PREPARATION AND CHEMICAL PROPERTIES OF ESTERS OF 1H- AND 2H-TETRAZOLYLACETIC ACIDS

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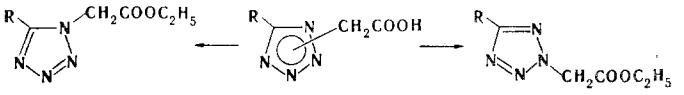
The alkylation of 5-R-tetrazoles with esters of haloacetic acids is a virtually unique method for the preparation of esters of 1H- and 2H-tetrazolylacetic acids [1]. However, this method has substantial limitations because of the difficulty involved in the separation of the resulting isomeric esters. At the same time, 1H- and 2H-tetrazolylacetic acids are obtained in high yields in the alkylation of 5-R-tetrazoles with chloroacetic acid, since the isolation of these compounds from the reaction mixture is carried out by ordinary recrystallization [2].

In this connection, we developed a simple and effective method for the preparation of isomeric esters of tetrazolylacetic acids by esterification of 1H-tetrazolylacetic (I) and 2H-tetrazolylacetic (II) acids with ethanol in the presence of 100% H_2SO_4.



III–IV a R=H; b R=CH_3

The use of lower concentrations of sulfuric acid leads to a sharp decrease in the yields of final products. Compound IIIa, with bp 95°C ($1.33 \cdot 10^{-4}$ hPa) was obtained in 84% yield. IR spectrum (KBr): 990, 1010, 1230, 1420, 1450, 1490 (tetrazole); 1280 (C–O); 1740 cm^{-1} (C=O). PMR spectrum (d_6-acetone): 9.40 (1H, s, CH), 5.50 (2H, s, CH_2), 4.20 (2H, q, CH_2), and 1.20 ppm (3H, t, CH_3). Compound IIIb, with mp 74-75°C, was obtained in 85% yield. IR spectrum (KBr): 1040, 1105, 1130, 1240, 1450, 1490 (tetrazole); 1280 (C–O); 1740 cm^{-1} (C=O). PMR spectrum (d_6-acetone): 5.42 (2H, s, CH_2), 4.20 (2H, q, CH_2), 2.53 (3H, s, CH_3), and 1.25 ppm (3H, t, CH_3). Compound IVa, with mp 52-53°C, was obtained in 85% yield. IR spectrum (KBr): 1030, 1050, 1210, 1430 (tetrazole); 1280 (C–O) 1750 cm^{-1} (C=O). PMR spectrum (d_6-acetone): 8.90 (1H, s, CH), 5.73 (2H, s, CH_2), 4.29 (2H, q, CH_2), and 1.25 ppm (3H, t, CH_3). Compound IVb, with bp 80-82°C (1.3 hPa), was obtained in 85% yield. IR spectrum (KBr): 1040, 1240, 1420, 1450, 1490 (tetrazole); 1280 (C–O) 1750 cm^{-1} (C=O). PMR spectrum (d_6-acetone): 5.61 (2H, s, CH_2), 4.30 (2H, q, CH_2), 2.50 (3H, s, CH_3), and 1.20 ppm (3H, t, CH_3).

Hydrazides V and VI and the corresponding amides VII and VIII were formed by the action of hydrazine and methylamine on esters IIIa and IVa. Compound V, with mp 117-119°C, was obtained in 86% yield. IR spectrum (KBr): 990, 1020, 1120, 1190, 1280, 1450, 1500, 1560 (tetrazole); 1685 (C=O); 1620, 3340, 3415 cm^{-1} (NH). PMR spectrum (d_6-acetone): 9.32 (1H, s, CH) and 5.32 ppm (2H, s, CH_2). Compound VI, with mp 118-120°C, was obtained in 70% yield. IR spectrum (KBr): 1010, 1050, 1150, 1210, 1430, 1570 (tetrazole); 1685 (C=O); 1630, 3100-3400 cm^{-1} (NH). PMR spectrum (d_6-acetone): 8.90 (1H, s, CH) and 5.75 ppm (2H, s, CH_2). Compound VII, with mp 157-159°C, was obtained in 85% yield. IR spectrum (KBr): 1115, 1190, 1260, 1280, 1490, 1560 (tetrazole); 1690 (C=O); 3320 cm^{-1} (NH). PMR spectrum (d_6-acetone): 9.20 (1H, s, CH), 5.30 (2H, s, CH_2), and 2.70 ppm (3H, d, CH_3). Compound VIII, with mp 99-100°C, was obtained in 76% yield. IR spectrum (KBr): 1060, 1110, 1220, 1260, 1420, 1460, 1525 (tetrazole); 1690 (C=O) 1600, 3340 cm^{-1} (NH). PMR spectrum (d_6-acetone): 8.80 (1H, s, CH), 5.40 (2H, s, CH_2), and 2.80 ppm (3H, d, CH_3).

The results of elementary analysis of all of the compounds obtained were in agreement with the calculated values.

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REACTION OF 2,3,4,6-TETRA-O-ACETYL-β-D-GALACTOPYRANOSYL ISOTHIOCYANATE WITH 4-AMINO-4-METHYL-2-PENTANONE

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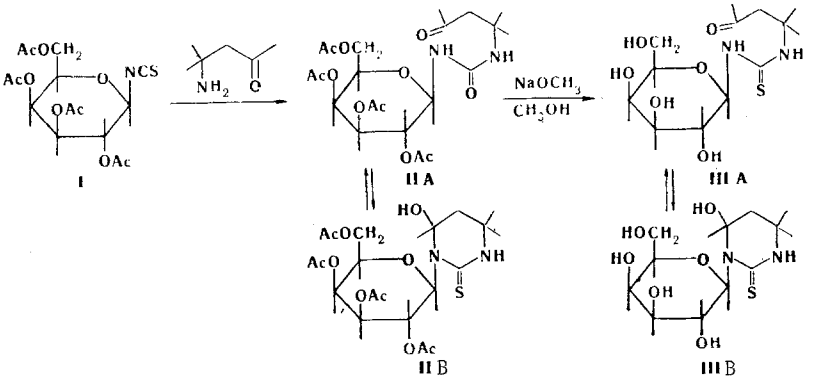
Hydroxyhexahydropyrimidine-2-thiones are structural analogs of the minor bases of nucleic acids, the products of their metabolism, and some medicinal preparations [1]. In order to study the structure, tautomerism, and new properties of substituted 4-hydroxyhexahydropyrimidine-2-thiones we undertook the structural modification of the latter by means of a sugar residue. As a model reaction we studied the reaction of 2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl isothiocyanate (I) [2] with 4-amino-4-methyl-2-pentanone [3] in benzene at 20°C, as a result of which we obtained N-glycoside II, with mp 89.5-91.0°C (from benzene), $[\alpha]_D^{22}$ 0.0, and $[\alpha]_{366}^{22}$ + 159.2 (c 1.1, $CHCl_3$), in 80% yield. Zemplen deacetylation of glycoside II gave III, with mp 92.0-93.5°C, $[\alpha]_D^{20}$ 0.0, and $[\alpha]_{366}^{20}$ + 4.6 (c 0.9, H_2O), in 60% yield after chromatography on silica gel in a $CHCl_3$—EtOH system (3:1).



A νC=O band at 1710 cm^{-1} is observed in the IR spectra of N-glycosides II and III recorded in mineral oil and in solution in $CHCl_3$. Signals of protons of, respectively, a CH_2C=O group at 3.16 and 3.40 ppm and of a CH_3C=O group at 2.10 and 2.12 ppm are present in the PMR spectra of II and III. The set of spectral data shows that in the crystalline state and in solution in $CDCl_3$ N-glycosides II and III have primarily the N_1-(β-D-galactopyranosyl)-N_3-(2-methyl-4-oxo-2-pentyl)thiourea structure (IIA, IIIA) with an acyclic structure of the aglycone, whereas the N_1-methylanalog, which is not bonded to a sugar residue, has a cyclic structure [4]. Thus the introduction of a sugar residue in the hydroxyhexahydropyrimidine-2-thione molecule destabilizes the cyclic structure of the heterocyclic compound.

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