Synthesis of new Schiff bases and nucleoside analogues derivatives derived from D- Glucose and their biological activity study

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Abstract

In this study new derivatives of Schiff bases and nucleoside analogues have been synthesized from the starting material D-glucose after a series of reactions. Derivative 1 was prepared from D-glucose then react with P-bromoacetophenone gave derivative 2 was reacted with dimethyl sulfoxide and acetic anhydride for dehydration a molecule of water gave 3. The spiro ring was prepared at 3-position from the reaction of 3 derivative with 1-phenyl-2 –thioureagave 4 . The protection group at 1 position was removed by using acetic acid fllowed by periodate oxidation to obtain 6. Reaction of 6 with hydrazide derivative at once and dtriazole derivative at another gave 8 and 9 respectively.

Compound 6 was reduced to gave derivative 7. The 1-hydroxylgroup was protected with benzoyl group by using benzoyl chloride to give the derivative 10. Derivative 10 treatment with a mixture of trifluoroacetic anhydride and acetic acid followed by the reaction with trifluoroacetic anhydride gave derivative 11. When derivative 11 treated with silylated uracil derivative the nucleoside analogue 12 was obtained when 11 allowed to react with mercuric theophylline salt in dry xylene, the nucleoside analogue 13 was obtained. The free nucleoside 14 and 15 were obtained when 12 and 13 were allowed to react with sodium methoxide in ethanol respectively. Compounds 8,9,14,15 were exhibited biological activity against E-coli bacteria. Compound 9 exhibited higher degree of activity than the others.

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تحضير مشتقات جديدة من قواعد شف ومماثلات النيوكليوسيد مشتقة من سكر الـD- كلوكوز ذات فعالية بايولوجية محتملة

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الخلاصة

تم في هذا البحث تحضير مشتقات جديدة من قواعد شف ومماثلات النيوكليوسيد - كلوكوز بعد مروره بسلسلة من التفاعلات، اذا تم مفاعلة المشتق Dمن المادة الأولية الـ .2- كلوكوز مع بارا- برمو اسيتوفينون للحصول على المشتق D المحضر من سكر الـ1 مع ثنائي مثيل السلفوكسيد وانهيدريد الخليك لغرض سحب جزيئة 2تم مفاعله المشتق . تم تحضير حلقة سبايرو في الموقع ثلاثة من مفاعله 3ماء للحصول على المشتق . ازيليت مجموعة الحماية في 4- ثايويوريا ليعطي المشتق 2- فنيل -1 مع 3المشتق الذي 6 باستعمال حامض الخليك يتبعها عملية أكسدة للحصول على المشتق2و1الموقع استخدم لتحضير المشتقات من قواعد شف ومماثلات النيوكليوسيد. تمت مفاعلة المشتق

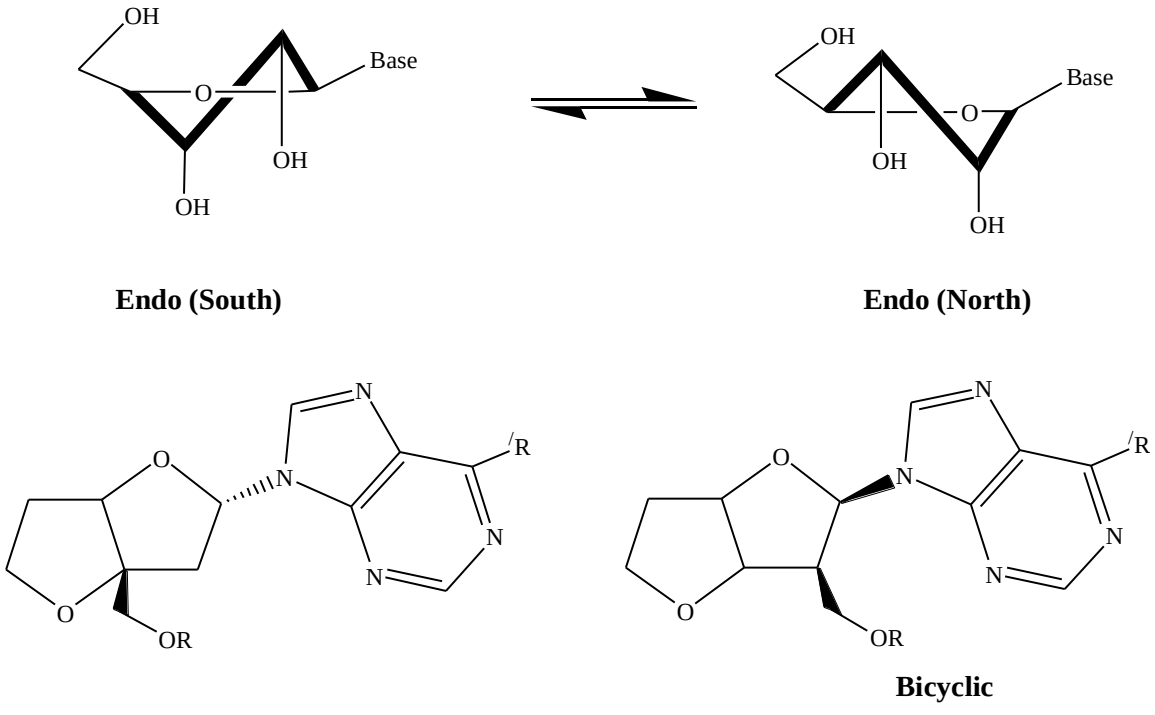
مع مشتق الهيدرازايد مرة ومع مشتق الترايزول مرة اخرى للحصول على المشتق 6 . تمت حماية مجموعة7 للحصول على المشتق 6 على التوالي. تم اختزال المركب 9و8 باستخدام كلوريد البنزوايل لتوفير الفرصة المناسبة لازاحة 1الهيدروكسيل في الموقع . عومل المبمزيج 10شتق 10 والذي اعطى المشتق 4 و3مجموعة الاسيتال في الموقع من حامض الخليك وثلاثي فلوريد الخليك تبعه التفاعل مع ثلاثي فلوريد انهيدريد الخليك مع مشتق السيلايل لليوراسيل اعطى مماثل 11. ان تفاعل المشتق 11لأعطاء المشتق . ان تسخين كل 13 مع ملح الزئبق للثيوفلين اعطى11. معاملة المشتق 12النيوكليوسيد مع ميثوكسيد الصوديوم في الميثانول اعطى مشتقات النيوكليوسيد 13و12من ضد 15,14,9,8 على التوالي. تمت دراسة الفعالية البايولوجية للمشتقات15و 14الحرة 9بكتيريا القولون وقد وجد ان لها فعالية بايولوجية وأكثرها فعالية المشتق.

Introduction

Structurally modified nucleosides represent an important class of medicinal compounds which have been found to behave as therapeutic agent and are currently used in pharmaceuticals as antitumour, antiviral, and antibiotic agent [1-5].

Nucleoside analogs of reverse transcriptase (NARTIs) occupied an essential position in treatment of HIV (Human Immuno deficiency Virus) and AIDS [6].

Mileina et al [7] have synthesized different derivatives of nucleoside analogues derived from cyclobutanone Figure (1)



R= O Bn, H

Ŕ= CL, NH_2

Figure (1)

Firas [8] has prepared some derivatives of spiro fused ring and imine at position 3 of D- glucofuranose Figure (2) and were all found to have biological activity.

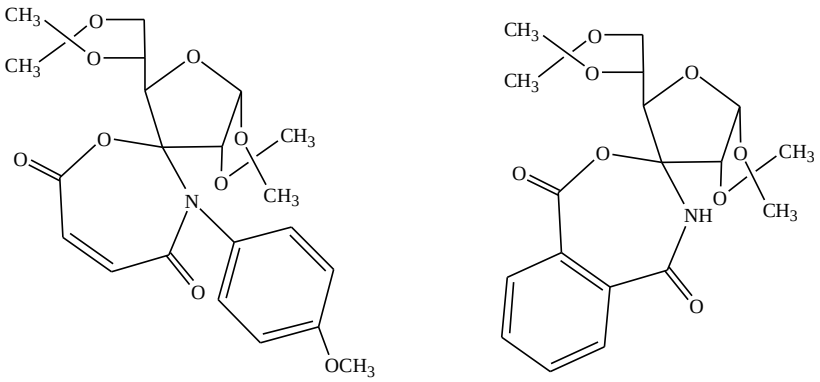
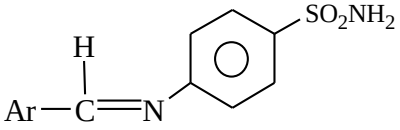


Figure (2)

Biocidalactivity of Schiff bases have also been well established. These have been attributed to the toxophoric C= N linkage in them [9].

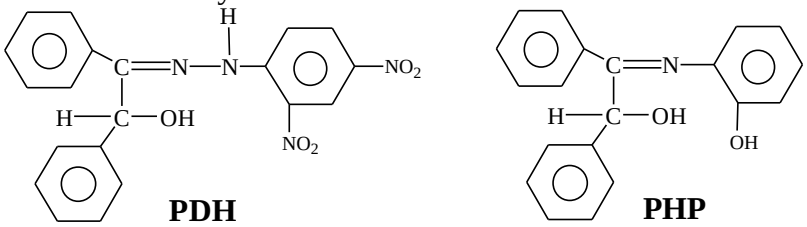
Santosh et al [10] have synthesized new derivative of Schiff bases of sulfone amide Figure (3) and were examined against bacteria and fungi and were all shown good biological activity.



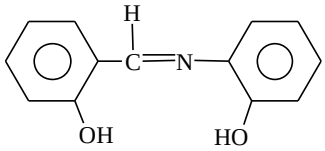
Ar= (C_6H_5-, 2-CL-C_6H_5-, 2-OH-C_6H_5-, 4-N$(CH_3)_2$- C_6H_5-, 3-NO_2- C_6H_5, 4-$OCH_3C_6H_5$)

Figure (3)

Jasmin et al[11] have studied the anticancer activities of three kinds of Schiff bases (PDH, HHP and PHP) figure (4) against *Ehrlichascities carcinoma* (EAC) cells in Swiss albino mice and they all found to be active.



PDH **PHP**



HHP

Figure (4)

In this study new derivatives of nucleoside analogues and Schiff bases were synthesized and study their biological activity.

Materials and methods

All chemical used were supplied from Merk chemical Fluka AG, BDH chemicals, Riedel. De Haen AG, Acros Organics, Janssen chemical and Hopkin and Williams. ^{1}HNMR spectra were recorded in Hitachi Perkin Emelr, R-24 B at 60MHz, elemental analyzer were carried out by using Carlo Erba/ Mod 1106 and Infrared spectra were recorded usingShimadzu 408. All synthesized compounds werepurified by column chromatography using silica gel (60-120) mesh. The biomaterials were obtained from Biomerieux Ltd.

Synthesis of 1,2:5,6 Di-*O*- isopropylidene- ∝-*D*- ribo- hexofuran- 3- ulose. 1

Compound 1 was used as starting material, this derivative was prepared from the reaction of diacetone glucose with dimethyl sulphoxide in acetic anhyoride according to the reference [12].

Synthesis of 1,2: 5,6 –Di- *O*- isopropylidene-3- *C*-p- bromobenzoyl methyl –∝-*D*- allo- hexo- Furanose. 2

To (50 ml) of absolute ethanol, sodium metal (0.2 g, 8.69 mmol) was added and the solution was stirring at room temperature for (20) minutes, p-bromoacetophenon (0.48g, 2.41 mmol) and 3- uoles 1 (3g, 10.52mmol) were added to the mixture of reaction. This reaction was further stirred for (48 h). tlc (benzene: ethylacetate 9.5: 0.5) showed that the reaction was complete. The ethanol was removed under reduced pressure and the brown syrup was diluted with water (20 ml) and extracted with chloroform. Combined organic layer dried over magnesium sulphate and the solvent removed togive 2 as syrup.

Synthesis of 3-p- Bromobenzoylethene- 1,2: 5,6- di- *O*- isopropylidene-∝- *D*. glucofuranose. 3

The mixture of dimethyl sulphoxide (50ml), acetic anhydride (25ml), compound 2 (4 g, 9.11 mmole) is made in a stoppered conical flask, and was stirred at room temperature for (48 h) and tlc (benzene: ether 9,1) showed that the reaction was complete. The mixture was diluted with ice water (60 ml) and the brown syrup was separated by the decantation and the syrup was washed with ice water (4×30 ml), followed by the extraction with chloroform. The organic layer was dried and the solvent was removed under reduced pressure to afford a syrup residue of derivative 3.

Synthesis of 1- [(1\,2*O*- Isopropylidene) ethyl] – 3,4- *O*- isopropylidene- 9- (4\- bromo phenyl) -2- oxa -6- aza phenyl -7- thionspiro [4,5] deca- 8- imine. 4

A mixture of 3 (5g, 11.38 mmol), 1- phenyl -2- thiourea (1.7g, 11.18 mmol) and (5-10 drops) of dietylamine dissolved in (100 mL) absolute ethanol, was refluxed for (72 hrs). The solvent was evaporated and the residue was diluted with water and extracted with chloroform (3×40 ml). The organic layer was dried over magnesium sulphate and the salvent was removed to give 4 as semi solid.

Synthesis of 1- [1\2\- Dihydroxy ethyl] – 3,4- *O*- isopropylidene-9- (4\-bromophenyl) -2- oxa-6-aza phenyl -7- thionspiro [4,5] deca -8- imine.5

A solution of 4 (4g, 6.98 mmol) in (66%) acetic acid (20ml) was storred for (24 hrs) at room temperature. The solution was evaporated under reduced pressure and the resulting residue was re- evaporated with toluene twice (25 ml) to give 5 as syrup.

Synthesis of 1- Aldehydomethyl -3,4-*O*- isopropylidene -9- (4\-bromo phenyl) -2- oxa- 6- aza phenyl -8- iminospiro [4,5] deca -7- thion. 6

To a well stirred solution of 5 (5g, 9.38 mmol) in ethanol (50 ml) was added a saturated solution of sodium hydrogen carbonate (14 ml) followed by a solution of sodium periodats (2g, 9.35 mmol) in (50 ml) water the solution has been stirred for (3 hrs) at room temperature. After which the excess sodium periodate was destroyed by adding few drops of ethylene glycol. The reaction mixture was extracted with chloroform (3×5), dried over anhydrous magnesium sulphate and the solvent was removed to give 6 as syrup.

Synthesis of 1- Hydroxymethyl -3, 4-*O*- isopropylidene -9- (4\- bromo phenyl) -2- oxa- 6- aza phenyl-8- iminospiro [4,5] deca -7- thion.7

The same procedure for preparation of 6 was followed and before extracted with chloroform sodium borohydride (0.5g, 13.21 mmol) was added to the resulting aldehydo derivative 6 with continuous stirring for (1 hour). The reaction mixture was filtrated and exctracted with chloroform (3×50 ml), dried over magnesium sulphate and evaporated under reduced pressure to give 7 as syrup.

Synthesis of 1-[3/, 4/, 5/, 6/ - Tetrahydropyrimidine- 2\ -thio- acetic acidhydrazone methyl] -3-4-*O*- isopropylidene -9- (p-bromophenyl) -2- oxa -6- aza phenyl- 8- iminospiro[4,5] deca -7- thion. 8

A hot ethanolicsoiution of compound 6 (4g, 7.98 mmol) was mixed with a solution of 3, 4, 5, 6, -tetrahydropyrimidine -2- thioacetichydrazide(1.5g, 7.97mmol) in (75 ml) ethanol, the hydrazide derivative was prepared according to the reference [13].

The resulting mixture was then refluxed for (6 hrs). The solvent was evaporated and the residue was diluted with water and extracted with chloroform (3×40 ml). The organic layer was dried and the solvent was removed to give 8 as syrup (^{1}HNMR ($CDCl_3$) δ: 1.3- 1.45 (6 H, 2s, $2CH_3$); 1.65 (2H, s, CH_2-10), 2.3 (2H, s, SCH_2CO); 2.6 (2H, t, CH_2- 3\pyr.); 2.9- 3.3 (2H, m, CH_2-4\pyr.); 3.4 (1H, s, NH pyr.); 3.7 (2H, t, CH2- 5\pyr.), 3.9- 4.2 (3H, m, H-1, H-4,H.1\); 5.6 (1H, d, H-3); 6- 6.4 (1H, b, NHCO); 6.7- 8.2 (9H, m, ArH).

Synthesis of 2-[5- Mercapto -4- (1/ -methylimino- 2/ , 3/ -*O*- isopropylidene- 9/ -p- bromophenyl- 2/-oxa- 6/-aza phenyl -8/- iminospiro [4,5] -7/-thio)- 1, 2, 4- triazol- 3- yl]- thiomethyl- 3, 4, 6- tetrahydropyrimidine. 9

Following the same procedure of the preparation of compound 8, the compound 6 (4g, 7.98 mmol) and derivative 2- [5- mercapto -4- amino- 1, 2, 4- triazol -3-yl] thiomethyl -3, 4, 5, 6- tetrahydorpyrimidine (2g, 8.19 mmol) were dissolved in

ethanol (80 ml), the triazol derivative was prepared according to the reference [13]. The reaction mixture was stirred under reflux for (8hrs) to give 9 as semi solid.

Synthesis of 1- Benzoylmethyl -3, 4- *O*- isopropylidine-9- (4′- bromophenyl)- 2- oxa- 6- oza phenyl -8- iminospiro [4,5] deca -7- thion.10

Compound 7 (5g, 9.94 mmol) in anhydrous benzene (75 ml) containing pyridine (8 ml) was benzoylated with benzoyl chloride (1.4 ml, 9.95 mmol). After stirring for (20 hrs) at room temperature, the mixture was poured into ice water (120 ml). The organic layer was separated and washed with water (3×40 ml), dried and evaporated to give 10 as syrup.

Synthesis of 1- Benzoylmethyl -9- (4′- bromophenyl) -2- oxa- 6- aza phenyl- 8- iminospiro [4,5] deca – 7- thionyl- 3,4- di- *O*-trifluoro- acetate. 11

Water (4 ml) and trifluoroacetic acid (25 ml) was added to a solution of 10 (4g, 6.58 mmol) in acetic acid (25 ml). The resltingmixture was stirred for (8hrs) atroom temperature. The reaction mixture was then neutralized with solidsodium hydrogen carbonate and extracted with dichloromethane (2×100 ml). The combined extracts were dried and the solvent was removed to give a syrup. This syrup was immediately treated with trifluoroacetic anhydride (5 ml) in a mixture of anhydrous benzene (50 ml) and anhydrous pyridine (8 ml) with stirring for (30 hrs) at room temperature. Ice water was added to the mixture and the organic layer was separated, dried and concentrated under reduced pressure. Traces of pyridine were removed by co- evaporation with dry toluene (2×30 ml) to give 11 as syrup.

Synthesis of 1 [1′- Benzolymethyl- 4′- *O*- trifluoroacetyt- 9′- (p- bromaphenyl)- 2′- oxa- 6′- aza phenyl -8′- iminospiro [4,5] deca -7′- thionyl] uracil. 12

Anhydrous stannic chloride (1 ml) and few pellets of molecular sive 4A was added to a mixture of 11 (3.0 g, 3.95 mmol) and silylateduracil (1g, 3.9 mmol) in (60 ml) of anhydrous dichloromethane. The silytatedurcil was synthesized by using the reference [4]. The mixture was stired at 20 Cº for (20 hrs). The reaction mixture was poured in to an excess of sodium bicarbonate solution and extracted with dichloromethane (3×50 ml). The organic layer was dried and removed to give 12 as syrup. ^{1}HNMR ($CDCl_3$).δ: 1.75 (2H, s, CH_2-10′); 2.6-3.1 (6H, m, H-1′, H-1′^{a}, H-1′^{b}, H-4′, H-4, H-5) ; 5.6(1H, d, H-3′); 6-6.3(1H, b, NH); 6.8- 8.3 (14H, m, ArH).

Synthesis of 7 [1′- Benzoylmethyl- 4′- *O*- trifluoroacelyl -9′- (p- bromophenyl)- 2′- oxa- 6′- azaphenyl -8′- iminospiro [4.5] deca- 7′- thionyl] theophylline. 13

The theophylline mercury salt was synthesized according to the reference [5]. This salt (0.96 g, 2.63 mmol) was powdered, suspended in (75 ml) sodium dried xylene and the solvent was distilled to remove the traces of water azeotropically. When the temperature of mixture was raised to 137Cº, the suspension was allowed to cool (below 50Cº). compound 11 (2g, 2.63 mmol) in xylene (25 ml) was added to the suspension and refluxed with stirring for (24 hrs). The traces of theophylline salt wasfiltreted from the hot xylene and washed with dichloro methane (20 ml). The organic layer was dried and removed to give acetylated nucleoside 13 as syrup.

Synthesis of 1 [1′- Hydroxymethyl) -4′- hydxoxy- 9′- (p- bromophenyl) -2′- oxa- 6′- azaphenyl- 8′- iminospiro [4,5] deca -7′- thionyl]. 14

Compound 12 (1g, 1.32 mmol) and sodium methoxids (0.6g, 11.11 mmol) were dissolved in ethanol (60 ml). The solution was stirred under reflux for (20 hrs). the solvent was removed to give 14 as syrop.

Synthesis of 7 [1′- Hydroxymethy -4′- hydroxyl -9′- (p- bromophenyl) -2′- oxa- 6′- azaphenyl -8′- iminospiro [4,5] deca -7′- thionyl] theophyllene. 15

Following the same procedure of preparation of compound 14, the compound 13 (0.5g, 0.6 mmol) and sodium methoxide (0.3 g, 5.55 mmol) were dissolved in ethanol (40 ml). The reaction mixture was stirred under reflux for (24 hrs) to give 15 as syrup.

Results and Discussion

The strategy used frothe synthesis new derivatives of Schiff bases and necleoside analogues was started with derivative 1 in a series of reactions [Scheme 1] and [Scheme 2].

Compound 2 was syuthesized by the reaction of p- bromoacetophenon with 3-ulose derivative [14]. The IR spectrum of 2 showed stretching bands at 3355 cm^{-1} and 1680 cm^{-1} for (OH) and (CO) respectively. Tables (1) and (2) showed the characteristic IR absorption bands and physical properties for all new derivatives.

Compound 3 was synthesized by the dehydration of 2 with DMSO/ Ac_2O [15]. The IR spectrum of 3 showed the disappearance of stretching band at 3355 cm^{-1} for hydroxyl group with appearance of stretching band at 1645 cm^{-1} for aliphatic (C=C). The $\propto$, β- unsaturated branched chain 3 undergoes 1,3- addition of the 1- phenyl -2-thiourea to give the spiroderivative 4 [8]. The IR spectrum of 4 showed the disapperauce of stretching bands at 1645 cm^{-1} and 1685 $cm^{-1}$for (C=C) and (CO) respectively with appearance of streatching bands at 1655 cm^{-1} and 1080 cm^{-1} for (C=N) and (C=S) respectively. To obtain the derivative 5, the ssopropylideneacetal at $c^{/}$-1 and $c^{/}$-2 was removed with acetic acid.

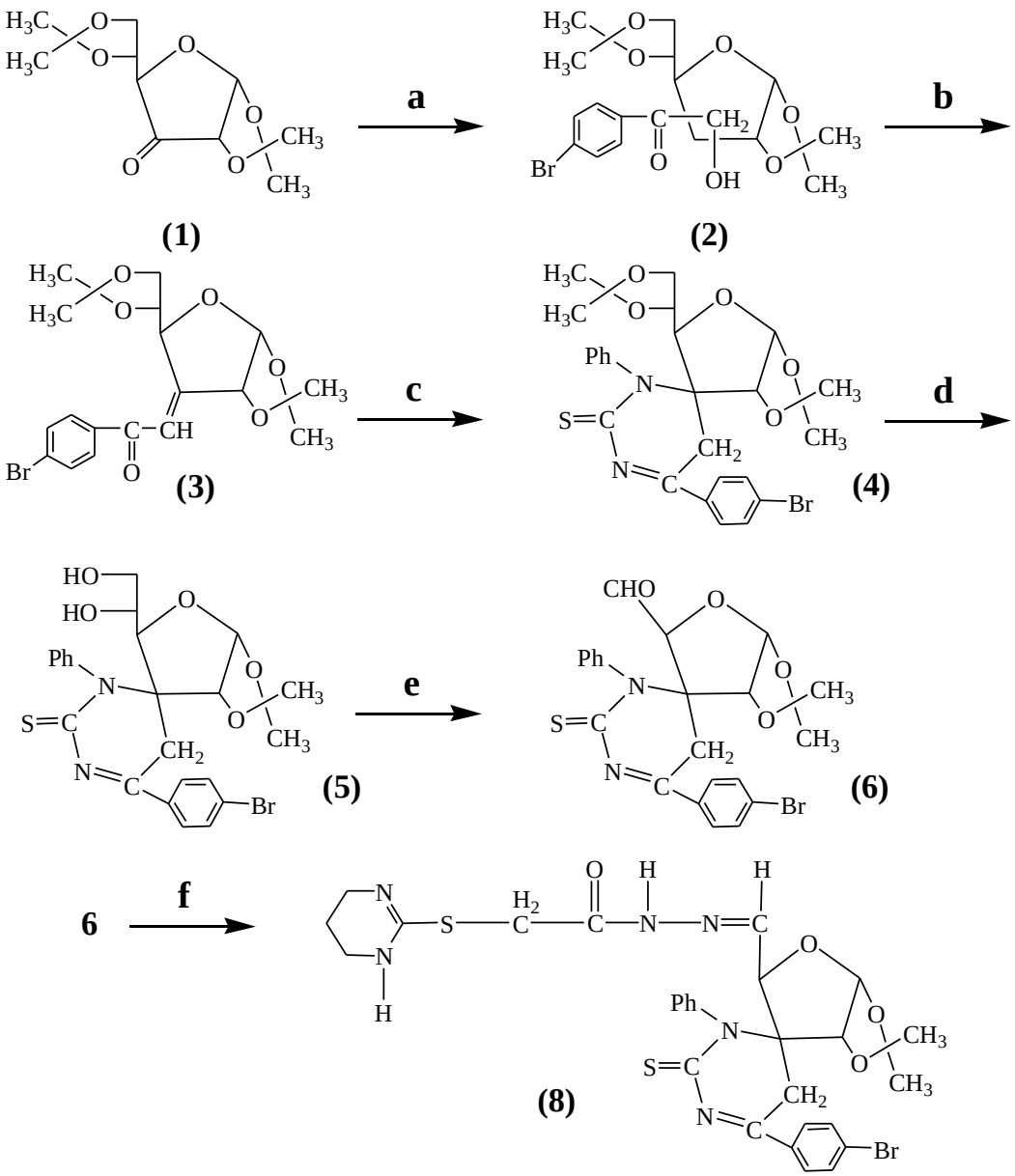
The IR spectrum of 5 showed a streatching band at 3380 cm^{-1} for (OH) groups. Oxidation of compound 5 with sodium periodate gave 6. The IR spectrum of 6 showed the disappearance of streatchig bands of (OH) groups with a appearance of stretching bond at 1680 cm^{-1} for (CO) group. The new Shiff bases derivatives were synthesized by the reaction of compound 6 with hydrazidederivative at once andtriazole derivative at another to gave 8 and 9 respectively. The ^{1}HNMRspectrum of 8 showed two singlet at 1.3- 1.45 for isopropylidene methyl groups, singlet at 2.3 for mrthylene group (S-CH_2CO), 2.6 triplet, 2-9-3.3 multiplet and 3.7 triplet for methylene groups at C- $3^{/}$, $4^{/}$, $5^{/}$forpyrimidinc ring respectively, 3.4 singlet for NH pyrimidine ring, 3.9- 4.2 maltiplet for H-1, H-4, H-$1^{/}$, doublet 5.6 for H-3; broad peak at 6-6.4for NHCO and multiplet signals at 6.7 -8.2 for aromatic rings protons. The reduction of compound 6 by sodium borohydride gave 7. The 1- hydroxyl group was protected with benzoyl group by using benzoylchloride to give the derivate 10. The IR spectrum of 10 showed a stretching band at 1710 cm^{-1} for (CO) group with disappearance of (OH) group at 3385 cm^{-1}. Compound 10 was treated with a mixture of trifluoroacetic acid and acetic acid followed by the reaction with trifluroacetic anhydride gave 11. Compound 11 was treated with silylated uracil [4] gave 12. The ^{1}HNMEspectrum of 12 showed a singlet at 1.75 for methylene group at C-$10^{/}$,

multiplet at 2.6-3.1 for H-$1^{/}$, H-$1^{/a}$, H-$1^{/b}$, H-4/, H-4, H-5), doublet at 5.6 for H-$3^{/}$, broad signal at 6-6.3 for NH uracil and multiplet at 6.8-8.3 for aromatic protons. Compound 13 was prepared by using the Koenigs- Knorr condensation method [12] treatment of compounds 12 and 13 with sodium methoxide in ethanol under reflux [14] gave 14 and 15 respestively. Compounds 8,9,14 and 15 exhibted a biological activity against E- coli bacteria. Compound 9 exhibited a higher degree of activity than the others (table 3).

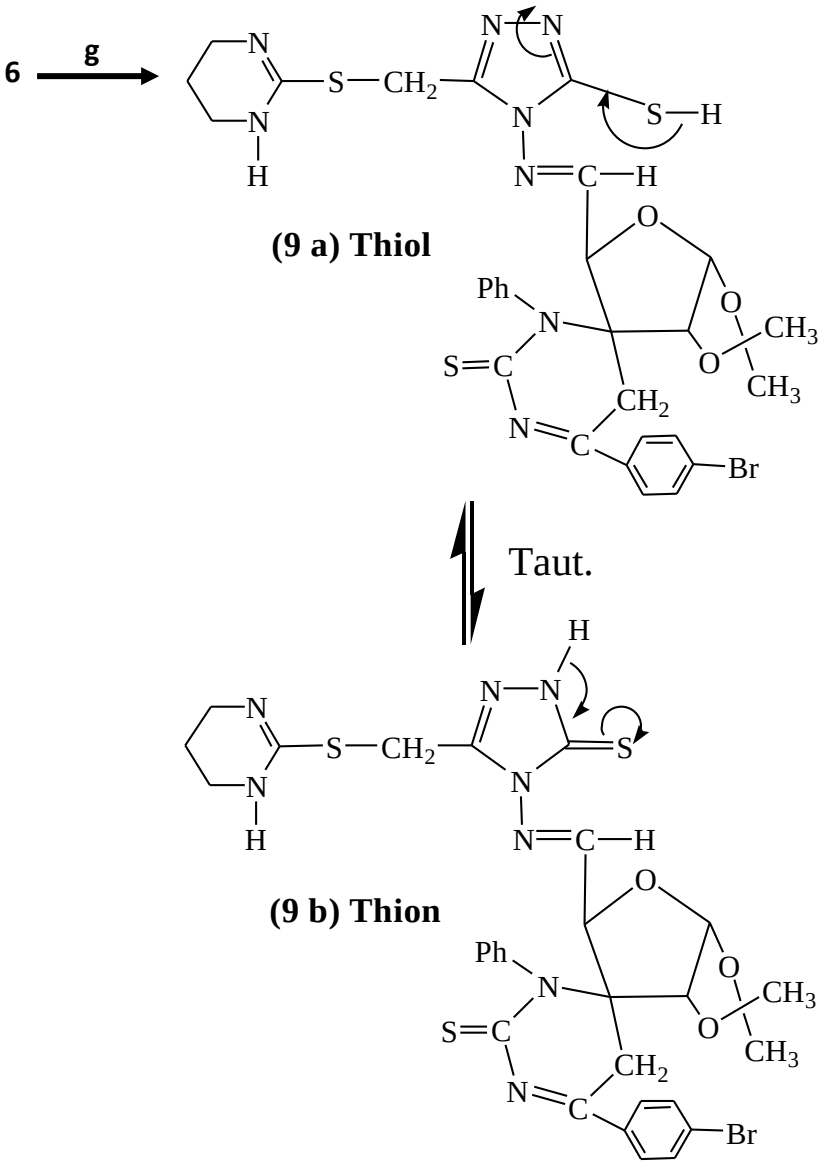
Conclusion

D-glucose has been chosen as a starting material for synthesis of nucleoside analogues since it is a readily available and comparatively inexpensive compound. In this study we have been used two principal approaches for construction of carbohydrate portion for modified nucleosides and Schiff bases. The strategy used for the synthesis of 8, 9, 14 and 15 was started with D-glucose in a series of reactions. The reason for selection of this synthetic route relative to other possible procedure for each step. Study of biological activity of these new derivatives showed that the derivative 9 exhibited higher degree of activity than the others. Due to these possible activity against HIV (Human Immuno Deficiency Virus) a preliminary test should be conducted.

(Scheme 1)

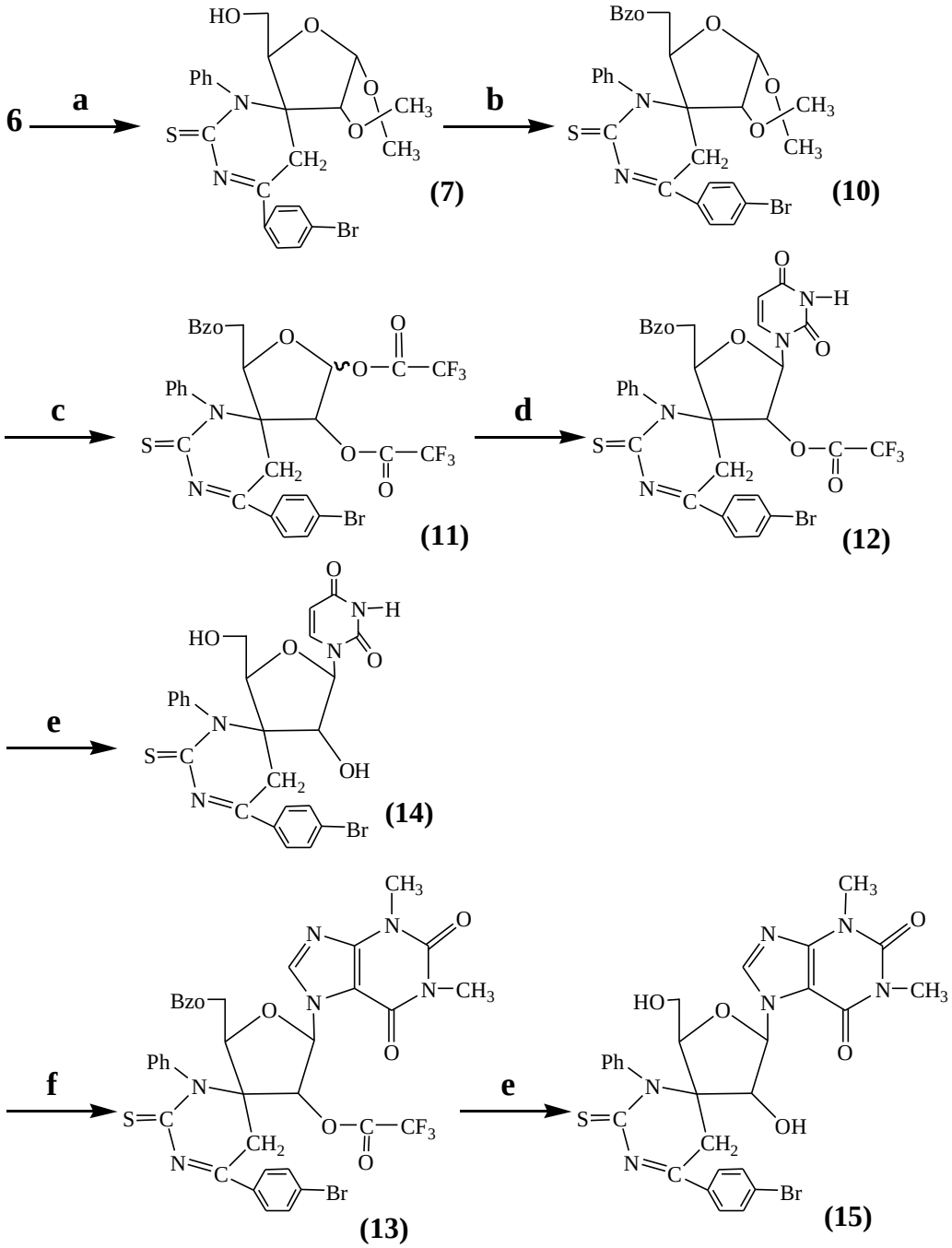


(Scheme 1)



a: p- Bromoacetophenon, Na, absolute C_2H_5OH.
b: DMSO, Ac_2O.
c: 1- Phenyl -2- thiourea, Diethylamine, absolute ethanol.
d: 66% AcOH ; e: $NaIO_4$
f: 3,4,5,6- tetrahydropyrimidine -2- thioacetichydrazide, C_2H_5OH
g: 2- [5- mercapto -4- amino -1,2,4. triazol -3- yl] thiomethyl- 3, 4, 5, 6- tetrahydropyrimidine, C_2H_5OH.

(Scheme 2)



a= $NaBH_4$
b= BzCL, Pyridine, Benzene
c= CF_3COOH, CH_3COOH, H_2O then $(CF_3CO)_2O$, Benzen Pyridine
d= Silylated Uracil, CH_2Cl_2
e=CH_3ONa, C_2H_5OH, Reflux
f=Theophylline, Mercuric Salt, Xylene, Δ

Table (1): Characteristic IR absorption bands of new derivatives

Compound No.	Infrared data ($\upsilon_{max}cm^{-1}$) (film)
2	(OH) 3355; (CO) 1680; (C=C) aromatic ring 1560-1690; (C=C) bending 815.
3	(C=C) stretching aliphatic 1645; (CO) 1685; (C=C) aromatic ring 1485-1615; (C=C) bending 810.
4	(C=N) 1655; (C=C) aromatic ring 1480-1660; (C=S) 1080; (C=C) bending 790.
5	(OH) 3380; (C=C) aromatic ring 1500-1630; (C=N) 1660; (C=S) 1085; (C=C) bending 670.
6	(C=N) 1655; (CO) 1680; (C=C)aromatic ring 1520-1600; (C=S) 1075; (C=C) bending 670.
7	(OH) 3385; (C=C) aromatic ring 1500-1620; (C=N) 1645; (C=S) 1080; (C=C) bending 810.
8	(NH) 3215; (CO) 1675; (C=N) 1660; (C=S) 1080; (C=C) aromatic ring (1595- 1630) (C=C) bending 815.
9	(NH) 3200; (NH) bending 1640; (C=N) 1615; (-N-C=S) 1490; (C=S) 1075; (C=C) aromatic ring (1500-1590); (C=C) bending 810
10	(CO) 1710, (C=C) aromatic ring 1480- 1610; (C=N) 1640; (C=S) 1085; (C=C) bending for p-substitution ring (C=C) bending for benzoyl ring 670.
11	(CO) for OB_2 1715, (CO) for CO_2Cf_3 1685; (C=N) 1645; (C=S) 1075; (C=C) aromatic ring 1450- 1610; (C=C) bending 810- 125.
12	(NH) 3380; (CO) for OBz and CO_2Cf_3 1710, 1680; (CO) for CONH 1670; (C=N) 1640; (C=S) 1080; (C=C) aromatic ring 1440- 1615; (C=C) bending 820, 710.
13	(CO) for OBz and CO_2Cf_3 1700, 1680; (CO) for ($CONCH_3$) 1675; (C=N) 1645; (C=S) 1080; (C=C) aromatic ring 1460-1625; (C=C) bending 810, 720.
14	(NH. OH) 3300, 3500; (CO) 1675; (C=N) 1660; (C=S) 1080; (C=C) aromatic ring 1500- 1615; (C=C) bending 800,710.
15	(OH) 3355, (CO) 1670; (C=N) 1645; (C=S) 1085; (C=C) aromatic ring 1460- 1620; (C=C) bending 810,700.

Table (2): Physical properties and elemental analysis for new derivatives.

Formula & comp. No.	Physical state	Rat of flow in thin lyer chromatography (tlc), R_f (solvent)	Elemental analysis calculated (found)			
			C%	H%	N%	Yield %
$C_{20}H_{25}O_7Br$ (2)	syrup	0.55 (benzene:ether 9:1)	52.51 (52.65)	5.47 (5.21)		66
$C_{20}H_{23}O_6Br$ (3)	syrup	0.48(benzene: methanol 9.5: 0.5)	54.66 (54.11)	5.23 (4.98)		52.5
$C_{27}H_{29}O_5N_2SBr$ (4)	Semi solid	0.77 (benzene: ether 9:1)	56.54 56.32	5.06 (4.99)	4.88 5.30	69.5
$C_{24}H_{25}O_5N_2SBr$ (5)	syrup	0.48(benzene:methanol 9.5:0.5)	54.03 (53.98)	4.69 (4.66)	5.25 (5.00)	55
$C_{23}H_{21}O_4N_2SBr$ (6)	syrup	0.61(benzene: n-hexane 9:1)	55.08 (54.9)	4.19 (4.25)	5.58 (5.62)	48
$C_{23}H_{23}O_4N_2SBr$ (7)	syrup	0.55 (benzene: methanol 9:0.5)	78.72 (78.51)	4.57 (4.32)	5.56 (5.22)	36.7
$C_{29}H_{31}O_4N_6S_2Br$ (8)	syrup	0.71 (benzene: methanol 9:05)	51.86 (52)	4.61 (4.44)	12.51 (12.86)	60.5
$C_{30}H_{31}O_3N_8S_3Br$ (9)	Semi solid	0.49 (benzene: ethylacetate 9.5:0.5)	49.51 (49.30)	4.26 (4.68)	15.40 15.73	75.8
$C_{30}H_{27}O_5N_2SBr$ (10)	syrup	0.36 (benzene: methanol 9:0.5)	59.30 (59.71)	4.44 (4.08)	4.61 (4.93)	55.5
$C_{31}H_{21}O_7N_2SBrF_6$ (11)	syrup	0.58 (benzene: ether 9:1)	49.01 (48.98)	2.76 (3.00)	3.68 (3.36)	63.6
$C_{33}H_{24}O_7N_4SBrF_3$(12)	syrup	0.4 (benzene: methanol 9: 0.5)	52.31 (52.65)	3.17 (3.41)	7.39 (7.21)	67.6
$C_{36}H_{28}O_7N_6SBrF_3$ (13)	syrup	0.33 (benzene: methanol 9: 0.5)	52.36 (52.11)	3.39 (3.71)	10.18 (9.96)	54.4
$C_{24}H_{21}O_5N_4SBr$ (14)	syrup	0.58 (benzene: methanol 9:0.5)	51.70 (52.00)	3.77 (3.45)	10.05 (10.38)	44.3
$C_{27}H_{25}O_5N_6SBr$ (15)	syrup	0.51 (benzene: methanol 9 0.5)	51.84 (51.60)	4 3.96	13.44 (13.68)	70.1

Table (3), Effect of antimicrobial agents on Escherichia Coli

Com. No.	Effect of new derivatives on the growth of E. coli bacteria												
	1	0.9	0.8	0.7	0.6	0.5	0.4	0.3	0.2	0.1	0.09	0.08	Conc. gm/ml
8	-	-	-	-	-	-	-	-	+				
9	-	-	-	-	-	-	-	-	-	-	-	+	
14	-	-	-	-	-	-	+						
15	-	-	-	-	-	-	-	-	-	+			
Blank	+												

(-) No growth

(+) Growth

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