1-NUCLEOSIDES OF 5-SUBSTITUTED 4-CHLORO-1,2,3-TRIAZOLES

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1-Nucleosides of 5-substituted 4-chloro-1,2,3-triazoles were produced by glycosylation of the corresponding triazoles by the method of fusion with tetra-O-acyl-D-ribofuranose in the presence of bis-p-nitrophenyl phosphate. The structure of the compounds obtained and their conformational peculiarities were studied by the methods of mass spectrometry and NMR spectroscopy.

In recent years considerable interest among synthetic chemists has been evoked by nucleosides of azoles, since highly active antineoplastic and antiviral compounds have been detected among them, for example, the drug preparation ribavirin (1-β-D-ribofuranosyl-5-carbamoyl-1,2,4-triazole), the antibiotic pyrazofurin [3(5)-β-D-ribofuranosyl-5(3)-carbamoylpyrazole], the highly active antineoplastic agent 2-β-D-ribofuranosyl-4-carbamoylthiazole, and others [1]. In view of this, it was of interest to obtain nucleosides of derivatives of 1,2,3-triazoles. Nucleosides of 1,2,3-triazoles containing, as a rule, one substituent in the heterocyclic base have been described; the most widespread method of producing such compounds is completion of the heterocyclic portion of the molecule on the basis of glycosylazides [2, 3]; moreover, there are studies on the glycosylation of derivatives of 1,2,3-triazoles [4, 5].

In this work we investigated the glycosylation of 5-substituted 4-chloro-1,2,3-triazoles by fusion with tetra-O-acyl-D-ribofuranose under vacuum in the presence of bis-p-nitrophenyl phosphate as the catalyst. The initial 5-cyano- (I) and 5-methoxycarbonyl-4-chloro-1,2,3-triazoles (II) were produced by transformation of 6-substituted 4-chloro-5-aminopyrmidines [6]. 4-Chloro-5-carbamoyl-1,2,3-triazole (III) was produced by saponification of the nitrile I with hydrogen peroxide in aqueous alkali.

When the nitrile I was fused with 1-O-acetyl-2,3,5-tri-O-benzoyl-β-D-ribofuranose (IV) under vacuum at 150°C in the presence of catalytic amounts of bis-p-nitrophenyl phosphate, a single reaction product was formed — 1-(2,3,5-tri-O-benzoyl-β-D-birofuranosyl)-4-chloro-5-cyano-1,2,3-triazole (VI) — with a yield of 97%. 1-(2,3,5-Tri-O-acetyl-β-D-ribofuranosyl)-4-chloro-5-cyano-1,2,3-triazole (VII) was produced with a yield of 86% by fusion of the nitrile I and tetra-O-acetyl-D-ribofuranose (V) at 120°C. Fusion of the heterocycles II or III with the acylribose IV was performed at 190°C on account of the high melting point of the heterocycles; it was accompanied by substantial resinification. 1-(2,3,5-Tri-O-benzoyl)-β-D-ribofuranosides of 4-chloro-5-methoxycarbonyl- (VIII) and 4-chloro-5-carbamoyl-1,2,3-triazoles (IX) were isolated with yields of 57 and 62%, respectively. Treatment of the nucleosides VIII and IX with sodium methylate in methanol to remove the protective groups leads to high yields of the ribosides X and XI. We succeeded in producing 1-β-D-ribofuranosyl-4-chloro-5-cyano-1,2,3-triazole (XII) (removal of the protective groups without affecting the CN group) only by treating the nitrile VII with Dowex 50 (H^+) resin at room temperature to the presence of silica gel in a 4:1 mixture of chloroform and methanol for 20 days. Removal of the acyl protection in compounds VI and VII by sodium methylate in methanol is accompanied by a simultaneous saponification of the CN group with the formation of the ester X. Analogously, treatment of compound VI with sodium ethylate in ethanol leads to 1-β-D-ribofuranosyl-4-chloro-5-ethoxycarbonyl-1,2,3-triazole (XIII). In the deblocking of the nitrile VI with a 10% aqueous solution of sodium hydroxide at room temperature for 10 min, the amide XI is formed, isolated in a 16% yield.

In the interaction of the nucleoside VI with hydrogen sulfide in methanol in the presence of triethylamine, 1-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)-4-chloro-5-thiocarbamoyl-

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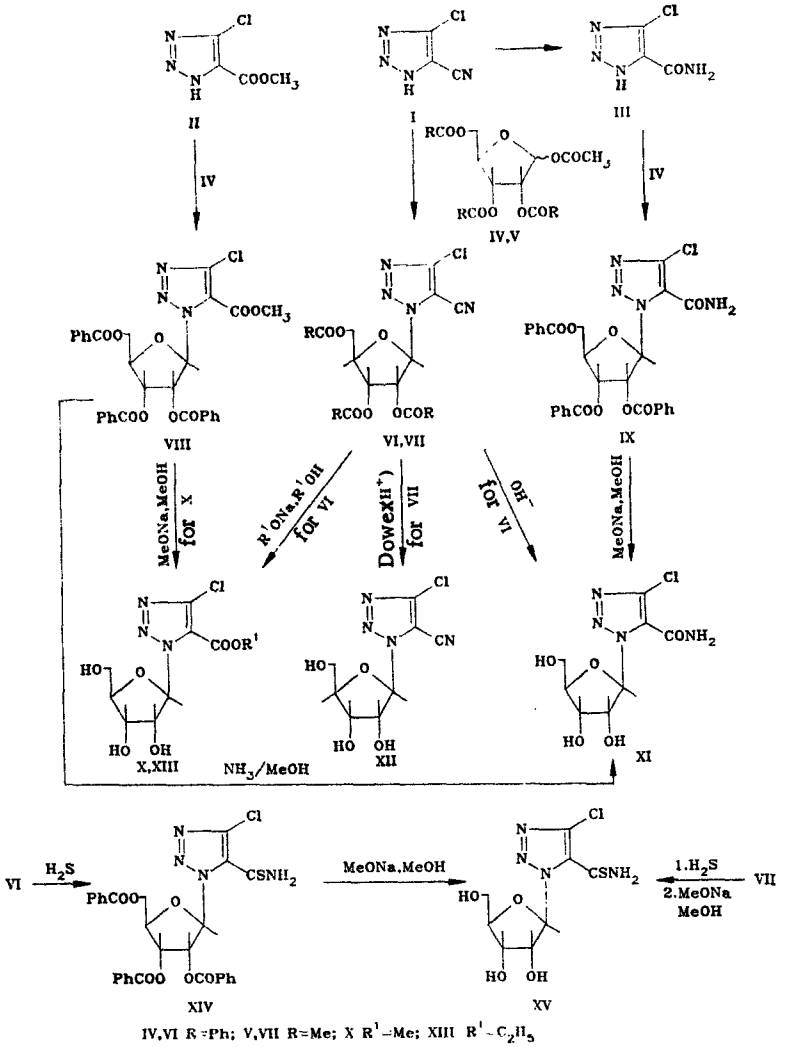
TABLE 1. Parameters of the PMR Spectra of Compounds VI-XI, XIII-XV

Compound*	Chemical shifts, δ, ppm								J, SSCC, Hz					
	1′-H	2′-H	3′-H	4′-H	5′-H	5″-H	CH_3	CH_2	$J_{1'2'}$	$J_{2'3'}$	$J_{3'4'}$	$J_{4'5'}$	$J_{4'5''}$	$J_{5'5''}$
VI	6,43	6,23	6,16	4,90	4,82	4,60	—	—	2,8	5,3	5,3	4,8	5,5	16,6
VII†	6,17	5,84	5,63	4,30—4,50		4,16	—	—	3,4	5,2	5,2			13,2
VIII	6,46	6,26	6,19	4,88	4,78	4,64	3,94	—	3,1	5,3	5,3	3,7	4,6	12,2
IX	6,42	6,30	6,18	4,89	4,82	4,63	—	—	3,3	5,3	5,3	3,7	4,40	12,3
X	5,97	4,59	4,41	4,13	3,77	3,66	3,94	—	3,3	4,9	4,9	3,8	5,6	12,2
XI	5,97	4,60	4,43	4,13	3,78	3,67	—	—	3,4	5,0	5,0	3,7	5,5	12,3
XIII	5,97	4,58	4,41‡	4,13	3,78	3,67	1,39	4,41†	3,3	4,9		3,8	5,7	12,1
XIV	6,43	6,30	6,17	4,91	4,82	4,65	—	—	3,1	5,2	5,2	3,5	4,2	12,2
XV	5,95	4,61	4,42	4,13	3,78	3,67	—	—	3,4	4,8	4,8	3,6	5,5	12,1

*Compounds VI-IX, XIV — solutions in $CDCl_3$, X, XI, XIII, XV — in CD_3OD.

†The spectrum was recorded on a Jeol JNM-MH-100 instrument (Japan).

‡The signals overlap.



1,2,3-triazole (XIV) is formed; by the action of sodium methylate in methanol it is converted to 1-β-D-ribofuranosyl-4-chloro-5-thiocarbamoyl-1,2,3-triazole (XV). Analogously, successive treatment of the nitrile VII with hydrogen sulfide and sodium methylate also leads to the compound XV. Ammonolysis of the ester VIII at room temperature yielded the amide XI. Thus, it was shown by mutual conversions of the nucleosides obtained that the direction of glycosylation of the triazoles I-III by tribenzoylacetylribofuranose IV and tetraacetylribofuranose V coincide.

TABLE 2. Mass Spectra of Compounds X and XII

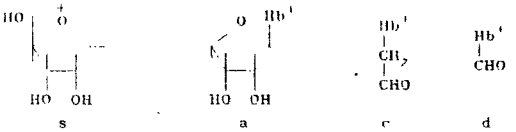
Ion	Compound X		Compound XII	
	m/z	intensity, %	*m/z*	intensity, %
M	293*	0,3	260*	0,25
M+1	294*	0,4	261*	0,2
S	133	10	133	23
S—H	132	15	132	20
b+H	—	—	128*	12
b+2H	162*	50	129*	30
a	263*	15	230*	12
c	204*	100	171*	100
d	—	—	157*	3
M—H_2O	—	—	242*	2,3
$C_3H_5O_2$	73	55	73	55

*Ions containing ^{35}Cl are marked.

The compounds obtained were characterized by the IR, UV, and PMR spectra. In the PMR spectra of the acyl derivatives VI, VIII, IX, and XIV (see Table 1), a regular weak-field shift of the resonance signals of the protons of the carbohydrate ring next to the protected hydroxyl groups is observed in comparison with the spectra of unprotected nucleosides X, XI, XIII, and XV. Somewhat larger values of $^3J_{2'3'}$ (5.2-5.3 Hz) and small values of $^3J_{4'5''}$ (4.2-4.6 Hz) were also noted for benzoates in comparison with unprotected nucleosides (4.9-5.0 and 5.5-5.7 Hz, respectively). For all the compounds under consideration, the constant $^3J_{1'2'}$ does not exceed 3.4 Hz, which confirms a β-configuration of the anomeric site in them on the basis of the general principles in the series of ribofuranosides [7]. On the whole, in the PMR spectra for all the compounds under discussion, with the exception of the benzoate VI, the values of the SSCC are close. This is evidence that replacement of the substituent in the 5-position of the aglycone has virtually no effect on the conformational state of the carbohydrate ring. In the PMR spectrum of compound VI the constant $^3J_{5'5''}$ differs somewhat from those in the spectra of other compounds. Evidently this compound has a somewhat different conformational equilibrium around the exocyclic $C_{(4')}$—$C_{(5')}$ bond.

The most difficult task for us was to establish the site of attachment of the glycosyl residue to the heterocycle. An attempt to convert the nitrile VII or the amide XI to the 1-(2,3,5-tri-O-acetyl-β-D-ribofuranosyl)-5-cyano-1,2,3-triazole or 1-β-D-ribofuranosyl-5-carbamoyl-1,2,3-triazole, respectively, described in the literature by hydrogenolysis over Pd/C at room temperature did not lead to the expected result (the starting materials were isolated). It would be noted that, in contrast to the corresponding heterocycles [8], the nucleosides that we obtained contain a nonmobile chlorine atom, and its replacement by other functional groups presents great difficulties.

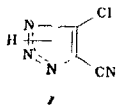
To establish the structure of the compounds synthesized, especially to determine the site of attachment of the ribose residue to 4,5-di-substituted triazoles I-III, we studied their mass spectra. It is known that the mass spectra of O-unprotected nucleosides contain peaks of fragments arising in the cleavage of the glycoside bond: the ion of the base $(b)^+$ exists primarily with one $(b + H)^+$ or two $(b + 2H)^+$ hydrogen atoms; the fragment of the carbohydrate residue $(s)^+$ usually has low intensity [9]. As a rule, a dehydration peak of $(M - H_2O)^+$ is observed; there is an elimination of CH_2OH group, which leads to the ion *a*. Moreover, ions **c** $(M - 89)^+$ and **d** $(B + 30)^+$ are formed; usually the ion $C_3H_3(OAc)_2$ (m/z = 157) and the ion $C_3H_5O_2$ (m/z = 73) are noted in the spectra.



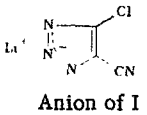
The ions observed in the mass spectra of the nucleosides X and XII are presented in Table 2. For all the ions containing Cl a characteristic isotope distribution is noted. Noteworthy is the high intensity of the ion **c** (taken as the base). In the mass spectrum of the ester X, together with the ion **c**, an ion with m/z = 172 $(c - H - OCH_3)^+$, an ion with m/z = 130 $(b - OCH_3)^+$, and others are noted.

In the mass spectrum of the nucleoside VII, as usual for O-acetylated nucleosides, the ion **s** (m/z = 259,100%) has high intensity. Fragments corresponding to successive elimina-

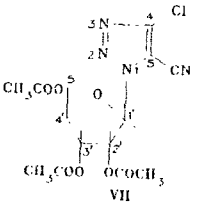
TABLE 3. Chemical Shifts of the ^{13}C Carbon Atoms of Compound I, Its Anion, and VII in DMSO-D_6



I



Anion of I



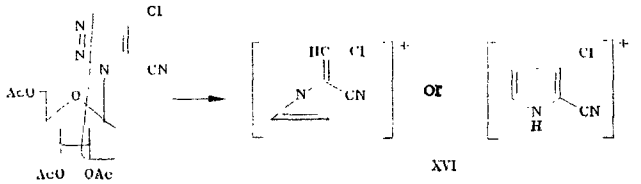
VII

Compound	CN	$C_{(4)}$	$C_{(5)}$	$C_{(1')}$	$C_{(2')}$	$C_{(3')}$	$C_{(4')}$	$C_{(5')}$	CH_3	C=O
I	118,43	139,41	110,20	—	—	—	—	—	—	—
Anion of compound I	118,68	139,70	110,57	—	—	—	—	—	—	—
VII	120,83	141,03	109,24	94,31	73,16	69,76	80,53	62,11	20,28; 20,14; 20,14	169,44; 169,05; 168,79
Δδ VII—I		+1,62	−0,96							
Δδ VII—XX		+1,33	−1,33							

tion of one and two molecules of acetic acid from M^+ [$(M - AcOH)^+$ m/z = 326 (1.5%) and $(M - 2AcOH)^+$, m/z = 266 (15%)] and then splitting out of ketene [$(M - 2AcOH - CH_2CO)^+$, m/z = 224 (30%)] are observed. Moreover, the peak of the ion $C_3H_7(OAc)_2$ with m/z = 157 (35%), the ion with m/z = 271 (35%) [$M - C_3H_7(OAc)_2 - CH_2CO]^+$, and the ion with m/z = 115 (40%) [$C_3H_7 \cdot (OAc)_2 - CH_2CO]^+$ are noted.

In contrast to the nucleosides X and XII, the spectrum of compound VII contains no peaks corresponding to the ions $(b + H)^+$ or $(b + 2H)^+$, but there is an intense peak with m/z = 126 (50%), formed with ejection of N_2 from the heterocycle and retaining the C_2H_3 fragment of the carbon skeleton.

It can be assumed that it contains an aziridine ring or is rearranged to pyrrole derivatives XVI. Its formation is evidently a multi-step process, including not only elimination of N_2 but also transfer of a proton from the carbohydrate fragment to the aglycone, splitting out of AcOH, and cleavage of the carbohydrate skeleton.



VII XVI

No other fragments associated with the decomposition of the aglycone are noted in the spectrum of the nucleoside VII. The formation of the fragment XVI, formed with the ejection of N_2, is evidence that the ribose residue is bonded in the N-1 or N-3 position; if it were at N-2, the elimination of N_2 would be impossible. The formation of an ion with ejection of N_2 was also noted for certain other 1-substituted 1,2,3-triazoles [10]. From the mass spectrum of compound I it follows that its molecular ion with m/z = 128 is rather stable (100%); there is an intense ion with m/z = 76, corresponding to the rearrangement ion $(HNNCCl)^+$. At the same time, ions with m/z = 100 and m/z = 102 are evidence of an ejection of N_2H, which, as was shown above, is observed in the decomposition of the nucleoside VII.

The question of whether glycosylation occurred at the N-1 or N-3 position of the substituted triazole was resolved by the method of ^{13}C NMR spectroscopy. In the ^{13}C NMR spectra of N-protected heterocycles, in comparison with the spectra of the corresponding anions or neutral heterocycles, a strong-field shift of the α-carbon atom (next to the substituted nitrogen atom) is observed, with a simultaneous shift of the resonance signal of the carbon atom in the β-position to the substituted nitrogen, in the weak-field direction [11]. The assignment of the resonance signals of $C_{(4)}$ and $C_{(5)}$ in the ^{13}C NMR spectra of the thiazoles I, VII, and the anion of the triazole I was performed considering the values of the chemical

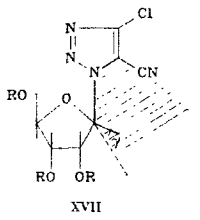
TABLE 4. UV and CD Spectra of Compounds X, XI, XIII, and XV

Compound	UV spectra		CD spectra	
	λ_{max}, nm	lg ε	λ_{max}, nm	$[\theta]_{max}$, mdeg·cm²/mole
X	240	3,91	238	−8100
XI	240	3,91	238	−9400
XIII	240	3,93	238	−8300
XV	253	3,91	251	−8100
	303	3,92	305	−1600

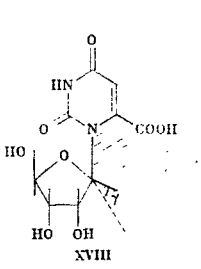
shifts of C-4 and C-5 in the spectra of unsubstituted 1,2,3-triazole and the additive contributions to the chemical shift of such substituents as Cl and the CN group [12]. The resonance signals of the carbon atoms of the ribofuranose residue in the glycoside VII were assigned according to the literature analogies [13].

A comparison of the ^{13}C NMR spectra of the triazole I and its riboside VII (see Table 3) showed that in the transition to the glycoside VII the signal of the carbon atom $C_{(5)}$ is shifted by 0.96 ppm in the strong-field direction, whereas the signal of the $C_{(4)}$ atom undergoes a weak-field shift ($\Delta\delta$ − 1.62 ppm). In a comparison of the ^{13}C NMR spectra of the anion of the triazole I, obtained from the heterocycle I by the addition of an equimolar amount of lithium hydroxide, and the riboside VII, the same patterns were noted — a strong-field shift of the signal of the $C_{(5)}$ carbon atom ($\Delta\delta$ − 1.33 ppm) and a weak-field shift of the signal of the $C_{(4)}$ carbon ($\Delta\delta$ − 1.33 ppm). On the basis of all the data obtained it can be concluded that the carbohydrate residue is situated at the $N_{(1)}$ atom of the aglycone.

We also recorded the high-resolution ^{13}C NMR spectrum of compound VII.* The data of the spectra permit a judgment of the conformation around the glycoside bond in the molecule of the nucleoside VII. In the spectrum recorded in DMSO-D_6 in the scanning range 600 Hz (600 passes, volume of the memory 16 K), it was found that the resonance signal of the $C_{(5)}$ carbon atom (109.24 ppm) has a vicinal constant $^3J_{C-5,\ H-1'}$ less than 0.5 Hz. Considering the nucleoside VII as an analog of 5,6-disubstituted pyrimidines, we suggested that the $N_{(1)}$—$C_{(5)}$ bond in the nucleoside VII is isoteric to the $N_{(1)}$—$C_{(6)}$ bond in pyridimes. By analogy with pyrimidines, we assume that the angle $\gamma = 0°$ corresponds to the conformation in which the $N_{(1)}$—$C_{(5)}$ and $C_{(1')}$—$H_{(1')}$ bonds are shielded (syn-conformation), while the region with values of γ = 90-270°is considered as the region of the anti-conformations. The small absolute value of the two-faced angle $C_{(5)}$—$N_{(1)}$—$C_{(1')}$—$H_{(1')}$ ≈ 45-50°, i.e., for the nucleoside VII the region of syn-conformations is the most populated in DMSO solution. Thus, the conformation of the nucleoside bond of the natural orotidine. The conformation and position of the angle γ of the nucleoside bond of the modified nucleoside and orotidine are presented schematically by formulas XVII and XVIII, respectively.



XVII



XVIII

In the ^{13}C NMR spectrum of compound VII (scanning region 600 Hz, 600 passes, 16 K), for the resonance signal of $C_{(4)}$ at 141.03 ppm, a long-range interaction constant equal to 0.8 Hz was also detected.

The UV spectra of compounds X, XI, and XIII virtually coincide, which is an indication of the closeness of the electronic structure of the chromophores of 5-substituted 1,2,3-triazoles. The UV spectrum of compound XV contains an absorption band at 303 nm, corresponding to $p \rightarrow \pi^*$ transition of the thioamide chromophore (the band is shifted hypsochromically to 295 nm in the transition from ethanol to H_2O), along with an absorption band at 253 nm, to which the $\pi \rightarrow \pi^*$ transitions of the triazole ring and the thioamide group contribute [17].

*The spectrum was recorded on a Bruker WH-360 instrument with working frequency 90.52 MHz.

In the circular dichroism spectra of compounds X, XI, and XIII (see Table 4) there is a characteristic negative Cotton effect (CE) at 238 nm, which is an indication that they have the same conformational shape. The CD spectrum of compound XV, together with the characteristic negative CE at 251 nm, also has a substantially less intense CE (negative) at 305 nm, probably corresponding to the less optically active $p \rightarrow \pi^*$ transition of the thioamide chromophore. The closeness of the characteristics of the PMR and CD spectra of the nucleosides of 1,2,3-triazoles obtained is evidence that a syn-conformation of the nucleoside bond is preferential for all these compounds.

EXPERIMENTAL

The PMR spectra were taken on a Bruker WH-360 instrument with a working frequency 360 MHz, internal standard tetramethylsilane. The ^{13}C NMR spectra were recorded on a Varian XL-100 instrument with working frequency 25.2 MHz. The IR spectra were recorded on a Perkin-Elmer 283 instrument in KBr tablets; the UV spectra were recorded on a Specord-UV-vis recording spectrophotometer in ethanol; the CD spectra were recorded on a Mark-IIIS-Jobin-Yvon instrument; for alcohol (EtOH) solutions $c = 1 \cdot 10^{-4}$ M. The mass spectra were recorded by the method of direct input into the ion source of a Hewlett-Packard HP-5985 mass spectrometer at a temperature of 35°C, followed by an increase in the temperature to 200°C at a rate of 20 deg/min. The electron energy was 70 eV. Silufol UV-254 was used for analytical thin-layer chromatography. Preparative chromatography was carried out on plates (40 × 20 cm) with an unfixed layer of LSL_{254} silica gel, 5-40 μ (Chemapol), with layer thickness 1 mm. The following systems were used for chromatography: A (chloroform–methanol, 5:1), B (chloroform–methanol, 10:1), C (benzene–acetone, 9:1), D (benzene–acetone, 8:1), E (benzene–acetone, 5:1).

4-Chloro-5-carbamoyl-1,2,3-triazole (III). To a solution of 0.5 g (3.8 mmoles) of the triazole I in 30 ml of water containing 0.42 g potassium hydroxide we added 7 ml hydrogen peroxide. The reaction mass was mixed at room temperature for 96 h, then acidified with hydrochloric acid to pH 1-2. The solvent was distilled off, the solid residue treated with 50 ml of boiling acetone. After the acetone was distilled off, 0.57 g (92%) of the crystalline compound III was obtained, mp 198-202°C (dec). According to the data of [18], mp 192-194°C. IR spectrum: 1694 (C=O); 1600 cm^{-1} (C–N). Found: C 24.5; H 2.1; N 38.9; Cl 24.2%. $C_3H_3ClN_4O$. Calculated: C 24.6; H 2.7; N 38.2; Cl 24.2%.

1-(2,3,5-Tri-O-benzoyl-β-D-ribofuranosyl)-4-chloro-5-cyano-1,2,3-triazole (VI). Portions of 0.05 g (0.48 mmole) of the nitrile I and 0.26 g (0.51 mmole) of the acylribose IV were fused under vacuum at 14 mm Hg at 150°C in the presence of 0.03 g bis-p-nitrophenyl phosphate for 40 min. The fusion was dissolved in 3 ml of chloroform, applied on eight plates, and chromatographed in system C. After elution from the silica gel with a chloroform–methanol mixture (4:1) and evaporation of the solvent, 0.26 g (97%) of the foamy substance VI, R_f 0.66 (C) was obtained. IR spectrum: 2225 cm^{-1} (CN).

1-(2,3,5-Tri-O-acetyl-β-D-ribofuranosyl)-4-chloro-5-cyano-1,2,3-triazole (VII). Portions of 0.38 g (3 mmoles) of the nitrile I and 0.95 g (3 mmoles) tetraacetyl-D-ribofuranose V were fused at 120°C. The conditions of the experiment and treatment were analogous to the production of compound VI. A total of 0.99 g (86%) of compound VII was formed as a colorless oil, R_f 0.40 (C). IR spectrum: 2225 cm^{-1} (CN).

1-(2,3,5-Tri-O-benzoyl-β-D-ribofuranosyl)-4-chloro-5-methoxy-carbonyl-1,2,3-triazole (VIII). Portions of 0.16 g (1 mmole) of the ester II and 0.50 g (1 mmole) of the acylribose IV were fused at 190°C. The experimental conditions and conditions of treatment were analogous to the production of compound VI. We obtained 0.36 g (56.6%) VIII in the form of a colorless oil, R_f 0.48 (C). IR spectrum: 1731 cm^{-1} (C=O).

1-(2,3,5-Tri-O-benzoyl-β-D-ribofuranosyl)-4-chloro-5-carbamoyl-1,2,3-triazole (IX). Under conditions analogous to the conditions of production of compound VIII, 0.14 g (1 mmole) of the amide III and 0.50 g (1 mmole) of the acylribose IV were fused. After chromatography in the system D, 0.37 g (62.7%) of compound IX was obtained in the form of a brown oil, R_f 0.19 (D).

1-β-D-Ribofuranosyl-4-chloro-5-methoxycarbonyl-1,2,3-triazole (X). A. A 0.39 g (0.64 mmole) portion of the nucleoside VIII was placed in 30 ml of a 0.1 N solution of sodium methylate in methanol. The solution was left at room temperature for 1.5 h. The excess alkali was neutralized with Dowex 50 (H^+) resin. The resin was filtered off, washed thoroughly with methanol, the filtrate evaporated, and the residue chromatographed on four plates in

system A. Yield 0.13 g (70%), R_f 0.45 (A). The compound represents a colorless oil, which crystallizes upon standing, mp 70–74°C. IR spectrum: 1739 cm^{-1} (C=O). Found: C 36.8; H 4.4; N 14.0%. $C_9H_{12}ClN_3O_6$. Calculated: C 36.8; H 4.1; N 14.3%.

B. A 0.47 g (0.88 mmole) portion of the nitrile VI was dissolved in 40 ml of a 0.1 N solution of sodium methylate in methanol and left at room temperature for 2.5 h, then treated as in the production of compound X according to method A. Yield 0.17 g (70.8%). Samples of the compound obtained by the two methods were identical according to the data of PMR and IR spectra, as well as in R_f values.

1-β-D-Ribofuranosyl-4-chloro-5-carbamoyl-1,2,3-triazole (XI). A. A 0.16 g (0.27 mmole) portion of the amide IX was dissolved in 15 ml of a 0.1 N solution of sodium methylate in methanol and left at room temperature for 0.5 h. It was treated analogously to compound X. Yield of XI 0.07 g (93%) in the form of a colorless oil, which crystallizes upon standing, mp 127–131°, R_f 0.24 (A). IR spectrum: 1608 (C–N); 1681 cm^{-1} (C=O). Found: C 34.4; H 4.5; N 19.8%. $C_8H_{11}ClN_4O_5$. Calculated: C 34.5; H 4.0; N 20.1%.

B. A 0.45 g (0.78 mmole) portion of the nitrile VI was dissolved in 5 ml of acetone, 5 ml of a 10% aqueous solution of sodium hydroxide was added, and the mixture left at room temperature for 10 min. It was treated analogously to compound X. After chromatography in system A, we obtained 0.03 g (16%) of the amide XI.

C. A 0.27 g (0.44 mmole) portion of the ester VIII was dissolved in 25 ml of dry methanol, saturated with ammonia, and left at room temperature for 4 h. The solvent was distilled off, the residue chromatographed on three plates in system A. Yield 0.03 g (25%). The identity of the compounds obtained by the three methods was demonstrated by the identity of their PMR and IR spectra and their R_f values.

1-β-D-Ribofuranosyl-4-chloro-5-cyano-1,2,3-triazole (XII). A 0.15 g (0.38 mmole) portion of the nitrile VII was dissolved in 15 ml of a 4:1 mixture of chloroform with methanol, 1 g of Dowex 50 (H^+) resin and 0.5 g silica gel were added, and the mixture was mixed at room temperature for 20 days. The resin was removed and washed thoroughly with methanol. The filtrate was concentrated to a volume of 3 ml, applied on four plates, and chromatographed in system A. We isolated 0.03 g (30%) of compound XII in the form of a colorless oil, R_f 0.60 (A), IR spectrum: 2225 cm^{-1} (CN).

1-β-D-Ribofuranosyl-4-chloro-5-ethoxycarbonyl-1,2,3-triazole (XIII). We dissolved 0.53 g (0.92 mmole) of the nitrile VI in 50 ml of a 0.1 N solution of sodium ethylate in ethanol. It was treated analogously to compound X. Yield of compound XIII 0.19 g (67.8%) in the form of a colorless oil, which crystallized upon standing, mp 81–83°C, R_f 0.39 (A). IR spectrum: 1731 cm^{-1} (C=O). Found: C 39.0; H 4.9; N 13.7%. $C_{10}H_{13}ClN_3O_6$. Calculated: C 39.1; H 4.6; N 13.7%.

1-(2,3,5-Tri-O-benzoyl-β-D-ribofuranosyl)-4-chloro-5-thiocarbamoyl-1,2,3-triazole (XIV). We dissolved 0.3 g (0.52 mmole) of the nitrile VI in 15 ml of absolute alcohol, containing 0.5 ml of dry triethylamine. A stream of dry hydrogen sulfide was passed into the solution; the course of the reaction was monitored by thin-layer chromatography. After 1 h the solvent was distilled off, the residue dissolved in chloroform (2 ml), applied on 18 plates, and chromatographed in system D. We obtained 0.37 g (68.5%) of compound XIV in the form of a yellow oil, R_f 0.43 (C). IR spectrum: 1450 cm^{-1} (C(S)NH_2). Found: C 55.4; H 3.7; Cl 8.2; S 5.0%. $C_{29}H_{23}ClN_4O_7S \cdot 0.25\ CHCl_3$. Calculated: C 55.6; H 3.7; Cl 9.0; S 5.1%.

1-β-D-Ribofuranosyl-4-chloro-5-thiocarbamoyl-1,2,3-triazole (XV). A. We dissolved 0.27 g (0.44 mmole) of the thioamide XIV in 20 ml of a 0.1 N solution of sodium methylate in methanol. It was treated analogously to compound X. After chromatography in system B, we obtained 0.11 g (84%) of compound XV in the form of a yellow oil, R_f 0.19 (B). Found: C 32.4; H 3.9%. $C_8H_{11}ClN_4O_4S$. Calculated: C 32.6; H 3.8%.

B. We dissolved 0.53 g (1.37 mmoles) of the nitrile VII in 20 ml abs. alcohol containing 0.6 ml dry triethylamine. A stream of dry hydrogen sulfide was passed into the solution for 2 h. The solvent was concentrated to a volume of 3 ml, applied on 10 plates, and chromatographed in system E with three passages of the solvent system. We isolated 0.47 g of a viscous oil, which, after drying over P_2O_5, was placed in 40 ml of a 0.1 N solution of sodium methylate in methanol. It was treated analogously to compound X. We isolated 0.27 g (67%) XV, identical according to the data of the PMR spectrum with the compound produced by method A.

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CONDENSED IMIDAZO-1,2,4-AZINES.

11.* THE REACTION OF 2,6-DIPHENYLIMIDAZO[1,2-b]-1,2,4-TRIAZINE WITH FORMALDEHYDE

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The structure of four main products contained in the reaction mixture obtained in the oxymethylation of 2,6-diphenylimidazo[1,2-b]-1,2,4-triazine was established by the method of chromato-mass spectrometry, with the enlistment of PMR spectroscopy.

We have shown [2] that 2,3,6-trisubstituted imidazo[1,2-b]-1,2,4-triazine readily enters into an electrophilic substitution reaction with the formation of substitution products at the $C_{(7)}$ atom of the bicycle.

In this work we consider the oxymethylation of 2,6-diphenylimidazo[1,2-b]-1,2,4-triazine (I) [3], which has two free positions in the ring (at the $C_{(3)}$ and $C_{(7)}$ atoms), which suggests the possibility of electrophilic substitution not only at the imidazole ring but also at the triazine fragment of the molecule.

*For communication 10, see [1].

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