

## Synthesis of New Carbohydrate Derivatives Via 1,3-Dipolarcycloaddition Reaction

A. Hussain K. Sharba\*, Yousif A. Al-Fattahi\*\* and Firyal W. Askar\*

\* Department of Chemistry, College of Science, Al-Mustansirya University, Baghdad-Iraq.

\*\* Department of Chemistry, College of Science, Baghdad University, Baghdad-Iraq.

Author to whom correspondence should be addressed ; E-mail: hussainirk@yahoo.com.

### Abstract

This work describes the synthesis of a new fructofuranosyl derivatives comprising 1,2,3-triazole, 1,2,3-triazoline or tetrazole rings via 1,3-dipolar cycloaddition reaction. To obtain these derivatives, 1,3,4,6-tetra-*O*-benzoyl- $\beta$ -D-fructofuranose (1) with free hydroxyl group at position-2 was prepared as the starting material. Reaction of compound (1) with 45% HBr solution in glacial acetic acid gave compound (2). The bromide (2) was then made to react with some nucleophiles ( $\text{NaN}_3$  and KCN) to give 1,3,4,6-tetra-*O*-benzoyl- $\beta$ -D-fructofuranosyl azide (3) and 1,3,4,6-tetra-*O*-benzoyl- $\beta$ -D-fructofuranosyl cyanide (4). Treatment of compound (3) with cinnamic acid, cinnamaldehyde, acrylic acid, acrylonitrile, acrylamide and maleic anhydride, gave the triazoline derivatives (5-10). Cycloaddition reaction was also carried out with propargyl chloride, propargyl alcohol and 1-hexyn-3-ol using  $(\text{ph}_3\text{P})_3\text{CuI}$  as a catalyst to give the triazole derivatives (12-14). Reaction of the cyanosugar (4) with arylsulfonyl azides gave the tetrazole derivatives (16-18). Antibacterial and antifungal activities of some novel synthesized compounds were studied and compared with that of two well known antibiotics (Ampicillin and Gentamycin).

### Introduction

In various publications it was found that 1,2,3-triazoles possess therapeutic values [1-3], they are synthetic intermediates in the preparation of medicinal compounds, and find numerous applications in the chemical industry [4]. Some 1,2,3-triazole derivatives have antibacterial [5], antifungal [6], antiviral [7], and anti-inflammatory activities [8]. Other 1,2,3-triazoles can be used as corrosion inhibitors [9,10].

Recently, 1,2,3-triazole links have emerged as a popular bridging units in carbohydrate chemistry because of the facile efficient method of their introduction, which referred to as "click chemistry". The later method is based on Cu(I)-catalyzed version of Huisgen's 1,3-dipolarcycloaddition of azido sugar to terminal alkynes and it has been successfully applied for the synthesis of various glycoconjugates including multivalent glycosides [11].

The development of tetrazoles chemistry has been largely associated with a wide scale of applications for these compounds in medicine, biochemistry [12], agriculture,

photography as well as robust binder system for high energy explosives [13].

Tetrazole compounds have also been employed as antibacterial [14], antiviral [15], antifungal, and anticonvulsive agents [16].

Hydrolysis of the benzoate groups of some novel compounds afforded a new carbohydrate derivatives containing 1,2,3-triazoline and 1,2,3-triazole, and such derivatives are expected to have high solubility in water and may possess biological activity.

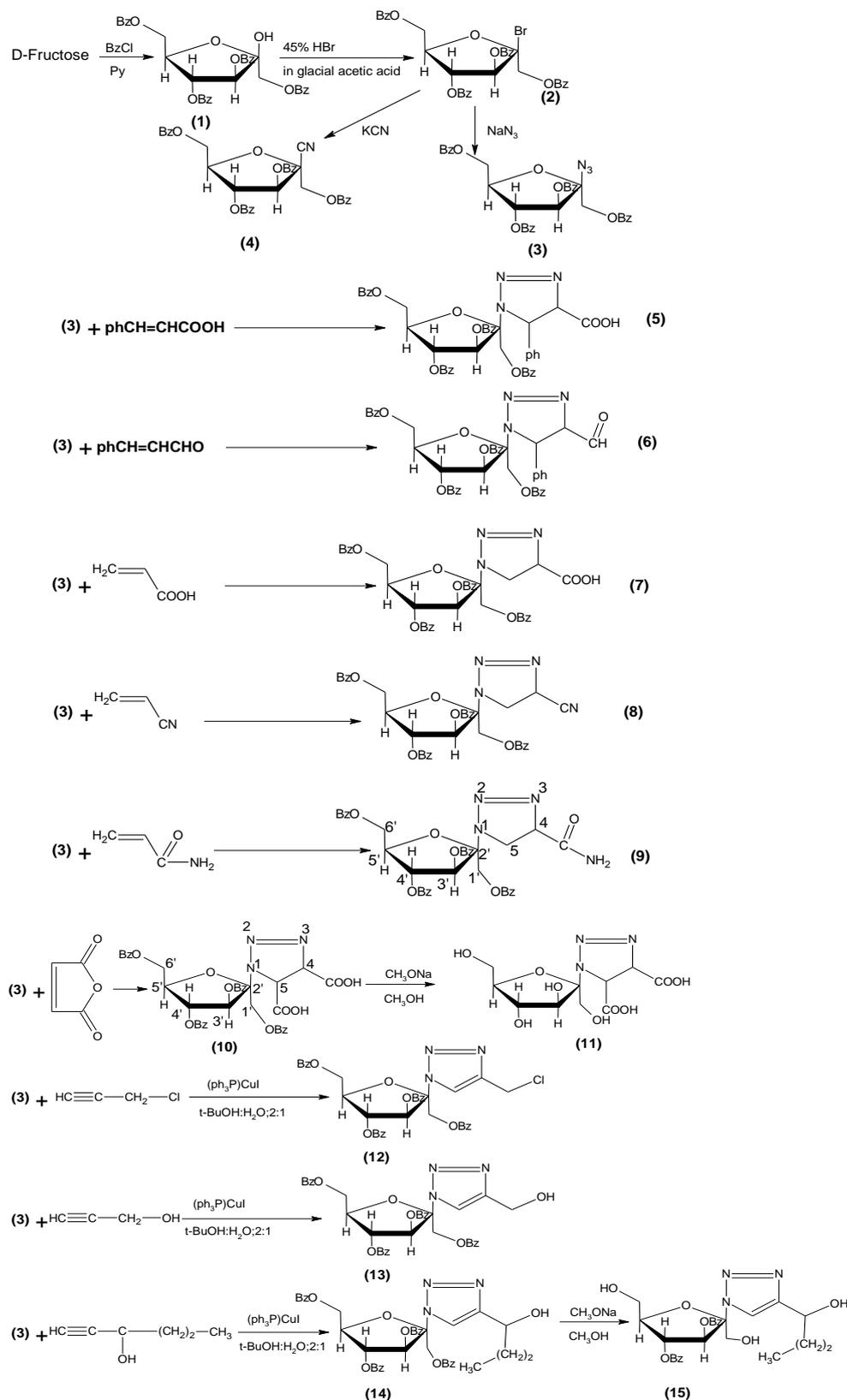
The presence of carbohydrate moiety side chain in drug may also overcome the frequently observed water insolubility problem, [17].

The activities were determined *in vitro* using disc diffusion method against staphylococcus aureus, Escherichia coli and three pathogenic strains of yeast (*Candida*) and fungus (*Aspergillus flavus* and *penicillium* spp.)

## Results and Discussions

Three types of new sugar-based monocyclic triazole, triazoline and tetrazole derivatives of D-fructose have been synthesized and characterized. These

compounds have been synthesized using [3+2] cycloaddition reaction. The reaction sequences are outlined in Schemes (1 and 2) from fructose:



Scheme (1).



FT-IR spectrum of the triazole (13) showed stretching bands at  $3400\text{ cm}^{-1}$  for the (OH) and the disappearance of ( $\text{N}_3$ ) band at  $2137\text{ cm}^{-1}$ . Using nitrile group as a dipolarophile the sugar substituted nitrile (4) readily participated in a [2+3] cycloaddition reaction with arylsulfonyl azide as 1,3-dipole, yielding five membered heterocyclic tetrazole systems. The IR absorption bands were utilized to characterize specific structure for compounds (16-18). The disappearance of the bands at  $2200\text{ cm}^{-1}$  and  $2137\text{ cm}^{-1}$  attributed to nitrile group and azide group stretching frequency is good evidence for the success of this reaction. In addition the IR spectrum of compounds (16) showed a stretching bands at  $1610\text{ cm}^{-1}$  for (C=N), at  $1370\text{ cm}^{-1}$ ,  $1160\text{ cm}^{-1}$  for ( $\text{SO}_2$ ), at  $1135\text{ cm}^{-1}$ ,  $1085\text{ cm}^{-1}$ ,  $1030\text{ cm}^{-1}$  for tetrazole ring [21] and at  $750\text{ cm}^{-1}$ ,  $690\text{ cm}^{-1}$  for mono substituted benzene ring.

The  $^1\text{H-NMR}$  spectrum of (17) showed a singlet at  $\delta$  2.4 integrated for three protons assigned to p-methyl group, while  $^{13}\text{C-NMR}$  spectrum showed signal at 20.5 ppm for methyl group of p- toluene. The signal at 151.3 assigned for C=N, while the carbonyls of the benzoate appeared at 165, 166, 166.5 and 167 ppm. The tetrazole (20) can be synthesized directly by a [3+2] dipolar cycloaddition between an azido sugar (3) and cyano compound such as (4). This reaction occurs through concerted and regioselective [22] cycloaddition with the formation of 2,5-disubstituted product as expected.

The IR spectrum of (20) showed the absence of the stretching bands for (CN) at  $2200\text{ cm}^{-1}$  and for ( $\text{N}_3$ ) at  $2137\text{ cm}^{-1}$  confirmed the formation of the tetrazole (20) with the appearance of band  $1610\text{ cm}^{-1}$  for (C=N) of the tetrazole ring.

Treatment of the some benzoylated sugar with catalytic amount of sodium methoxide under reflux afforded the free heterocyclic derivatives (11, 15, 19, and 21). The IR spectrum of (11) showed stretching band at  $3300\text{ cm}^{-1}$  for hydroxy groups, while the UV ( $\text{H}_2\text{O}$ ) spectrum agreed with free deblocked sugar (11), since the  $\lambda_{\text{max}}$  at 233 nm due to  $\pi\text{-}\pi^*$  transition of the benzoate group was absent.

## Biological Screening: Antimicrobial Activity

### Tests

The biological activity of some of the prepared compounds was tested against one strain of Gram +ve bacteria (*Staphylococcus aureus*), Gram -ve bacteria (*Escherichia coli*), yeast (*Candidas*) and fungi (*Aspergillus flavus*).

Disc sensitivity test [23] was employed for the *in vitro* study for anti bacterial and anti fungal studies. This method involves the exposure of the zone of inhibition toward the diffusion of microorganism on agar plate. The plates were incubated for 24 hrs. at  $37\text{ }^\circ\text{C}$ , the zone of inhibition of bacterial growth around the disc was measured.

In order to complete this study, some of the new compounds were tested for their *in vitro* growth inhibitory activity against yeast (*Candidas*) and a pathogenic fungi i.e. *Aspergillus flavus*, *Penicillium spp* on potato dextrose agar medium, then incubated at  $30\text{ }^\circ\text{C}$  for 72 hrs. The resulted are presented in Table (1), all tested compounds were less active than Ampicilline and Gentamycine against the Gram positive staphy. aureus. Compounds (11, 12, 18, and 21) were nearly as active as the antibiotics against the Gram negative E. Coli with (21) being the most active. Moreover compounds (11, 12, 15, and 21) show similar activity against the yeast (*Candidas*) as two antibiotics taken as standard for comparison. Compounds (12, 15, 16, 18, and 21) were more active than Ampicilline and Gentamycine against the pathogenic fungi *Spergillus flavus*, while compounds (11, 15, and 21) were more active against *penicillium spp* than the two antibiotics.

**Table (1)**  
**Results of antimicrobial activities of the compounds ( $10^{-3}$  mg. mL<sup>-1</sup>).**

Compound	Staph. Aurous	E. Coli	Candidas	Asp. flavus	Penici. spp
Control (DMSO)	–	–	–	–	–
Ampicillin	17	24	20	10	22
Gentamycin	20	22	22	17	24
6	–	8	10	10	20
11	8	20	20	17	19
12	10	20	20	20	30
15	10	15	20	20	25
16	8	15	15	20	22
18	10	20	15	15	20
19	8	15	15	20	20
21	10	25	20	20	25

Where:

6-8 mm: (+)                      10-20 mm: (+++)  
 8-10 mm: (++)                20-30 mm: (++++)

## Experimental General:

Melting points were recorded using Electrothermal 9100 melting point apparatus and are uncorrected. The IR spectra (KBr discs or thin films) were recorded on a Perkin-Elmer 1310 infrared spectrophotometer, or a Shimadzu FTIR-800.

UV spectra were recorded on UV-Visible Varian UV-Cary-100 spectrophotometers. <sup>1</sup>H-NMR and <sup>13</sup>C-NMR spectra were recorded on Varian Gemini 200BB spectrometer (200MHz) in Lodz University, Poland, on a Bruker-300 at 300 MHz for proton nucleus and 75 MHz for carbon nucleus in Al-Albait University, Jordan and on a 400 MHz in Hanover University, Germany. Tetramethylsilane was used as an internal reference and CDCl<sub>3</sub> as solvent. (TLC) was performed on aluminum plates precoated with silica-gel f<sub>254</sub>, supplied by Merck. Column chromatography was carried out with silica-gel 60 (Fluka). Spots were detected with iodine vapor.

## Synthesis of Compounds

### Preparation of 1,3,4,6-Tetra-O-benzoyl-β-D-fructofuranose (1), [18]:

Anhydrous D-fructose (2g, 11.11 mmol) was suspended in a mixture of dry CH<sub>2</sub>Cl<sub>2</sub> (30 mL) and dry pyridine (5 mL). To this mixture benzoyl chloride (7 mL) was added dropwise, then was heated with continuous stirring for 4 hrs, at (55-60 °C). TLC [CH<sub>2</sub>Cl<sub>2</sub>:MeOH; 8:2] indicated completion of the reaction. The mixture was poured over ice-water then extracted with CH<sub>2</sub>Cl<sub>2</sub> (3×15 mL). The organic phase was washed with (10 mL) (5% HCl) solution and then with (5% Na<sub>2</sub>CO<sub>3</sub>) solution (10 mL). The CH<sub>2</sub>Cl<sub>2</sub> layer was dried with anhydrous sodium sulphate and the solvent was evaporated to dryness in *vacuo* to give a syrup that crystallized from absolute ethanol to give white crystals (5.1 g, 77% yield), m.p. (121-122 °C), lit.[18] (122-123 °C), IR (KBr disc) 3450 cm<sup>-1</sup> (OH), 1710 cm<sup>-1</sup> (C=O).

**Preparation of 1,3,4,6-Tetra-O-benzoyl- $\beta$ -D-fructofuranosyl bromide (2), [24]:**

Glacial acetic acid (5 mL) was added to a solution of tetrabenzoyl fructofuranose (1) (2g, 3.36 mmol) and (45%) hydrogen bromide in glacial acetic acid (5 mL). The mixture was stirred for 30 min. and left for 6 hrs. at room temperature, after that the mixture was left to stand at (5 °C) overnight. The reaction was monitored by TLC [ $\text{CHCl}_3$ :MeOH; 8:2] and the mixture was then neutralized with saturated aqueous sodium bicarbonate solution and extracted with  $\text{CH}_2\text{Cl}_2$  (3 $\times$ 15 mL). The combined extracts were dried with anhydrous sodium sulphate, filtered and evaporated to dryness in vacuo to give a brown syrup (1.5 g, 66% yield), IR (film)  $1720\text{ cm}^{-1}$  (C=O),  $650\text{ cm}^{-1}$  (C-Br).

**Preparation of 1,3,4,6-Tetra-O-benzoyl-2-azido-2-deoxy- $\beta$ -D-fructofuranose (3):**

Compound (2) (1 g, 1.48 mmol) and excess of sodium azide were added to DMF (20 mL). The mixture was heated with stirring at (50-60 °C) for 20 hrs. The reaction was monitored by TLC [Benzene:MeOH; 8:2]. The reaction mixture was poured onto ice-cold water and extracted with chloroform (3 $\times$ 15 mL), then dried with anhydrous sodium sulphate. The solvent was evaporated to give a syrup (0.8 g, 86% yield),  $R_f = 0.6$  [ $\text{CHCl}_3$ :MeOH; 8:2], FTIR (film)  $2137\text{ cm}^{-1}$  ( $\text{N}_3$ ),  $1720\text{ cm}^{-1}$  (C=O).

**Preparation of 1,3,4,6-Tetra-O-benzoyl-2-cyano-2-deoxy- $\beta$ -D-fructofuranose (4):**

To a solution of compound (2) (1g, 1.48 mmol) in  $\text{CHCl}_3$  (30 mL), potassium cyanide (0.3 g) and tetrabutylammonium iodide (0.1 g) were added. The resulting mixture was refluxed with continuous stirring overnight. TLC [ $\text{CHCl}_3$ :MeOH; 8:2] showed that the reaction was complete. The reaction mixture was poured onto ice-cold water and extracted with chloroform (3 $\times$ 15 mL), then dried with anhydrous sodium sulphate, the chloroform layer was evaporated to give a syrup (0.75 g, 84% yield),  $R_f = 0.55$  [ $\text{CHCl}_3$ :MeOH; 9:1], FTIR (film)  $2200\text{ cm}^{-1}$  (CN),  $1714\text{ cm}^{-1}$  (C=O).

**General method for the synthesis of arylsulfonyl azides:**

Arylsulfonyl chloride and excess sodium azide were heated with stirring in acetone (50 mL). The reaction mixture was monitored by TLC [ $\text{CHCl}_3$ :ethyl acetate; 8:2]. When the reaction was completed, excess of sodium chloride was removed by filtration and evaporation of the organic solvent gave the desired product as solid or oil.

IR spectral data showed a band at  $2137\text{ cm}^{-1}$  ( $\text{N}_3$ ) and  $1365\text{ cm}^{-1}$ ,  $1170\text{ cm}^{-1}$  ( $\text{SO}_2$ ), with the disappearance of (C-Cl) band at  $740\text{ cm}^{-1}$ .

**General procedure for cycloaddition reaction of azidosugar with selected alkenes:****Preparation of compounds (5-10):**

A mixture of the azidosugar (3) (0.5 g, 0.803 mmol) and alkene (0.803 mmol) was heated with stirring in dioxane (20 mL) and monitored by TLC [benzene:MeOH; 9:1] until it indicated completion of reaction. The mixture was poured onto ice-cold water (50 mL), then extracted with chloroform (3 $\times$ 15 mL) and the chloroform of the extract was evaporated to give a syrupy product.

**1-(1',3',4',6'-Tetra-O-benzoyl- $\beta$ -D-fructofuranose-2'-yl)-4-carboxy-5-phenyl-1H-1,2,3-triazoline (5)**

$R_f = 0.41$  [ $\text{CH}_2\text{Cl}_2$ :MeOH; 8:2]; IR (film)  $3400\text{ cm}^{-1}$  (COOH),  $1720\text{ cm}^{-1}$  (C=O); UV ( $\text{CHCl}_3$ ) ( $\lambda_{\text{max}}$ , nm): 240, 362.

**1-(1',3',4',6'-Tetra-O-benzoyl- $\beta$ -D-fructofuranose-2'-yl)-4-formyl-5-phenyl-1H-1,2,3-triazoline (6):**

$R_f = 0.38$  [ $\text{CH}_2\text{Cl}_2$ :MeOH; 8:2]; IR (film)  $2800\text{ cm}^{-1}$  ( $\overset{\text{O}}{\parallel}{\text{C}}-\text{H}$ ),  $1730\text{ cm}^{-1}$  (C=O of benzoate),  $1690\text{ cm}^{-1}$  (C=O of aldehyde); UV( $\text{CHCl}_3$ ) ( $\lambda_{\text{max}}$ , nm): 246, 370.

**1-(1',3',4',6'-Tetra-O-benzoyl- $\beta$ -D-fructofuranose-2'-yl)-4-carboxy-1H-1,2,3-triazoline (7):**

$R_f = 0.43$  [ $\text{CH}_2\text{Cl}_2$ :MeOH; 8:2]; IR (film)  $3450\text{ cm}^{-1}$  (COOH),  $1724\text{ cm}^{-1}$  (C=O).

***1-(1',3',4',6'-Tetra-O-benzoyl-β-D-fructofuranose-2'-yl)-4-cyano-1H-1,2,3-triazoline (8):***

$R_f = 0.46$  [ $\text{CH}_2\text{Cl}_2$ :MeOH; 8:2]; IR (film)  $2220\text{ cm}^{-1}$  (CN),  $1715\text{ cm}^{-1}$  (C=O).

***1-(1',3',4',6'-Tetra-O-benzoyl-β-D-fructofuranose-2'-yl)-4-carbamoyl-1H-1,2,3-triazoline (9):***

$R_f = 0.3$  [ $\text{CH}_2\text{Cl}_2$ :MeOH; 8:2]; FTIR (film)  $3354, 3199\text{ cm}^{-1}$  ( $\text{NH}_2$ ),  $1724\text{ cm}^{-1}$  (C=O),  $1674\text{ cm}^{-1}$  (C=O amide).

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ (ppm): 2.89 (2H, d, H-5), 4.4-4.9 (6H, m, H-4, H-6', 6', H-1', 1', H-5'), 5.65-5.82 (2H, m, H-4', H-3'), 5.85-6.05 (2H, m,  $\text{NH}_2$ ), 7.15-8.20 (20H, m, 4BzO).

***1-(1',3',4',6'-Tetra-O-benzoyl-β-D-fructofuranose-2'-yl)-4,5-dicarboxy-1H-1,2,3-triazoline (10):***

$R_f = 0.28$  [ $\text{CH}_2\text{Cl}_2$ :MeOH; 8:2]; FTIR (film)  $3354\text{ cm}^{-1}$  (COOH),  $1726\text{ cm}^{-1}$  (C=O), UV( $\text{CHCl}_3$ ) ( $\lambda_{\text{max}}$ , nm): 233.

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ (ppm): 4.2-5.1 (5H, m, H-4, H-5, H-6', 6', H-5'), 5.5-6.1 (4H, m, H-1', 1', H-4', H-3'), 7.1-8.2 (20h, m, 4BzO), 10.5 (2H, s, COOH);  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ (ppm): 64, 65, 65.9, 67, 69 and 80 ( $\text{C}_6'$ ,  $\text{C}_1'$ ,  $\text{C}_4'$ ,  $\text{C}_3'$ ,  $\text{C}_5'$ ,  $\text{C}_2'$ ), 83 (C-triazole), 128-133 (C-aromatic), 166-168.5, 176.1, 176.3 (COOH).

***General procedure for Cu-catalyzed cycloaddition (Click reaction) of some terminal alkynes with azidosugar (3):******Preparation of compounds (12-14):***

Compound (3) (0.1g, 0.161 mmol) was dissolved in (20 mL) of (t-BuOH:H<sub>2</sub>O; 2:1) and terminal alkyne (0.161 mmol) (propargyl chloride, propargyl alcohol and 1-hexyn-3-ol) was added followed by the addition of ( $\text{ph}_3\text{P}$ )<sub>3</sub>CuI (0.1 g) as a catalyst. The mixture was then refluxed with stirring for 20 hrs. TLC showed that the reaction was complete. The mixture was poured onto ice-cold water, then extracted with chloroform (3×15 mL) and the solvent was evaporated to give the triazole as a syrup.

***1-(1',3',4',6'-Tetra-O-benzoyl-β-D-fructofuranose-2'-yl)-4-chloromethyl-1H-1,2,3-triazole (12):***

72% yield;  $R_f = 0.32$  [ $\text{CH}_2\text{Cl}_2$ :MeOH; 8:2]; FTIR (film)  $1724\text{ cm}^{-1}$  (C=O),  $1600\text{ cm}^{-1}$  (C=C),  $711\text{ cm}^{-1}$  (C-Cl).

***1-(1',3',4',6'-Tetra-O-benzoyl-β-D-fructofuranose-2'-yl)-4-hydroxymethyl-1H-1,2,3-triazole (13):***

64% yield;  $R_f = 0.39$  [ $\text{CH}_2\text{Cl}_2$ :MeOH; 8:2]; FTIR (film)  $3400\text{ cm}^{-1}$  (OH),  $1712\text{ cm}^{-1}$  (C=O),  $1604\text{ cm}^{-1}$  (C=C).

***1-(1',3',4',6'-Tetra-O-benzoyl-β-D-fructofuranose-2'-yl)-4-(1-hydroxybutyl)-1H-1,2,3-triazole (14):***

52% yield;  $R_f = 0.28$  [ $\text{CH}_2\text{Cl}_2$ :MeOH; 8:2]; FTIR (film)  $3460\text{ cm}^{-1}$  (OH),  $1715\text{ cm}^{-1}$  (C=O),  $1615\text{ cm}^{-1}$  (C=C).

***General procedure for cycloaddition of cyanosugar (4) with arylsulfonyl azides:******Preparation of compounds (16-18):***

The cyanosugar (4) (0.2 g, 0.253 mmol) was dissolved in toluene (20 mL) and arylsulfonyl azide (0.253 mmol) was added. The mixture was heated at (70-75 °C) in an oil-bath for 90 hrs. TLC [ $\text{CH}_2\text{Cl}_2$ :MeOH; 8:2] indicated the completion of the reaction. The mixture was poured onto ice-cold water and extracted with chloroform (3×15 mL). The organic layer was dried with anhydrous  $\text{Na}_2\text{SO}_4$ , then the solvent was evaporated to give a syrup, which was purified on a column of silica-gel using [ $\text{CH}_2\text{Cl}_2$ :Ethyl acetate; 8:2] as eluent.

***2-(Benzenesulfonyl)-5-(1',3',4',6'-tetra-O-benzoyl-β-D-fructofuranose-2'-yl)-2H-tetrazole (16):***

59% yield;  $R_f = 0.24, 0.18$  [ $\text{CH}_2\text{Cl}_2$ : Ethyl acetate; 9:1]; IR (film)  $1725\text{ cm}^{-1}$  (C=O),  $1610\text{ cm}^{-1}$  (C=N),  $1372, 1160\text{ cm}^{-1}$  ( $\text{SO}_2$ ) and  $1135, 1085$  and  $1030\text{ cm}^{-1}$  for the tetrazole ring.

***2-(p-Toluenesulfonyl)-5-(1',3',4',6'-tetra-O-benzoyl-β-D-fructofuranose-2'-yl)-2H-tetrazole (17):***

77% yield;  $R_f = 0.2, 0.15$  [ $\text{CH}_2\text{Cl}_2$ : Ethyl acetate; 8:2]; IR (film)  $1715\text{ cm}^{-1}$  (C=O),  $1380, 1172\text{ cm}^{-1}$  ( $\text{SO}_2$ ),  $1612\text{ cm}^{-1}$  (C=N),  $1130, 1090$  and  $1040\text{ cm}^{-1}$  for tetrazole.

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ (ppm): 2.4 (3H, s,  $\text{CH}_3$ ), 4.95 (2H, H-6', 6'), 5.15 (2H, s, H-1', 1'), 5.38 (1H, H-5'), 5.59 (1H, d, H-4'), 5.88 (1H, d, H-3'), 7.40-8.15 (24H, m, 4BzO, Ar);  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ (ppm): 20.5 ( $\text{CH}_3$ ), 58.2, 65.15, 69.0, 71.12, 76 and 85 ( $\text{C}_4'$ ,  $\text{C}_5'$ ,  $\text{C}_6'$ ,  $\text{C}_1'$ ,  $\text{C}_3'$  and  $\text{C}_2'$ ), 128.5-135.6 (C-aromatic), 137 (C-SO<sub>2</sub>), 138 (Ar-CH<sub>3</sub>), 151.3 (C=N), 165-

$\begin{array}{c} \text{C-Bz} \\ || \\ \text{O} \end{array}$   
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**2-(*m*-Nitrobenzenesulfonyl)-5-(1',3',4',6'-tetra-*O*-benzoyl- $\beta$ -D-fructofuranose-2'-yl)-2H-tetrazole (18):**

57% yield;  $R_f = 0.19, 0.14$  [ $\text{CH}_2\text{Cl}_2$ : Ethyl acetate; 9:1]; FT-IR (film) 1728  $\text{cm}^{-1}$  (C=O), 1602  $\text{cm}^{-1}$  (C=N), 1352, 1176  $\text{cm}^{-1}$  (SO<sub>2</sub>), 1533, 1379  $\text{cm}^{-1}$  (NO<sub>2</sub>), for tetrazole 1122, 1097 and 1070  $\text{cm}^{-1}$ .

**2,5-Bis(1',3',4',6'-tetra-*O*-benzoyl- $\beta$ -D-fructofuranos-2'-yl)-2H-tetrazole (20):**

The azidosugar (3) (0.1 g, 0.151 mmol) was dissolved in (20 mL) of toluene and cyanosugar (4) (0.1g, 0.165 mmol) was added. The mixture was heated at (60-70 °C) with continuous stirring for 40 hrs. TLC [ $\text{CHCl}_3$ : MeOH; 9:1] showed that the reaction was complete. The mixture was poured onto ice-cold water, then extracted with chloroform (3×15 mL). The organic layer was dried with anhydrous Na<sub>2</sub>SO<sub>4</sub>, then evaporated to give a syrup (0.07 g, 35% yield);  $R_f = 0.12$  [ $\text{CH}_2\text{Cl}_2$ :MeOH; 8:2]; IR (film) 1730  $\text{cm}^{-1}$  (C=O), 1610  $\text{cm}^{-1}$  (C=N).

**General procedure for hydrolysis of benzoate groups in triazole, triazoline and tetrazole derivatives:**

The benzoylated compound (0.1 g) in (0.01 M) methanolic sodium methoxide (20 mL) was refluxed with stirring for 1.5 hrs. Neutralization with amberlite IR(120) (H<sup>+</sup>) resin was achieved and the mixture was filtered. The filtrate was evaporated to dryness and the product was purified by a column of silica-gel 60. The column was eluted with [ $\text{CHCl}_3$ : MeOH; 8:2]. The major fraction was evaporated to give an amorphous powder.

**1-( $\beta$ -D-fructofuranos-2'-yl)-4,5-dicarboxy-1H-1,2,3-triazoline (11):**

M.p. (190-193 °C); 72% yield;  $R_f = 0.3$  [ $\text{CH}_2\text{Cl}_2$ : MeOH; 8:2]; IR (KBr disc) 3300  $\text{cm}^{-1}$  (OH of COOH), UV(H<sub>2</sub>O) ( $\lambda_{\text{max}}$ , nm): 317.

**1-( $\beta$ -D-fructofuranos-2'-yl)-4-(butyl-1-ol)-1H-1,2,3-triazole (15):**

M.p. (200-203 °C); 75% yield;  $R_f = 0.46$  [ $\text{CHCl}_3$ : MeOH; 6:4]; IR (KBr disc) 3440  $\text{cm}^{-1}$  (OH).

**2-(*m*-Nitrobenzenesulfonyl)-5-( $\beta$ -D-fructofuranos-2'-yl)-2H-tetrazole(19):**

M.p. (182-184 °C); 68% yield;  $R_f = 0.35$  [ $\text{CHCl}_3$ : MeOH; 5:5]; IR (KBr disc) 3350  $\text{cm}^{-1}$  (OH), 1360, 1180  $\text{cm}^{-1}$  (SO<sub>2</sub>), 1602  $\text{cm}^{-1}$  (C=N).

**2,5-Bis( $\beta$ -D-fructofuranos-2'-yl)-2H-tetrazole (21):**

M.p. (212-215 °C); 80% yield;  $R_f = 0.23$  [ $\text{CH}_2\text{Cl}_2$ : MeOH; 6:4]; FT-IR (KBr disc) 3433  $\text{cm}^{-1}$  (OH), 1600  $\text{cm}^{-1}$  (C=N).

**References**

- [1] Y.S. Sanghvi, B.K. Bhatta Charya, G.D. Kini and S.S. Matsumoto, J. Med. Chem., 33 (1990) 336.
- [2] G. Biagi, I. Giorgi, O. Livi and A. Lucacchini, J. Pharm. Sci., 82 (1993) 893.
- [3] A. Bascal, L. Holden-Dye, R.J. Willis and S.W.G. Smith, J. Parasitology, 112 (1996) 253.
- [4] C. Peto, G. Batta, Z. Gyorgdeak and F. Szaricskai, J. Carbohydr. Chem., 15 (1996) 465.
- [5] G.S. Gadaginamath, S.A. Patil and A.S. Shydligeri, Ind. J. Chem., 35(B) (1996) 681-684.
- [6] M.M. Pearson, P.D. Rogers and S.W. Chapman, Ann. Pharmacother., 37(3), (2003) 420-32.
- [7] C.H. Chu, X.W. Sun, L. Sun and Z.Y. Zhang, J. Chin. Chem. Soc., 46 (1999) 229.
- [8] P.K. Kadaba, P.J. Stevenson and P. Nunane, Bio Org. Med. Chem., 4(2) (1996) 165.
- [9] A.M.S. Abdennabi, A.I. Abdalhadi and S.T. Abu-Orabi, Anti Corrosion Methods and Materials, 45 (1998) 103.

## الخلاصة

- [10] S.T. Abu-Orabi, *Molecules*, 7 (2002) 302-314.
- [11] Sergey A. Nepogodiev, Simone Dedola, Laurence Marmuse, Marcelo T. de Oliveira and Robert A Field, *Carbohydrate Research* 342, (2007) 529-540.
- [12] G.I. Koldaskii and V.A. Ostrovskii, *Khim. Geterotsikl. Soedin*, 6 (1985) 557-858.
- [13] G.I. Koldoskii, V.A. Ostrovskii and V.S. Poplavskii, *Advances in Tetrazole's Chemistry (Review)*, *Khim. Geterotsikl. Soedin*, 10, (1981) 1299-1326.
- [14] G.D. Chaitanya and R.D. Shah, *Molecules*, 7 (2002) 554-565.
- [15] T. Himanshui, R. Olsen-Carl-E and P. Ashok-K, *Bio. Org. Med. Chem.*, 10(4), (2002) 963-8.
- [16] P.K. Kadabe and M.M. Morgan, *Bio. Med. Pharamacother.*, 49(7-8) (1995) 381.
- [17] A.A Jarrahoup, M. Shekarriz and A. Taslimi, *Molecules*, 9 (2004), 29-38.
- [18] P. Brigl and R. Schinle, *Ber.*, 67 (1934) 754.
- [19] R.M. Silverstein, G.C. Basler and T.C. Morrill, "Spectroscopic identification of Organic Compounds", John Wiley and Sons, Inc., New York, 4<sup>th</sup> Ed. (1980).
- [20] V.V. Rostovtsev, L.G. Freen, V.V. Fokin and K.B. Sharpless, *Angew. Chem. Int. Ed.*, 2002, 114, 2708-2711.
- [21] M.M. Ismail, M. Abass and M.M. Hassan, *Fourth International Electronic Conferences on Synthetic Organic Chemistry (ECSOC-4)*, [www.mdpi.org/escoc40htm](http://www.mdpi.org/escoc40htm), September, 1-30 (2000).
- [22] R. Huisgen, *J.Org. Chem.*, 33 (1968) 2291-2297.
- [23] M.R. Atlas, E. Alfres, Brown and C. Lawrence Parks, "Laboratory Manual Experimental Microbiology, Mosby-Year Book Inc. (1995).
- [24] R.K. Ness and H.G. Fleteher, *J. Am. Chem. Soc.*, 75 (1953) 2619.
- [25] Taken in part from ph.D. thesis of F. W. Askar, Al-Mustansirya University, Baghdad.

يتضمن هذا العمل تحضير مشتقات كاربو هيدراتية جديدة تحتوي حلقة 3,2,1-ترايازول، 1,2,3-ترايازولين و حلقة تترازول بطريقة تفاعل الاضافة ثنائية القطب 1 و 3 الحلقيّة.

للحصول على هذه المشتقات ، حضر 1، 3، 4، 6-رباعي-O-بنزويل-D-β-فركتوفورانونوز (1) الذي يحتوي على مجموعة هيدروكسيل حرة في الموقع 2-كمادة اولية. عند معاملة (1) مع (HBr 45%) المذاب في حامض الخليك الثلجي نحصل على بروميد -D-β-فركتوفورانونوسيل(2)، بعد ذلك تم مفاعلة (2) مع عدد من الكواشف الباحثة عن النواة مثل ازيد الصوديوم ، و سيانيد الصوديوم ليعطي 1، 3، 4، 6-رباعي-O-بنزويل-β-D-فركتوفورانونوازيد (3) 1، 3، 4، 6-رباعي-O-بنزويل-D-β-فركتوفورانونوسيانيد(4). عند معاملة (3) مع حامض السينامك، سينمالديهيد، حامض الاكريليك، اكريليك نايتريل، اكريل اماید و انهيدريد المالبك حيث يتم الحصول على مشتقات التترازولين(5-10).

و عند اجراء تفاعل الاضافة الحلقيّة 1 و 3 بين ازيد السكر (3) و كلوريد البروبرجيل و كحول البروبرجيل و 1-هيكساين-3-اول، باستخدام ((ph3P)3CuI) كعامل مساعد تم الحصول على مشتقات التترازول (12-14). تفاعل سيانيد السكر (4) مع اريل سلفونيل ازيد اعطى عدد من مشتقات التترازول (16-18).

تم تقويم الفعالية المضادة للبكتريا و الفطريات

لبعض المركبات المحضرة و مقارنتها مع

نوعين من المضادات الامبسلين و جنتاميسين

(Ampicillin and Gentamycin).