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Preliminary Communication

Nitrogen Bridged Anhydro- and Unsaturated Isocytidines

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The synthesis of hitherto unknown 4′,5′-unsaturated isocytidine III along with the formation of nitrogen bridged 2,5′- VI and 2,4′- X anhydro derivatives were accomplished. The stereospecific hydrogenation of 2-benzamido vinylether II and 5′-iodoisocytidine VIII yielded corresponding lyxo- VII and ribo- IX isomers.

The nucleoside antibiotic angustmycin A containing a 4′,5′-double bond considerably stimulated the investigations toward the synthesis of 4′,5′-unsaturated adenosine and uridine derivatives.

We now report that the mild base — catalyzed E2 elimination[1] of *p*-toluenesulphonate from 2-*N*-benzoyl-5′-0-*p*-tolylsulphonyl-2′,3′-0-isopropylideneisocytidine (I), m. p. 169—171 °C, yields 2-*N*-benzyl-1-(2,3-0-isopropylidene-5-deoxy--β-D-erythropent-4-enofuranosyl) isocytosine (II), m. p. 163—164 °C (80%). The n. m. r. spectrum of II (in $CDCl_3$) showed doublets at $\tau = 5.13$ and 5.37 ($J = 2.5$ Hz) assigned to 4′-exomethylene protons. The debenzoylation of II in methanolic ammonia afforded 4′,5′-unsaturated isocytidine III, m. p. 116—118° (84%).

The tosylisocytidine I, prepared from 2-benzamido derivative (IV; m. p. 178—179 °C), was converted into the (*N*)-2,5′-anhydro-2-*N*-benzoylisocytidine (V), m. p. 279—286° (dec., sintered at 135 °C) (59%). The debenzoylation of anhydro compound V with *t*-BuOK-DMSO yielded (*N*)-2,5′-anhydro-1-(5-deoxy--2,3-0-isopropylidene-β-D-ribofuranosyl) isocytosine (VI), m. p. 285—287 °C (dec.) (95%). The n. m. r. spectra of V and VI in $CDCl_3$ revealed significant differences in chemical shifts for 5′a,b geminal protons. The 2-benzamido derivative V shows two quartets at $\tau = 4.88$ and 6.83 ($J_{a,b} = 15.0$, $J_{a,4'} = 2.5$, $J_{b,4'} = 1.2$ Hz) and debenzoylated compound VI at $\tau = 5.97$ and 6.71 ($J_{a,b} = 14.5$, $J_{a,4'} = 2.5$, $J_{b,4'} = 1.8$ Hz).

In the course of the present research the n. m. r. spectral data reported for (*N*)-2,5′-anhydroisocytidine[2] are in good accordance with those of 2′,3′-0-isopropylidene derivative VI.

The 2-benzamido vinylether II was hydrogenated in a stereospecific manner[3] to 2-*N*-benzoyl-1-(5-deoxy-2,3-*O*-isopropylidene-α-L-lyxopentofuranosyl) isocytosine (VII), m. p. 128—129 °C (95%), $[\alpha]_D^{21} = +13.5°$ (*c* 0.88, MeOH). According to hydrogenation procedure of Benz et al.[4] 5′-iodoisocytidine VIII, m. p. 125—126° unambiguosly afforded isomeric 5′-deoxyisocytidine (IX), m. p.

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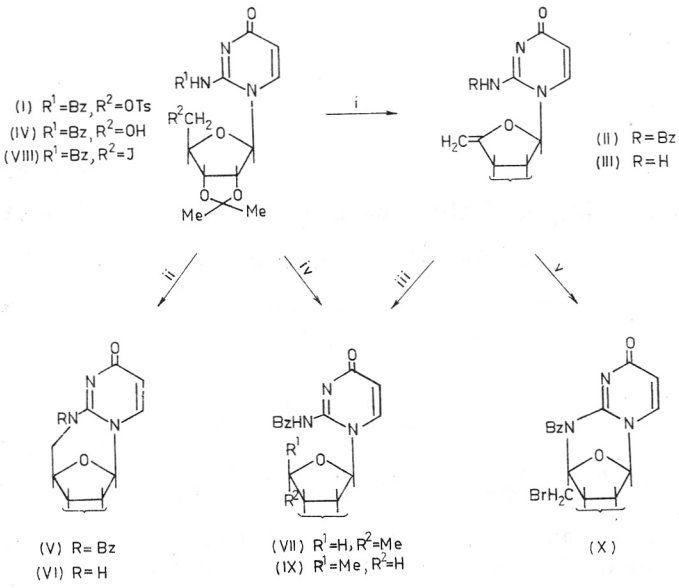

Reagents: (i) *t*-BuOK—*t*-BuOH; (ii) *t*-BuOK—*t*-BuOH—Py;
(iii) [H_2] Pd—C, MeOH; (iv) NaOH—EtOH;
(v) Br_2—$CHCl_3$

143—145 °C (67%), $[\alpha]_D^{18} = +57.9^0$ (*c* 0.7, MeOH). The n. m. r. spectra of lyxo-VII and ribo- IX nucleosides showed the signals centred at $\tau = 8.52$(d) and 8.56(d) assigned to 5′-methyl protons.

When the chloroform solution of isocytidine vinylether II was allowed to react with bromine[5] at —10 °C, foamy (*N*)-2,4′-anhydro-2-*N*-benzoyl-1-(5--deoxy-5-bromo-2,3-*O*-isopropylidene-α-L-lyxopentofuranosyl) isocytosine (X), was isolated in 35% yield, $[\alpha]_D^{21} = +117.0^0$ (*c* 0.47, MeOH). The n. m. r. spectrum of X in $CDCl_3$ evidenced (*N*)-2,4′-anhydro structure by diagnostic sharp singlet at $\tau = 4.42$ attributed to the anomeric 1′ proton and two doublets centred at $\tau = 5.76$ and 6.10 ($J = 12$ Hz) corresponding to the 5′ geminal protons.

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SAŽETAK

Dušikom premošteni anhidro- i nezasićeni izocitidini

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Izvršena je sinteza dosad nepoznatog 4′,5′-nezasićenog izocitidina III kao i dušikom premoštenih 2,5′- VI i 2,4′- X anhidro derivata. Stereospecifično hidriranje 2-benzamido 4′,5′-nezosićenog izocitidina (II) i 5′-jodoizocitidina (VIII) daje odgovarajuće likso- VII i 5′-deoksiribo- IX izomere.

Struktura i stereokemija nepoznatih spojeva određena je na osnovu n. m. r. spektara, optičkih rotacija i elementarne analize.

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