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Synthesis of Nucleotide α-Amino Acids via New Branched Chain Sugar

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ABSTRACT

This work includes synthesis of new N-substituted nucleotide α-amino acids, in order to obtain these derivatives; 3-keto sugar derivative was subjected to a modified strecker-type reaction, where by different primary aromatic amine with cyanide ion were introduced successfully, and new α-aminonitriles were thus obtained in good yields.

Base hydrolysis of sugar α-aminonitriles by using (35 %) aqueous sodium hydroxide solution, at reflux temperature gave the desired sugar α-amino acids. FTIR spectroscopy was utilized for characterization of synthesized compounds.

In order to synthesis the new nucleotides, the branched chains sugars modified to either active forms as acetyl sugar derivative or (1-bromosugar derivatives). When use 1-bromosugar the conversion include the hydrolysis to the corresponding diol, acetylation with acetic acid/acetic anhydride in acidic to furnished the acetylated sugar, bromination, forming 1-bromo, that was subjected to condensations with mercury base salts to gives aprtected nucleotides. DE blocking of these groups with (CH_3ONa / CH_3OH produced nucleotides free analogue type of (2′,3)-dideoxye-(3′,3)-amine carboxyl - pyrano).

Keywords: Nucleotide, Nucleoside Analoges, Hexo pyranoside, Thyophylline, Indole

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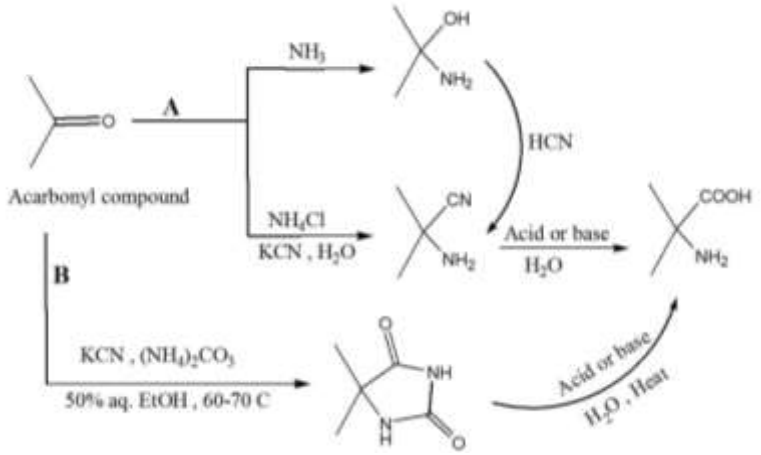
INTRODUCTION

The biochemistry of brancheds-chain sugars nucleotides that are analogous of natural occurring's and synthetics show a kinds of biochemical activities (Roedern *et al* ,2003), for example Remdesivir is active against EVD (Ebola Virus Disease) (Travis *et al,* 2016), Marburg disease and used in recent year in chemotherapy as drug for COVID-19 and herpes viruses (Liying *et al* ,2002) and the synthetic 3′ -C-methylsubstituted cytidines and 2′ and 3′ -C-methyl substituted adenosines are efficacy antivaccinias agent in mice [2] and also inhibit the growth of KB cells in vitro (Sanghvi *et al,* 2004), others synthetics 2′ -C and 3′ -C-brancheds-chains nucleotides inhibition the growths of tumors cell (Rosenthal and Baker 1973), different bacterias and also inhibition of a different kind of enzyme biosystems (Roedern *et al,* 2003). In this research the Michael addition of cyanide ion to the carbon-nitrogen double bond of unsaturateds C=N, brancheds chains sugars to produced the required products (Szarek *et al,* 1982).

The target products, 3′[C-(brancheds-chains)] amino acids nucleotides, were analogues of nucleotides moiety (Dondoni, 2000, 1998; Yoshimura, 1984).

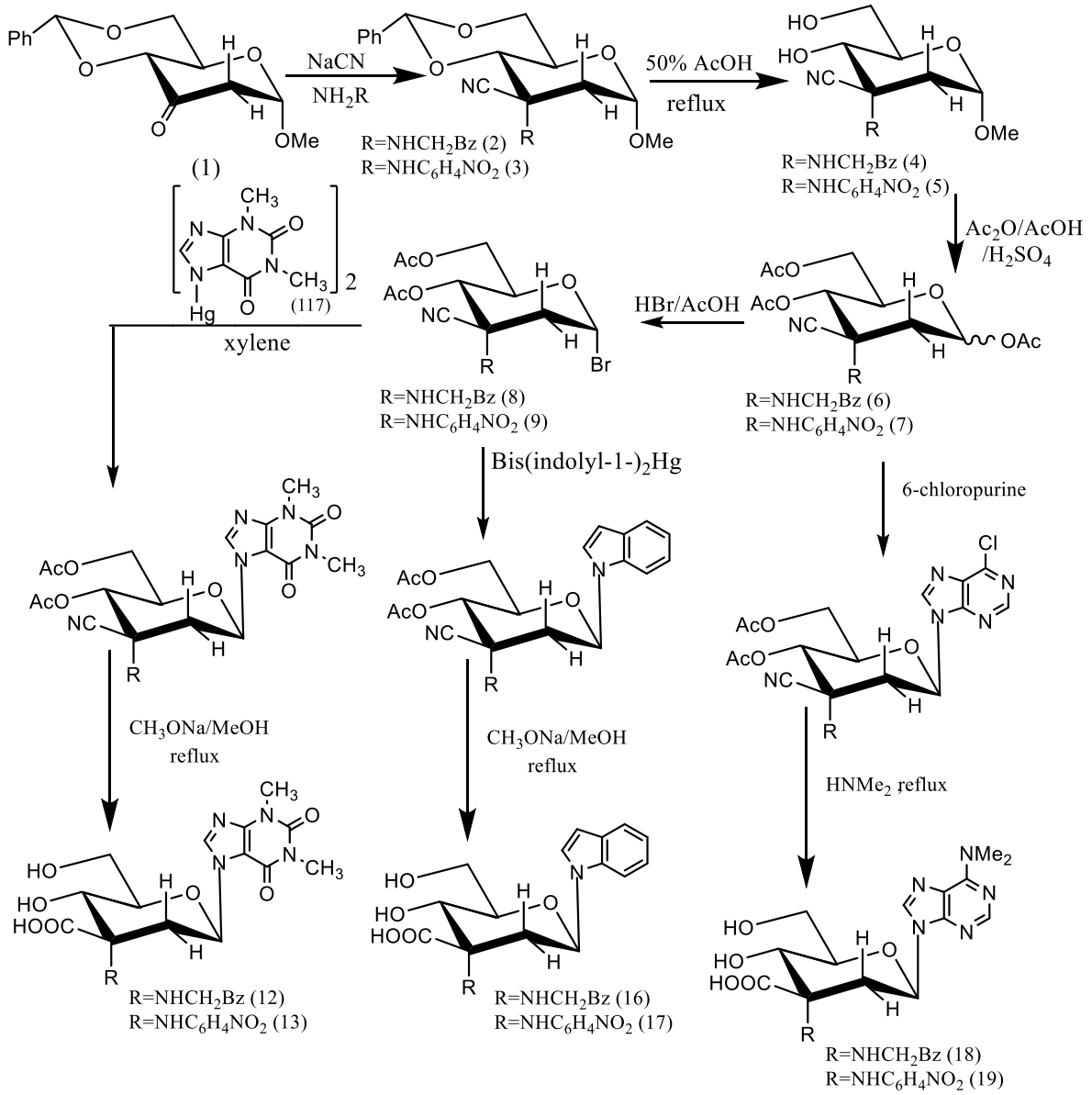
One class of sugar α-amino acids, is of special interest, since they mimic many of naturally occurring compounds, and they also became an attractive goal in the area of peptodomimetic studies (Baker *et al,* 1965)for designing new powerful drugs, as well as, new model compounds for specific enzymetic studies (Grisebach, 1978).

One of the oldest and reliable routes to wards α-amino acids is the treatment of the a carbonyl compound (aldehyde or ketone) with ammonia and then with hydrogen cyanide to form the α-amino nitrile; the so-called streacker synthesis (Lawton *et al*, 1969). The α-amino acids, is then obtained by the acid or base hyrolysis of the α-amino nitrile. Also, the Bucherer-bergs synthesis (Roedern *et al,* 2003) provides hydantoin; the direct precursor of α-amino acids. That is, when a carbonyl derivative is allowed to react with two moles of potassium cyanide and four moles of ammonium carbonate in 50% aqueous alcoholic warm solution, the hydantion usually be isolated on cooling. The α-amino acid will then be obtained by base or acid hydrolysis of the hydantoin. (Scheme 1)



Scheme 1: The general strecker synthesis (A), and the Bucherer- Bergs synthesis (B) of α-amino acid

The synthetic route was started with [methyl(4, 6)-*O*- benzyldene-2-deoxy-(α-*D)*-eryth -hexopyrnosi- de-3-ulose) in a series of reaction (Schemes A)



APPARATUS

1- Infrared Spectrophotometer

(SHIMADZU) FT-IR-8400s spectrophotometer. Solid samples were run in KBr disc, Liquid were run as smears.

2- Nuclear Magnetic Resonance Spectrophotometer were determined FT-NMR: 300 MHz in DMSO, $CDCL_3$ with tetramethyl silane as internal standard.

3- Micro Element Analysis (CHNO) was carried out in the Central Laboratories Euro Vector EA 3000 A.

MATERIALS

All materials that used from Fluka, BDH and Merck company, and Were Used without further purification.

3.1: [Methyl (2-deoxy-(4,6)-*O*-Benzyldene-(α-*D*)-erythhexopyranoside-3-uloses(1)

The deoxy-sugars [Methyl(2-deoxye (4,6)-*O*-Benzyldene-α-*D*-ribo-hexopyranoside](Baker and Buss, 1965) About (2.5 g, 9.46 mmole) is dissolve in a mixtures of anhydrous DMSO (30 mL) and acetic anhydride (20 cm^3). at room temperatures, After stirring for 35-50 hr., TLC (chloroform-ethere 1:1) to indicate the complete of reaction. then dilute of The mixture with ice water, (80 cm^3) and washe the result yellow syrup with ice water, (3x25 cm^3) then followed by using chloroform (3x25 cm^3) for extractions .drying combined organic extracts over anhydrous sodiume sulphate,then solvent was evaporatede to afford syrup residue to 3-keto-derivative (1) in 62% yields: R_f = 0.8 ($CHCl_3$: ether 1:1).

3.2: Amino-cyanation Procedure; synthesis of compounds (2,3) (Kennedy, 1988)

A solution of blocked Keto sugar (1) (2 mmole) in just sufficient ethanol were add for solution of sodiume metabisulfite (0.8 g, 4, mmole) in water (1 cm^3), and mixture were stirred vigorously to about 40 min at 38-42º; during which time a slurry of the Bisulfite adduct was formed. A solution of the amine (2 mmole) in ethanol (1cm^3) were add, and stirring were continued to 35-65 min, at 38-42º. reaction vessel were then immersed in an ice bath inside the hood, and 0.2 g (4 mmole) of sodium cyanide was added. the vessel was tighted, at room temperature, with continue of stirring, until TLC (ether-petroleum-ether; 3:1) that indicate completion of a reaction. Then dilute of reaction mixture with chloroform-water (10 cm^3 each) was done, and extractions of the aqueous layers with chloroform (3x15 cm^3). the combined chloroforme solutions was washe successively with brine (2x15 cm^3), and water (10 cm^3), dried ($MgSO_4$), filtere, and evaporate to bear mixture of α-aminonitriles were synthesized by using the selected amines (Strecker, 1850; Ware, 1950).

3:b Procedure for the Hydrolysis of α-aminonitriles (4,5)[11]

To a 5 cm^3 of 35 % aqueous sodium hydroxide solution, were added 100 mg of α-aminonitriles, and about 1 cm^3 from ethanol . The resulting mixtures were stirred and boiled in reflux until the liberation of the ammonia gas had ceased (16 hours). The opened reaction vessel was heated for a few minutes to ensure liberating of the residual ammonia. then cool the reaction mixture to ambient temperatures, and filtere off. the basic filtrate were dilute with about 3 cm^3 of water, treated with Zerolite 255 (H^+) resin, and evaporated to dryness, to became the product as a light-browne-solid. The last was dissolved at boiling methanol containing a little charcoal, filtered hot, and water about (30 cm^3) was then add to the cooled filtrate whereupon α-amino acid crystallized out as a white solid.

The following α-amino acid derivatives were obtained by using the above hydrolysis procedure (Strecker, 1850; Ware, 1950).

3:2 Methyl-(4,6)-*O*-Benzyldene-3-*C*-cyano-3-benzylamine-(2,3)-dideoxye-(**α**–*D*)-arabino-hexopyranoside (2) & Methyl-(4,6)-*O*-Benzyldene-(2,3)-dideoxye-3-*C*-cyano-3-p-nitroanline-(**α**–*D*)-arabino-hexopyranoside (3)

Starting from the protected keto deoxy sugar (1) (0.76g, 2mmole), benzylamine 0.2 cm^3 was used, and the reaction completed during 16 hours after the addition of sodium cyanide. The solution was isolated as a yellow to give (2) as thick syrup, Yield 0.38 g (52.8 %). R_f 0.18, FTIR (film): 3321 cm^{-1} (-N-H), 2150 cm^{-1} (-C≡N).

The compound (3) was prepared under similar conditions as for (2) Starting from the compound (1), benzylamine 0.1 cm^3 (0.1 g, 1 mmole) was used, and reactions completes during 16 hours after the addition of sodium cyanide. The solution were separatrd as a pale, thick syrup. Yields 0.41 gm (72%). R_f 0.16, FTIR (film): 3331 cm^{-1}, (-N-H), 2182 cm^{-1}, (-C≡N).

3:3 Methyl-(2,3)-dideoxye-3-*C*-cyano-3-benzylamine-**α**–*D*-arabino-hexo pyranoside (4) & Methyl-(2,3)-dideoxy-3-*C*-cyano-3-p-nitroanline-(**α**–*D*)-arabinohexopyranoside (5)

(0.5 g, 1.5 m mole) of protected deoxy-sugars derivatives (2) were dissolve in 48 % aqueous CH_3COOH (8 cm^3) and heating the solution under reflux for about 0.5 hr., the thin layer chromatography examinations at this stages indicate that reaction were completed. about (12 cm^3) of water were add then extractions with chloroform (3x25 cm^3), then drying combinede organic phase over anhydrous magnesiume sulphates and under reduced pressure were evaporated to gives (4) (0.32 g, 79 %) as a paly yellow syrup: FTIR (as afilm), 3382 cm^{-1} broad band of (O-H), R_f 0.15 ($CHCl_3$: EtOH 1:0.5).

Removed of Benzyldene groups from (3) followed by the same procedure for preparation of compounds (4) afford (5) as an off-white syrup (0.0.542 g, 80 %): 3452 cm^{-1} broad band of (O-H), 2182 cm^{-1} weak band of (C≡N), 1573 cm^{-1}, 1512 cm^{-1} (NO_2) R_f 0.3 ($CHCl_3$: EtOH 8:2); FT-IR (film).

3:4 (1,4,6)-tri-*O*-Acetyle-3-*C*-cyano-3-benzylamine-(2,3)-dideoxye-*D*-arabino-hexopyranose (6) & (1,4,6)-tri-*O*-Acetyle-3-*C*-cyano-3-p-nitroanline-(2,3)-dideoxye-*D*-arabinohexopyranose (7)

To a solution of blocked derivative (4) (0.81 g, 2 mmole) in glacial CH_3COOH (3 cm3) and $(CH_3CO)_2O$ (2.5 cm^3) H_2SO_4 (0.02 cm^3) were add, at room temperature Then stirr The result solutions for about 24 h. by TLC Reaction were present to be complete then dilute the mixture with (20 cm^3) of water, followed by using of chloroform (3x15 cm^3) for extractions, under reduced pressure occures drying over magnesium sulphate and evaporate yielding (0.78 g, 65 %) of (6) as a paly yellow syrup: FT.IR (K.Br disk), 2120 cm^{-1} weak band of (C≡N), 1755 cm^{-1} carbonyl group(C=O),R_f, 0.16 ($CHCl_3$: MeOH 1:0.4).

under the similar conditions as for (4) Acetylation of (5) until gives (7) as an white-off solid as (0.816 g, 71 %): R_f, 0.18 ($CHCl_3$: MeOH 1:0.4); FT-IR (KBr disk), 2152 cm^{-1}weak band of (C≡N), 1756 cm^{-1} carbonyl group(C=O).

3:5 (4,6)-di-*O*-Acetyle-3-*C*-cyano-3-benzylamine-(2,3)-dideoxye-*D*-arabinohexopyranosyl-**α**-bromide (8) & (4,6)-di-*O*-Acetyle-(2,3)-dideoxy-3-*C*-cyano-3-p-nitroanline-*D*-arabino-hexopyranosyl-**α**-bromide (9)

The acetylated sugar (6) (1 g, 0.423mmole) were treat with 55 % (W/V) HBr in CH3COOH (10 cm^3). still The mixture was kept at 0^0 in 1 hr until TLC indicate reactions completions then poure at an ice-cold chloroform (40 cm3), and wash with ice water (3x20 cm^3) and then removing the remaining acids using saturated aqueous solution of sodium bicarbonates. At final neutralization and wash with ice waters (30 cm^3) all organics layer were dry in pure sodiume sulphates and solvents were evaporate by rotary evaporator to gives (8) as asyrup (0.436 g, 45.56 %). The final sugars-

substituted bromide (8) were used in direct in prepare of nucleotides: R_f 0.45 (Me_2CO: $CHCl_3$ 1:1).
The Brominations of (7) were synthesize under as for as prepare compound (6) to formed (9) as a syrup (0.482 g, 51.13 %): R_f, 0.38 ($CHCl_3$: C_6H_6 4:1).

3:6 7(4′,6′)-di-*O*-Acetyle-2′,3′-dideoxye-3′-*C*-cyano-3-benzylamine-(*β-D*)-arabinohexopyranosyltheophylline (10) & 7(4′,6′)-di-*O*-Acetyle-2′,3′-dideoxye-3′-*C*-cyano-3-p-nitroanline-(*β-D*)-arabinohexopyranosyltheophylline (11)
Thoroughly dried, finely powdered mixture of The theophylline mercury salt (0.3g, 0.533 mmole) were suspende in (75 cm^3) xylene that dry on sodium in celite (1 g) and remove trace of water azeotropically by distille off of solvent. When the temperature of were raise to 135 ^{0}C, the residues of suspensions were cold (in 55 ^{0}C). The protected sugars (8) (0.5 g, 1.25 mmole) in dry xylenes that addation and allowed to refluxes in strong stirrings for 2 h. To indicates complete reactions by using TLC (chloroform-ether 9:1) which was filter from the hot xylene suspensions and wash with DCM (10 cm^3). Washing with (2x10 cm^3) of 18% potassium iodide of organic layer to remove the remaining trace of the mercurice salts, then wash with water (2x10 cm^3) drying over anhydrous magnesium sulphate to remove solvent to gives acetylated nucleotides (10) (0.162 g, 29.25 %)
The compound (11) under same conditions as for (10) to yields were prepared (0.156 g, 29.28% yields).

3:7 7-(2′,3′)-Dideoxye-3′-*C*-benzylamine –(β-*D*)-3-arabinohexopyranosonic acid) theophylline (12) & 7-(2′,3′)-Dideoxye-3′-*C*-p-nitroanline-(β-*D*)- -3-arabinohexo pyranosonic acid) theophylline (13)
A mixture of (0.165 g, 0.312 mmole) of protected nucleotides (10) in (10 cm^3) of 0.1M sodiume methoxides were reflux with stirring of 1 hr. TLC (DCM: EtOH 4:1) show that the reactions was complete, using acetic acid to neutralize of the solution and evaporate until dryness, the residues was recte by partitione between chloroform and water and the aqueous phase were evaporate by rotatory evapor. Then residues was dissolve by CH_3OH (10 cm^3) and then used a columne of silica by chromatographe on using 9:1 CH_2Cl_2-CH_3OH as developer to afford (0.119g, 72.55 %) the nucleotides (12) was crystallize from C_2H_5OH-ether: R_f 0.3 (DCM: EtOH 8:2); mp 208-210 ^{0}C .
H^1NMR: (Data) in δ Delta (ppm) : 1.88(6H, s, $(NCH_3)_2$, 7.826 (6H, m, H-arom), 3.45 (2H, tt, 2′-H_a, 2′- H_b), 3.342 (1H, mm, 5'-H), 3.66 (1H, dd, 1'-H), 3.75-3.88 (2H, dd, 6'-H_a , 6'-H_b) ,4.88 (1H, dd, 4'-H), 3.22 (2H, ss, 2-OH), 10.22 (1H, s, COOH), 4.345 (1H, s, $NHCH_2$); ^{13}C-NMR (Data) in δ Delta (ppm) : 25.66 (C-3'), 29.56 (C-2') 73.15-74.55 (C-4', C-5' and C-1'), 63.88 (C-6'), 185.33 (COOH), 33.8, 35.6 (CH_3- N)$_2$-), 142.22 and 148.4 (C-4, C-5),
Analyt. Calcd. to the $C_{21}H_{25}N_5O_7$(12): C, 54.90; H, 5.45; N, 15.25. Founded: C, 54.72; H, 5.52; N, 15.29.
The compound (13) under same conditions as for (12) to yields were prepared (0.115 g, 71.22% yields).
H^1NMR: (Data) in δ Delta (ppm) : 1.85(6H, s, $N(CH_3)_2$, 7.724 (5H, m, H-arom), 3.347 (2H, tt, 2′-H_a, 2′- H_b), 3.423 (1H, mm, 5'-H), 3.466 (1H, dd, 1'-H), 3.57-3.69 (2H, dd, 6'-H_a , 6'-H_b) ,4.83 (1H, dd, 4'-H), 3.12 (2H, ss, 2-OH), 10.5 (1H, s, COOH), 4.34 (1H, s, NHarom); ^{13}C-NMR (Data) in δ Delta (ppm) : 25.66 (C-3'), 29.56 (C-2') 73.15-74.55 (C-4', C-5' and C-1'), 63.88 (C-6'), 181.67 (COOH), 71.67 (C-NO_2), 33.88, 37.6 $(CH_3)_2$ N-), 145.33 and 149.5 (C-4, C-5),
Analyt. Calcd. to the $C_{20}H_{22}N_5O_7$(13): C, 54.05; H, 4.95; N, 15.76. Founded: C, 54.45; H, 4.74; N, 15.88.

3:8 1-(4′,6′)-di-*O*-Acetyle-(2′,3′)-dideoxye-3′-*C*-cyano-3-benzylamine-(β-*D*)-arabinohexopyranosylindole (14) & 1-(4′,6′)-di-*O*-Acetyl-(2′,3′)-dideoxye-3′-*C*-cyano-3-*p*-nitroanline-(β-*D*)-arabinohexopyranosylindole (15)
Depending on same procedures for synthesis in compounds (10 and 11) the protecting sugars-bromide (8) (0.48, 1.2 mmole) and under reflux in xylenes with indole Hg (II) salts (0.5 g, 1.2 mmole) for 60 min. to gives (14) as syrup. (0.290 g, 54 %): R_f, 0.44 ($CHCl_3$: $(Et)_2O$ 9:1) and compounds (15) as syrup. (0.28 g, 55 %): R_f, 0.41 ($CHCl_3$: $(Et)_2O$ 9:1)

3:9 1-(2′,3′)-Dideoxye--3′-*C* -3-benzylamine-β-*D*-arabino-3-hexopyranosonic acid) Indole (16) & 1-(2′,3′-Dideoxye--3′-*C*-3-*p*-nitroanline-β-*D*-arabino-3-hexopyranosonic acid) Indole (17)
The above compounds were prepareds under the same conditions as in (12 and 13) to produced (16) as a white off crystals. (0.08 g, 52%): R_f, 0.48 (dichloromethane: ethanol 8:2); mp 165 ^{0}
H^1NMR: (Data) in δ Delta (ppm) : 7.23-7.42(6H, m, ,aromatic indole) 7.85 (6H, m, H-arom), 3.33 (2H, tt, 2′-H_a, 2′- H_b), 3.45 (1H, mm, 5'-H), 3.88 (1H, dd, 1'-H), 3.93-3.98 (2H, dd, 6'-H_a , 6'-H_b) ,4.85 (1H, dd, 4'-H), 3.25 (2H, ss, 2-OH), 10.66 (1H, s, COOH), 4.56 (1H, s, $NHCH_2$); ^{13}C-NMR (Data) in δ Delta (ppm) : 27.68 (C-3'), 28.44 (C-2') 75.15-76.55 (C-4', C-5' and C-1'), 65.94 (C-6'), 180.22 (COOH), 33.8, 35.6 (C-N), and 127.56 – 145 (C-aromatic)
Analyt. Calcd. to the $C_{22}H_{24}NO_5$(16): C, 69.11; H, 6.28; N, 3.67. Founded: C, 69.20; H, 6.30; N, 3.75.
compound (17) as a white solid crystals. (0.075 g, 51%): R_f, 0.45 (dichloromethane: ethanol 8:2); mp 172 ^{0}
H^1NMR: (Data) in δ Delta (ppm) : 7.12-7.55(6H, m, ,aromatic indole) 7.66 (6H, m, H-arom), 3.45 (2H, tt, 2′-H_a, 2′- H_b), 3.63 (1H, mm, 5'-H), 3.92 (1H, dd, 1'-H), 3.95-3.99 (2H, dd, 6'-H_a , 6'-H_b) ,4.88 (1H, dd, 4'-H), 3.11 (2H, ss, 2-OH), 10.42 (1H, s, COOH), 4.22 (1H, s, NHarom); ^{13}C-NMR (Data) in δ Delta (ppm) : 28.55 (C-3'), 26.66 (C-2') 76.88-77.86 (C-4', C-5' and C-1'), 66.95 (C-6'), 183.25 (COOH), 35.8, 37.6 (C-N), and 128.56 – 147 (C-aromatic)
Analyt. Calcd. to the $C_{21}H_{21}N_2O_7$(17): C, 61.02; H, 5.09; N, 6.78 Founded: C, 61.42; H, 5.05; N, 6.63.

3:10 6-*N,N*-Dimethylamino-9-(2′,3′)-Dideoxye--3′-*C*-3-benzylamine-β-*D*-arabino- hexopyranosonic acid) purine (18) and 6-*N,N*-Dimethylamino-9-(2′,3′)-Dideoxye--3′-*C*-3-p-nitroaniline-β-*D*-arabino-hexopyranosonic acid) purine (19) (Rosenthal , Baker 1973)
A mixtures of (0.75 g, 1 mmole) of compounds (6) and (0.35 g, 1.01 mmole) of 6-chloropurine was heated at (158°, 0.4 bar) in oil bath for about 5 min. then follow by other

further heating at (158°, 0.4 bar) to 42 min. all melts was extracte with (3×25 cm^3) of DCM and the solution was extract. The extracted was evaporation and filtrate to gave a residue which was separations by column chromatographe on 50 gm of silicai grades II usings (4:2 C_6H_6-$CH_3COOC_2H_5$) as developers and crystallization the sold in ethanol to become (0.63 g, 69.2%) of nucleotides, then dissolve in anhydrous dimethyle amine (45 cm^3) and store in -9 ° at 30 days, then evaporate dimethyle amine and dissolve in ether (20 cm^3) after decante in ethanole and allow to stands in 0° at 30 hr. to crystallize nucleotides by chromatographic of mothers liquors on columns of thin layer chromatography silicai gels using C_2H_5OH-DCM (1:9) recrystallization of nucleotides in ethanole to gave pure compound (0.065g, 70.2%) as a pale yellow crystal.: R_f, 0.45 (DCM: EtOH 9:1); mp 152 ^{0}C and (17) as a paly yellow crystals. (0.091 g, 62%): R_f, 0.35 (DCM: EtOH 9:1); mp 165 ^{0}C

H^1NMR: (Data) in δ Delta (ppm) : 1.77 (6H, s, $N(CH_3)_2$, 7.565 (7H, m, H-arom), 3.533 (2H, tt, 2'-H_a, 2'- H_b), 3.682 (1H, mm, 5'-H), 3.722 (1H, dd, 1'-H), 3.76-3.85 (2H, dd, 6'-H_a , 6'-H_b) ,4.67 (1H, dd, 4'-H), 3.23 (2H, ss, 2-OH), 11.34 (1H, s, COOH), 4.225 (1H, s, $NHCH_2$); ^{13}C-NMR (Data) in δ Delta (ppm) : 27.65 (C-3'), 30.99 (C-2') 75.18-76.58 (C-4', C-5' and C-1'), 65.81 (C-6'), 188.44 (COOH), 35.6, 37.8 $(CH_3)_2$N), 144.22 and 145.8 (C-4, C-5),

Analyt. Calcd. to the $C_{21}H_{26}N_6O_5$(18): C, 57.01; H, 5.88; N, 19.00. Founded: C, 57.12; H, 5.56; N, 18.86

H^1NMR: (Data) in δ Delta (ppm) : 1.55 (6H, s, $N(CH_3)_2$, 7.46 (7H, m, H-arom), 3.223 (2H, tt, 2'-H_a, 2'- H_b), 3.872 (1H, mm, 5'-H), 3.447 (1H, dd, 1'-H), 3.22-3.708 (2H, dd, 6'-H_a, 6'-H_b), 4.77 (1H, dd, 4'-H), 3.55 (2H, ss, 2-OH), 10.44 (1H, s, COOH), 4.47 (1H, s, NHarom); ^{13}C-NMR (Data) in δ Delta (ppm) : 28.44 (C-3'), 29.88 (C-2') 74.75-77.65 (C-4', C-5' and C-1'), 66.85 (C-6'), 182.45 (COOH), 72.55 (C-NO_2), 35.34, 37.5 $(CH_3)_2$ N-), 147.22 and 148.65 (C-4, C-5),

Analyt. Calcd. to the $C_{20}H_{23}N_6O_7$(19): C, 52.29; H, 5.01; N, 18.30. Founded: C, 52.62; H, 5.32; N, 18.22.

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