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Baghdad Science Journal **Vol.13(3)2016**

DOI: http://dx.doi.org/10.21123/bsj.2016.13.3.0531

Synthesis of Some New Nucleoside Analogues Containing Seven Membered Ring and Studying Their Biological Activity

Thanaa Mahdi Al-Mouamin ***SurorAbdulrahman Mahdi***
Omar Abdulateef Mohammed ***Yasmeen H. Muhamad***

Department of Chemistry, College of Science, University of Baghdad, Al-Jaderia, Baghdad-Iraq

E-mail:surchem_82@yahoo.com

Received 17/5/2015
Accepted 20/12/2015

Abstract:

In this work, a series of new Nucleoside analogues (D-galactopyranose linked to oxepanebenzimidazole moiety) was synthesized via multisteps synthesis.

The first step involved preparation of two benzimidazoles 2-styrylbenzimidazole and 2-(phenyl ethynyl) benzimidazole via reaction of phenylenediamine with cinnamic acid or β-phenyl propiolic acid. Electrophilic addition of the prepared benzimidazoles by three anhydrides in the second step afforded (4-6) and (14-16) which in turn were treated with *1,2,3,4-di-O*-isopropylidene galactopyranose in the third step to afford a series of the desirable protected nucleoside analogues (7-9) ,(17-19)which after hydrolysis in methanolic sodium methoxidein the fourth step afforded the free nucleoside analogues (10-12) and (20-22) .The synthesized compounds were identified by FT-IR and some of them by ^{1}H-NMR and^{13}C-NMR.

The synthesized oxepane nucleoside analogues were screened for their antibacterial activity against three types of bacteria including *Staphylococcusaureus* ,*Bacillus*(gram positive) and*E.coli* (gram negative) bacteria repectively.

Key words: Nucleoside, oxepane nucleoside, isopropyledenegalactopyranose.

Introduction:

Oxepane diones that are heterocyclic compounds with seven-membered oxycyclic are found in a number of natural products such as zoapatanol ,regiolenyne and breveral [1]. Nowaday they have been receiving more attention for their wide range of biomedical applications as cytotoxicity against cancer cell lines, antimicrobial activity and inhibition of several enzyme activities [2]. Also they applied as achemotherapeutic used to treat advanced brain tumors[3],[4].

On the other hand, benzimidazole has an important chemical entity in pharmaceuticals [5]. Benzimidazole derivatives possess antibacterial effects, antifungal activity, HIV inhibitors,

antiviral effects, antihypertensive agents, antiulcer activity, antiproliferative activity, antitumor activity, antioxidant agents[6].In another approach nucleoside analogues have found to be important moiety in creation of novel medical compounds. Even though, they have been studied a long time ago, there is still a great potential development of new therapeutic agents as antiviral compounds to treat diseases caused by HIV and hepatitis [7], antimicrobial agents [8], anticancer agents [9], [10].These observations inspire us to synthesis new nucleoside analogues containing oxepane and bezimidazole as a anucleobase and galactose as a asugar moiety which shows good biological activities against three types of bacteria.

Materials and Methods:

Melting points were recorded using Gallenkhamp electro thermal melting point apparatus. FT-IR spectra were recorded on SHIMADZU FT-IR 8400 fourier transform intrared spectrophotometer using KBr disc or thin films. 'H-NMR spectra were recorded on Brukerspectrospin ultra shield magnet 300MHz instrument using Me_4Si as the internal standard and DMSO-d6 as solvent.TLC plates were used with an aluminum backing (0.2mm, 60 F_{254}), the reactions were monitored by TLC and visualized by development of the TLC plates. Incubator Heraeus D-63450 (Germany) model was used for incubation samples for biological study.

1- Synthesis of *1,2:3,4-di-O*-isopropylidene-D-galacto pyranose (1)

Zinc chloride (8.87g, 88mmol) was partially dissolved in (125ml) acetone and (0.4ml) concentrated sulfuric acid was added at room temperature to give a clear solution. (10g, 56mmol) D-galactosewas added in one portion and the resulting white suspension was stirred for 6 hours at room temperature. Asuspension of (20g ,189mmol) sodium carbonate in (30 ml) water added to the yellow reaction mixture at 0° C in medium sized portions. The suspension was allowed to stir for 30 min before filtration and solvent removal in vacuo to give the crude product as tallow oil below the aqueous layer. The organic fraction was separated from the aqueous layer, followed by further extraction with (3x50 ml) diethylether. The organic layer was dried over sodium sulfate [11], and the solvent removed in vacuo to yield *1,2:3,4-di-O*-iso propylidene-D-galactso (1) as a pale yellow syrup (87%),Rf=0.23 (Et_2O).

2- Synthesis of 6-Bromo-*1,2:3,4-di-O*-isopropylidene-D-galacto pyransoe(2)

The sugar(1) (20g ,76.9 mmol) was treated with 50% (w/v) hydrogen bromide in acetic acid (52.5 ml). The solution was kept in 0°C unitl TLC in indicated reaction completion (generally within one hour), then poured into an ice-cold chloroform (35 ml) , washed with iced water (3x25 ml) and then with saturated aqueous solution of sodium bicarbonate to remove the remaining acid [12] . After a find wash with iced water (25 ml) the organic phase was dried over anhydrous sodium sulphate to give (2) as syrup (43%) the isolated sugar bromide (2) was used directly for the nucleoside synthesis : Rf 0.43 (Et_2O: EtOH 1:1), yield 43%.

3- Synthesis of 2-Styryl benzimidazole (3)

Cinnamic acid (2.96 g ,20 mmol) was dissolved in(25 ml) absolute ethanol ,*O*-phenylenediamine(2.16 g ,20 mmol)was added. The mixturewas refluxed for 12h using water bath. then cooled and poured onto (50ml) ice-cold water

containing (1ml) of concentrated HCl,scratched for 15 min, filtered [13][14].Dried and recrystallized from ethanol to give (2) as yellow precipitate, yield 75% .

4- Synthesis of benzimidazol-2-yl oxepane-4,7-diones (4-6)

compound (3) (1 mmol) was placed in round bottomed flask; (succinic ,phthalicor maleic) anhydride (1 mmol) in (10 ml) benzene wasadded,then refluxed on water bath for 1 hour the solvent was evaporated and the solid precipitated was recrystalized from tetrahydro furan (THF). Physical properties of compounds (4-6) are listed in Table (2).

5-Synthesis of 6-(N-(phenyl oxepane -4,7-dione -3-yl) benzimidazolyl)- *1,2,3,-di-O-* isopropylidene galactopyranoses (7-9)

(1.08 mmol) isopropylidene sugar bromide (2) was dissolved in (10 ml) of dried xylene, then (0.533 mmol) benzimidazolyl derivatives (4-6) were added and refluxed with vigorous stirring for one hour [12]. TLC (chloroform ether 9:1), the result mixture was cooled to room temperature then filtred and washed with (5 ml) ethanol then dried to give after silica gel column chromatography the protected nucleoside [12]. Physical properties of componneds (7-9) are listed in Table (3).

6-Synthesis of 6-(N-(phenyl oxepane -4,7-dione -3-yl) benzimidazoyl) galactopyranoses (10-12)

A solution of (0.292 mmol) of the protected nucleoside (7-9) in (7 ml) of 0.1 M methanolic sodium methoxide was refluxed with stirring for half hour TLC (chloro form : ethanol 8:2) showed that the reaction was complete. The mixture was neutralized with acetic acid and evaporated to dryness. The residue was partitioned between water and chloroform and the aqueous phase was evaporated to dryness in vacuo. The reside was dissolved in methanol (3 ml) and then chromatographed on a column of silicagel using 9:1 chloroform – methanol as developer [12]. Afforded free nucleoside analogueswas purified by recrystalization from ethanol-ether. Physical properties of compounds (10-12) are listed in Table (4).

7- Synthesis of 2-(phenyl ethynyl) benzimidazole (13)

The titled compound was prepared by following the same procedure used in preparation of 2-cinnamoylbenzimidazole except using of β-phenyl propiolic acid instead of cinnamic acid. The product was purified by recrystallization from elhanol yield 73%.

8- Synthesis of benzimidazolyl -2,3-didehydo oxepane -4,7-diones (14-16).

The titled compounds were prepared following the same procedure used in the preparations of compounds (4-6) except using of 2-(phenyl ethynyl) instead of 2-styryl benzimidazole. The final products was purified by recrystallization from tetrahydrofuran (THF) physical properties of compounds (14-16) are listed in Table(9).

9- Synthesis of 6-(N-(phenyl -2,3-didehdro oxepane -4,7 dione -3-yl) benzimidazolyl) – *1,2,3,4-di-O-*isopropylidene galactopyranoses (17-19).

The titled compounds were prepared by following the same procedure used in the preparations of compounds (7-9) except using of benzimidazolyloxcpane

-4,7-dions(14-16) instead of compounds (4-6). The final products were purified by recrystallization from chloroform physical properties of compounds (17-19) and they are listed in Table (10).

10- Synthesis of 6-(N-(phenyl -2,3-didehydro oxepane -4,7-dione -3-yl) benzimidazolyl) galactopyranoses(20-22)

The titled compounds were prepared following the same procedure used in the preparation of compounds (10-12) using of protected nucleosides (17-19)instead of (7-9). The product was recrystallized from ethanol ether. Physical properties of compounds (20-22) were listed in Table (11).

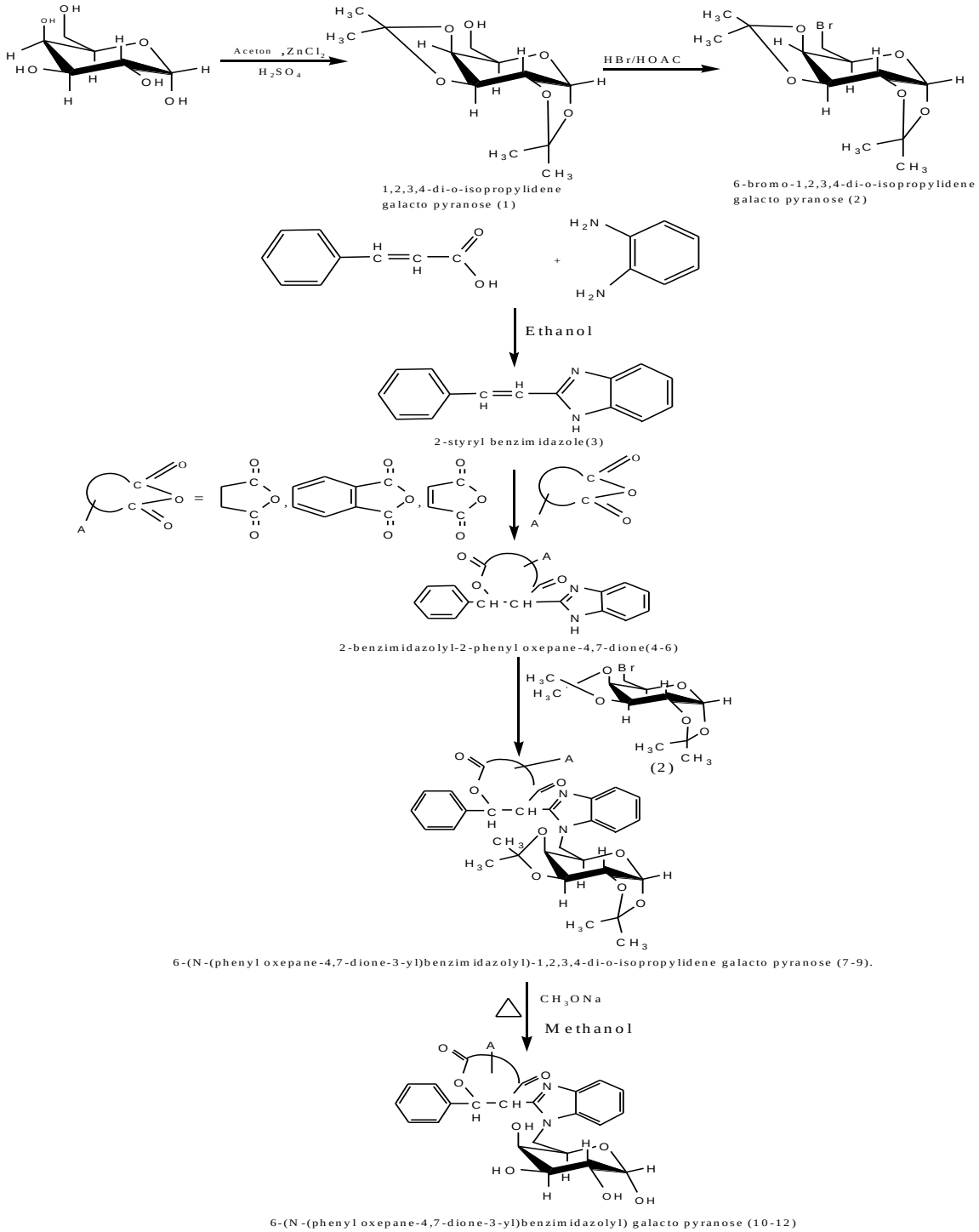
11- Microbiological test:

Nutrient agar was added to (1L) of distilled water in suitable conical flask with stirring and heating until complete dissolving then the flask was stoppered by cotton and the medium was sterilized in an autoclave for 20 minutes at (121°) under pressure at 15 pound/inch. The medium was placed in petridishes about (20 ml) for each one and was left to cool and solidified. The studied bacteria and fungi were placed on the nutrient agar surface using the loop and by streaking processor then the discs saturated with tested compound solutions. The samples were incubated for 24 hours at 37°C [15].

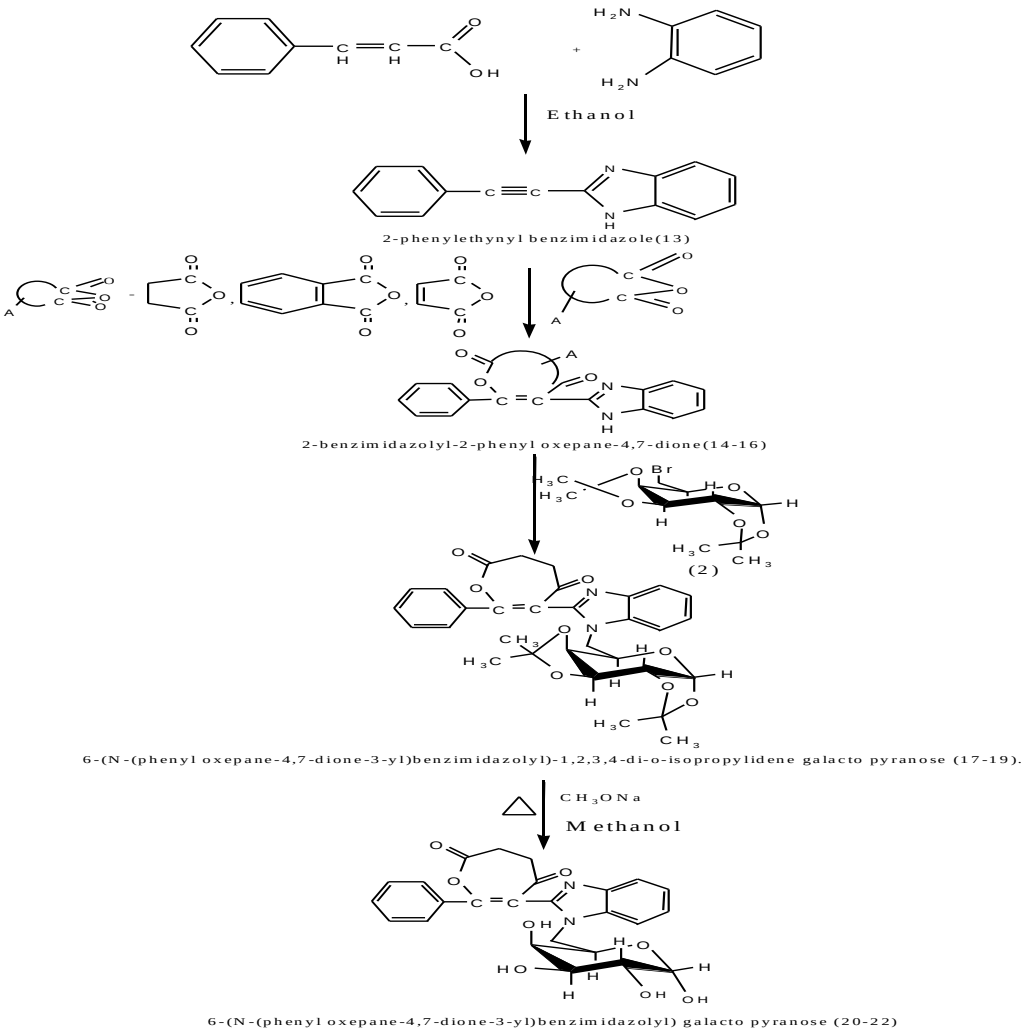
Results and discussion

The synthetic route was started with 2- styrylbenzimidazole (3) and 2-(phenyl ethynyl) benzimidazole (13) which were synthesized from condensation reaction of phenylenediamine withequimolar quantity of cinnamic acid or β - Phenyl propiolic acid respectively via Debus – Radziszewski, reaction.

Thesetwocompoundswere reacted with different acid anhydrides (succinic, phthalic, and maleic) to give new substituted oxepanedione derivatives (4-6) and (14-16) subjected to nucleophilic substitution reaction with bromo sugar (2)to give new protected nucleoside analogues (7-9) and (17-19) respectively to obtain our synthetic goal. The free nucleoside analogues play an important role in treatment of tumor cell and as antiviral drugs.Benzimidazole and oxepane (oxepine) ring also have abroad spectrum of biological activities. The overall work steps show in Scheme (1) and Scheme (2).



Scheme (1):Synthesis of 6-(N-(phenyl oxepane -4,7-dione -3-yl) benzimidazoyl) galactopyranoses (10-12)



Scheme (2) :Synthesis of 6-(N-(phenyl -2,3-didehydro oxepane -4,7-dione -3-yl) benzimidazolyl) galactopyranoses(20-22)

The reaction of D- galactose with aceton in presence of anhydrous zinc chloride and sulfuric acid afforded *1,2:3,4, - di – O–* isopropylidene - D- galactopyranose (1) in high yield. FT- IR spectrum of (1) showed absorption band at (3458) cm^{-1} assigned to ν (O-H) while this band was disappeared in FT- IR spectrum of 6-Bromo– *1,2:3,4 – di – O-* isopropylidenegalactopyranose (2) with an absorption band at (698) cm^{-1} due to ν(C-Br) group [16] ,^{1}H-NMR spectrum of compound (2) showed two singlet signals at (δ= 0.9 and 1.1) ppm belong to protons of four methyl group ,singlet signal at (δ= 2.5) ppm belong to (CH-Br)and signals at (δ= 3.3-4) ppm belong to (CH-OR) proton ,^{13}C-NMR spectrum showed signals at (δ= 39.1- 39.9) ppm belong to carbon of four methyl ,signals at (δ= 61.6)ppm and (δ= 65.9)ppm belong to ($\underline{C}H_2$-OR) and signal at (δ= 40.2)ppm belong to ($\underline{C}H_2$-Br). This indicated the formation 6- bromo – *1,2,3,4 – di – O –* isopropylidenegalactopyranose (2). On the other hand two α, β-unsaturated carboxylic acids named cinnamic acid and β - phenyl Propiolic acid were condensed with *O* – Phenylenediamine to afford 2- styrylbenzimidazole (3) and

2- (β - phenyl ethynyl) benzimidazole (13) in the first step. FT – IR spectra of (3) and (13) showed appearance of several bands,ν(C=N) benzimidazole ,ν (C-N) benzimidazol and ν (N-H) benzimidazol at , (1589-1577)cm^{-1} (1313-1319)cm^{-1} and (3325-3444) cm^{-1} respectively , and absence of ν (O-H) . ^{1}H-NMR spectrum of compound (3) showed signal at (δ= 2.3)ppm belong to (N-H)proton ,douplet signal at (δ= 6.2,6.3)ppm belong to (CH=CH) vinylic protons and multiplet signals at (δ= 7.03-7.48)ppm belong to aromatic protons .^{13}C-NMR spectrum of compound (3) showed signal at (δ= 39.97)ppm belong to (C-NH) carbon ,two signals at (δ= 114.2 , 119.1)ppm belong to (C=C) vinylic carbon , signals at (δ= 122.44 – 143.89)ppm belong to (C-C) aromatic carbon and signal at (δ= 168)ppm belong to (C=N) carbon.

The second step involved synthesis of oxepanedionebenzimidazole (4-6) and 2,3, -didehydrooxepanedionebenzimidazole (14-16) via reaction of acid anhydride (succinic, phthalicand maleic anhydride) with Compound 2- styrylbenzimidazole (3) or 2 – (β - phenyl ethynyl) benzimidazole (13). FT – IR spectra of (4-6) and (14-16) gave absorption bands at (1685-1693)cm^{-1} , (1700 – 1733) cm^{-1} attributed to ν(C=O) ketone and ν (C=O) ester respectively; besides the absence of ν (C=O)anhydride at (1800-1840) cm^{-1} indicated the success of addition reaction of anhydride (4-6) and (14-16) which subjected to anucleophilic substitution by treating with 6 – bromo– *1,2,3,4- di – O-* isopropylidene - D – galactopyranose (2) in the third step to afford 6 – (N – (phenyl oxepane – 4,7 – dione – 3 – yl) benzimidazolyl) – *1,2,3,4. Di – O –* isoproplidenegalactopyaroses (7-9) and 6- (N- (phenyl – 2,3 – didehydrooxepane – 4,7 – dione – 3- yl) benzimidazole) – *1,2,3,4 – di-O-* isopropylidenegalactopyranoses (17-19).

TheFT–IR spectrum showed disappearance of bands ν (C-Br) ,ν (N-H) benzimidazole with appearance of bands at (1271 – 1342)cm^{-1} attributed to ν(C-N) nucleoside. ^{1}H-NMR spectrum of compound (5), showedsignal at (δ=2.3)ppm belongs to (N-H) proton, signal at (δ=2.74)ppm belongs to (CH-C=O) proton, signal at (δ= 3.6)ppm belongs to (CH-O-C=O) proton, multiplet signals at (δ= 6.5-7.9)ppm belong to aromatic protons ,^{13}C-NMR showed singletsignal at (δ= 28.74)ppm belongs to (CH-C=O) carbon ,signal at (δ= 39.9)ppm belongs to (CH-CH) carbon ,multiplet signals at (δ=128.12-143.87)ppm belong to aromatic carbon and signal at (δ= 173.56)ppm belong to (C=N) carbon.

For synthesis of 6- (N – (phenyl oxepane – 4, 7 – dione – 3 – yl) benzimidazolyl) galactoPyranoses (10-12) and 6- (N- (phenyl – 2,3 – didehydro – oxepane – 4,7- dione – 3- yl) benzimidazolyl) galactopyranoses (20-22) in the fourth step , (7-9) and (17-19) were allowed to hydrolize by methanolic Sodium methoxide at reflux temperature . FT – IR spectrum of (10-12) and (20-22) showed appearance of absorption band at (3350-3357)cm^{-1} assigned to ν (O-H) glycolic and absence of ν (C-O-C) ether , other absorption bands to (10-12) and (20-22)

Were (1340) cm^{-1}, (1579-1580)cm^{-1}, (1280-1311)cm^{-1}, (1695-1716)cm^{-1}due toν (C-N) nucleoside,ν (C=N) imidazole ,ν (C-N) imidazole ,ν (C=O)oxepane respectively. Other details of FT- IR spectral data of the prepared mentioned compounds are listed in Tables (5,6,7,8) and (12,13,14). On the other hand structures of Compound (11) were confirmed also by ^{1}H- NMR spectrum which showed signal at (δ= 1.9)ppm belong to (CH_2-NR_2) proton signal at (δ= 2.5)ppm belong to (CH-C=O) proton,signal at (δ= 3.6)ppm belong to (CH-O-C=O) proton.

^{13}C-NMRspectrum of compound (11) showed signal at (δ= 28.23)ppm belongs to (CH-C=O) carbon, signal at (δ= 38.91)ppm belongs to (CH_2-NR_2) carbon and signal at (δ= 67.40)ppm belongs to (CH-O-C=O) carbon.

Microbiological test

The prepared nucleosides are screened for their antibacterial activity against three types of bacteria *Bacillu*, *Staphylococcusaureus* (gram positive) and *E.coli*(gram negative) . They showed different biological activities against these bacteria as shown in Table (15). The result showed a high antibacterial activity of the prepared nucleosidesagaist gram negative more than gram positive, thus compounds (7-12),(17-22) showed highantibacterial activity against *E.coli*. Also antibacterial activity of the prepared nucleosides depends on nature of substituents in their molecules, thus compounds (17),(18) and (20) which are substituted phenyl ethynyl showed a high antibacterial activity against *Staphylococcus aureus*also compounds (8) and (19) have a high antibacterial activity against this bacteria. Other compounds showed a moderate activity against this bacteria. Finally, compounds (7),(18) and(21) showed a high antibacterial activity against *Bacillus*,compounds (9) ,(20) and(22) showed no activity against this bacteria; other compounds showed a moderate activity against this bacteria.

Table (15) inhibition zones to compounds (7-12), (17-22) in mm

Comp. No.	Gram negative	Gram positive	
	E.Coli	***Bacillus***	***Staphylococcus aureus***
7	**14**	**12**	**11**
8	**16**	**10**	**12**
9	**15**	**N**	**11**
10	**14**	**7**	**11**
11	**16**	**11**	**11**
12	**12**	**11**	**13**
17	**16**	**11**	**15**
18	**15**	**14**	**14**
19	**15**	**11**	**12**
20	**11**	**N**	**13**
21	**13**	**12**	**11**
22	**12**	**N**	**11**

N = No inhibition , Inhibition zone (5-7)mm = Slightly active , Inhibition zone (8-11)mm = Moderately active, Inhibition zone >12mm Highly active

Table (1) physical properties of the prepared compounds (1) , (2) , (3) , (13).

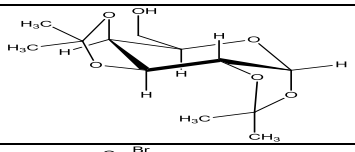
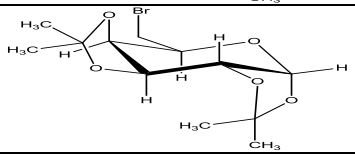
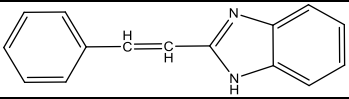
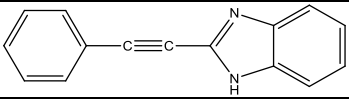
Comp. No.	Compound Structure	Color	Rf solvent system	Yield %	m.p C^0
1		Pale yellow syrup	Diethyl ether-ethanol	87	b.p= 119
2		Brown syrup	Diethyl ether-ethanol	43	b.p= 104
3		Pale gray	Ethanol-acetone	75	124-126
13		Pale yellow	Ethanol-acetone	77	92-94

Table (2) physical properties of Substituted oxepane 4,7-diones (4-6).

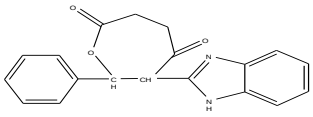
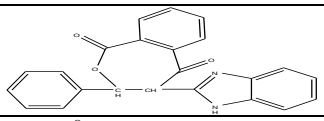
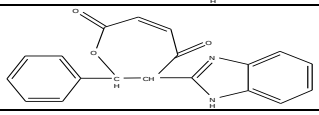
Comp. No.	Compound Structure	Color	Yield %	m.p C^0	Recrystallization solvent
4		Deep brown	70	82-84	THF
5		Grayish-white	73	173-176	THF
6		Off white	66	126-128	THF

Table (3) physical properties of oxepane benzimidazole isopropylidene- D - galactopyranose (7-9) .

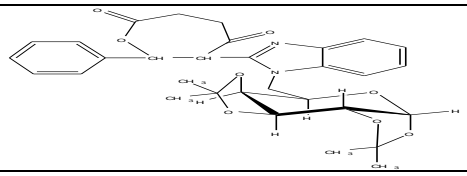
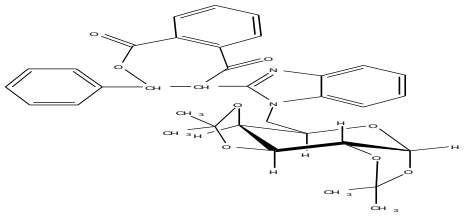
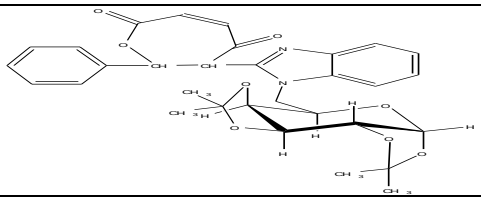
Comp. No.	Compound Structure	Color	Yield %	m.p C^0	Recrystallization solvent
7		Dark brown	48	72-74	Chloroform
8		Brown	57	112-114	Chloroform
9		Deep brown	43	100-102	Chloroform

Table (4) physical properties of oxepane benzimidazoleβ- D – galactopyranose (10-12)

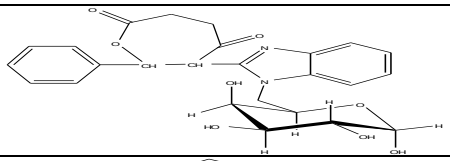
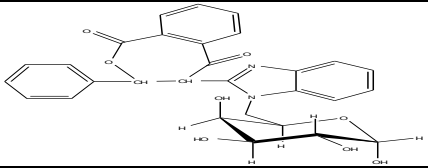
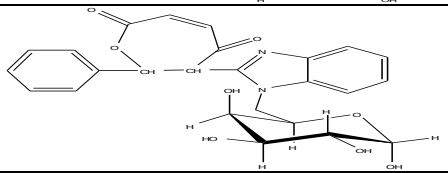
Comp. No.	Compound Structure	Color	Yield %	m.p C^0	Recrystallization solvent
10		Pale yellow	75	240 dec	Ethanol- ether (1:1)
11		Pale yellow	82	225 dec	Ethanol- ether (1:1)
12		Pale yellow	78	230 dec	Ethanol- ether (1:1)

Table (5) FT-IR spectral data (cm^{-1}) of compounds (1), (2), (3), (13).

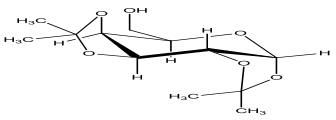
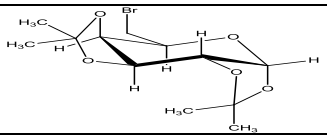
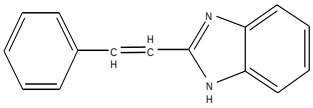
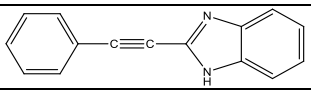
Comp. No.	Compound Structure	ν(O-H)	ν(C-O-C)	ν(C-O) alcohol	ν(C-H)	ν(C-C)
1		3458	1166	1070	2977	1002
2		**ν(C-Br)**	**ν(C-O-C)**	**ν(C-O)**	2925	1041
		698	1122	1072		
3		**ν(N-H)**	**ν(C=C) vinylic**	**ν(C=C) aromatic ν(C=N) imidazole**	**ν(C-N) imidazole**	**ν(C-H) aromatic**
		3325	1629	1589	1286 1313	3066
13		3444	**ν(C≡C)** alkyne 2115	1635 1577	1319	3056

Table (6) FT-IR spectral data (cm^{-1}) of subistituted oxepane-4,7-dione (4-6)

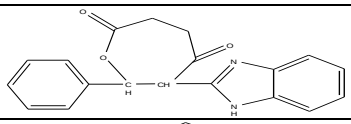
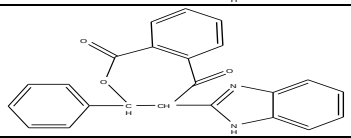
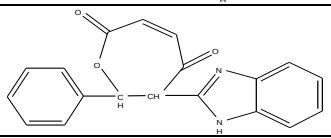
Comp. No.	Compound Structure	ν(C=O) ketone	ν(N-H) imidazole	ν(C=C) Aromatic ν(C=N) imidazole	ν(C-N) imidazole	ν(C=O) ester	ν(C-H) aromatic
4		1693	3207	1631 1577	1286 1313	1728 1712	3024
5		1685	3450	1629 1577,1596	1286 1311	1733	3020
6		1685	3200	1629 1577,1598	1284 1311	1710	3026

Table (7) FT-IR spectral data (cm^{-1}) of oxepane benzimidazole isoprpylidene galactopyranose (7-9)

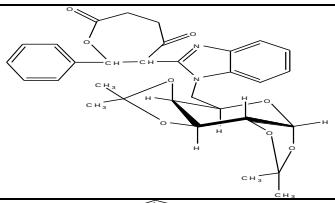
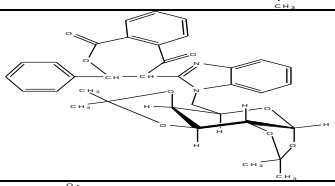
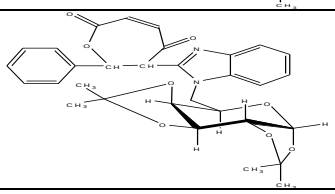
Comp. No.	Compound Structure	ν(C-N) imidazole ν(C-N) nucleoside	ν(C=O) ester	ν(C=O) ketone	ν(C-O) isopropylidine	ν(C-H) aromatic	ν(C=C) Aromatic ν(C=N) imidazole
7		1288,1311 1330	1700	1693	1074	3053 3026	1631 1577
8		1286,1315 1342	1700	1683	1100	3024 3060	1631 1577
9		1286 1311	1728	1689	1072	3064	1629 1577

Table (8) FT-IR spectral data (cm^{-1}) of oxepane benzimidazole galactopyranose (10-12)

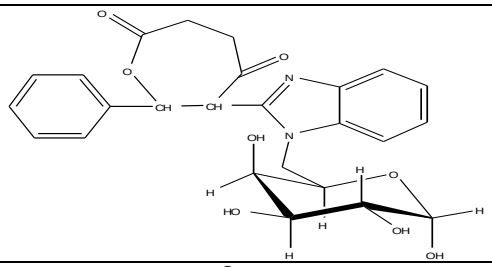
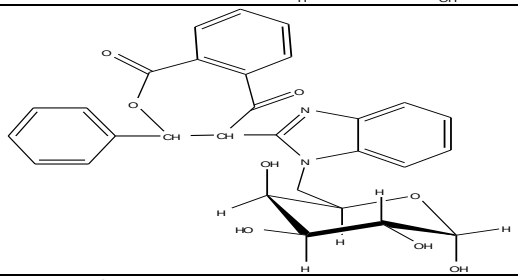
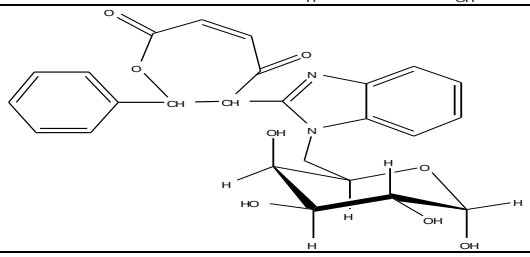
Comp. No.	Compound Structure	ν(O-H)	ν(C-N) nucleoside	ν(C=N) imidazole	ν(C-N) imidazole	ν(C=O) Oxepane
10		3442	1340	1576	1280	1731
11		3475	1345	1573	1290	1700
12		3417	1342	1580	1292 1319	1710

Table (9) physical properties of Substituted didehydrooxepane 4,7-diones (14-16).

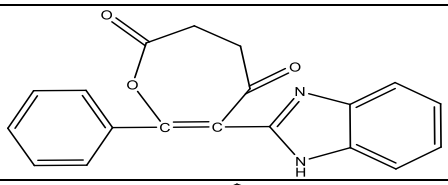
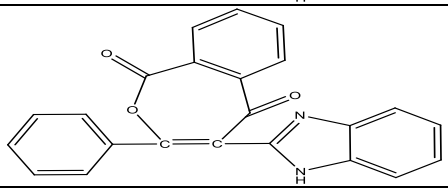
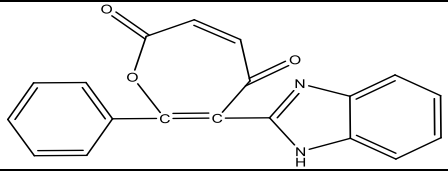
Comp. No.	Compound Structure	Color	Yield %	m.p C^0	Recrystallization solvent
14		Gray	72	102-104	THF
15		Light brown	79	117-118	THF
16		Green	70	170-172	THF

Table (10) physical properties of didehydrooxepane benzimidazole isopropylidene- D -galactopyranose (17-19) .

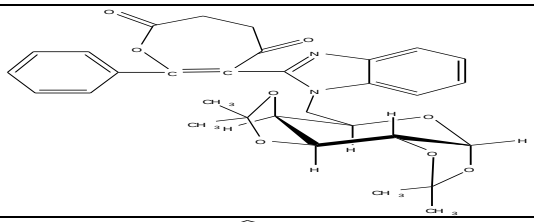
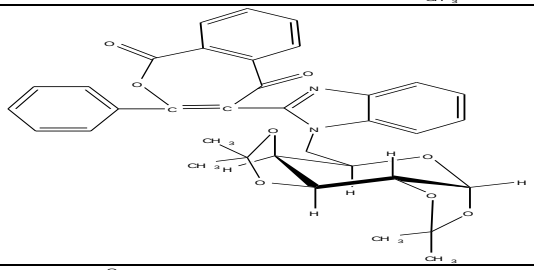
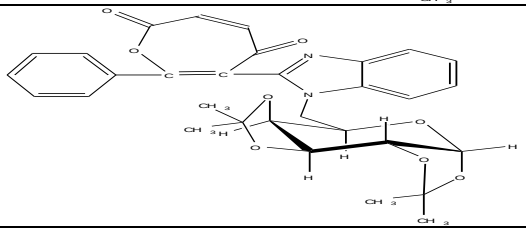
Comp. No.	Compound Structure	Color	Yield %	m.p C^0	Recrystallization solvent
17		Deep brown	52	110-112	Chloroform
18		Brown	60	96-98	Chloroform
19		Gray	47	130-132	Chloroform

Table (11) physical properties of didehydrooxepane benzimidazole galactopyranose (20-22) .

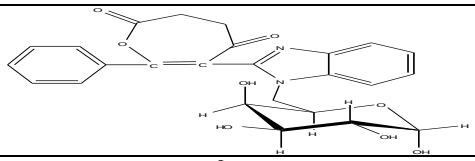
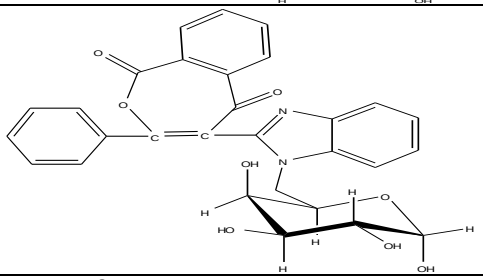
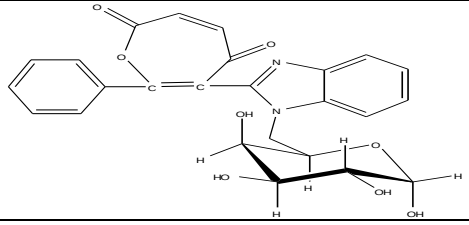
Comp. No.	Compound Structure	Color	Yield %	m.p	Recrystallization solvent
20		Brown	73	225 dec	Ethanol-ether (1:1)
21		Light brown	79	232 dec	Ethanol-ether(1:1)
22		Light brown	71	120 dec	Ethanol-ether(1:1)

Table (12) FT-IR spectral data (cm^{-1}) of didehydrooxepane benzimidazole (14-16)

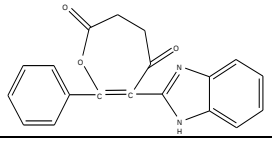
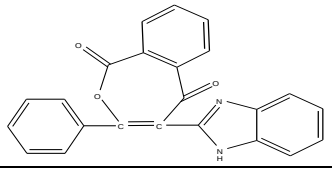
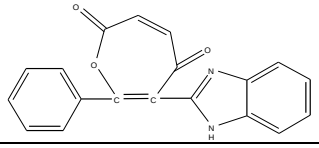
Comp. No.	Compound Structure	ν(N-H) imidazole	ν(C=O) ester	ν(C=O) keton	ν(C=C) Aromatic ν(C=N) imidazole	ν(C=C) vinylic	ν(C-N) imidazole	ν(C-H) aromatic
14		3444	1710	1685	1631 1570	1660	1319	3024 3056
15		3390	1700	1687	1631 1583	1665	1313	3024 3058
16		3467	1701	1683	1631 1570	1660	1315	3024 3060

Table (13) FT-IR spectral data (cm^{-1}) of didehydrooxepane benzimidazole isoprpylidene galactopyranose (17-19)

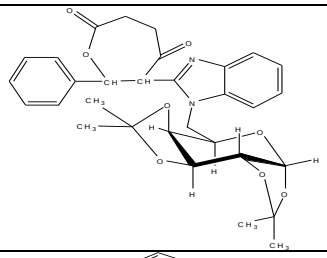
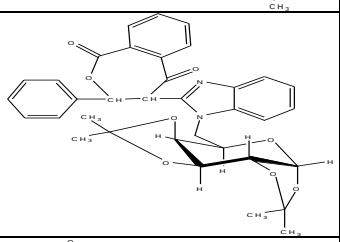
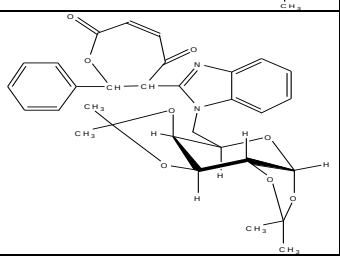
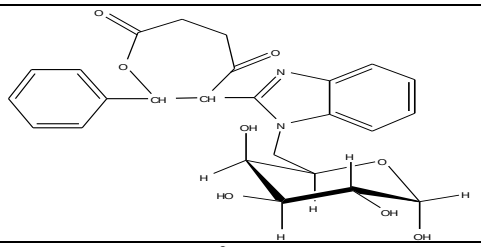
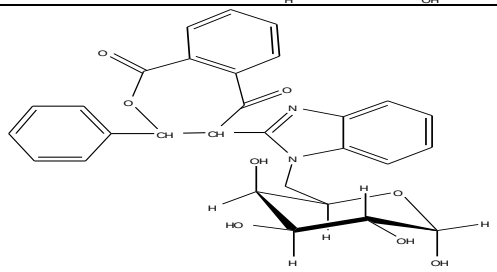
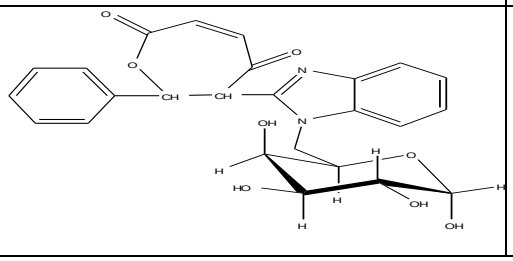
Comp. No.	Compound Structure	ν(C-N) imidazole ν(C-N) nucleoside	ν(C=O) ester	ν(C=O) ketone	ν(C-O) isopropylidine	ν(C=H) aromatic	ν(C=C) Aromatic ν(C=N) imidazole	ν(C=C) vinylic
17		1280,1311 1340	1705	1691	1074	3068	1629 1577	1660
18		1284,1313 1334	1715	1693	1072	3064	1629 1580	1665
19		1286,1313 1344	1707	1695	1072	3026 3060	1631 1577	1660

Table (14) FT-IR spectral data (cm^{-1}) of didehydrooxepane benzimidazole galactopyranose (20-22)

Comp. No.	Compound Structure	ν(O-H)	ν(C-N) nucleoside	ν(C=N) imidazole	ν(C-N) imidazole	ν(C=O) oxepane
20		3355	1340	1580	1286 1311	1716 1706
21		3350	1340	1579	1280 1300	1710
22		3357	1340	1580	1294	1695

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تحضير بعض نظائرالنيوكليوسيداتالجديدة المرتبطة بحلقة سباعية ودراسة فعاليتها البايلوجية

ثناء مهدي المؤمن **سرور عبد الرحمن مهدي**
عمر عبد اللطيف محمد **ياسمين حكمت محمد**

قسم الكيمياء، كلية العلوم، جامعة بغداد.

الخلاصة:
تضمن البحث تحضير سلسلة من النيوكليوسيدات الجديدة (دي كالكتوبايرنوز مرتبطة بمكونة اوكسبينبنزاميدازول) من خلال اجراء عدة خطوات.
تضمنت الخطوة الأولى تحضير اثنين من البنزاميدازولات هما 2-ستايريل بنزاميدازول و2-فنيل ايثاينيلبنزاميدازول من خلال تفاعل ثنائي امين فنيلين مع حامض السيناميك او حامض بيتا-فنيل بروبيوليك. اما في الخطوة الثانية فقد تم تفاعل إضافةالكتروفيل الى البنزاميدازولات المحضرة وذلك بمفاعلتها مع ثلاث حوامض انهدريد وبذلك تم الحصول على المركبات (4-6) و(14-16) اللاتي تمت معاملتها لاحقا في الخطوة الثالثة مع 4,3-2,1- ثنائي-اورثو-ايزوبربيليدينلانتاج سلسلة من النيوكليوسيدات المحجوزة ا (7-9) و(17-19) على التوالي. اما في الخطوة الرابعة فقد تم التحلل القاعدي للمركبات الناتجة من الخطوة الثالثة باستخدام ميثوكسيد الصوديوم الميثانولي وبذلك تم الحصول على سلسلة من النيوكليوسيدات الحرة المرغوبة (10-12) و (20-22) على التوالي.تم تشخيص المركبات المحضرة باطيافFT-IR والبعض منها باطيافH-NMR^{1} و C-NMR^{13} .
درست الفعالية البايلوجية لنيوكليوسيدات الاوكسبين المحضرة ضد ثلاث أنواع من البكتريا هي (ستافيلوكوكاساوريس) و(باسيلاس) الموجبة لصبغة غرام و (أشرشياكولاي) السالبة لصبغة غرام.

الكلمات المفتاحية: نيوكليوسيد ،اوكسبيننيوكليوسيد ، ايزوبروبيليدينكالكتوبايرنوز.