isomers with Eu(fod)$_3$ show that the two high-field lines of the AB quartet are broadened more than the low-field lines. If one takes into account the stereoselective effect of the electronegativity and the orientation of the X and Y heteroatoms (determined through phase angle $\phi = \theta - 120°$) on the vicinal constant $^3J_{HH'} = f(\theta,\phi)$ in the $-XHC_{4'(6')}-C_{5'}H'Y$ fragment [8], the high-field lines can be assigned to axial $H_A$ and $H_{A'}$ protons. The fact is that the vicinal $^3J_{4a5e}$ constant for these protons should be greater (∿2.9 Hz) than the $^3J_{4e5e}$ constant (∿2 Hz).* Thus it may be asserted that in the investigated series of compounds when there is no axial alkyl or alkoxy substituent attached to the $C_{2'}$ atom, the axial and equatorial 4'- and 6'-H protons do not display inversion of the nuclear magnetic shielding constant; this has heretofore been stated more than once [4].

To establish the configuration of the compounds we determined the spatial orientation of the substituents attached to the $C_{2'}$, and $C_{5'}$ atoms. If the pyrimidine ring is axial, the resonance of the 5'-$H_e$ methylidyne proton with allowance for the broadening of the lines from quadruple relaxation of the $^{14}N$ nucleus should be displayed in the form of a broad line with half width $\Delta\nu_{1/2} \sim 2(^3J_{4a5e}+^3J_{4e5e}) \sim 8$ Hz (for the Lorentz form of the NMR lines). In the case of an equatorial conformation of the pyrimidine ring the resonance of the 5'-$H_a$ proton would show up in the form of a triplet of triplets with $^3J_{4a5a} \sim 10$ Hz and $^3J_{4e5a} \sim 5$ Hz [4]. In the spectra of all of the investigated II-V the signal of the 5'-H proton is observed in the form of a broad singlet with half width $\Delta\nu_{1/2}$[Eu(fod)$_3$] 8.5 Hz [when Eu(fod)$_3$ is added, the signal of the 5'-H proton, which in all cases is superimposed on the other resonance lines, is shifted to low field in such a way that it excludes superimposition of the bands (see Fig. 1)]. This constitutes absolutely definitive proof for an axial orientation of the pyrimidine ring in II-V.

The establishment of the orientation of the substituents attached to the second steric center ($C_{2'}$) requires a detailed analysis of the spectral peculiarities of each compound.

In the spectrum of III the 2'-H methylidyne proton resonates in the form of a doublet at 4.41 ppm ($^3J_{HH'} = 6.6$ Hz). This value of the chemical shift is typical for an axial proton attached to $C_{2'}$ in 2-alkyl-1,3-dioxanes [9]; consequently, the substituent attached to $C_{2'}$ in III is equatorial, and the compound is the cis isomer.

By comparing the spectra of stereoisomeric IVa and IVb, which contain a 2'-ethoxy group, it may be seen that the chemical shifts of the protons attached to the $C_{2'}$ atom differ by $\Delta\delta = 0.2$ ppm (see Table 2). Since in 1,3-dioxanes, which exist in the chair conformation, the chemical shifts of the methylene protons attached to $C_2$ do not experience inversion, the $\delta_H = 5.54$ ppm line, inasmuch as it is shifted to lower field, must be assigned to an equatorial proton. Consequently, the high-melting isomer (mp 177-180°C) has a trans configuration, and the low-melting isomer (mp 158-160°C) has a cis configuration. Let us note that the axial orientation of the ethoxy group in IVa, which is evidently stabilized by an anomeric effect [10], has a pronounced effect on the chemical shifts of the axial $H_A$ and $H_{A'}$ protons attached to the $C_{4'}$ and $C_{6'}$ atoms and leads to inversion of the chemical shifts of the methylene protons attached to these carbon atoms (see Table 2 and Fig. 1). Somewhat similar examples in 1,3-diheterocycles have been previously established [11].

A trans configuration can be assigned to high-melting stereoisomer Va (mp 200-206°C) with $R^1 = OC_2H_5$ and $R^2 = CH_3$ on the basis of a formal spectral feature: The form of the resonance of the five protons of the 1,3-dioxane ring is absolutely identical to the form of the resonance of the corresponding protons in IVa. If one takes into account the manifestation of the $\alpha$ effect of the equatorial methyl group, the close values of the $\alpha$-$OCH_2$ and $\beta$-$CH_3$ chemical shifts for the ethoxy group in IVa and Va and the identical $^3J_{CH_2CH_3}$ constants of 7.0 Hz may serve as a second argument in favor of an axial orientation of the ethoxy group.

Low-melting isomer Vb is characterized by exceptionally low solubility in $CDCl_3$; its solubility is improved somewhat in a mixture of $CDCl_3$ and $CD_3OD$ (3:2) but is still low, and the lines can be recorded with difficulty after accumulation of the signals with a pulse NMR

*The evidence for an equatorial orientation of the 5'-H proton is discussed below.

spectrometer with Fourier transformation; Vb is destroyed during the time required to record the spectrum. Nevertheless, the spectral peculiarities that can be recorded (Table 2) make it possible to assume that the methyl group attached to $C_2$, is axial and that the ethoxy group is equatorial, i.e., Vb has a cis configuration.

The dioxane ring in II exists in a chair conformation, as indicated by, in addition to the spectral features discussed above, the nonequivalence of the methyl groups [$\Delta\delta_{ae}(CH_3)$ = 0.08 ppm]. Consequently, one of the methyl groups is axial. It is precisely this fact that gives rise to inversion of the chemical shifts of the $H_A$ and $H_B$ protons. This fact is manifested quite clearly when the Eu(fod)$_3$ shift reagent is added in a concentration of 0.005 mole/liter. In the latter system the broad line of the 5'-H methylidyne proton, which previously coincides with the low-field component of the AB quartet, is shifted to low field and has half width $\Delta_{\nu 1/2} \sim 8$ Hz (Fig. 2), whereas the signals of the protons of the gem-dimethyl grouping merge. However, this does not mean weakening of the conformational rigidity of the dioxane ring but constitutes evidence for a change in the puckered character of the ring in the case of coordination of II with the $Eu^{3+}$ ion, evidently at the $C_4$=O group of the pyrimidine ring; the stereoselective spin-spin slitting of the low-field components of the AB quartet ($^3J_{4a5e}$ = 3.0 Hz) is retained in this case.

To confirm the data obtained and in order to make a more detailed study of the conformations of the pyrimidine and dioxane rings, as well as their mutual orientations, we investigated the molecular-crystal structure of II by x-ray diffraction analysis.

A three-dimensional model of the molecule with designation of the atoms and indication of the interatomic distances, bond angles, and dihederal angles between the planar fragments of the II molecule is presented in Fig. 3.

The uracil fragment in the II molecule exists in the diketo form that is normal for uracil. The $C_4$—$O_4$ bond length, which is 1.24 Å, is somewhat increased as compared with the $C_2$—$O_2$ bond (1.21 Å ) as a consequence of the participation of the $O_4$ atom in an intermolecular hydrogen bond. Similar lengthening of the C=O bond occurs in the uracil [12] and 1-methyluracil [13] molecules for the oxygen atoms that participate in intermolecular hydrogen bonds. The geometry of the uracil fragment in II within the limits of 0.02 Å and 2° (except for the somewhat shortened $N_3$—$C_4$ bond length of 1.35 Å ) corresponds to that in the uracil [12], 1-methyluracil [13], and uridine [14] molecules.

The pyrimidine ring in the II molecule is virtually planar (see the A plane in Fig. 3). The $O_2$ and $C_5$' atoms deviate from the A plane on the same side by 0.047 and 0.040 Å , respectively. The deviations of the analogous $O_2$ and $C_1$' atoms in the uridine molecule [14], for example, are 0.073 and 0.066 Å.

Within the limits of experimental error, the $N_1$—$C_5$' bond length in the II molecule (1.50 Å ) corresponds to the length of the glycoside bond in the uridine molecule (1.497 and 1.483 Å ) [14]. The geometry of the 1,3-dioxane ring in the II molecule is close to the geometry of dioxane in the 9-(2-ethoxy-1,3-dioxan-5-yl)adenine molecule [15], as well (except for the endocyclic bond angles at the oxygen atoms) as in the trans and cis isomers of 6-chloro-9-(2-ethoxy-1,3-dioxan-5-yl)purine [16, 17] and other dioxane derivatives [18, 19]. The endocyclic bond angles at the oxygen atoms in the II molecule, which are 114°, somewhat exceed the values of the corresponding angles (110-112°) found in [16-19].

Calculations showed that the pairs of $O_1$' and $C_4$' and $O_3$' and $C_6$' atoms deviate from mean-square plane C in the opposite direction by an average value of 0.26 Å . The planarity of the fragment formed by the $C_1$', $O_3$', $C_4$', and $C_6$' atoms, which is twisted about the diagonal, is thereby disrupted. The deviations of the $C_2$' and $C_5$' atoms from the C plane are, respectively, 0.64 and 0.61 Å and are directed in the opposite direction. The planar B and D fragments form dihedral angles of 43.9 and 50.7° with the C plane. Consequently, the dioxane ring has a somewhat distorted chair conformation.

The torsion angles of the 1,3-dioxane fragment are presented in Fig. 4. The difference in the torsion angles along the $O_1$'—$C_6$' and $O_3$'—$C_4$' bonds, which amounts to 8.3°, characterizes the deviation of the conformation of the 1,3-dioxane fragment from the ideal chair conformation, which upon the whole is more flattened than in the structures mentioned above [15-19].

The 1,3-dioxane ring in the II molecule exists in an anti conformation with respect to the uracil residue with torsion angles $C_6$—$N_1$—$C_5$'—$C_6$' = —32.5° and $C_6$—$N_1$—$C_5$'—$C_4$' = 90.5°. The

pyrimidine ring is oriented axially with respect to the dioxane ring. The dihedral angle between the average planes of the uracil and dioxane fragments is 87.5°.

In the II molecule it was observed that the distance between the proton attached to the $C_6$ atom and the $O_{1'}$ atom of the dioxane ring is less than the sum of the van der Waals radii and, with respect to its parameters [$H(C_6)...O_{1'}$ = 2.25, $C_6...O_{1'}$ = 3.05 Å, and $\angle C_6\text{-}H...O_{1'}$ = 141°] corresponds to a rather rarely encountered hydrogen bond of the C–H...O type [20]. It should be noted that an intramolecular hydrogen bond with participation of the 7-H proton of the uracil residue was previously observed in uridine [14] and 1-(5-nitro-2,4-dihydroxypyrimidinyl)-β-D-ribofuranic acid [21] molecules.

The projection of the structure on the ac plane is shown in Fig. 5. The molecules are joined in chains directed along the *a* axis by means of intermolecular hydrogen bonds $H(N_3)...O_4$ = 1.98 Å ($N_3...O_4$ = 2.83 Å, $< N_3\text{-}H...O_4$ = 174.3°). The remaining intermolecular contacts are no smaller than their average statistical values indicated in [22].

## EXPERIMENTAL

Thin-layer chromatography (TLC) was carried out on 0.25-mm thick DC-Fertigplatten Kieselgel 60F-254 analytical plates. Preparative TLC was accomplished on 2-mm thick PSC-Fertigplatten Kieselgel 60F-254 plates in a chloroform–ethanol sy-tem (9:1) with development in UV light with an UPM apparatus. The IR spectra of mineral oil suspensions of the compounds were recorded with a UR-10 spectrometer. The NMR spectra of solutions in $CDCl_3$ were recorded with a Varian HA-100 spectrometer with hexamethyldisiloxane as the internal standard.

The experimental set of intensities was obtained with a Syntex $P2_1$ diffractometer with monochromatic (obtained with a graphite monochromator) copper emission with a colorless 0.37 × 0.20 × 0.15 $mm^3$ single crystal. The crystals had the composition $C_{10}H_{14}N_2O_4$ and were monoclinic: a = 7.051(1), b = 8.757(2), c = 18.022(3) Å, V = 1112.7(3) $Å^3$, M = 226.25, $d_{calc}$ = 1.35 $g \cdot cm^{-3}$, $\mu(Cu\ K_\alpha)$ = 9.0 $cm^{-1}$, Z = 4, space group $P2_12_12_1$, $F_{ooo}$ = 480.

The intensities of 788 independent reflections were measured by the θ/2θ scanning method up to $2\theta_{max}$ = 150°. A total of 731 reflections with $I \geq 2\sigma_I$ was used in the calculations. The structure was elucidated by the XTL system for the determination of structures. Normalization of the structural factors was carried out with allowance for the known geometry of the fragments of the molecule. The model was found by a direct method by means of the MULTAN program [23]. The structure was refined by the method of least squares within the total matrix approximation, anisotropically for the nonhydrogen atoms and isotropically for the hydrogen atoms up to R = 0.035. The coordinates of the atoms are presented in Table 3. The standard deviations of the bond lengths and angles did not exceed 0.01 Å and 0.5°.

1-(2,2-Dimethyl-1,3-dioxan-5-yl)uracil (II). A mixture of 0.74 g (4 mmole) of I, 10 ml of dry acetone, and 0.01 g of Dowex-50 in the $H^+$ form was refluxed for 1 h, after which it was filtered (the precipitate contained starting uracil I). The filtrate was evaporated, and the residue was crystallized from absolute ethanol to give 0.1 g (11%) of product.

1-(2-Isopropoxy-1,3-dioxan-5-yl)uracil (III). A mixture of 0.74 g (4 mmole) of I, 0.3 g (4 mmole) of isobutyraldehyde, 10 ml of dry benzene, and Dowex-50 in the $H^+$ form (10% of the starting aldehyde) was refluxed in a flask equipped with a Dean-Stark trap until water separation ceased. The hot mixture was filtered, the filtrate was evaporated, and the residue was crystallized successively from heptane and absolute ethanol to give 0.29 g (30%) of product.

1-(2-Ethoxy-1,3-dioxan-5-yl)uracil (IVa,b). A solution of 0.74 g (4 mmole) of I in a mixture of 5 ml of acetic anhydride and 5 ml of orthoformic ester was refluxed for 15 min, after which the solvent was removed by distillation, and the residue was crystallized from absolute ethanol to give 0.84 g (92%) of a mixture of IVa and IVb. Separation on TLC preparative plates in a chloroform–ethanol system (9:1) and elution of the pure isomers with chloroform gave trans and cis isomers IVa and IVb (Table 1) in a ratio of 5:3.

1-(2-Methyl-2-ethoxy-1,3-dioxan-5-yl)uracil (Va,b). A solution of 0.74 g (4 mmole) of I in a mixture of 5 ml of acetic anhydride and 5 ml of orthoformic ester was refluxed for 15 min, after which the solvent was removed by distillation, and the residue was crystallized from absolute ethanol to give 0.80 g (80%) of a mixture of Va and Vb. Separation on TLC preparative planes in a chloroform-ethanol system (9:1) and elution of the pure isomers with

chloroform–ethanol (1:1) gave the trans and cis isomers in a ratio of 40:1 (Table 1).

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