Kirkuk University Journal /Scientific Studies (KUJSS)
Volume 11, Issue 3, September 2016 , p.p(1-14)
ISSN 1992 – 0849

Synthesis and Antibacterial activities of some Arabinofuranose-Schiff bases Derivatives

Mohsin O. Mohammed AL-Shwany
Kirkuk University / College of Science / Chemistry Dept.
Althker1@yahoo.com

Received date : 22 / 11 / 2015 **Accepted date : 11 / 1 / 2016**

ABSTRACT

As a continuous research for the discovery of new antibacterial agents due to the developing resistance toward conventional antibiotics, we reported a convenient synthetic approach for the preparation of methyl-α-D-arabinofuranoside shiff-bases. A series of arabinose-Shiff bases were prepared through the trityl protection of the primary hydroxyl group of methyl-α-D-arabinofuranoside, benzoylation, the removal of the trityl protective group, tosylation, azidation, conversion to the amine in the presence of triphenylphosphine, condensing reaction with a variety of aromatic aldehydes, and subsequent debenzoylation. New compounds were characterized by ^{1}H NMR and FTIR spectroscopy. Synthesised compounds were screened for antibacterial activity against several bacterial strains namely, Escherichia coli; Staphylococcus aureus; Bacillus subtilis; Candida albicans; Aspergillus niger, and they showed enhanced antibacterial activity.

Keywords: *Arabinose, Shiff-base, Antibacterial, iminosaccharides*

Kirkuk University Journal /Scientific Studies (KUJSS)
Volume 11, Issue 3, September 2016 , p.p(1-14)
ISSN 1992 – 0849

تحضير ودراسة الفعالية البايولوجية لبعض مركبات الاربينوفيورانوز – قواعد شيف

محسن عمر محمد الشواني

قسم الكيمياء / كلية العلوم / جامعة كركوك

Althker1@yahoo.com

تاريخ استلام البحث: ٢٢ / ١١ / ٢٠١٥ تاريخ قبول البحث: ١١ / ١ / ٢٠١٦

الملخص

مع استمرار البحوث لاكتشاف المضادات البكتيرية الجديدة، نتيجة مقاومة البكتريا للمضادات الحيوية التقليدية، تم تحضير مشتقات قواعد شيف جديدة لمركب الاربينوفيورانوز. تم التحضيرعن طريق حماية مجموعة الهيدروكسيل الاولية لمركب الاربينوس بواسطة ثلاثي فنيل ميثان (التريتايل) ،حماية مجاميع الهيدروكسيل الثنائية بالبنزوايل، ازالة التريتايل واستبدالها بالتولوين سلفونايل كلورايد، استبدال التوزليت بالازايد واختزال الاخيرة الى الامين عن طريق معاملتها بثلاثي فنيل فوسفين. تمت معاملة الاربينوس–الامين مع ٧ الديهايدات اروماتية لتحضير قواعد شيف (9a–g) واتبعتها ازالة مجاميع البنزوايل ليعطي المركب النهائي (10a–g) . جميع المركبات المحضرة تم تشخيصها باستخدام الطرائق الطيفية ^{1}H NMR و FTIR .تم فحص الفعالية البايولوجية لجميع المركبات المحضرة ضد بعض اصناف من البكتيريا المرضية *E. coli*, *S. aureus*, *B. subtilis*, C. albicans, *A. niger* وجميعها اظهرت فعالية مميزة للتثبيط.

الكلمات الدالة: الاربينوس؛ قواعد شيف؛ المضادات البكتيرية؛ ايمينوسكرايد.

Kirkuk University Journal /Scientific Studies (KUJSS)
Volume 11, Issue 3, September 2016 , p.p(1-14)
ISSN 1992 – 0849

1. INTRODUCTION

Schiff bases are known as imine or azomethine. Structurally these are nitrogen analogue of an aldehyde or ketone[1],[2]. Schiff bases are formed by the condensation of aldehydes and the amine group. Compound containing imines bases have been found to stand extensive application in organic synthesis, in addition, several of these molecules display significant pharmacological activities such as antimicrobial, antimalarial, antitubercular, anticancer, antihelmintic, antioxidant, analgesic and antiinflammatory[3],[4],[5]. Many studies have illustrated that aromatic nucleus Schiff bases had significant bioactivities[6]. Carbohydrates are biologically important substrate. Their chemical modification can provide new compounds and materials with interesting physicochemical and biological properties[7]. Inulin consists primarily of *β*-fructosylfructose units, always presented in furanose form[8]. Study showed that inulin Schiff bases derivatives containing benzene, have antifungal activity against different kinds of phytopathogens and exhibit higher inhibition indices than inulin. These data established that the chemical modification of inulin would lead to an enhancement of the biological activity against some plant pathogenic fungi[9]. Arabinofuranose (Ara*f*) is a very common structural constituents of polysaccharide present in many lower organisms including bacteria[10],[11], parasites[12], and fungi[13]. Polysaccharide of Ara*f* are major components of the cell wall of mycobacterial, including the human pathogens *Mycobacterium tuberculosis* and *Mycobacterium leprae*[14]. The ability of the organism to make these polysaccharides is crucial to its survival and pathogenicity[15]. Chemical synthesis of the structural fragments of these polysaccharide is holding current appeal, as the synthetic fragments play significant roles not only in probing the biosynthetic pathway by which these glycans are assembled[16], but also in exploring new oligosaccharide-based inhibitors that target the enzymes[17]. Looking at the role of Ara*f*, Schiff base and carbohydrate in medicinal chemistry, it was planned to synthesis some diverse shiff bases of Ara*f* using different aromatic aldehydes in alkaline medium and evaluation their antibacterial activities.

2. MATERIAL AND METHODS

Melting points were measured using a Gallenkamp melting point apparatus. Infra-red spectra were recorded as KBr discs (solids) or thin films on NaCl windows using a Perkin Elmer 1600 series FTIR spectrometer. NMR spectra were recorded on Bruker Avance 400

Kirkuk University Journal /Scientific Studies (KUJSS)
Volume 11, Issue 3, September 2016 , p.p(1-14)
ISSN 1992 – 0849

spectrometer. Chemical shifts are quoted in δ relative to the trace resonance of proton chloroform (δ_H 7.27 ppm).

2.1. Methyl 5-*O*-trityl-α-D-Ara*f* 3

Freshly prepared HCl solution in MeOH (resulting from mixing acetyl chloride (6 mL) in MeOH (90 mL) at 0 ºC) was added to a stirred solution of D-(-) arabinose (15.0 g, 99 mmol) in anhydrous MeOH (300 mL). Stirring was continued overnight at room temperature, when a clear solution was obtained. The mixture was neutralized by adding pyridine to pH 7-8. The solvent was evaporated to give a residue which was purified by column chromatography eluting with chloroform: acetone (3:5) to give a colourless oil, methyl-α,β-D-Ara*f* (**1**) (12.9 g, 78%) in a ratio (α : β; 3:2). Trityl chloride (19.2 g, 23 mmol) and DMAP (7.5 g, 63 mmol) were added to a stirred solution of methyl-α,β-D-Ara*f* (**1**) (9.3 g, 60 mmol) in anhydrous pyridine (100 mL) and the mixture was stirred at room temperature overnight then heated on oil bath at 70 ºC for 4 hrs. The mixture was cooled to room temperature and poured into ice/water (500 mL). The organic phase was separated and the aqueous phase was extracted with ethyl acetate (3×300 mL). The combined organic layers were washed with aq. $NaHCO_3$ solution (5%, 300 mL), dried over $MgSO_4$ and the solvent was evaporated. The residue was purified by column chromatography on silica eluting started from 10% to 50% hexane/ethyl acetate gave the title compound as a colorless oil (**3**) (9.9 g, 42%) and 5–*O*-trityl-β-D-Ara*f* (**4**) (6.9 g, 29%). The mixture of anomers were showed δ_H (400 MHz, $CDCl_3$) and IR identical to the literature[18],[19].

2.2. Methyl 2,3-di-*O*-benzyl-α-D-Ara*f* (5)

Benzoyl chloride (168.6 mL, 1.18 mmol) in anhydrous pyridine (150 mL) was added to a stirred solution of (**3**) (9.9 g, 23.6 mmol) at 0 ºC. The reaction mixture was allowed to reach room temperature and stirred at 40 ºC for 1.5 h then TLC showed no starting material was left, the mixture was cooled to 0 ºC and ice chips (150 g) was added. The mixture was diluted with ethyl acetate (150 mL), then the organic layer was separated and washed firstly with water (150 mL), sodium bicarbonate (150 mL) and finally with brine (150 mL), dried over ($MgSO_4$) and the solvent was evaporated under reduced pressure. Traces amount of pyridine was removed by co-evaporation with toluene. The result compound was dissolved in CH_2Cl_2:MeOH (1:1, 300 mL), and TsOH-H_2O (15.1 g, 79.3 mmol) was added. After stirring

Kirkuk University Journal /Scientific Studies (KUJSS)
Volume 11, Issue 3, September 2016 , p.p(1-14)
ISSN 1992 – 0849

at room temperature for 12 h, the reaction was quenched with Et_3N (15 mL). The solvent was evaporated under reduced pressure to give the residue which was purified by column chromatography on silica eluting with petrol/ethyl acetate (4:1) to give (**5**) (10.2 g, 78%), which showed δ_H (400 MHz, $CDCl_3$): 7.40 – 7.28 (10H, m), 4.95 (1H, s), 4.61 (1H, d, *J* 12.0 Hz), 4.54 (1H, d, *J* 12 Hz), 4.53 (1H, d, *J* 12 Hz), 4.50 (1H, d, *J* 12 Hz), 4.18 – 4.12 (1H, m), 4.02 – 3.96 (2H, m), 3.85 (1H, dd, *J* 2.8, 12.1 Hz), 3.65 (1H, dd, *J* 4.1, 12.1 Hz), 3.40 (3H, s), 2.93 (1H, br. s); IR, cm^{-1}: br. 3466, 3089, 3064, 3031, 2925, 1725, 1605, 1454, 696, 739. All data were identical to the authentic sample [19],[20].

2.3. Methyl 2,3-di-*O*-benzoyl-5-*O*-p-toluensulfonyl-α-D-Ara*f* (6) [20]

p-Toluene sulfonyl chloride (12.2 g, 64.2 mmol) was added to a stirred solution of compound (**5**) (10.2 g, 29.5 mmol), pyridine (15 mL, 190 mmol) and DMAP (catalytic amount) in dry CH_2Cl_2 (100 mL) at 0 ºC. The mixture was stirred and the temperature was allowed to rise to room temperature, the stirring was continued overnight. TLC showed no starting material was left and the reaction mixture was diluted with ethyl acetate (100 mL), the organic layer was separated and the aqueous layer was re-extracted with ethyl acetate (2×300 mL). The combined organic layers were washed with water (150 mL), brine (150 mL), dried over ($MgSO_4$) and the solvent was evaporated, the residue was purified by column chromatography on silica eluting with hexane/ethyl acetate (4:1) affording the title compound (**6**) (13.26 g, 90%), which showed δ_H (400 MHz, $CDCl_3$): 7.8 (2H, d, *J* 8.2 Hz), 7.41 – 7.25 (12H, m), 4.85 (1H, s), 4.22 – 4.15 (1H, m), 4.12 (2H, br. d, *J* 4.6 Hz), 3.94 (1H, br. d, *J* 2.6 Hz), 3.81 (1H, dd, *J* 2.7, 5.9 Hz), 3.33 (3H, s), 2.42 (3H, s); IR, cm^{-1}: 3064, 3032, 2916, 1741, 1454, 1365, 1177, 815.

2.4. Methyl 2,3-di-*O*-benzoyl-5-azido-5-deoxy-α-D-Ara*f* (7)

Sodium azide (5.0 g, 0.9 mmol) was added to a stirred solution of (**6**) (13.0 g, 24.6 mmol) in dry DMF (150 mL) at room temperature under nitrogen atmosphere. The reaction mixture was stirred at 70 ºC for 16 h. The reaction mixture was diluted with Et_2O (200 mL) and poured into ice cold water (250 mL), the organic layer was separated and the aqueous layer was re-extracted with Et_2O (3×150 mL). The combined organic layers were washed with saturated solution of $NaHCO_3$ (3×150 mL), brine (1×150 mL), dried over ($MgSO_4$) and the solvent was evaporated under reduced pressure to give the azide (**7**) as a white solid (10.7 g,

90%). M.p. 175–177 °C; which showed δ_H (400 MHz, $CDCl_3$): 7.31 – 7.14 (10H, m), 4.75 (1H, s), 4.24 – 4.17 (1H, m), 4.15 (2H, br. d, *J* 4.7 Hz), 3.97 (1H, br. d, *J* 2.8 Hz), 3.85 (1H, dd, *J* 2.8, 6.0 Hz), 3.35 (3H, s); IR, cm^{-1}: 3064, 3022, 2917, 1740, 1452, 1368, 1178, 815.

2.5. Methyl 2,3-di-*O*-benzoyl-5-amino-5-deoxy-α-D-Ara*f* (8)

To a stirred solution of compound (**7**) (10 g, 25 mmol) in (200) mL of anhydrous DMSO, Ph_3P (7 g, 26 mmol) was added and the reaction mixture was stirred for 24 h at room temperature. Water (10 mL) was added to the mixture and the solution was stirred for a further 24 h. The reaction mixture was poured into 500 mL acetone and the product was collected, washed 3 times by ethanol and acetone, and dried in vacuum to give the azide (**8**) (6.1 g, 90%). M.p. 229–231 °C; which showed δ_H (400 MHz, $CDCl_3$): 7.41 – 7.10 (10H, m), 4.85 (1H, s), 4.27 – 4.19 (1H, m), 4.55 (2H, br. d, *J* 4.7 Hz), 4.0 (1H, br. d, *J* 2.8 Hz), 3.95 (1H, dd, *J* 2.8, 6.0 Hz), 3.46 (3H, s); IR, cm^{-1}: 3437, 3110, 3081, 3052, 2930, 2850, 1730, 1590, 1375, 1190, 756.

2.6. General procedure for the synthesis of Schiff bases of Ara*f* (10a-g).

To a solution of compound (**8**) (0.005 mol) in methanol (20 mL), the corresponding aldehyde (0.02 mol) was added. To this mixture, KOH (0.1 % in methanol) was added to adjust the pH of the solution between 7-8 and then the mixture respectively was refluxed for 4 h. After completion reflux, Schiff base (**9a-g**) was separated out on removal of the solvent at room temp. The final compound was subjected to a hydrolysis by adding sodium methoxide (0.1 M, in methanol, 6.0 mL) to a stirred solution of compounds of (**9a-g**) (0.01 g) in dry MeOH : CH_2Cl_2 (1:1, 8 mL) at room temperature and the reaction mixture was stirred for 5 h then TLC showed no starting material was left. The reaction mixture was neutralized with Amberlite IR-120 (H^+), the resin was filtered off and the solvent was removed under reduced pressure to give a residue which was purified by column chromatography on silica eluting with dichloromethane/methanol (5:1) to afford the desired compound (**10a-g**). Synthesised compounds were proved by ^{1}HNMR and IR spectroscopy.

2.6.1. Methyl 2,3-di-*O*-benzoyl-5-deoxy-5-(3-nitrobenzylidenamino)-α-D-Ara*f* (10a)

Yield: 74.8%; M.p.: 210–212 ºC; δ_H (400 MHz, $CDCl_3$): 8.48 (1H, t, *J* 1.4, 2-Ar-*H*), 8.32 (1H, s, -C*H*=N), 8.20 (1H, dt, *J* 7.4, 1.4, 4-Ar-*H*), 7.92 (1H, dt, *J* 7.5, 1.2, 6-Ar-*H*), 7.58 (1H,

Kirkuk University Journal /Scientific Studies (KUJSS)
Volume 11, Issue 3, September 2016 , p.p(1-14)
ISSN 1992 – 0849

t, *J* 7.5, 5-Ar-*H*), 4.56 – 4.45 (2H, m, 1`,4`-H), 4.14 (1H, dd, *J* 12.5, 6.7, 5`b-H), 4.05 (1H, m, 2`-H), 3.60 (1H, dd, *J* 12.4, 6.8, 5`a-H), 3.39 – 3.28 (4H, m, 2`-H, OCH_3), 2.05 (1H, s, OH), 1.73 (1H, s, OH). IR, cm^{-1}: 3401 (*v*O-H), 3000 (*v*C-$H_{arom.}$), 2830 (*v*C-$H_{aliph.}$), 1660 (*v*C=N), 1530 (*v*NO_2), 1230 (*v*C-N), 820-680 (1,3-disubs. ring).

2.6.2. Methyl 2,3-di-*O*-benzoyl-5-deoxy-5-(4-nitrilebenzylidenamino)-α-D-Ara*f* (10b)

Yield: 80.0%; M.p.: 220–222 ºC; δ_H (400 MHz, $CDCl_3$) 8.33 (1H, s, -C*H*=N), 7.73 (2H, d, *J* 7.6, Ar-*H*), 7.65 (2H, d, *J* 7.5, Ar-*H*), 4.49 (1H, s, 1`-H), 4.43 (2H, m, 2`-H, 4`-H), 4.12 (1H, dd, *J* 7.3, 4.5, 5`b-H), 3.91 (1H, dd, *J* 12.4, 7.3, 5`a-H), 3.75 (2H, m, O*H*,3`-H), 3.34 (3H, s, OCH_3), 1.58 (1H, s, O*H*); IR, cm^{-1}: 3370(*v*O-H), 3000 (*v*C-$H_{arom.}$), 2860 (*v*C-$H_{aliph.}$), 1640 (*v*C-C), 1530 (*v*NO_2), 2240 (*v*C=N), 1230 (*v*C-N), 810 (1,4-disubs. ring).

2.6.3.Methyl2,3-di-*O*-benzoyl-5-deoxy-5-(2,4,6-trihydroxybenzylidenamino)-α-D-Ara*f* (10c)

Yield: 85.0%; M.p.: 175–177 ºC; δ_H (400 MHz, $CDCl_3$) 8.20 (1H, s, -C*H*=N), 7.38 (2H, m, 2O*H*), 5.91 (2H, m, Ar-*H*), 4.62 (1H, dt, *J* 8.7, 7.3, 4`-H), 4.49 (1H, s, 1`-H), 4.08 (1H, dd, *J* 12.4, 7.3, 5`a-H), 4.03 (1H, m, 5`b-H), 3.93 – 3.84 (2H, m, 2`, 3`-H), 3.34 (3H, s, OCH_3), 2.30 (1H, s, O*H*), 1.79 (1H, s, O*H*); IR, cm^{-1}: 3420 (*v*O-H), 3100 (*v*C-$H_{arom.}$), 2910-2860 (*v*C-$H_{aliph.}$), 1600 (*v*C=C), 1210 (*v*C-O), 1330 (*v*O-H), 2240 (*v*C=N), 1270 (*v*C-N), 800 (2,4,6-trisubs. ring).

2.6.4. Methyl 2,3-di-*O*-benzoyl-5-deoxy-5-(4-phenylbenzylidenamino)-α-D-Ara*f* (10d)

Yield: 75.0%; M.p.: 151–153 ºC; δ_H (400 MHz, $CDCl_3$) 8.17 (1H, s, -C*H*=N), 7.53 (6H, m, Ar-*H*), 7.31 (2H, t, *J* 7.3, Ar-*H*), 7.25 – 7.19 (1H, m, Ar-*H*), 4.42 (1H, td, *J* 7.3, 1.1, 4`-H), 4.34 (1H, s, 1`-H), 4.25 (1H, m, 2`-H), 4.05 (1H, m, 3`-H), 4.03 – 3.94 (2H, m, 5`b-H, O*H* ), 3.66 (1H, dd, *J* 12.5, 7.2, 5`a-H), 3.19 (3H, s, OCH_3), 1.44 (1H, s, O*H*); IR, cm^{-1}: 3401 (*v*O-H), 3000 (*v*C-$H_{arom.}$), 2910 (*v*C-$H_{aliph.}$), 2860 (*v*C-$H_{aliph.}$), 1650 (*v*C=C), 1340 (*v*O-H),, 1212 (*v*C=O), 811 (1,4-disubs. ring).

2.6.5.Methyl2,3-di-*O*-benzoyl-5-deoxy-5-(5-methylpyridylmethyleneamino)-α-D-Ara*f* (10e)

Yield: 71.0%; M.p.: 160–162 ºC; δ_H (400 MHz, $CDCl_3$) 8.36 (1H, s, -C*H*=N), 7.90 (1H, t, *J* 7.5, Py-*H*), 7.68 (1H, dd, *J* 7.5, 1.6, Py-*H*), 7.43 (1H, dd, *J* 7.5, 1.5, Py-*H*), 5.55 (1H, s, 1`-

Kirkuk University Journal /Scientific Studies (KUJSS)
Volume 11, Issue 3, September 2016 , p.p(1-14)
ISSN 1992 – 0849

H), 4.60 (1H, dt, *J* 8.9, 5.9, 4`-H ), , 4.18 (1H, br. d, *J* 4.4, 2`-H), 3.95 (1H, dd, *J* 12.4, 5.9, 5`b-H), 3.81 (1H, br. d, *J* 4.8, 3`-H), 3.60 (1H, dd, *J* 12.5, 5.9, 5`a-H), 3.34 (3H, s, OCH_3), 2.60 (3H, s, -CH_3), 2.39 (1H, s, O-*H*), 1.92 (1H, s, O-*H*); IR, cm^{-1}: 3401 (*v*O-H), 3200 (*v*C-$H_{arom.}$), 2920 (*v*C-$H_{aliph.}$), 2860 (*v*C-$H_{aliph.}$), 1600 (*v*C=C), 1340 (*v*O-H), 1290 (*v*C-N).

2.6.6. Methyl 2,3-di-*O*-benzoyl-5-deoxy-5-(2-thienylmethyleneamino)-α-D-Ara*f* (10f)

Yield: 64.2%; M.p.: 187–189 ºC; δ_H (400 MHz, $CDCl_3$) 8.05 (1H, s, -C*H*=N), 7.41 (1H, dd, *J* 7.5, 1.6, Ar-*H*), 7.28 (1H, dd, *J* 7.5, 1.5, Ar-*H*), 7.04 (1H, t, *J* 7.5, Ar-*H*), 4.47 (1H, s, 1`-H), 4.44 (1H, dd, *J* 5.7, 1.9, 3`-H), 4.17 (1H, dd, *J* 4.9, 3.9, 2`-H), 3.98 (1H, dd, *J* 12.4, 7.5, 5`a-H), 3.93 (1H, dd, *J* 12.3, 5.5, 5`b-H), 3.89 – 3.83 (1H, m, 4`-H), 3.29 (3H, s, OCH_3), 2.29 (1H, s, O-*H*), 2.14 (1H, s, O-*H*); IR, cm^{-1}: 3401 (*v*O-H), 3010 (*v*C-$H_{arom.}$), 2860 (*v*C-$H_{aliph.}$), 1630 (*v*C=C), 1340 (*v*O-H), 730-710 (*v*C-S).

2.6.7. Methyl 2,3-di-*O*-benzoyl-5-deoxy-5-(3-indolylmethyleneamino)-α-D-Ara*f* (10g)

Yield: 64.0%; M.p.: 155–157 ºC; δ_H (400 MHz, $CDCl_3$) 8.37 (1H, s, -C*H*=N), 7.68 – 7.59 (2H, m, Ar-*H*), 7.41 – 7.36 (2H, m, Ar-*H*), 7.32 – 7.20 (2H, m, Ar-*H*), 5.60 (1H, s, 1`-H), 4.75 (1H, dt, *J* 8.9, 5.8, 4`-H), 4.29 – 4.22 (1H, m, 3`-H), 4.11 (1H, dd, *J* 12.4, 5.8, 5`a-H), 3.88 (1H, m, 2`-H), 3.70 (1H, dd, *J* 12.4, 5.8, 5`b-H), 3.40 (3H, s, OCH_3), 2.60 (1H, s, O-*H*), 2.01 (1H, s, O-*H*); IR, cm^{-1}: 3401 (*v*O-H), 3200 (*v*C-$H_{arom.}$), 2990 (*v*C-$H_{aliph.}$), 2860 (*v*C-$H_{aliph.}$), 1610 (*v*C=N), 1630 (*v*C=C), 1210 (*v*C-N), 830-730 (1,2-disubs. ring).

3. ANTIMICROBIAL ACTIVITY

The *in vitro* antimicrobial activity of the synthesized compounds was tested against several pathogenic representatives: EC, *Escherichia coli;* SA, *Staphylococcus aureus;* BS, *Bacillus subtilis;* CA, Candida albicans; AN, *Aspergillus niger*. All microorganisms used were obtained from the culture collection. The antimicrobial screening, which is the first stage of antimicrobial drug discovery, was performed by the disc diffusion method Disc[15]. Media for disc sensitivity tests were nutrient agar and Muller-Hinton agar (MHA), purchased from Difco, (USA). The nonsterile powder of the tested compounds was dissolved in sterile DMSO to yield 2 µg mL^{-1} passed through 0.2 µm membrane filter (Millipore Corp., USA). The filtrates were dispensed as 2 mL samples into sterile, small screw-capped vials and kept stored at -15 °C. DMSO as a solvent showed no inhibition zones.

Kirkuk University Journal /Scientific Studies (KUJSS)
Volume 11, Issue 3, September 2016 , p.p(1-14)
ISSN 1992 – 0849

4. RESULY AND DISCUSSION

4.1.CHEMISTRY

The general synthetic strategy employed to obtain the target compounds is depicted in Scheme (1). It describes the synthesis of methyl 2,3-di-*O*-benzoyl-5-amino-5-deoxy-α-D-Ara*f* (**8**) according to literature procedures, D-(-)-arabinose was treated with freshly prepared HCl (0.22 N), generated *in situ* by addition of acetyl chloride to anhydrous methanol at 0 °C, and then worked-up with pyridine to give methyl-α, β-D-Ara*f* (**1**) Scheme (1) with predominant formation of the α-anomer (α/β, 3:2). Separation of the two anomers of (**1**) was carried out by tritylation of the mixture followed by column chromatography to give methyl 5-*O*-trityl-α-D-Ara*f* (**3**) (42%) and methyl 5-*O*-trityl-β-D-Ara*f* (**4**) (29%). Compound (**3**) was perbenzoylated to protect the two secondary hydroxyl groups using benzoyl chloride in dry pyridine, then the primary hydroxyl group was deprotected by using TsOH-H_2O in CH_2Cl_2:MeOH (1:1), affording compound (**5**) in 78% yield, Scheme (1). Structures of all the synthesised compound were proved by ^{1}HNMR and IR spectroscopy. The primary hydroxyl group in the compound (**5**) was tosylated by reaction with *p*-toluenesulfonyl chloride (TsCl) in dry pyridine and catalytic DMAP in dry CH_2Cl_2 at 0 ºC, to afford the tosylate (**6**) in 90% yield. Compound (**6**) was treated with (NaN_3, DMF) at 70 °C for 16 h, to give the azide (**7**) in 90% yield. FTIR and NMR data confirmed the structures of (**6**) and (**7**). Conversion of the azide (**7**) to the corresponding amine (**8**) was done by treated (**7**) with Ph_3P in DMSO for 24 h which afforded methyl 2,3-di-*O*-benzoyl-5-amino-5-deoxy-α-D-Ara*f* (**8**) in a good yield. Compound (**8**) was converted to its Schiff bases (**9a−g**) by refluxing with a variety of aromatic aldehydes in alkaline medium Scheme (1). Finally, the removal of the benzoyl protective groups have been done via the conventional NaOMe in MeOH to generate the amide analogues (**10a–g**) in general good yields (64–85%). Figures (1) and (2) shows the ^{1}HNMR spectra for the compounds (**3**) and (1**0f**), respectively.

Kirkuk University Journal /Scientific Studies (KUJSS)
Volume 11, Issue 3, September 2016 , p.p(1-14)
ISSN 1992 – 0849

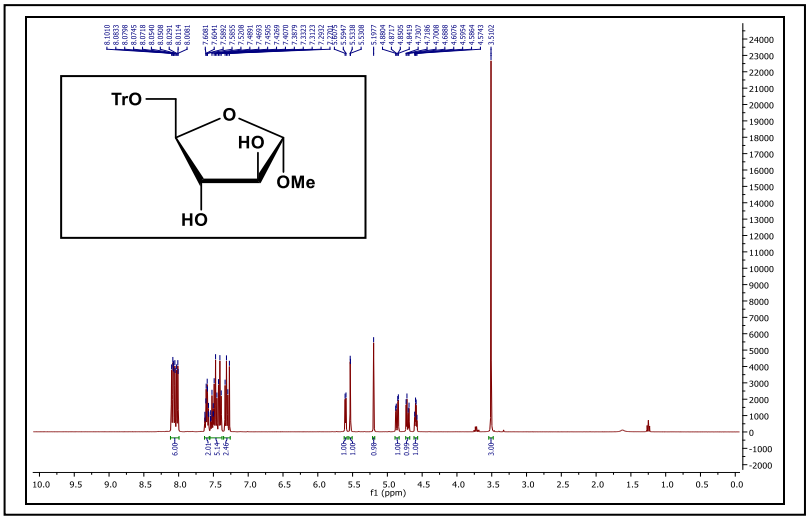


Fig. (1): ^{1}HNMR spectrum for compound (**3**)

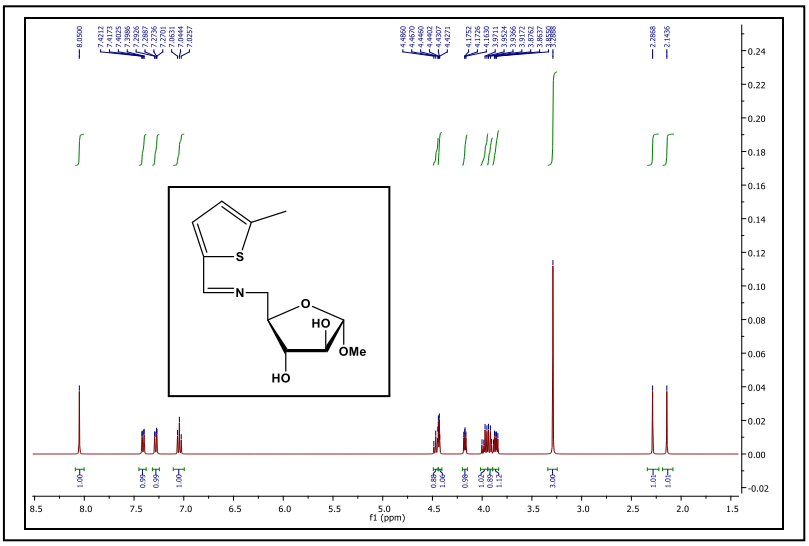
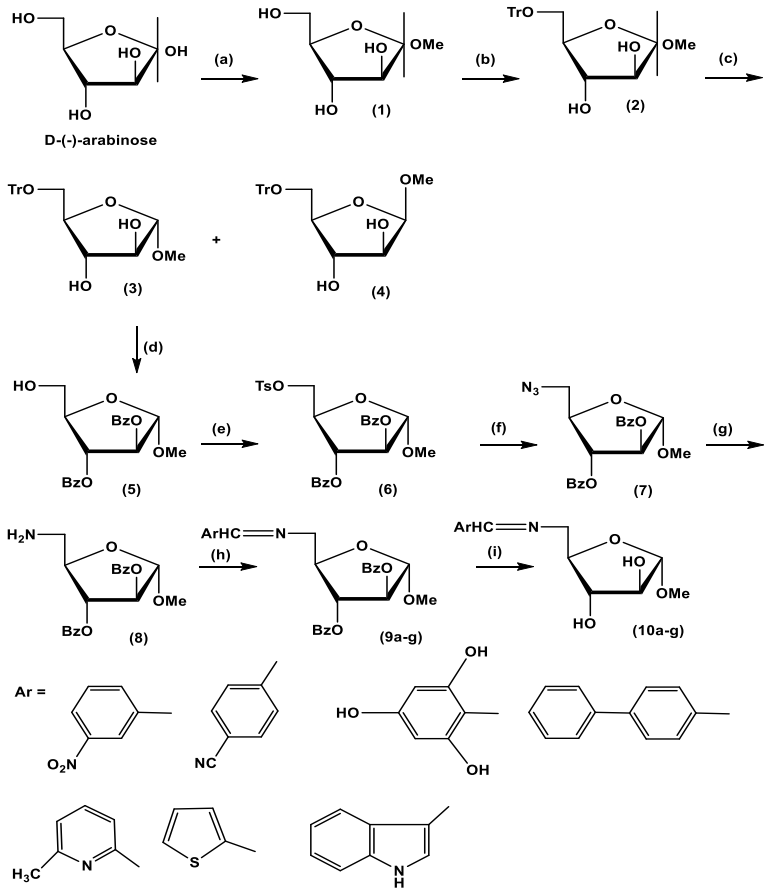


Fig. (2): ^{1}HNMR spectrum for compound (**10f**)

Kirkuk University Journal /Scientific Studies (KUJSS)
Volume 11, Issue 3, September 2016 , p.p(1-14)
ISSN 1992 – 0849



Scheme (1): Synthesis of the target compounds (**10a–g**). Reagents and conditions: (a) MeOH, HCl; (b) TrCl, DMAP, Py, 70 °C, 4 h; (c) column chromatography; (d) (1) PhCOCl, 0 to 40 °C, 1.5 h; (2) TsOH-H_2O, CH_2Cl_2/MeOH (1/1), rt, 12 h; (e) TsCl, DMAP, Py, 0 °C, 3 h; (f) NaN_3, DMF, 70 °C, 16 h; (g) Ph_3P, DMSO, 24 h; (h) ArCOH, KOH, reflux, 4 h; (i) MeONa, 0.12 M, MeOH, rt, 5 h.

4.2. BIOLOGICAL SCREENING

Determination of the antimicrobial activities of the new compounds was carried out *in vitro* by the the Disc diffusion method against test microorganisms stated in Table (1). The antimicrobial activity was evaluated by measuring the inhibition zone diameter observed. It is obvious that our synthesized compounds showed significant activity against the tested microorganisms with inhibition zones ranging from 10 to 30 mm. However, the compounds differ significantly in their activity against test microorganisms.

Kirkuk University Journal /Scientific Studies (KUJSS)
Volume 11, Issue 3, September 2016 , p.p(1-14)
ISSN 1992 – 0849

Table (1): Antimicrobial activity of some synthesized compounds

	Microorganisms[a]				
Compounds[c]	**EC**	**SA**	**BS**	**CA**	**AN**
10a	19 [b]	23	20	22	18
10b	19	14	25	18	20
10c	20	26	10	18	20
10d	22	24	10	13	10
10e	25	30	22	18	15
10f	16	18	20	24	17
10g	15	12	10	15	18

[a] Test microorganisms: EC, *Escherichia coli;* SA, *Staphylococcus aureus;* BS, *Bacillus subtilis;* CA, Candida albicans; AN, *Aspergillus niger*.

[b] Inhibition zone diameter in millimetres.

[c] $\gamma = 25\ \mu g\ mL^{-1}$ in DMSO.

DMSO has no values for negative control.

5. CONCLUSION

In conclusion, we have achieved the synthesis of novel Shiff bases of Ara*f* (**10a-g**) derived from methyl 2,3-di-*O*-benzoyl-5-amino-5-deoxy-α-D-Ara*f* and different aromatic aldehydes in good yields. Their antimicrobial activities were studied against various microorganisms, and the results showed that the synthesized derivatives had antibacterial activities. More tests and assays on these compounds are in progress.

References

[1] R. Synthesis, A. Activity, and O. F. Some, "***amgoth srinivas nayak and neerati venu madhav***" *Acta Chim. Pharm. Indica*, vol. 4, no. 1, pp. 63–67, 2014.

[2] A. Sandala, R. Suthakaran, A. Vema, A. Ravindernath, K. S. K. R. Patnaik, and F. Pharmacy, "***Docking Studies and Synthesis Of 5-benzimidazole-1-yl-methyl –[1 , 3 , 4] oxadiazole-2-thiol and their derivatives***" *Int. J. Res. Dev. Pharm. life Sci.*, vol. 2, no.

3, pp. 432–438, 2013.

[3] H. Pajouhesh and G. R. Lenz, "***Medicinal chemical properties of successful central nervous system drugs***" *NeuroRx*, vol. 2, no. 4, pp. 541–53, Oct. 2005.

[4] S. M. Alwan, "***Synthesis and preliminary antimicrobial activities of new arylideneamino-1,3,4-thiadiazole-(thio/dithio)-acetamidocephalosporanic acids***" *Molecules*, vol. 17, no. 1, pp. 1025–38, Jan. 2012.

[5] A. Aliabadi, E. Eghbalian, and A. Kiani, "***Synthesis and evaluation of the cytotoxicity of a series of 1,3,4-thiadiazole based compounds as anticancer agents***" *Iran. J. Basic Med. Sci.*, vol. 16, no. 11, pp. 1133–8, Nov. 2013.

[6] M. S. Karthikeyan, D. J. Prasad, B. Poojary, K. Subrahmanya Bhat, B. S. Holla, and N. S. Kumari, "***Synthesis and biological activity of Schiff and Mannich bases bearing 2,4-dichloro-5-fluorophenyl moiety***" *Bioorganic Med. Chem.*, vol. 14, pp. 7482–7489, 2006.

[7] N. Sachdev, A. K. Singh, A. Shrivastava, Y. Katre, and A. A. P. Khan, "***Mechanistic study of oxidation of d-arabinose by N-bromophthalimide in presence of micro-amount of chloro-complex of Ru(III) as a homogeneous catalys***t" *Arab. J. Chem.*, no. 0, 2014.

[8] T. M. Rogge and C. V Stevens, "***Facilitated synthesis of inulin esters by transesterification***" *Biomacromolecules*, vol. 5, no. 5, pp. 1799–803, Jan. 2004.

[9] Z. Guo, Q. Li, G. Wang, F. Dong, H. Zhou, and J. Zhang, "***Synthesis, characterization, and antifungal activity of novel inulin derivatives with chlorinated benzene***" *Carbohydr. Polym.*, vol. 99, pp. 469–473, 2014.

[10] P. J. Brennan and H. Nikaido, "***The envelope of mycobacteria***" *Annu. Rev. Biochem.*, vol. 64, pp. 29–63, Jan. 1995.

[11] B. Lindberg and L. Kenne, "***The Polysaccharides, Vol. 2; Academic: New York, 1985 p 287. (b) Lindberg, B***" *Adv. Carbohydr. Chem. Biochem*, vol. 48, p. 279, 1990.

[12] R. de Lederkremer and W. Colli, "***Galactofuranose-containing glycoconjugates in trypanosomatids***" *Glycobiology*, vol. 5, p. 547, 1995.

[13] S. Notermans, G. H. Veeneman, C. W. E. M. van Zuylen, P. Hoogerhout, and J. H. van Boom, ***"(1→5)-linked β-d-galactofuranosides are immunodominant in extracellular polysaccharides of Penicillium and Aspergillus species***" *Mol. Immunol.*, vol. 25, no.

10, pp. 975–979, Oct. 1988.

[14] P. Brennan, "***Structure, function, and biogenesis of the cell wall of Mycobacterium tuberculosis***" *Tuberculosis*, vol. 83, no. 1–3, pp. 91–97, Feb. 2003.

[15] Y. L. Janin, "***Antituberculosis drugs: ten years of research***" *Bioorg. Med. Chem.*, vol. 15, no. 7, pp. 2479–513, Apr. 2007.

[16] N. L. Rose, G. C. Completo, S.-J. Lin, M. McNeil, M. M. Palcic, and T. L. Lowary, "***Expression, purification, and characterization of a galactofuranosyltransferase involved in Mycobacterium tuberculosis arabinogalactan biosynthesis***" *J. Am. Chem. Soc.*, vol. 128, no. 20, pp. 6721–9, May 2006.

[17] A. K. Pathak, V. Pathak, W. J. Suling, J. R. Riordan, S. S. Gurcha, G. S. Besra, and R. C. Reynolds, "***Synthesis of deoxygenated α(1→5)-linked arabinofuranose disaccharides as substrates and inhibitors of arabinosyltransferases of Mycobacterium tuberculosis***" *Bioorg. Med. Chem.*, vol. 17, no. 2, pp. 872–881, Jan. 2009.

[18] A. K. Sanki, J. Boucau, P. Srivastava, S. S. Adams, D. R. Ronning, and S. J. Sucheck, "***Synthesis of methyl 5-S-alkyl-5-thio-D-arabinofuranosides and evaluation of their antimycobacterial activity***" *Bioorg. Med. Chem.*, vol. 16, no. 10, pp. 5672–82, May 2008.

[19] A. N. Cuzzupe, R. Di Florio, and M. A. Rizzacasa, "***Enantiospecific Synthesis of the Phospholipase A 2 Inhibitor (−)-Cinatrin B***" *J. Org. Chem.*, vol. 67, no. 13, pp. 4392–4398, Jun. 2002.

[20] A. Ishiwata, H. Akao, Y. Ito, M. Sunagawa, N. Kusunose, and Y. Kashiwazaki, "***Synthesis and TNF-alpha inducing activities of mycoloyl-arabinan motif of mycobacterial cell wall components***" *Bioorg. Med. Chem.*, vol. 14, no. 9, pp. 3049–61, May 2006.

AUTHOR

Mohsin O. Mohammed AL-Shwany received B.Sc. and MSc degrees in Chemistry from Al-Mustansriya University / Baghdad-Iraq, in 1997 and 2000, respectively. He joined Sulimani University / Facility of Agriculture - Fundamental science department from 2004 till now. He received Ph.D. in Bioorganic synthesis from Bangor University in UK in 2014.