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GLYCOSYLINDOLES IX. I-β-D-RIBOFURANOSYLINDOLE 5′-PHOSPHATE

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In a previous paper we have reported the synthesis of an indole analogue of nucleosides (I-β-D-ribofuranosylindole)[I]. Now, the synthesis of indole analogue of nucleotides, namely I-β-D-ribofuranosylindole 5′-phosphate is described.

The parent compound I-β-D-2,3-di-O-acetylribofuranosylindole /I/[I] was phosphorylated by the action of diphenylphosphoryl chloride in pyridine at 37-40° during 70hr. I-β-D-2,3-Di-O-acetylribofuranosylindole 5-diphenylphosphate was isolated (47%) by column chromatography on hydrated silicic acid in benzene-ether system (9:2), the fractions being controlled by TLC method in the same system (R_f0.3). II was identified by microanalysis (Found C 62.I7, H 4.85, N 2.68, P 5.45%. $C_{29}H_{28}NO_9P$ requires C 6I.73,H 4.99, N 2.48, P 5.47%). NMR spectrum of II in CD_3OD, determined using an JNM 4HI00 instrument with operating frequency of I00 mc, gave the signals in the lower field (phenyl and indole nuclear protons), the doublet at δ 6.27 ppm (anomeric proton, J=5.8c/s), the signals at δ 5.45-5.60ppm (C′-2 and C′-3 protons), the signals at δ 4.30-4.60ppm (C′-4 and C′-5 protons), the signals at δ 2.0ppm and 2.I5ppm (acetyl groups). The protons at C′-5 are coupled with P (J=7.0c/s).

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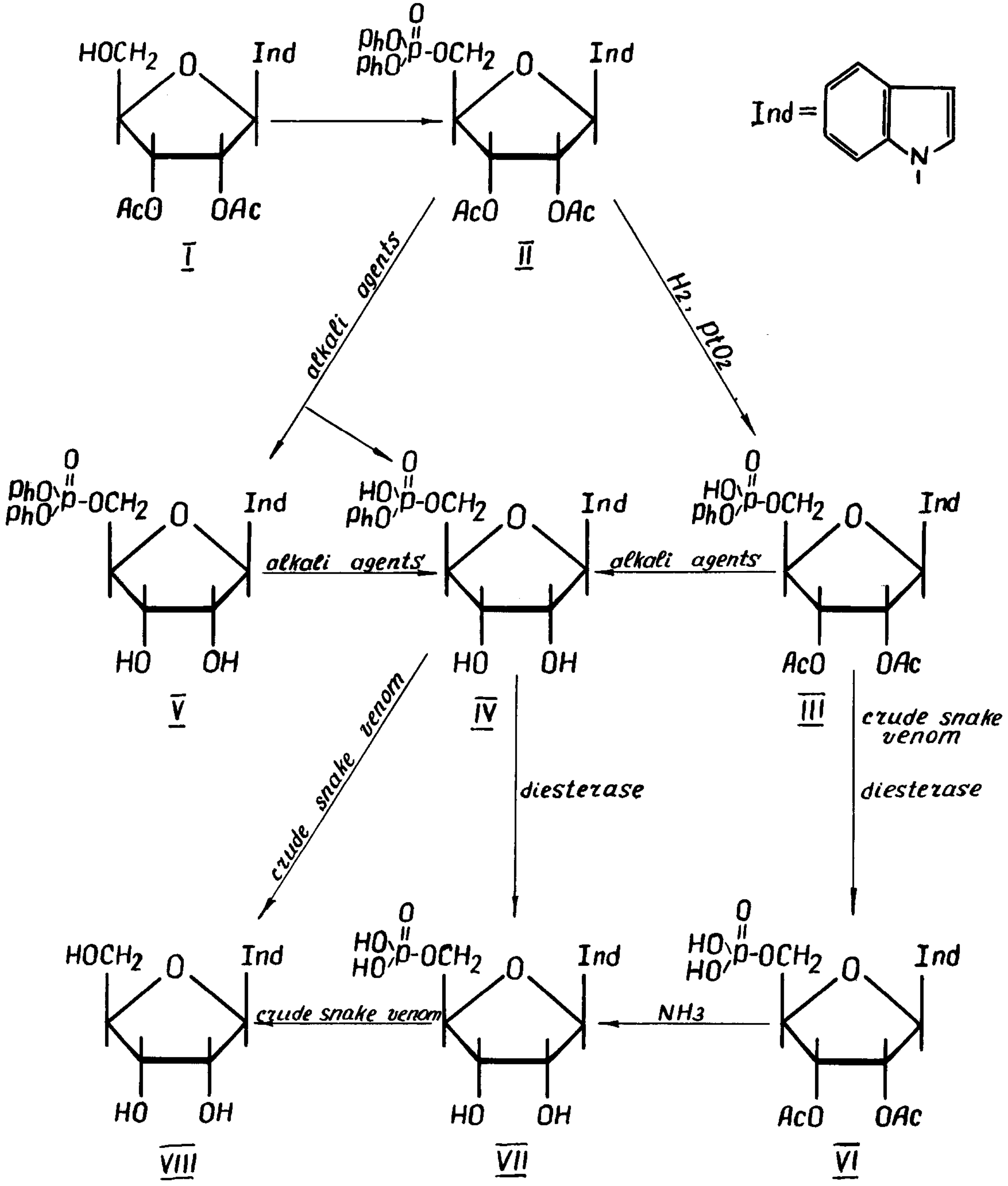
Hydrogenation of II with Adams platinum oxide yielded only the amorphous monophenylester /III/, the structure of which was confirmed by NMR spectrum and electrophoresis (see table). The mixture of I-β-D-ribofuranosylindole $5'$-monophenylphosphate /IV/ and I-β-D-ribofuranosylindole $5'$-diphenylphosphate /V/ was formed by the action of alkali agents (aq. methanolic ammonia, aq. methanolic NaOH, $NaOCH_3$ in CH_3OH, incubation for 2-4 days with alkali buffer at pH 9.2). The structures of these compounds were established by electrophoresis (see table). IV was also obtained by alkali hydrolysis of III.

I-β-D-2,3-Di-O-acetylribofuranosylindole 5-phosphate /VI/ was obtained by incubation of III with crude snake venom or purified phosphodiesterase, obtained from Vipera lebetina, in the presence of $Mg^{\oplus}$ at 37° in carbonate - bicarbonate buffer (pH 9.2).

The treatment of VI with methanolic ammonia gave I-β-D-ribofuranosylindole $5'$-phosphate /VII/. "A more convenient route for the preparation of VII is as follows: II was treated with aq. methanolic ammonia and the resulting mixture of IV and V without separation was incubated with phosphodiesterase at 37° in carbonate - bicarbonate buffer (pH 9.2) in the presence of $Mg^{\oplus}$. VII was extracted with methanol from the zone of electrophoretic papergramm. The methanolic solution was evaporated and the residue was dissolved in water and treated with DAWEX 50 ($H^{\oplus}$). Aq. ammonia was added to filtrate (pH 9.0), and evaporation of the solution yielded VII as amorphous ammonium salt (25% starting from II). Its structure was established by the electrophoresis (see table) and NMR spectrum. NMR spectrum (CD_3OD) gave the signals in lower field (protons of indole nucleus), doublet at δ 6.00ppm (anomeric proton, J=5.5c/s) and the signals at δ 4.0-4.4ppm (C'-2,C'-3, C'-4 and C'-5 protons). Acceptable integrated intensities were obtained.

Both VII and IV when treated with crude snake venom yielded I-β-D-ribofuranosylindole /VIII/, the structure of which was confirmed by comparing with authentic sample of VIII by TLC and paper electrophoresis (see table).


HOCH2
Ind
AcO
OAc
I
PhO
PhO
P-OCH2
Ind
AcO
OAc
II
Ind =
N
alkali agents
H2, PtO2
PhO
PhO
P-OCH2
Ind
HO
OH
V
alkali agents
HO
PhO
P-OCH2
Ind
HO
OH
IV
alkali agents
HO
PhO
P-OCH2
Ind
AcO
OAc
III
crude snake venom
diesterase
crude snake venom
diesterase
HOCH2
Ind
HO
OH
VIII
crude snake venom
HO
HO
P-OCH2
Ind
HO
OH
VII
NH3
HO
HO
P-OCH2
Ind
AcO
OAc
VI

TABLE

E VALUES OF THE VARIOUS DERIVATIVES OF I-β-D-RIBOFURANOSYLINDOLE

Substance	a	b	c	d	f
II	0.0	0.0	0.0	0.0	-
III	0.46	0.46	-	0.37	I.0
IV	0.46	0.46	0.5I	0.66	I.0
V	-	0.26	0.20	0.37	0.0
VI	-	0.90	0.85	0.66	I.0
VII	0.92	0.90	0.85	I.0	I.0
VIII	0.0	0.07	0.20	0.27	0.0

E of uridine 5-phosphate =I.0. a.Triethylammonia - bicarbonate buffer pH 7.5, 9.5 v/cm, 4 hr. b. Phosphate buffer pH 8.9, 6.5 v/cm, 4 hr. c.Carbonate - bicarbonate buffer pH 9.2, 7.5 v/cm, 4 hr. d. Boric acid - borax buffer pH 9.2, 7.5 v/cm, 4.5 hr. f.Acetate buffer pH 3.6, 7.5v/cm,4.5 hr.

By the electrophoresis or TLC the zones were detected with the p-$(CH_3)_2NC_6H_4CHO$ in methanolic HCl (the specific reagent for indole derivatives).

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References

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