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Synthesis of New Nucleoside Analogues From Benzimidazole and Evaluation of Their Antimicrobial Activity

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Abstract:

Our goal in this research, some new nucleoside analogues was synthesized. Starting from ∝-*D* glucose which was converted to per acetylated *β-D* gluco pyronoside then converted to active from(1-Bromo Sugar (2) as a sugar moiety.The base moiety 2-substituted benzimidazole was prepared from condensation of phenylene diamine with different aromatic aldehydes, which were subjected to amino alkylation via Mannich reaction forming new nucleobase derivatives.

Condensation of nucleobase with bromo sugar through nucleophilic substitution of anomeric carbon with nitrogen forming new protected nucleoside analogues then hydrolyzed with sodium methoxide in methanol to obtain our target, the free nucleoside analogues.

All prepared compound were identified by FT-IR Spectroscopy and some of them with H^1 –NMR and C^{13}-NMR Spectroscopy.

The synthesized nucleoside analogues were screened for their antibacterial activity in vitro against four types of bacteria including, *Bacillus Staphylococcus, aureus* (Gram Positive), *E.Coli and Pseudoman* as (Gram Negative).Also were screened against four types of Fungi (*Aspergines flurs, Aspergillus fumgntnts, Aspergillus niger and pencillum)*.

Key words: Nucloside analogues, Benzimidazole

Introduction:

Nucleoside analogues have proven to be a highly successful class of anti-viral[1], anti-cancer,anti-tumerand chemotherpeutic agent[2].

At the last decads, Nucleosides have six-membered carbohydrate moiety have been evaluated for their potential antiviral[3], and antibiotic properties, also as building block in nucleic acid Synthesis[4]. Nucleosides are large class of agents that include drugs for several diseases.

The Synthesis and development of glycosidase inhibitors have been the focus of attention, because of their vital role played by carbohydrates invairety of biological processes.

Benzimidazole ring is an important pharmaccophore in modern drug discover [5], compounds that exhibit

functionality of benzimidazole and Its derivatives have been used in the area of pharmaceutical[6], these good and high profile applications of compound with benzimidazoles structures have prompted extensive studies for their method of synthesis. Modifications of the benzimidazole ring System that have made the studies of anthelmintic activity have provided [7]. The most active drugs for anti-cancer, anticoagulant [8], anti-viral [9], anti-inflammatory, anti-hypertensive and anti-tumor [10].

Based on the above significances, our research focus on synthesis of new nucleoside analogues containing 2-substituted benzimidazole as anucleobase through Mannich base [11].

Materials and Methods:

The quality of all these chemical supplied from BDH England, and Fluga Merk,Pure materials used without purification.

Experimental instruments:

Melting points were recorded by Gallen Kamp, England, Melting point apparatus and were uncorrected. Infrared spectra were recorded using SHMADZU,FT-IR.$8400_{(S)}$ Spectrophotometer (Japan) as a thin film or KBr disk. ^{1}H-NMR and ^{13}C-NMR spectra were recorded with the help of ultra-high field 400 MHZ Avance III400 Bruker, Germany. At isfhon-University, Using Me_4Si as the internal standard and DMSO-d_6 as a solvent, and was appeared at 2.5 PPM in ^{1}H-NMR AND 40.45 in ^{13}C-NMR spectrum. TLC plates were used with an aluminum backing (0.2mm, 60 F_{254}).

Preparation of β -D- glucose penta acetate [12]

∝ -D- glucose (1g,0.0055 mole) and (0.8g,0.00975 mole) of unhydrouse sodium acetate was dissolved in (6 ml) acetic anhydride then refluxed on water bath with stirring for (2h), then pour the reaction mixture on to (50 ml) of ice – cold. Filtered and recrystallized from ethanol to afford compound (1) as a white crystal.

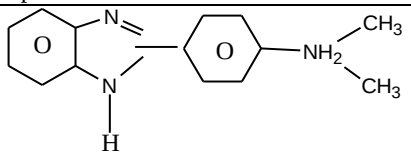
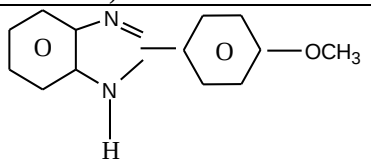
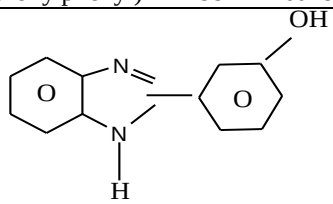
Synthesis of 1- bromo acetylated sugar [13].

The acetylated sugar (0.380 g, 1.08 m mole) was dissolved in (3ml) of (50%) hydrogen bromide in glacial acetic acid which was added at (0 °C). the solution was kept at (0 °C) for one hour, and finally at room temperature for (15) min. washed with ice – water (2x 15 ml) and then with saturated aqueous solutions of sodium bicarbonate to remove the remaining acid. After finial wash with ice – water (20 ml), the organic phase was dried over $MgSO_4$ and solvent was removed to give compound (2) as a syrup. The isolated sugar bromide (2) was used directly for the nucleoside synthesis.

General method for synthesis of 2-Substituted phenyl .1.H. benzimidazole (3-5) [13].

A mixture of substituted aromatic aldehyde (0.01 mole) and (1.08 (g) .0.01 mole) of ∘-phenylendiamine in (4 mL) DMF for (4 h) using (0.312 g, 0.01 mole) $NaHSO_3$ as ring closing agent. The precipitate obtained after cooling recrystallized from DMF.

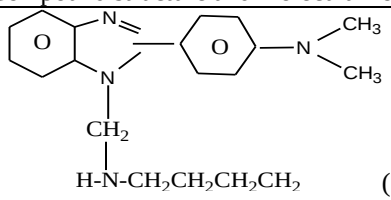
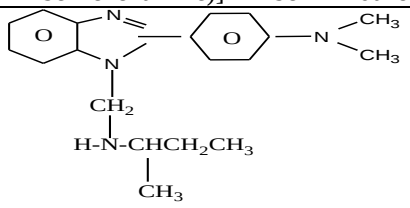
Table (1) physical properties of compound(3-5)

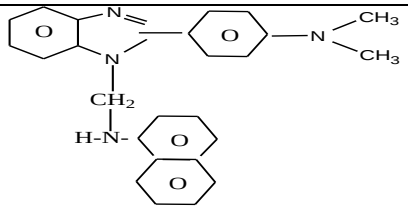
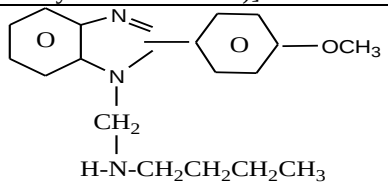
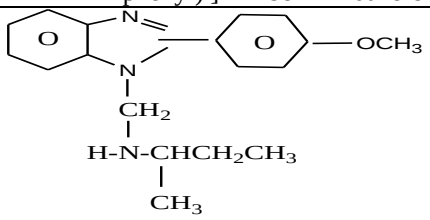
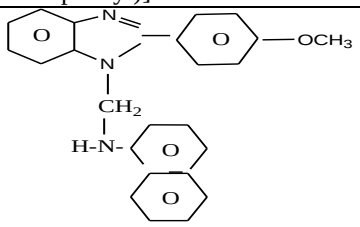
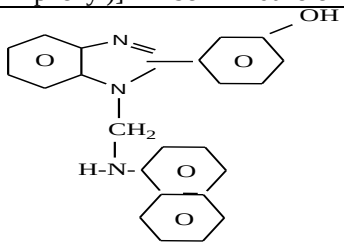
Comp. No.	Compound structure and molecular formula	M.P °C	Color	Yield
3	 2(N,N dimethyl benzene amine)1H- benzimidazole (237)	Dec. 180-182	Pale yellow	48%
4	 2(4-methoxy phenyl) 1H- benzimidazole (224)	190--192	Pale Gray	46%
5	 2(3-hydroxy phenyl) 1H- benzimidazole(210)	194-196	Pale green	95%

General procedure for synthesis of Mannish bases (6-12) [14].

To a solution of benzimidazole derivatives, (0.0054) in methanol (10 mL) and (1 mL)of 5% diluted HCl. The primary amine (0.0054 mole) and (0.3186 g, 0.0054 mole), formaldehyde were added, then refluxed on water bath (3h). The product formed after cooling. Then filtered, dried over anhydrous sodium sulphate and the solvent was removed to give the Mannich product (6-12).

Table (2) physical properties of compound (6-12)

Comp. No.	Compound structure and molecular formula	M.P °C	Color	Yield
6	 1-[Methylene-N-1-butyl-2-(4-N,N dimethyl benzene amine)]1H- benzimidazole (322)	Dec. 223	White	48%
7	 $C_{20}H_{26}N_4$ 1-[Methyenel-N-2-butyl amine-2-(4-N,N dimethyl benzene amine)]1H- benzimidazole (322)	210-213	Pale Brown	61%

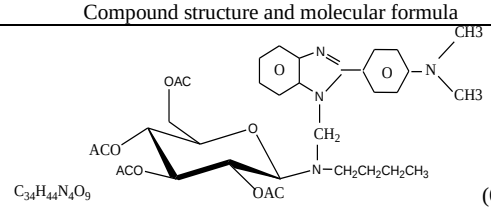
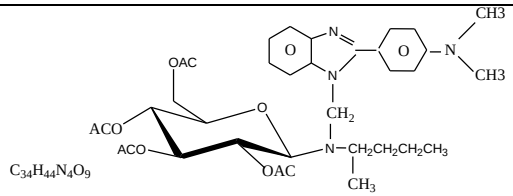
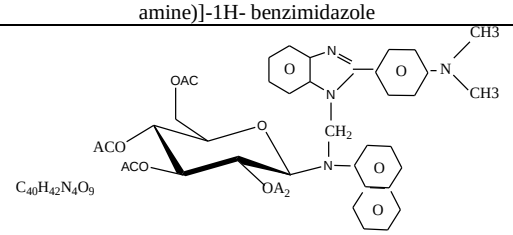
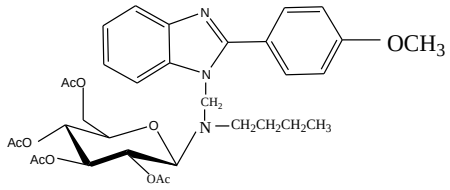
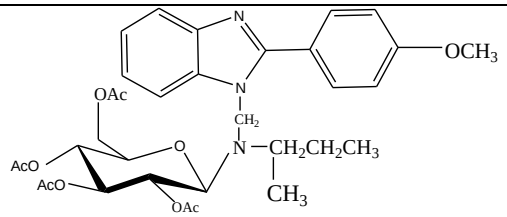
8	 $C_{26}H_{24}N_4$ (392) 1-[Methylene-N-1-Naphthyl amine 2-(4-N,N-dimethyl benzene amine)]1H- benzimidazole	Dec. 281	Pale Pinkie	93.3%
9	 $C_{14}H_{23}N_3O$ (309) [Methylene l-N-1- butyl amine] 2(4-methoxy phenyl)]1H- benzimidazole	Dec. 200	Off-White	34%
10	 $C_{19}H_{23}N_3O$ (309) 1-[Methylene-N-2- butyl] -2-(4-methoxy phenyl)]1H- benzimidazole	196-194	Farbe Grau	37%
11	 $C_{25}H_{21}N_3O$ (379) 1-[Methylene-N-1- naphthyl amine -2-(4-methoxy phenyl)]1H- benzimidazole	Dec. 234	Purple	75%
12	 $C_{25}H_{21}N_3O$ (365) 1-[Methylene-N-1- naphthyl amine 2-(3-hydroxy phenyl)]1H- benzimidazole	160-162	purple	62.2%

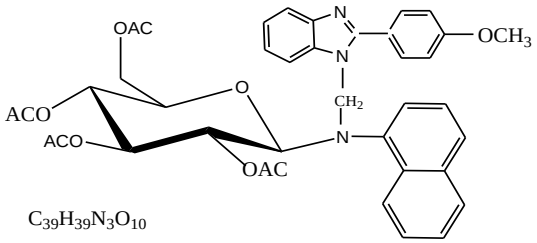
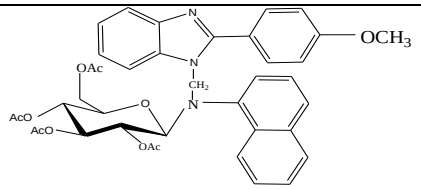
General procedure for synthesis of protected nucleoside analogues (13-9) [15]

Mannich base (0.00098 mole) (11-16) was finally powdered and suspended in (25 ml) dried *O*- xylen, and the solvent was practically distilled off to remove trace of the water. When the temperature of the mixture was raised to 137°C. The residual suspension allowed cool below (50°C). The acetylated sugar bromide (0.00098

mole) was dissolved in dried xylen, then added to the Mannich base solution and refluxed with vigor's stirring for (1h). The organic layer was washed (2➡5 ml) with water and dried over anhydrous Sodium sulphate. The solvent was removed to give the acetylated nucleoside as a syrup (13-19).

Table (3) physical properties of compound (13-19)

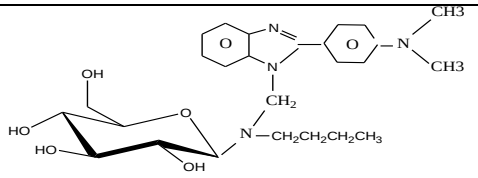
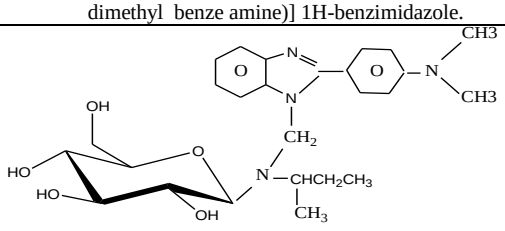
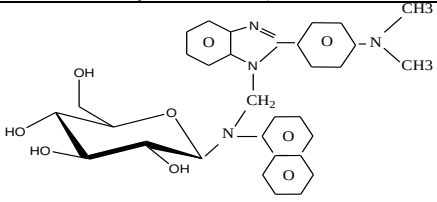
Comp. No.	Compound structure and molecular formula	M.p °C	color	yield
13	 $C_{34}H_{44}N_4O_9$ (652) 1-[Methylene-N-(2',3',5',6tetra-*O*- acetyl-*B*- gluco pyronosyl amine)-2-(4-N,N-dimethyl benzene amine)]-1H-benzimidazole	Dec 182	gray	72%
14	 $C_{34}H_{44}N_4O_9$ (652) 1-[Methylene -N-2-butyl-N-(2',3',4',6'-tetra-*O*- acetyl(-*B*-*D*-gluco pyronosyl amine)-2-(4-N,N-dimethyl benzene amine)]-1H- benzimidazole	Dec 182	gray	72%
15	 $C_{40}H_{42}N_4O_9$ (652) 1-[Methylene -N-1-naphthyl-N-(2',3',4',6' -tetra-*O*- acetyl-*B*-*D*- gluco pyronosyl amine)-2(-4-N,N-dimethyl benzene amine)]-1H- benzimidazole	166-168	Off-white	78%
16	 $C_{33}H_{41}N_3O_{10}$ (639) 1-[methyenel-N-1-butyl-N-(2',3',4',6'-tetra-*O*- acetyl-*B*-*D*-gluco pyronosyl amine)-2(-methoxy phenyl)]1H-benzimidazole	syrap	Deep orange	65-67%
17	 $C_{33}H_{41}N_3O_{10}$ (639) 1-[Methylene-N-1-butyl-N-(2',3',4',6'-tetra-*O*- acetyl-*B*-*D*-gluco pyronosyl) amine-2(-methoxy phenyl)]1H-benzimidazole	syrap	orange	65-67%

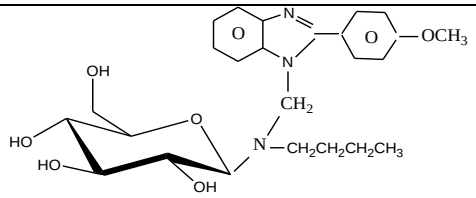
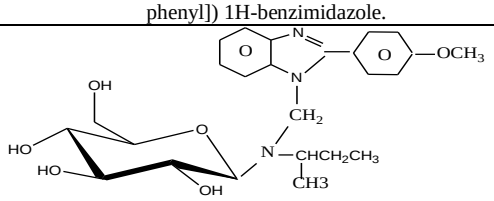
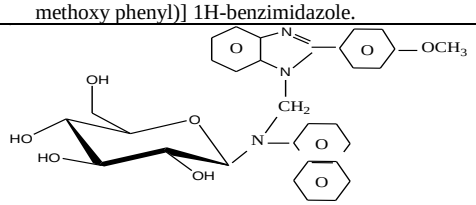
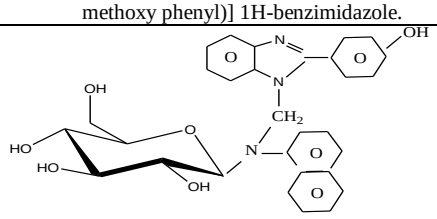
18	 $C_{39}H_{39}N_3O_{10}$ [Methylene-N-1- naphthyl -N-(2', 3', 5', 6' -tetra-*O*- acetyl- β -*D*-gluco pyronosyl amine)-2-(4-methoxy phenyl)]1-H benzimidazole	Dec. 158	brown	56%
19	 $C_{38}H_{37}N_3O_{10}$ (456) 1-[Methylene -N-1- naphthyl -N-(2',3',5',6' -tetra-*O*- acetyl-*B-D*- gluco pyronosyl amine)-2-(3- Methoxy phenyl)]1H-benzimidazole	160-162	purple	62.2%

General procedure for hydrolysis of nucleoside analogues (20-26) [16]

A solutuin of (0.00026 mole) of the blocked nucleoside analogues in (7 ml) of (0.1m) methanolic sodium methoxide was refluxed with stirring for (0.5 h).The mixture was neutralized with acetic acid and evaporated to dryness. The aqueous phase evaporated to dryness under vacuum ,to obtain free nucleoside (20-26).

Table (4) physical properties of compound (20-26)

Comp. No	Compound structure and molecular formula	M.p °C	Color	Yield %
20	 $C_{26}H_{36}N_4O_5$ (484) 1-[Methylene-N-1-butyl-N-*(B-D*-gluco pyranosy l amine)-2-(4-N,N dimethyl benze amine)] 1H-benzimidazole.	80-82	Reddish brown	70%
21	 $C_{26}H_{36}N_4O_5$ (484) 1-[Methylene-N-2-butyl-N-(*B-D*-gluco pyranosyl amine)-2-(4,N,N dimethyl benze amine)] 1H-benzimidazole.	Syrup	white	72%
22	 $C_{32}H_{34}N_4O_5$ (554) 1-[Methylene-N-1-naphthyl-N-(*B-D*-gluco pyranosyl amine)-2-(4,N,N dimethyl benze amine)] 1H-benzimidazole	118-120	Deep pink	75%

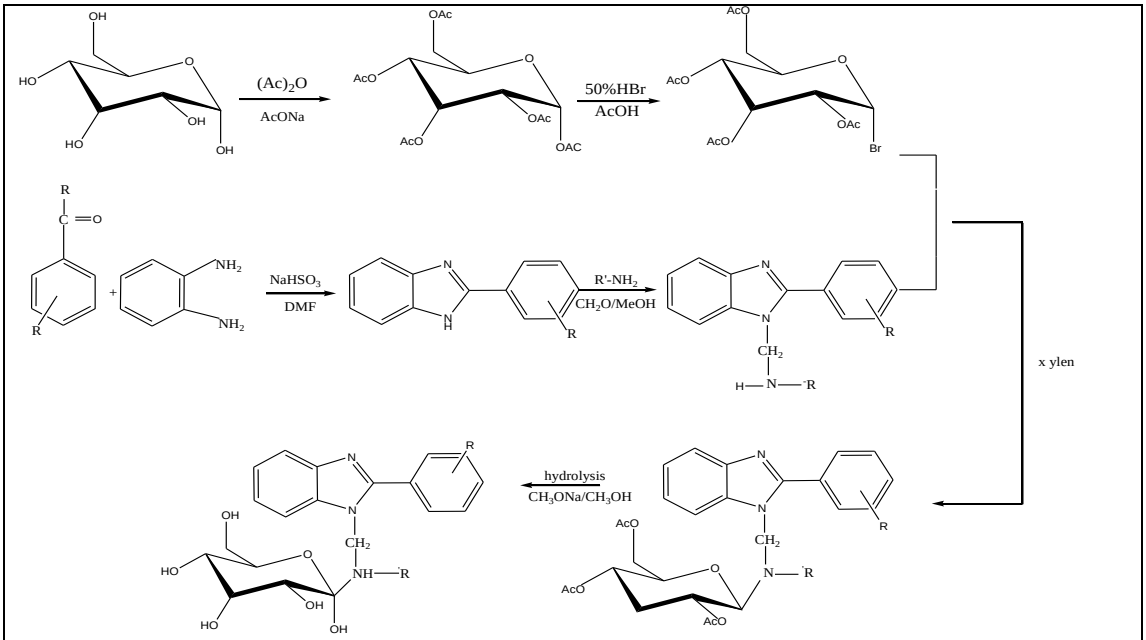
23	 $C_{25}H_{33}N_3O_6$ (471) 1-[Methylene-N-1- butyl-N-(B-D-glucopyranosyl amine)-2-(4- methoxy phenyl]) 1H-benzimidazole.	Dec. 226	Off white	75%
24	 $C_{25}H_{33}N_3O_6$ (471) 1- [Methylene-N-2- butyl-N-*B-D*-gluco pyranosyl amine)-2(4-methoxy phenyl)] 1H-benzimidazole.	Syrup	white	66%
25	 $C_{31}H_{31}N_3O_6$ (541) 1-[Methyenel-N-1- naphthyl-N-[(*B-D*-gluco pyranosyl amine)-2-(4-methoxy phenyl)] 1H-benzimidazole.	Dec. 158	Brown	56%
26	 $C_{30}H_{29}N_3O_6$ (527) 1-[methyl-N-1 Naphthyl-N- (*B-D*-gluco pyranosyl amine)-2(3-hydroxy Phenyl)] 1H-benzimidazole.	Dec. 220	Off-white	62%

Biological activity

This test was performed by the disk diffusion method. Nutrient agar was added to (1L) of distilled water in suitable conical flask with stirring and heating unite complete dissolving then the disk was stoppered by cotton and the medium was sterilized in an autoclave for (20) minutes at (121) °C under pressure at (15) pound inch. The medium was placed in an-petridises about (20) mL for catch one was left to cool and solid filed. Agar plates was surface inculcated uniformly with 600 mL from both culture of tested microorganism. The impregnated disk were placed on the medium suitably spaced apart and the plates incubated at (5°C) for (1 h) to permit good diffusion and then transferred to an incubator at (37) °C for (24 h) for bacteria and (72 h) for fungi. The inhibition zones caused by virus compounds on the microorganisms were examined.

Results and Discussion:

The most common modification of nucleosides represent on important of medicinal compounds which have been found to behave as another agent and are currently used pharmaceuticals as antitumor, antiviral and antibiotics agents. Thus our target is to synthesize a new modified nucleoside analogues.



R:4-N$(CH_3)_2$,3-OH,4-OCH_3
R':1-butyl,2-butyl,1-naphtyl

Scheme (1) synthetic route for synthesis of nucleoside analogues.

Table (5) FT-IR data cm^{-1} for compounds (3-26)

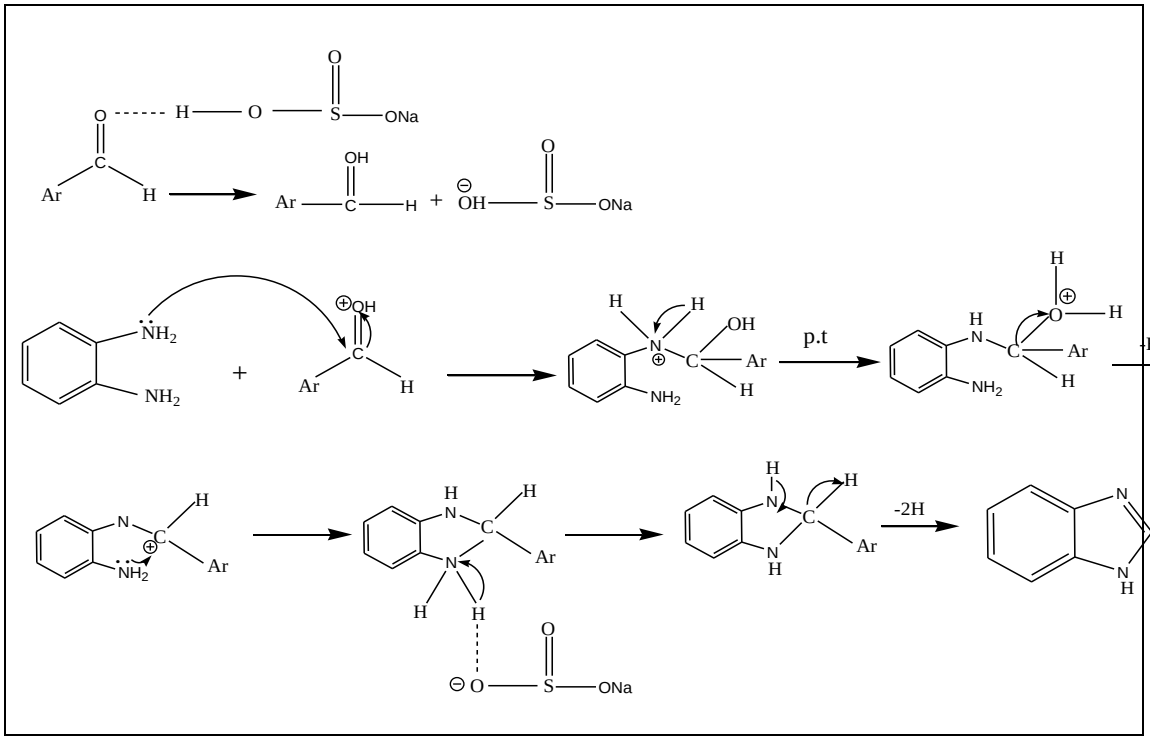
Comp No.	V(O-H)	V(N-H)	V(C-H)	V(C-H) aromatic	V(C=N) Aliphatic	V(C=C) aromatic	V(C=O)	Others
3		3460	3051	2914	1676	1610		
4		3400	3055	2962	1681	1610		C-O-C 12012
5	3440	3226	3051	-	1660	1583		
6		3428	3047	2954	1606	1512		C-N 1373
7		3402	3049	2920	1608	1512		C-N 1373
8		3371-3400	3110	2914	1606	1517		
9		3430	3051-3070	2885-2966	1610	1583		C-O-C 1218
10		3419	3079	2929-2958	1610	1500		C-N 1317
11		3325	3056	2926	1608-1629	1508		C-N-C 1305
12	3444	3326	3049	2931	1654	1581		
13			3054	2911	1600	1514	1697	C-N 1373
14			3014	2920	1610	1490	1755	C-N-C 1375
15			3114	2920	1612	1490	1755	C-O 1093
16	3340 Broad		3010	2923	1604	1454	1703	C-N 1348
17	-		3064	2925	1608	1575	1685	
18			3016	2920	1654	1515	1724	
19	3421	-	3016	2920	1654	1581	1755	
20	3431		3065	2925-2983	1650	1458		
21	3438		3109	2923	1612	1569		
22	3421		3058	2923	1598	1562		
23	3429		3000	2931	1573	1419		
24	3434		3003	2931-2958	1610	1458		
25	3386		3060	2921	1600	1515		
26	2423		3010	2900	1573	1411		

The synthetic rout was started with *D*-glucose as a sugar moiety and a new benzimidazole derivatives containing Mannich base as a base moiety, in a series of reaction steps. Scheme 1.

D-glucose was protected with acetic anhydride in the presence of sodium acetate afforded *B*-*D*-glucose penta acetate (1) which was brominated using hydrogen bromide in glacial acetic to give acetylated sugar bromide (2). Compounds (1 and 2) were confirmed by their physical properties due to the literature.

The FT-IR spectrum of compounds (1) showed several characteristic bands mainly the stretching band of carbonyl of acetyl group at 1744 cm^{-1} while compound (2) showed in addition to the carbonyl band the appearance of (C- Br) band at 780 $cm^{-1.}$

On the other band benzimidazole is an important pharacophore due to its biological activities (18,19) , therefore, it was chosen as anucleobase, which was synthesized by condensation of phenylenediamine with substituted benzaldehyde using sodium with hydrogen sulfite as ring closing agent, according to the suggest mechanism showed in Scheme(2)



Scheme(2) suggested mechanism of 2-substituted 1H- benzimidazol formation

Physical properties of the prepared compounds (3-5) the FT-IR are listed in Table (3-5) showed a stretching bands between (3226-3460) for amine in additional to amino group the stretching band at (3440) cm^{-1} for phenolic hydroxyl group to compound (5).

The FT-IR spectrum for compounds (6-12) Mannich bases in Table (5) showed stretching bands between (3199-3430) cm^{-1} for amine group, while compound (12) in addition to the amine showed stretching band at (3440) cm^{-1} for OH phenolic, all these data are listed in Table (5).

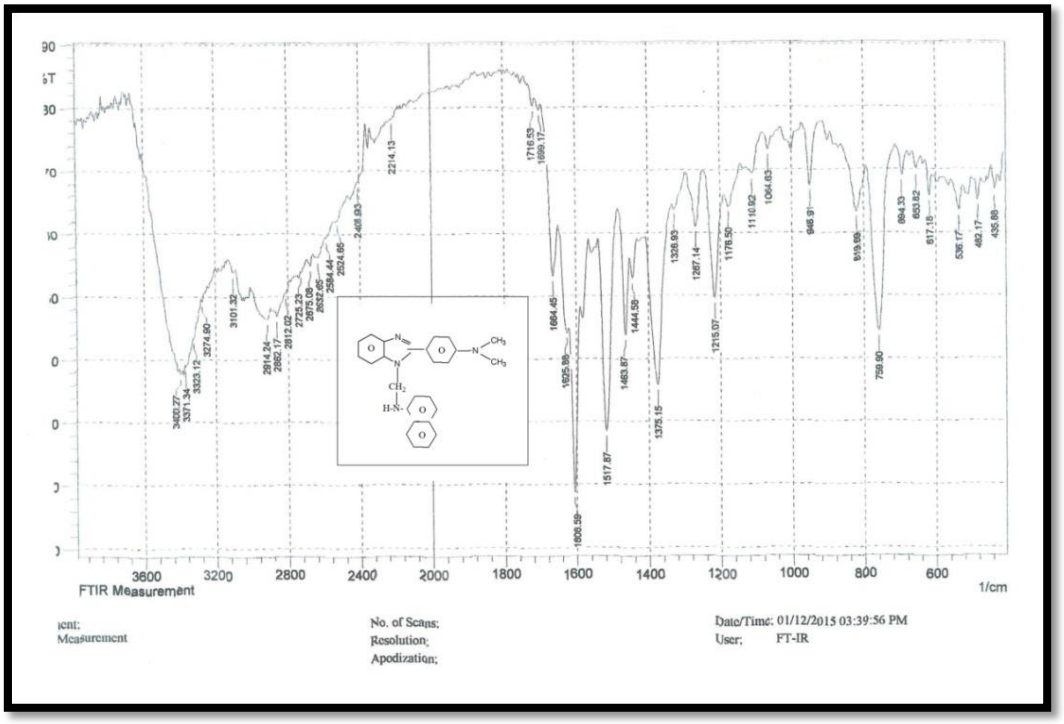


Fig.(1): FT-IR spectrum for compound (8)

To achieve our synthesis target nucleoside analogues, the 1- bromo sugar (2) was coupled with modified nucleobase (6-12) afforded the new blocked nucleoside(13-19)the FT-IR spectrum of compounds (13-19). Table (3) shows the characteristic bands at (1573-1654) for ν (C=N) further evidence is the appearance of carbonyl absorbance at (1685-1755) also disappeared band at (3226-4460) cm^{-1} for N-H (3340-3421) cm^{-1} respectively for compound 16 and 19 due to (OH) phenolic group .

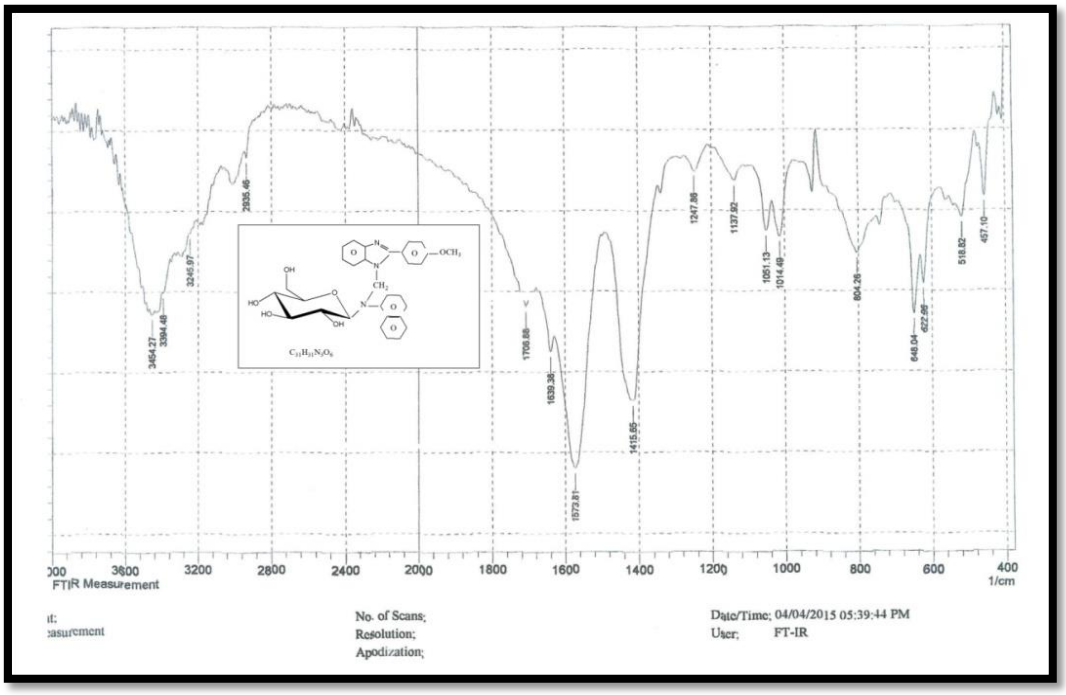


Fig. (2): FT-IR spectrum for compound (25)

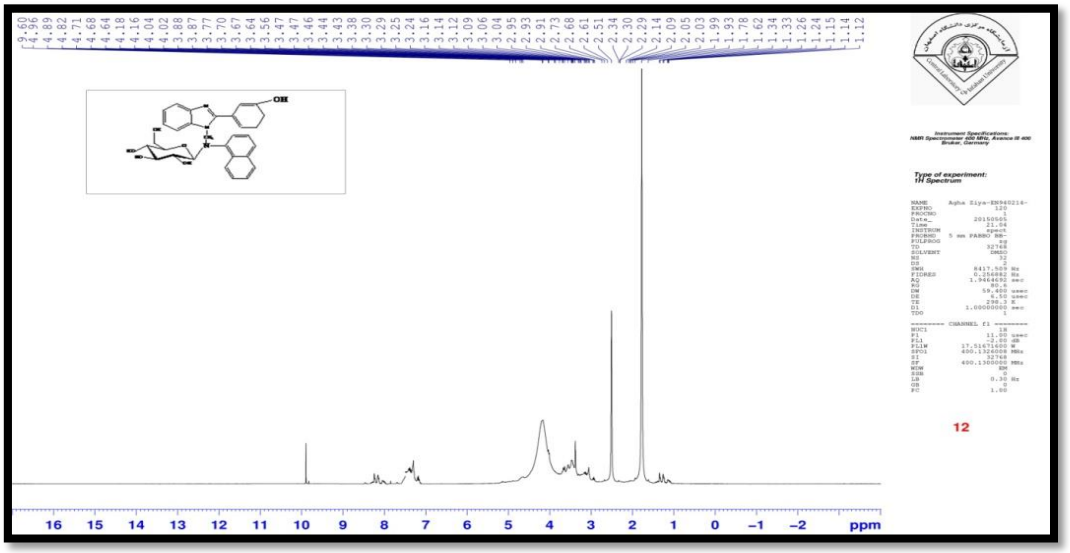


Fig. (3): ^{1}H-NMR spectrum for compound (26)

To achieve our synthetic target, the free nucleoside analogues (20-26) Table (4) were de blocked with methanolic sodium methoxide to afford our synthetic goal the free nucleoside analogues.

The FT-IR of free nucleoside analogues (20-26) showed in addition of the above bands, the disappearance of carbonyl bands and appearance of hydroxyl bands between (3386-3434) cm^{-1} which is a good evidence for hydrolysis of blocked nucleosides Figure(1,2).

The ^{1}H-NMR spectrum of compound (15) showed a singlet signal at (2.0-2.09) ppm (4S, 12H) for 4 CH_3 acetyl proton; also showed a singlet signal at (2.29) ppm for (6H) CH_3-N (two methyl group); and (3.71-3.78) ppm doublet belong to d, 2H, H_6^1 , $H_6^=$sugar protons; while the singlet singal at (4.5) PPM refers to δ 2H methylene CH_2-N protons; multiplet at 4.71-5.37 ppm assigned to (4H,H_5^-,H_4^-,H_3^-, H_2^-sugar protons. While doublet a signal appeared at (6.0-6.01) for 1H H_1^- sugar protons and multiplet at (6.9-8.9) PPM refers to (15 H aromatic protons.

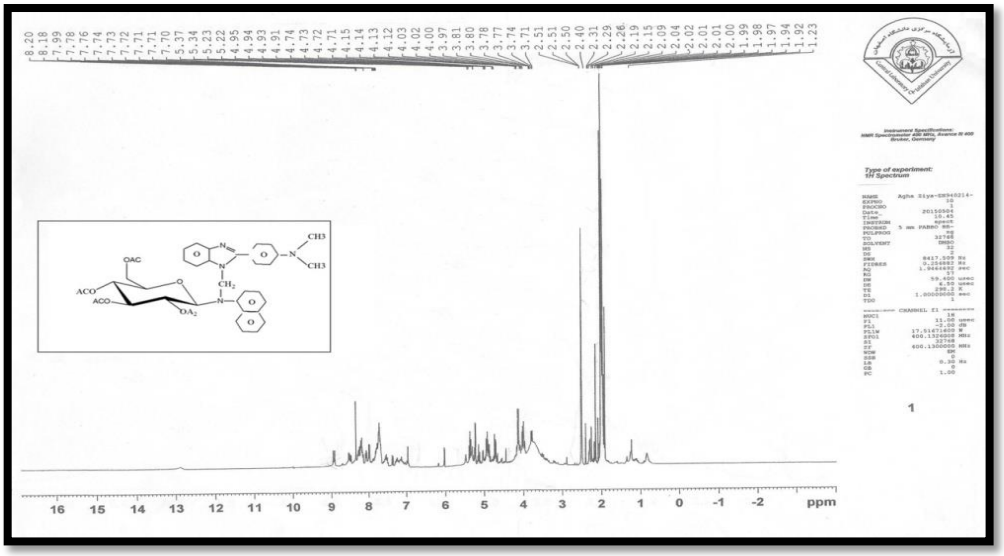
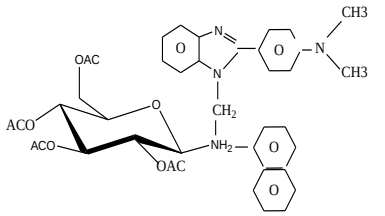
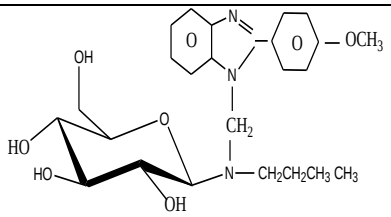
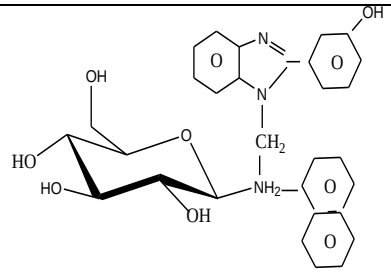


Fig. (4): ^{1}H-NMR spectrum for compound (15)

Table(6):^{1}H-NMR spectra data for compounds (15,23 and 26) in δ ppm

Comp. no.	Compound structure	H-NMR spectral data (⇦ppm)
15		2.0-2.09(s,12H,4CH_3actyal) ;2.24(s,6H,2CH_3-N); 3.71-3.78(d ,2H,H_6^- ,$H_6^=$ sugar) ; 4.5(s,2H,N-CH_2-N) ;4.71-5.37(m,4H,H_5^- ,H_4^- , ,H_3^- , ,H_2^- , sugar protons) ; 6.0-6.01(d,1H, ,H_1^-);6.9-8.9 (m,15H aromatic)
23		1.08-1.1(t,3H,CH_3 CH_2) ; 1.23-1.26(m,2H,CH_3 CH_2) 1.33-1.39(m,2H,CH_2 CH_2 CH_2); 2.33-2.34(t,2H,N-CH_2-CH_2) ; 3.4(3.4(s,4H,OH hydroxy sugar protons; 4.41-4.42 (d,2H, ,H_6^-, ,$H_6^=$ sugar); 4.84 (s,3H,OCH_3)4.67-4.75 (m,4H, ,H_5^-, ,H_4^-, ,H_3^-, ,H_2^- sugar protons) 5.01 (s,2H,N-CH_2-N; 5.12-5.13(d11H, ,H_1^-)
26		3.1-3.2(D,2H, ,H_6^- , ,$H_6^=$ sugar protons); (3.3 -3.7 s 4H 4OH); 3.8 (s-2H CH_2-N . (3.71-4.22 m 5H ,H_5^-,H_4^-, ,H_3^-, ,H_2^-, ,H_1^- sugar protons;(7.1-8.6) m 15 H aromatic protons.

The ^{1}H-NMR spectrum of compound (23) showed the appearance triplet at (1.08-1.1) for 3H CH_3 methyl protons belong to CH_3-CH_2 (1.23-1.26) ppm signal assigned to multiplet a signal for 2H CH_3CH_2; multiplet signal at (1.33-1.39) ppm refers to methylene protons (CH_2-CH_2-CH_2); Also triplet 2H for methylene protons (N-CH_2-CH_2); A singlet signal at (3.4) ppm for (4H, 4OH) sugar protons; while double signal appeared at (4.67-4.75) that belong to 2H, H_6^- , $H_6^=$, sugar); singlet signal appeared at (4.48) ppm for (3H, OCH_3 protons); sugar protons (m, 4H, H_5^-, H_4^-, H_3^-, H_2^-) appeared at (4.67-4.75) ppm. A singlet signal appeared at (5.01) ppm for methylene protons (N-CH_2-N); signal appeared at 5.12-5.13 ppm belong toH_1^-, and multiplet asignal at 7.01-8.9 ppm refers to (8H) aromatic proton.

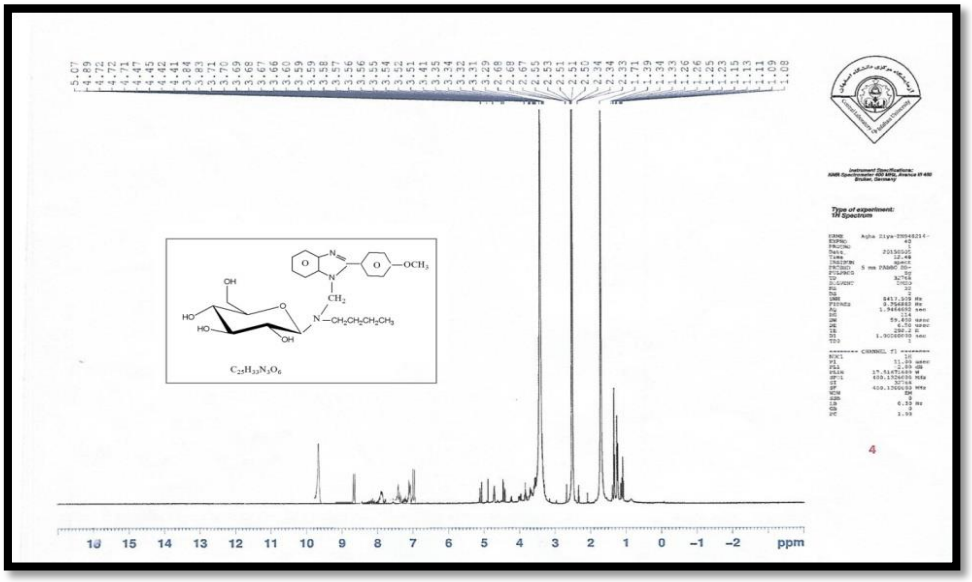
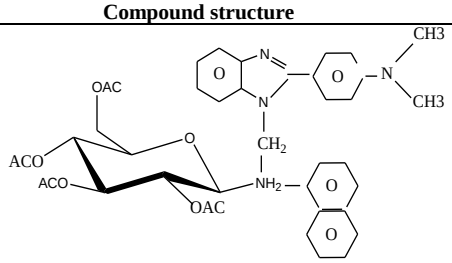
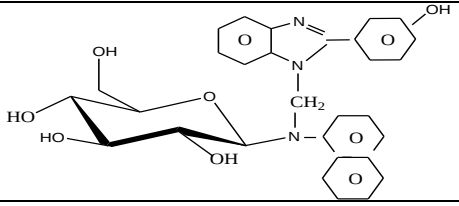


Fig (5): ^{1}HNMRspectrum of compound (23)

confirmed also by ^{1}H-NMR spectrum showed doublet signals at (3.1-3.2) ppm (d 2H H_6^-,$H_6^=$) sugar protons; while singlate signale at (3.3 -3.7 δ, 4H,4OH); singlete signal showed at (3.8 2H CH_2-N) for methylene protons; while (3.7-4.22 m 5H H_5^-,H_4^-, H_3^-, H_2^-,H_1^-) sugar protons; (7.1-8.6) ppm multiplet signals for (15H) Aromatic protons; (9.8) ppm singlet signal refers to OH phenolic proton Figure(3-5).

Table (7) ^{13}C-NMR spectra data for compound (15, 26) in δ PPM.

Comp no	Compound structure	^{B}C-NMR Spectra data sppm
15		20.27-20.60(4C,4CH_3acety); 20.7820.99 (2C, CH_3N); 66.2 (1C,C_6 sugar); 68.4-79.17(4C C_5, C_4, C_3, C_2 Sugar carbons); 90.9(1C,C_1 sugar; 93 (1C,N-CN); 121-130(22C,aromatic; 169.3 -169.63 (4C, carbonyl); 170.01(1C imidazole)
26		55.87-56.2 (1C, C'$_6$ sugar); 60.95-69.94 (4C, C'$_5$, C'$_4$, C'$_3$, C'$_2$ sugar); 103.87 1C, ethylene (N-CH_2-N); 116.4-133.4 22C aromatic)(173.91 1C imidazole)

The ^{13}C – NMR Spectra of compound (15), showed 20.27 – 20.60 ppm belong to 4C, 4CH_3 for acetyl; signal at 20.78 – 20.99 ppm refers to two carbons methyl groups (2C, 2CH_3-N): 66.2 ppm belong to (1C, C_6 sugar): 93.66 ppm singal refers to methylene carbons (1C N-CH_2-N): also 121-130 ppm assigned to 22 C aromatic carbons: 169.3 – 169.63 ppm assigned to (4C belong to 4C carbonyl group); and 170.01 ppm belong to (1C, imidazole).

The ^{13}C- NMR spectrum of compound (26) showed signal at 55.87 – 56.2 ppm belong to (1C',C_6, sugar cabron): 60.95-69.94 ppm refers to (4C,

C_5^- , C_4^- , C_3^- , C_2^-) sugar cabons: so 103.87 PPM refers to methyene carbon (N-CH_2-N) .
While 116.4-133.4 ppm belong to (22 C) aromatic carbons: and asignal 173.91 ppm assigned to (1C) imidazle.The disappeared of carbonyl signal (give good evidence for hydrolysis of blocked nucleoside analogues) Figure(6).

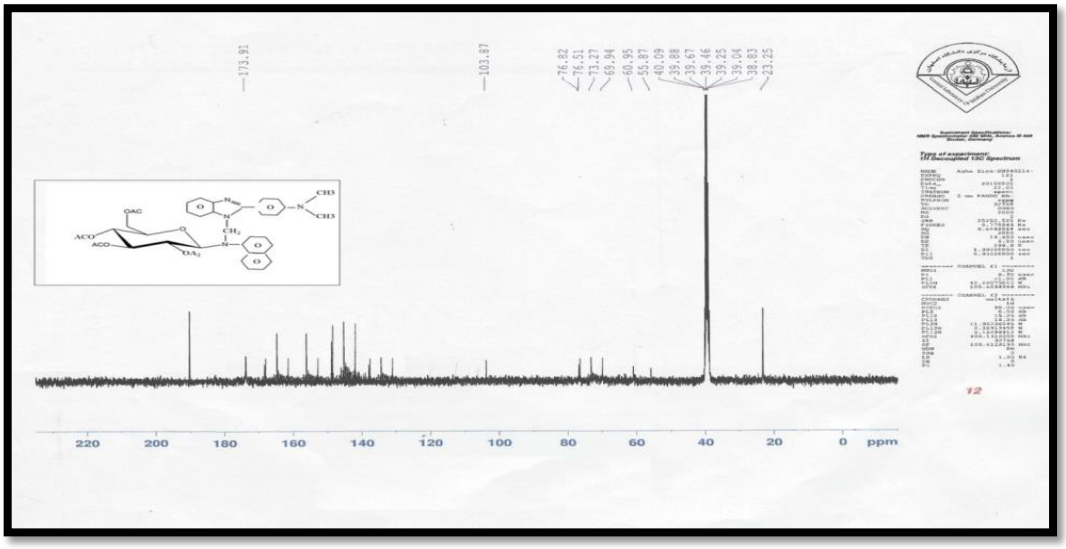


Fig. (6) C^{13}- NMR spectrum of compound (15)

Table (8): inhibition zones for compound (22,24,26)

Comp. no.	Gram positive Bacillus subtilis Staphlylossccus aurea		Gram negative E. coli Pseudomonas aeruginosa		spergins flursA	Aspergillus fumgntnts	Aspergills niger	pencillum
Control DMSO	-	-	-	-	-	-	-	-
22	10	-	-	-	-	-	-	-
24	10	-	-	-	-	-	-	-
26	14	-	9	9	-	-	-	-

Microbiological test:

Compounds (22, 24, 26) showed good or moderated activates against ***Bacillus subtilis*** , while these compounds showed zero activity against ***Staphylococcus aureus***. , so (22,24, 26) compounds showed zero activity against ***E. coli*** and ***Pseudomonas Aeruginosa,*** but (26) compound showed moderate activity against ***E. coli*** and ***Pseudomonas Aeruginosa*** .The difference of biological activity refers to different substituent in the compounds. On the other hand, all these compounds were completely inactive against four types of fungi namely (***Asperginesflurs, Aspergillusfumgntnts, Aspergillusniger and pencillum***) which indicate the specify of the action of the nucleoside analogues as anti – bacterial but not against fungi, that is accordance to the literature [17].

Conclusions:

Nucleoside analogues are important medical materials; therefor, new nucleoside analogues were synthesized from benzimidazole derivatives contanining Mannich basses which also have a broad spectrum of biological applications. The nucleoside analogues are characterized on the basis of analytical and spectra data. Screening of these compounds against two types of

gram positive and two types of gram negative, showed a good and moderate activity. And inactive against four types of fungi.

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تحضير مماثلات نيو كلوسيدات جديدة من إلبنزايمدازول ودراسة فعاليتها البايولوجية

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الخلاصة :

يهدف البحث، تحضير بعض مماثلات النيكلوسيدات بدءاً من (1) الفا- D- كلكوز والذي تم تحويله الى الاسيله الكاملة لبيتا-D- كلكوز ثم تحويله الى الصيغة الفعالة1- بروموسكر(2). أما الجزء القاعدي 2- بنزإيميدازول المعوض/تم تحضيره من خلال تكاثف O- فنلين ثنائي الأمين مع مختلف الديهايدات الاروماتية ومن ثم مفاعلتها مع امينيات احادية مختلفة بوجود الفورمالديهايد من خلال تفاعل مانخ حيث تم الحصول على قواعد نايتروجينية جديدة (5-3). والتي تم تكثيفها مع المركب(2) من خلال تفاعل تعويض نيكلوفيلي للحصول على نيكلوسيدات محمية جديدة (19-13) والتي عند تحللها بمنيوكسيد الصوديوم في الميثانول اعطت نيكلوسيدات حرة جديدة(26-20). جميع المركبات المحضرة ثم تشخيصها بتقنية طيف FT-IR الموجبة والبعض منها عن طريق الرنين النووي المغناطيسي للبروتون والكاربون 13. كذلك تقييم الفعالية البايولوجية للمركبات خارج الخلية مع اربعة انواع من البكتريا اثنان من البكتريا الموجبة , (*Bacillas subtilis*, Staphylococcus)واثنان من البكتريا السالبة(*E.Coli* ,*Pseudomonas Aeruginosa*). وكذلك تم تشخيصها ضد اربعة انواع من الفطريا (A*spergines flurs, Aspergillus fumgntnts, Aspergillus niger and pencillum*) .

الكلمات المفتاحية : مماثلات النيوكلوسيدات وبنزاميدال.