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

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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-β-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 (NaN_3 and KCN) to give 1,3,4,6-tetra-*O*-benzoyl-β-D-fructofuranosyl azide (3) and 1,3,4,6-tetra-*O*-benzoyl-β-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 $(ph_3P)_3CuI$ 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 posses 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], antifungicial, and anticonvulsive agents [16].

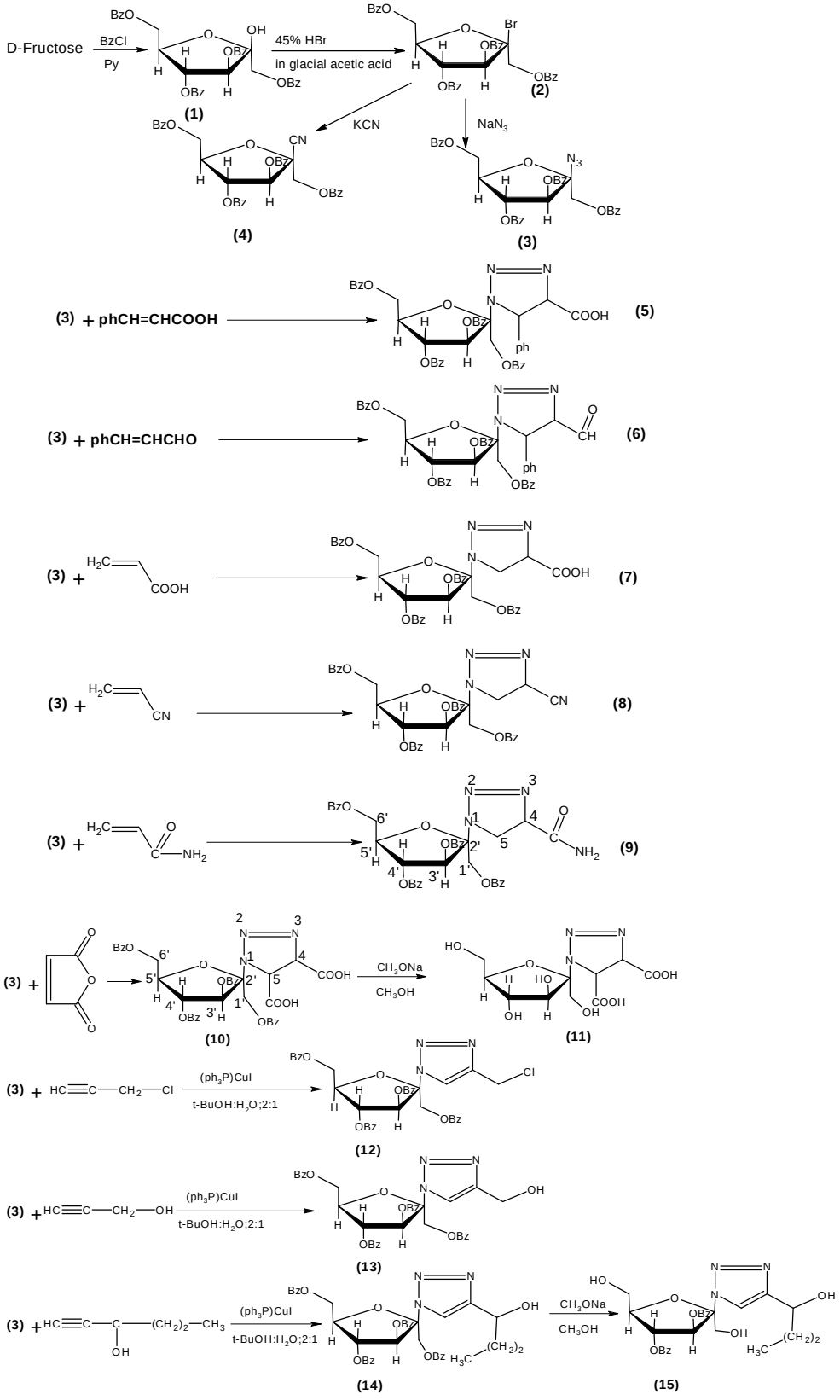
Hydrolysis of the benzoate groups of some novel compounds afforded a new carbohydrate derivatives containing 1,2,3-triazoline and 1,2,3-triazole, and such derivatives are expected to have high solubility in water and may possess biological activity.

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

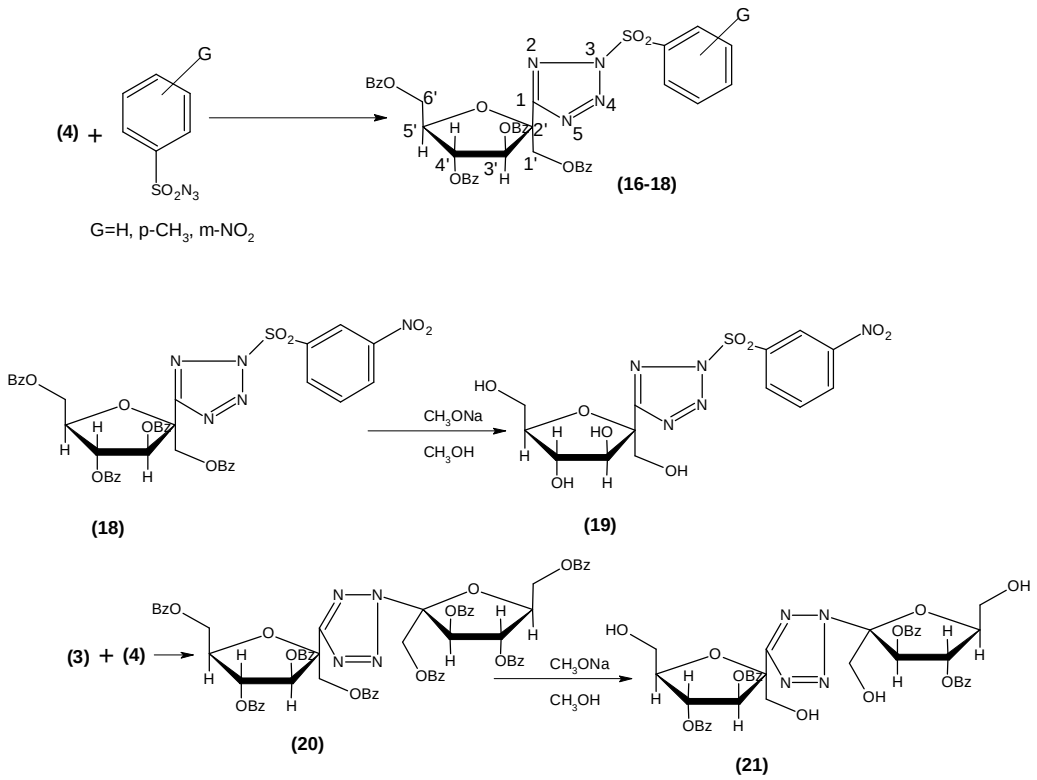
The activities were determined *in vitro* using disc diffusion method against staph-aureus, Eschericha coli and three pathogenic strains of yeast *(Candida)* and fungus (Aspergillus flaveus and pencillium spp.)

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).



Scheme (2).

D-Fructose was first converted to 1,3,4, 6-tetra- *O*- benzoyl- β- D- fructofuranose (1). According to reported method [18] when compound (1) was treated with 45% HBr solution in glacial acetic acid it gave 1,3,4,6-tetra-*O*-benzoyl-β-D-fructofuranosyl bromide (2). Treatment of the benzoylated bromide with sodium azide afforded sugar azide (3). The FTIR spectrum of (3) showed stretching band at 2137 cm^{-1} indicating the presence of an azido group with disappearance of the (C-Br) stretching band at 650 cm^{-1}.

To prepare the 1,2,3-triazoline derivatives, the azidosugar (3) entered 1,3-cycloaddition reaction with cinnamic acid, cinnamaldehyde, acrylic acid, acrylonitrile, acrylamide and maleic anhydride, which gave the triazoline derivatives (5-10) as indicated by the disappearance of (N_3) vibration band. The FTIR spectrum of (5) showed a characteristic band at 3450-3000 cm^{-1} due to hydroxyl group of the carboxylic acid, while compound (8) showed a stretching band at 2220 cm^{-1} for the nitrile group and compound (9) showed a split broad band at 3354 cm^{-1} and at 3199 cm^{-1} which was assigned to the asymmetric and symmetric stretching bands of NH_2 function, [19]. The ^{1}H-NMR spectrum of compound (9) showed the signals at δ 5.85-6.05 ppm assigned to protons of NH_2. Proton for triazoline ring H-5 appeared at δ 2.89 ppm.

The FT-IR spectrum of compound (10) showed a broad stretching band at 3600-3200 cm^{-1} due to the hydrogen bonded of acid hydroxyl group. FT-IR data gave good evidence that the cyclic anhydride has undergone ring opening during work up to give dicarboxylic acid. Furthermore, the ^{1}H-NMR spectrum showed a signal at 10.5 ppm and ^{13}C-NMR spectrum showed a signal at 170.2 ppm indicating the presence of carboxylic acid.

The 1,2,3-triazoles (12-14) were successfully obtained via cycloaddition reaction of the azido sugar (3) with propargyl chloride, propargyl alcohol and 1-hexyn-3-ol using $(ph_3P)_3CuI$ as catalyst. The thermal reaction leads to the formation of the disubstituted triazole isomers and need long reaction time while the copper (I)-catalyzed reaction selectively produces the 1,4-isomer in high yields. This assignment is quite compatible with the reported results of Rostovtsev and his co-workers on the addition of benzyl azide to phenyl propargyl ether, [20].

FT-IR spectrum of the triazole (13) showed stretching bands at 3400 cm^{-1} for the (OH) and the disappearance of (N_3) band at 2137 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 cm^{-1} and 2137 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 cm^{-1} for (C=N), at 1370 cm^{-1}, 1160 cm^{-1} for (SO_2), at 1135 cm^{-1}, 1085 cm^{-1}, 1030 cm^{-1} for tetrazole ring [21] and at 750 cm^{-1}, 690 cm^{-1} for mono substituted benzene ring.

The ^{1}H-NMR spectrum of (17) showed a singlet at δ 2.4 integrated for three protons assigned to p-methyl group, while ^{13}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 cm^{-1} and for (N_3) at 2137 cm^{-1} confirmed the formation of the tetrazole (20) with the appearance of band 1610 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 cm^{-1} for hydroxy groups, while the UV (H_2O) spectrum agreed with free deblocked sugar (11), since the λ_{max} at 233 nm due to π-π* 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 aurous*), Gram –ve bacteria (*Eschericha 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 °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*, *Penicillum spp* on potato dextrose agar medium, then incubated at 30 °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. aurous. 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 comparision. 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 pencillum spp than the two antibiotics.

Table (1)
Results of antimicrobial activities of the compounds (10^{-3} mg. mL^{-1}).

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. ^{1}H-NMR and ^{13}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. Tetramethyl-silane was used as an internal reference and $CDCl_3$ as solvent. (TLC) was performed on aluminum plates precoated with silica-gel f_{254}, 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-b-D-fructofuranose (1), [18]:*

Anhydrous D-fructose (2g, 11.11 mmol) was suspended in a mixture of dry CH_2Cl_2 (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_2Cl_2:MeOH; 8:2] indicated completion of the reaction. The mixture was poured over ice-water then extracted with CH_2Cl_2 (3×15 mL). The organic phase was washed with (10 mL) (5% HCl) solution and then with (5% Na_2CO_3) solution (10 mL). The CH_2Cl_2 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^{-1} (OH), 1710 cm^{-1} (C=O).

Preparation of 1,3,4,6-Tetra-O-benzoyl-b-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 [$CHCl_3$:MeOH; 8:2] and the mixture was then neutralized with saturated aqueous sodium bicarbonate solution and extracted with CH_2Cl_2 (3×15 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 cm^{-1} (C=O), 650 cm^{-1} (C-Br).

Preparation of 1,3,4,6-Tetra-O-benzoyl-2-azido-2-deoxy-b-D-fructo-furanose (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 (3×15 mL), then dried with anhydrous sodium sulphate. The solvent was evaporated to give a syrup (0.8 g, 86% yield), R_f = 0.6 [$CHCl_3$:MeOH; 8:2], FTIR (film) 2137 cm^{-1} (N_3), 1720 cm^{-1} (C=O).

Preparation of 1,3,4,6-Tetra-O-benzoyl-2-cyano-2-deoxy-b-D-fructofuranose (4):

To a solution of compound (2) (1g, 1.48 mmol) in $CHCl_3$ (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 [$CHCl_3$:MeOH; 8:2] showed that the reaction was complete. The reaction mixture was poured onto ice-cold water and extracted with chloroform (3×15 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 [$CHCl_3$:MeOH; 9:1], FTIR (film) 2200 cm^{-1} (CN), 1714 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 [$CHCl_3$: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 cm^{-1} (N_3) and 1365 cm^{-1}, 1170 cm^{-1} (SO_2), with the disappearance of (C-Cl) band at 740 cm^{-1}.

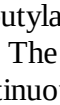
General procedure for cycloaddition reaction of azidosugar with selected alkenes: Preparation of compounds (5-10):

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 (3×15 mL) and the chloroform of the extract was evaporated to give a syrupy product.

1-(1',3',4',6'-Tetra-O-benzoyl-b-D-fructofuranose-2′-yl)-4-carboxy-5-phenyl-1H-1,2,3-triazoline (5)

R_f = 0.41 [CH_2Cl_2:MeOH; 8:2]; IR (film) 3400 cm^{-1} (COOH), 1720 cm^{-1} (C=O); UV ($CHCl_3$) (λ_{max}, nm): 240, 362.

1-(1',3',4',6'-Tetra-O-benzoyl-b-D-fructofuranose-2′-yl)-4-formyl-5-phenyl-1H-1,2,3-triazoline (6):

R_f = 0.38 [CH_2Cl_2:MeOH; 8:2]; IR (film) 2800 cm^{-1} (), 1730 cm^{-1} (C=O of benzoate), 1690 cm^{-1} (C=O of aldehyde); UV($CHCl_3$) (λ_{max}, nm): 246, 370.

1-(1',3',4',6'-Tetra-O-benzoyl-b-D-fructofuranose-2′-yl)-4-carboxy-1H-1,2,3-triazoline (7):

R_f = 0.43 [CH_2Cl_2:MeOH; 8:2]; IR (film) 3450 cm^{-1} (COOH), 1724 cm^{-1} (C=O).

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

R_f = 0.46 [CH_2Cl_2:MeOH; 8:2]; IR (film) 2220 cm^{-1} (CN), 1715 cm^{-1} (C=O).

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

R_f = 0.3 [CH_2Cl_2:MeOH; 8:2]; FTIR (film) 3354, 3199 cm^{-1} (NH_2), 1724 cm^{-1} (C=O), 1674 cm^{-1} (C=O amide).

^{1}H-NMR ($CDCl_3$) δ(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, NH_2), 7.15-8.20 (20H, m, 4BzO).

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

R_f = 0.28 [CH_2Cl_2:MeOH; 8:2]; FTIR (film) 3354 cm^{-1} (COOH), 1726 cm^{-1} (C=O), UV($CHCl_3$) (λ_{max}, nm): 233.

^{1}H-NMR ($CDCl_3$) δ(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}C-NMR ($CDCl_3$) δ(ppm): 64, 65, 65.9, 67, 69 and 80 (C_6', C_1', C_4', C_3', C_5', 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_2O; 2:1) and termial alkyne (0.161 mmol) (propargyl chloride, propargyl alcohol and 1-hexyn-3-ol) was added followed by the addition of $(ph_3P)_3CuI$ (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-b-D-fructofuranose-2'-yl)-4-chloromethyl-1H-1,2,3-triazole (12):

72% yield; R_f = 0.32 [CH_2Cl_2:MeOH; 8:2]; FTIR (film) 1724 cm^{-1} (C=O), 1600 cm^{-1} (C=C), 711 cm^{-1} (C-Cl).

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

64% yield; R_f = 0.39 [CH_2Cl_2:MeOH; 8:2]; FTIR (film) 3400 cm^{-1} (OH), 1712 cm^{-1} (C=O), 1604 cm^{-1} (C=C).

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

52% yield; R_f = 0.28 [CH_2Cl_2:MeOH; 8:2]; FTIR (film) 3460 cm^{-1} (OH), 1715 cm^{-1} (C=O), 1615 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 [CH_2Cl_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 Na_2SO_4, then the solvent was evaporated to give a syrup, which was purified on a column of silica-gel using [CH_2Cl_2:Ethyl acetate; 8:2] as eluent.

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

59% yield; R_f = 0.24, 0.18 [CH_2Cl_2: Ethyl acetate; 9:1]; IR (film) 1725 cm^{-1} (C=O), 1610 cm^{-1} (C=N), 1372, 1160 cm^{-1} (SO_2) and 1135, 1085 and 1030 cm^{-1} for the tetrazole ring.

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

77% yield; R_f = 0.2, 0.15 [CH_2Cl_2: Ethyl acetate; 8:2]; IR (film) 1715 cm^{-1} (C=O), 1380, 1172 cm^{-1} (SO_2), 1612 cm^{-1} (C=N), 1130, 1090 and 1040 cm^{-1} for tetrazole.

^{1}H-NMR ($CDCl_3$) δ(ppm): 2.4 (3H, s, 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}C-NMR ($CDCl_3$) δ(ppm): 20.5 (CH_3), 58.2, 65.15, 69.0, 71.12, 76 and 85 (C_4',C_5′, C_6', C_1', C_3' and C_2'), 128.5-135.6 (C-aromatic), 137 (C-SO_2), 138 (Ar-CH_3), 151.3 (C=N), 165-167 (C(=O)-Bz).

2-(m-Nitrobenzenesulfonyl)-5-(1',3',4',6'-tetra-O-benzoyl -b-D-fructofuranose-2'-yl)-2H-tetrazole (18):

57% yield; R_f = 0.19, 0.14 [CH_2Cl_2: Ethyl acetate; 9:1]; FT-IR (film) 1728 cm^{-1} (C=O), 1602 cm^{-1} (C=N), 1352, 1176 cm^{-1} (SO_2), 1533, 1379 cm^{-1} (NO_2), for tetrazole 1122, 1097 and 1070 cm^{-1}.

2,5-Bis(1',3',4',6'-tetra-O-benzoyl-b-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 [$CHCl_3$: 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_2SO_4, then evaporated to give a syrup (0.07 g, 35% yield); R_f = 0.12 [CH_2Cl_2:MeOH; 8:2]; IR (film) 1730 cm^{-1} (C=O), 1610 cm^{-1} (C=N).

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

The benzolayted 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^+) 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 [$CHCl_3$: MeOH; 8:2]. The major fraction was evaporated to give an amorphous powder.

1-(b-D-fructofuranos-2′-yl)-4,5-dicarboxy-1H-1,2,3-triazoline (11):

M.p. (190-193 °C); 72% yield; R_f = 0.3 [CH_2Cl_2: MeOH; 8:2]; IR (KBr disc) 3300 cm^{-1} (OH of COOH), UV(H_2O) (λ_{max}, nm): 317.

1-(b-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 [$CHCl_3$: MeOH; 6:4]; IR (KBr disc) 3440 cm^{-1} (OH).

2-(m-Nitrobenzenesulfonyl-5-(b-D-fructofuranos-2'-yl)-2H- tetrazole(19):

M.p. (182-184 °C); 68% yield; R_f = 0.35 [$CHCl_3$: MeOH; 5:5]; IR (KBr disc) 3350 cm^{-1} (OH), 1360, 1180 cm^{-1} (SO_2), 1602 cm^{-1} (C=N).

2,5-Bis(b-D-fructofuranos-2'-yl)-2H-tetrazole (21):

M.p. (212-215 °C); 80% yield; R_f = 0.23 [CH_2Cl_2: MeOH; 6:4]; FT-IR (KBr disc) 3433 cm^{-1} (OH), 1600 cm^{-1} (C=N).

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الخلاصة

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

للحصول على هذه المشتقات، حضر 1، 3، 4، 6-رباعي-O-بنزويل-β-D-فركتوفيورانوز (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 -β-D-فركتوفيورانوسيل(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-فركتوفيورانوازيد (3) 1، 3، 4، 6- رباعي-O-بنزويل-β-D-فركتوفيورانوسيانيد(4). عند معاملة (3) مع حامض السينامك, سينمالديهايد, حامض الاكريليك, اكريليك نايتريل, اكريل امايد و انهيدريد الماليك حيث يتم الحصول على مشتقات الترايزولين(5-10).

و عند اجراء تفاعل الاضافة الحلقية 1و 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 الترايزول(12-14). تفاعل سيانيد السكر (4) مع اريل سلفونيل ازايد 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) .