DINUCLEOSIDE MONOPHOSPHATES BASED ON 1-(3-HYDROXYPROPYL)-URACIL*

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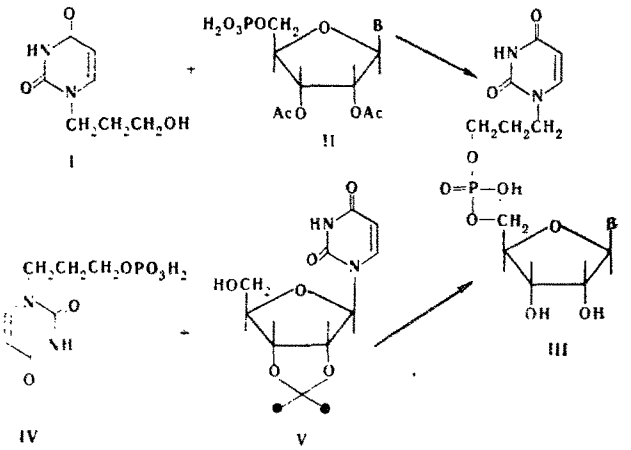
We have expressed the assumption that analogs of substrates that have increased (as compared with natural substrates) conformational mobility are of interest as inhibitors of enzyme reactions and as instruments for the investigation of the mechanism of the action of enzymes [2]. In fact, analogs of nucleosides of a similar type have proven to be powerful inhibitors of protein synthesis in a ribosomal system [3]. The synthesis and study of the inhibitor properties of conformationally mobile analogs of dinucleoside phosphates (DNP) could be a further development of this approach. The present communication is devoted to the synthesis of such analogs in which one of the monomer units — 1-(3-hydroxypropyl)uracil — has greater conformational mobility than the natural compound and does not display chiral properties.



II, III a B = uracil; b B = cytosine; c B = adenine, d B = guanine; e B = hypoxanthine

Because of the achiral character of one of the monomers, the compounds obtained seem of special interest for the study of the nature of the circular dichroism spectra of oligonucleotides; this is a problem for the theoretical meaning of which there is currently no single point of view both with respect to the fundamental inadequacies of the existing theoretical concept [4, 5] and also in connection with the absence of new experimental data.

EXPERIMENTAL

Completely acylated ribonucleoside monophosphates IIa-e were condensed with 1-(3-hydroxypropyl)uracil [6] by a modified method [7]. The reaction of 3 mmole of monophosphate II with 4.5 mmole of uracil I in the presence of 6 mmole of mesitylenesulfonyl chloride was carried out in absolute pyridine at room temperature for 3 h. After the protective groups had been removed by means of a solution of ammonia in methanol, the reaction mixture

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TABLE 1. DNP Analogs Based on 1-(3-Hydroxypropyl)uracil

Compound	UV spectrum, λ_{max}, nm (ε)			Electrophoretic mobility*	Yield, %
	pH 1	pH 7	pH 13		
IIIa	265 (18300)	265 (18300)	264 (14100)	0,54	72
IIIb	273 (20800)	269 (19000)	268 (21000)	0,49	67
IIIc	259 (21300)	261 (21300)	261 (21000)	0,45	73
IIId	260 (18700)	257 (18400)	265 (18400)	0,49	68
IIIe	253 (17500)	251 (17000)	257 (19400)	0,57	74

*Relative to uridine 5'-monophosphate.

was applied to a column filled with Dowex 1 × 4 (Cl^- form), and the products were eluted with a linear gradient of lithium chloride (from 0 to 0.1 M). The fraction containing dinucleoside monophosphate III was vacuum evaporated to dryness, and the lithium salt was isolated by precipitation with a mixture of absolute alcohol and acetone (1:5). Compound IIIa was also obtained by condensation of 1-(3-hydroxypropyl)uracil 3'-phosphate (IV) with 2,3-O-isopropylideneuridine (V) under the described conditions. The compounds obtained are presented in Table 1.

The compounds obtained were chromatographically and electrophoretically homogeneous.

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