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C-Furyl glycosides, I: Synthesis and antimicrobial evaluation of *C*-furyl glycosides and chalcones derived therefrom

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Abstract New *C*-furyl glycosides were synthesized in order to increase the number of compounds screened for antimicrobial activity. The antimicrobial activity showed that the bromo as well as the nitro derivatives were the most active compounds.

Keywords *C*-Furyl glycosides; *N*-Glycosides; Chalcones; Antimicrobial activity.

Introduction

The high throughput screening techniques are rapid methods to screen combinatorial assemblies for lead molecules, which become the main place for many drug discovery programs. Considerable attention has been devoted to the synthesis of *C*-glycosyl compounds owing to their biological interest, their natural occurrence, and synthetic utility [1]. Among naturally occurring *C*-glycosyl compounds, aryl *C*-glycosyl derivatives are useful as enzyme inhibitors [2] and present in a variety of biologically important natural products as papulacandins, pluramycins, vineomycin, gilvocarcin V, and urdamycin A, which are recognized for their various biological activities including antibiotic, antitumoral, and antiplatelet aggregation activities [3]. In addition, they are used as a model in enzymatic and metabolic studies; indeed it has been shown that the conformational differences between the *O*- or *N*-glycosides and the C-linked analogues are minimal [4]. Moreover, *C*-glycosides are essentially more inert to degradation and therefore possess high resistance to enzymatic hydrolysis [5]. A large number of *C*-glycosides [6] of considerable biological and chemical interest have been found to possess a substituted tetrahydrofuran moiety. *C*-Furyl glycosides are useful precursors for the synthesis of many *C*-glycosyl antibiotics [7]. In addition to their enzyme-inhibitory activities, these compounds are potential drug candidates for new therapeutics [8]. They have also been used as peptidomimetics that adopt interesting secondary structures because of the rigidity generated by the presence of furan moiety [9]. On the other hand, furan ring systems are potential drugs for new therapeutic strategies and exhibit a wide spectrum of biological activities [10–14].

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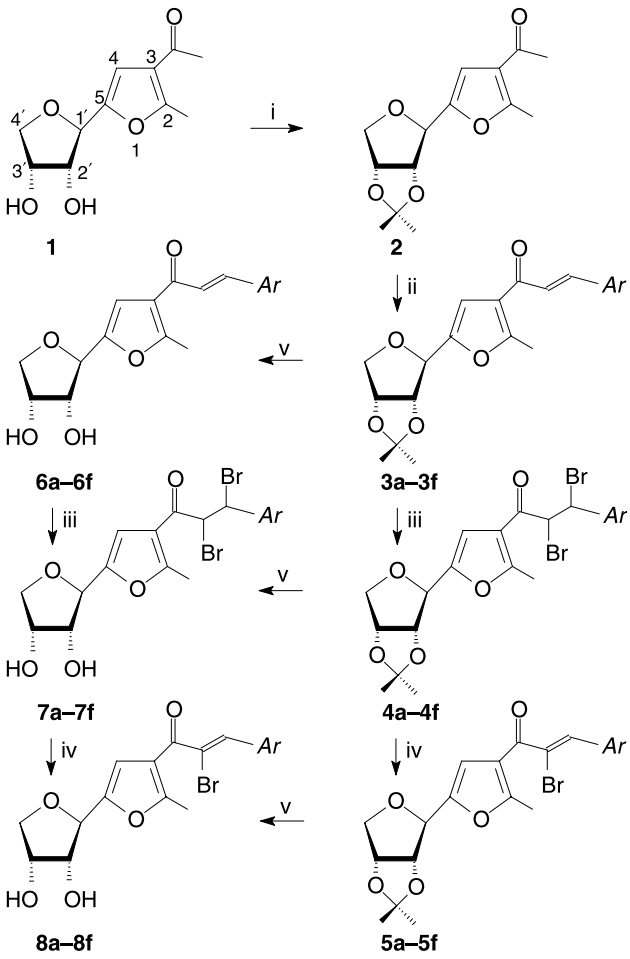
Results and discussion

Chemistry

The starting material 3-acetyl-5-*C*-(l,4-anhydro-β-D-erythro-tetrofuranosyl)-2-methylfuran (**1**) [15]

was synthesized by treatment of D-glucose with pentane-2,4-dione in the presence of 10 mol% indium(III) chloride in water at 80°C. A solution of **1** in acetone/2,2-dimethoxypropane/*p*-toluene sulfonic acid afforded after stirring 3-acetyl-5-*C*-(2,3-*O*-isopropylidene-l,4-anhydro-β-D-*erythro*-tetrofuranosyl)-2-methylfuran (**2**) in 80% yield. The ^{1}H NMR spectrum showed four singlets at $\delta = 1.28$, 1.49, 2.20, and 2.56 ppm for the isopropylidene, 2-*Me*, and 3-*Ac* groups. The two doublets of doublets at $\delta = 3.80$ and 4.10 ppm correspond to H-4′$_a$ and H-4′$_b$, while the signals of H-2′ and H-l′ appeared as two doublets at $\delta = 4.60$ and 4.80 ppm. The singlet at $\delta = 6.50$ ppm corresponds to H-4. Chalcones **3a**–**3f** were synthesized by a base catalyzed *Claisen-Schmidt* condensation reaction [16] of **2** and substituted aldehydes. The method is attractive since it specifically generates the (*E*)-isomer. From ^{1}H NMR spectra, all chalcones were geometrically pure and with *trans*-configuration ($J_{H\alpha-H\beta} = 15.5$ Hz). Saturation of the double bond results in loss of the anti-inflammatory and antimicrobial activity [17, 18]. So, bromination of chalcones was carried out by adding bromine drop wise to the clear solution of **3a**–**3f** in $CHCl_3$ to afford the corresponding 2,3-dibromochalcones **4a**–**4f**. Monobromo derivatives could be obtained from the corresponding dibromochalcones according to the method described by *Holla et al.* [19]. So, treatment of **4a**–**4f** with dry benzene in the presence of Et_3N afforded **5a**–**5f**. Deprotection of **3**–**5** with 70% *Ac*OH at reflux temperature afforded the corresponding deprotected derivatives **6**–**8**. Their ^{1}H NMR spectra showed the disappearance of the isopropylidene group in all cases (Scheme 1).



3–8	*Ar*
a	phenyl
b	2-bromo phenyl
c	4-bromo phenyl
d	2,4-dibromo phenyl
e	2-fluoro phenyl
f	3-nitro phenyl

(i) 2,2-Dimethoxypropane/acetone; (ii) *Ar*CHO/KOH/*Et*OH; (iii) $Br_2/CHCl_3$; (iv) Et_3N/benzene; (v) 70% *Ac*OH/reflux

Scheme 1

Antimicrobial activity

The newly synthesized compounds were tested for their antimicrobial action [20] against four different bacterial species namely, *Pseudomonas* sp. (*Gram* negative bacterium), *Bacillus subtilis* (*Gram* positive bacterium), *Bacillus cereus* (*Gram* positive bacterium), and *Streptomyces* sp. (one of the important actinomycetes). All the tested compounds exhibited different degrees of antibacterial activities or inhibitory actions. The most susceptible organisms were the two *Gram* positive bacteria (*Bacillus subtilis* and *Bacillus cereus*) followed by *Streptomyces* sp., while the lowest inhibitory effect was encountered in the case of *Pseudomonas* sp. The highest degrees of inhibition were recorded for compounds **6c**, **6d**, **6f**, **8c**, **8d**, and **8f** followed by **1**, **6a**, **6b**, **6e**, **8a**, **8b**, and **8e**, while the lowest degree of inhibition was recorded for the dibromochalcones **7a**–**7f** (Table 1). The results were compared to amoxicillin (penicillin) as a reference drug.

Table 1 Antimicrobial activity of the newly synthesized compounds **6–8**

Compd no.	*Pseudomonas* sp.	*Bacillus subtilis*	*Bacillus cereus*	*Streptomyces* sp.
Amoxicillin (Penicillin)	−	++	+++	+
1	+	++	+++	+
6a	+	++	++	+
6b	+	++	++++	+
6c	+	++++	++++	+
6d	+	++++	++++	++
6e	+	++	+++	+
6f	+	++++	++++	+
7a	+	+	+	+
7b	+	++	+	+
7c	+	++	+	++
7d	+	++	+	++
7e	+	++	+	+
7f	+	++	+	++
8a	+	++	++	+
8b	+	++	+++	++
8c	+	++++	++++	+
8d	+	++++	++++	+
8e	+	++	+++	+
8f	+	++++	++++	++

− No antimicrobial effect; + Low antimicrobial effect (4 mm); ++ Moderate antimicrobial effect (8–10 mm); +++ High antimicrobial effect (15–18 mm); ++++ Complete antimicrobial effect (20–22 mm)

Experimental

General

Melting points were determined using a *Kofler* block instrument. TLC was performed on plastic plates Silica Gel 60 F254 (E. Merck, layer thickness 0.2 mm). NMR spectra were recorded on a Bruker AC 250 FT NMR spectrometer at 250 MHz for ^{1}H NMR with *TMS* as an internal standard. ES mass spectra were obtained from an Esquire 3000plus iontrap mass spectrometer from Bruker Daltonics. The microanalyses were performed at the microanalytical unit, Cairo University, Egypt, and were found to agree favorably with the calculated values. Antimicrobial activity of the synthesized compounds was conducted at the Botany Department, Faculty of Science, Menoufia University, Shebin El-Koam, Egypt.

3-Acetyl-5-C-(2,3-O-isopropylidene-1,4-anhydro-β-D-erythrofuranosyl)-2-methylfuran (**2**, $C_{11}H_{18}O_5$)

A solution of 3.0 g **1** (13.3 mmol) in 40 cm^3 dry acetone, 4 cm^3 2,2-dimethoxypropane, and 0.2 g *p*-toluene sulfonic acid was stirred for 1 h at 0°C. The reaction mixture was stirred at 25°C for overnight. The resulting solution was neutralized with pyridine and evaporated to a yellow oil. This oil was partitioned between 20 cm^3 H_2O and 20 cm^3 of ether. The water layer was extracted twice with 20 cm^3 portions of ether, and the combined ether extracts were dried over Na_2SO_4. Evaporation under reduced pressure yielded 2.83 g (80%) as a white foam. ^{1}H NMR ($CDCl_3$, 250 MHz): $\delta = 1.28$ (s, CH_3), 1.49 (s, CH_3), 2.20 (s, CH_3), 2.56 (s, $COCH_3$), 3.80 (dd, $J = 3.2$, 10.4 Hz, H-4′$_a$), 4.10 (dd, $J = 4.8$, 10.4 Hz, H-4′$_b$), 4.30 (m, H-3′), 4.60 (d, $J = 6.4$ Hz, H-2′), 4.80 (d, $J = 6.4$ Hz, H-l′), 6.50 (s, H-4) ppm; MS (ESI): $m/z = 289$ [M$^+$ + Na].

*General procedure for the preparation of chalcones **3a–3f***

To a solution of 2.66 g **2** (10 mmol) in 20 cm *Et*OH, an aqueous solution of 10 cm^3 10% NaOH was added. The resulting solution was heated to 80°C and substituted benzaldehydes (10 mmol) were added with constant stirring. The reaction mixture was kept stirring at this temperature for 3–4 h, cooled to room temperature, and was allowed to stand overnight. The solid product separated was collected by filtration, dried, and recrystallized from ethanol to give **3a–3f** in 78–82% yields.

(E)-1-[5-C-(2,3-O-Isopropylidene-1,4-anhydro-β-D-erythrofuranosyl)-2-methylfuran]-3-phenylprop-2-en-1-one (**3a**, $C_{21}H_{22}O_5$)

White foam (80%); ^{1}H NMR ($CDCl_3$, 250 MHz): $\delta = 1.25$ (s, CH_3), 1.52 (s, CH_3), 2.21 (s, CH_3), 3.77 (dd, $J = 3.2$, 10.4 Hz, H-4′$_a$), 4.08 (dd, $J = 4.8$, 10.4 Hz, H-4′$_b$), 4.25 (m, H-3′), 4.55 (d, $J = 6.4$ Hz, H-2′), 4.77 (d, $J = 6.4$ Hz, H-l′), 6.45 (s, H-4), 7.60 (d, $J = 15.5$ Hz, COC*H*=CH), 7.74–7.89 (m, *Ar*–H), 7.92 (d, $J = 15.5$ Hz, COCH=C*H*) ppm; MS (ESI): $m/z = 377$ [M$^+$ + Na].

(E)-1-[5-C-(2,3-O-Isopropylidene-1,4-anhydro-β-D-erythrofuranosyl)-2-methylfuran]-3-(2-bromophenyl)prop-2-en-1-one (**3b**, $C_{21}H_{21}BrO_5$)

Yellow foam (81%); ^{1}H NMR ($CDCl_3$, 250 MHz): $\delta = 1.26$ (s, CH_3), 1.54 (s,CH_3), 2.23 (s, CH_3), 3.79 (dd, $J = 3.2$, 10.4 Hz, H-4′$_a$), 4.12 (dd, $J = 4.8$, 10.4 Hz, H-4′$_b$), 4.26 (m, H-3′), 4.59 (d, $J = 6.4$ Hz, H-2′), 4.81 (d, $J = 6.4$ Hz, H-l′), 6.49 (s, H-4), 7.62 (d, $J = 15.5$ Hz, COC*H*=CH), 7.70–7.80 (m, *Ar*–H), 7.94 (d, $J = 15.5$ Hz, COCH=C*H*) ppm; MS (ESI): $m/z = 455/457$ [M$^+$ + Na].

(E)-1-[5-C-(2,3-O-Isopropylidene-1,4-anhydro-β-D-erythrofuranosyl)-2-methylfuran]-3-(4-bromophenyl)prop-2-en-1-one (**3c**, $C_{21}H_{21}BrO_5$)

Yellow foam (82%); ^{1}H NMR ($CDCl_3$, 250 MHz): $\delta = 1.28$ (s, CH_3), 1.52 (s, CH_3), 2.20 (s, CH_3), 3.75 (dd, $J = 3.2$, 10.4 Hz, H-4′$_a$), 4.10 (dd, $J = 4.8$, 10.4 Hz, H-4′$_b$), 4.29 (m, H-3′), 4.66 (d, $J = 6.4$ Hz, H-2′), 4.87 (d, $J = 6.4$ Hz, H-l′), 6.53 (s, H-4), 7.70 (d, $J = 15.5$ Hz, COC*H*=CH), 7.75–7.84 (m, *Ar*–H), 7.97 (d, $J = 15.5$ Hz, COCH=C*H*) ppm; MS (ESI): $m/z = 455/457$ [M$^+$ + Na].

(E)-1-[5-C-(2,3-O-Isopropylidene-1,4-anhydro-β-D-erythrofuranosyl)-2-methylfuran]-3-(2,4-dibromophenyl)prop-2-en-1-one (**3d**, $C_{21}H_{20}Br_2O_5$)

Yellow foam (80%); ^{1}H NMR ($CDCl_3$, 250 MHz): $\delta = 1.25$ (s, CH_3), 1.50 (s, CH_3), 2.25 (s, CH_3), 3.83 (dd, $J = 3.2$, 10.4 Hz,

H-4′$_a$), 4.17 (dd, $J = 4.8$, 10.4 Hz, H-4′$_b$), 4.33 (m, H-3′), 4.62 (d, $J = 6.4$ Hz, H-2′), 4.87 (d, $J = 6.4$ Hz, H-l′), 6.55 (s, H-4), 7.72 (d, $J = 15.5$ Hz, COC*H*=CH), 7.79–7.88 (m, *Ar*–H), 7.99 (d, $J = 15.5$ Hz, COCH=C*H*) ppm; MS (ESI): $m/z = 533/535$ [$M^+ + Na$].

(E)-1-[5-C-(2,3-O-Isopropylidene-1,4-anhydro-β-D-erythro-furanosyl)-2-methylfuran]-3-(2-fluorophenyl)prop-2-en-1-one (**3e**, $C_{21}H_{21}FO_5$)
White foam (78%); ^{1}H NMR ($CDCl_3$, 250 MHz): $\delta = 1.23$ (s, CH_3), 1.50 (s, CH_3), 2.19 (s, CH_3), 3.78 (dd, $J = 3.2$, 10.4 Hz, H-4′$_a$), 4.10 (dd, $J = 4.8$, 10.4 Hz, H-4′$_b$), 4.27 (m, H-3′), 4.56 (d, $J = 6.4$ Hz, H-2′), 4.79 (d, $J = 6.4$ Hz, H-l′), 6.52 (s, H-4), 7.60 (d, $J = 15.5$ Hz, COC*H*=CH), 7.76–7.87 (m, *Ar*–H), 7.95 (d, $J = 15.5$ Hz, COCH=C*H*) ppm; MS (ESI): $m/z = 395$ [$M^+ + Na$].

(E)-1-[5-C-(2,3-O-Isopropylidene-1,4-anhydro-β-D-erythro-furanosyl)-2-methylfuran]-3-(3-nitrophenyl)prop-2-en-1-one (**3f**, $C_{21}H_{21}NO_7$)
Pale yellow foam (79%); ^{1}H NMR ($CDCl_3$, 250 MHz): $\delta = 1.28$ (s, CH_3), 1.54 (s, CH_3), 2.24 (s, CH_3), 3.78 (dd, $J = 3.2$, 10.4 Hz, H-4′$_a$), 4.09 (dd, $J = 4.8$, 10.4 Hz, H-4′$_b$), 4.33 (m, H-3′), 4.63 (d, $J = 6.4$ Hz, H-2′), 4.84 (d, $J = 6.4$ Hz, H-l′), 6.51 (s, H-4), 7.72 (d, $J = 15.5$ Hz, COC*H*=CH), 7.80–8.35 (m, *Ar*–H, COCH=C*H*) ppm; MS (ESI): $m/z = 422$ [$M^+ + Na$].

*General procedure for the preparation of 2,3-dibromochalcones **4a–4f***
Bromine (1.6 g, 10 mmol) was added dropwise with vigorous stirring to a solution of **3a–3f** (10 mmol) in 10 cm^3 $CHCl_3$ over 30 min. After complete addition of Br_2, the reaction mixture was allowed to stand for 1 h. The dibromo derivatives were precipitated, filtered off, and washed with 3×10 cm^3 ether to remove the excess of Br_2. Recrystallization from ethanol afforded **4a–4f** in 80–82% yields.

1-[5-C-(2,3-O-Isopropylidene-1,4-anhydro-β-D-erythro-furanosyl)-2-methylfuran]-2,3-dibromo-3-phenylpropan-1-one (**4a**, $C_{21}H_{22}Br_2O_5$)
Yellow foam (81%); ^{1}H NMR ($CDCl_3$, 250 MHz): $\delta = 1.29$ (s, CH_3), 1.55 (s, CH_3), 2.24 (s, CH_3), 3.70 (dd, $J = 3.2$, 10.4 Hz, H-4′$_a$), 4.04 (dd, $J = 4.8$, 10.4 Hz, H-4′$_b$), 4.33 (m, H-3′), 4.63 (d, $J = 6.4$ Hz, H-2′), 4.78 (d, $J = 6.4$ Hz, H-l′), 5.66 (d, $J = 2.5$ Hz, CH), 5.79 (d, $J = 2.5$ Hz, CH), 6.53 (s, H-4), 7.72–7.84 (m, *Ar*–H) ppm; MS (ESI): $m/z = 535/537$ [$M^+ + Na$].

1-[5-C-(2,3-O-Isopropylidene-1,4-anhydro-β-D-erythro-furanosyl)-2-methylfuran]-2,3-dibromo-3-(2-bromo-phenyl)propan-1-one (**4b**, $C_{21}H_{21}Br_3O_5$)
Yellow foam (80%); ^{1}H NMR ($CDCl_3$, 250 MHz): $\delta = 1.26$ (s, CH_3), 1.61 (s, CH_3), 2.26 (s, CH_3), 3.66 (m, H-4′$_a$), 4.09 (m, H-4′$_b$), 4.29 (m, H-3′), 4.60 (d, $J = 6.4$ Hz, H-2′), 4.74 (d, $J = 6.4$ Hz, H-l′), 5.58 (d, $J = 2.5$ Hz, CH), 5.72 (d, $J = 2.5$ Hz, CH), 6.48 (s, H-4), 7.42–7.69 (m, *Ar*–H) ppm; MS (ESI): $m/z = 615/617$ [$M^+ + Na$].

1-[5-C-(2,3-O-Isopropylidene-1,4-anhydro-β-D-erythro-furanosyl)-2-methylfuran]-2,3-dibromo-3-(4-bromo-phenyl)propan-1-one (**4c**, $C_{21}H_{21}Br_3O_5$)
Yellow foam (82%); ^{1}H NMR ($CDCl_3$, 250 MHz): $\delta = 1.24$ (s, CH_3), 1.59 (s, CH_3), 2.25 (s, CH_3), 3.68 (m, H-4′$_a$), 4.08 (m, H-4′$_b$), 4.22 (m, H-3′), 4.55 (d, $J = 6.4$ Hz, H-2′), 4.70 (d, $J = 6.4$ Hz, H-l′), 5.53 (d, $J = 2.5$ Hz, CH), 5.67 (d, $J = 2.5$ Hz, CH), 6.45 (s, H-4), 7.38–7.59 (m, *Ar*–H) ppm; MS (ESI): $m/z = 615/617$ [$M^+ + Na$].

1-[5-C-(2,3-O-Isopropylidene-1,4-anhydro-β-D-erythro-furanosyl)-2-methylfuran]-2,3-dibromo-3-(2,4-dibromo-phenyl)propan-1-one (**4d**, $C_{21}H_{20}Br_4O_5$)
Yellow foam (81%); ^{1}H NMR ($CDCl_3$, 250 MHz): $\delta = 1.23$ (s, CH_3), 1.54 (s, CH_3), 2.22 (s, CH_3), 3.65 (m, H-4′$_a$), 4.03 (m, H-4′$_b$), 4.27 (m, H-3′), 4.54 (d, $J = 6.4$ Hz, H-2′), 4.70 (d, $J = 6.4$ Hz, H-l′), 5.55 (d, $J = 2.5$ Hz, CH), 5.68 (d, $J = 2.5$ Hz, CH), 6.43 (s, H-4), 7.55–7.70 (m, *Ar*–H) ppm; MS (ESI): $m/z = 693/695$ [$M^+ + Na$].

1-[5-C-(2,3-O-Isopropylidene-1,4-anhydro-β-D-erythro-furanosyl)-2-methylfuran]-2,3-dibromo-3-(2-fluoro-phenyl)propan-1-one (**4e**, $C_{21}H_{21}Br_2FO_5$)
Yellow foam (80%); ^{1}H NMR ($CDCl_3$, 250 MHz): $\delta = 1.22$ (s, CH_3), 1.52 (s, CH_3), 2.20 (s, CH_3), 3.60 (m, H-4′$_a$), 4.09 (m, H-4′$_b$), 4.23 (m, H-3′), 4.52 (d, $J = 6.4$ Hz, H-2′), 4.66 (d, $J = 6.4$ Hz, H-l′), 5.50 (d, $J = 2.5$ Hz, CH), 5.67 (d, $J = 2.5$ Hz, CH), 6.49 (s, H-4), 6.92–7.10 (m, *Ar*–H), 7.52–7.65 (m, *Ar*–H) ppm; MS (ESI): $m/z = 553/555$ [$M^+ + Na$].

1-[5-C-(2,3-O-Isopropylidene-1,4-anhydro-β-D-erythro-furanosyl)-2-methylfuran]-2,3-dibromo-3-(3-nitro-phenyl)propan-1-one (**4f**, $C_{21}H_{21}Br_2NO_7$)
Yellow foam (80%); ^{1}H NMR ($CDCl_3$, 250 MHz): $\delta = 1.26$ (s, CH_3), 1.56 (s, CH_3), 2.21 (s, CH_3), 3.55 (m, H-4′$_a$), 4.00 (m, H-4′$_b$), 4.22 (m, H-3′), 4.51 (d, $J = 6.4$ Hz, H-2′), 4.68 (d, $J = 6.4$ Hz, H-l′), 5.61 (d, $J = 2.5$ Hz, CH), 5.70 (d, $J = 2.5$ Hz, CH), 6.45 (s, H-4), 7.47–7.59 (m, *Ar*–H), 8.10 (s, *Ar*–H) ppm; MS (ESI): $m/z = 580/582$ [$M^+ + Na$].

*General procedure for the preparation of 2-bromochalcones **5a–5f***
Triethylamine (4.04 g, 40 mmol) in 30 cm^3 dry benzene was added to a solution of **4a–4f** (10 mmol) in 100 cm^3 dry benzene with stirring. The reaction mixture was stirred at room temperature for 24 h. After removal of the separated triethylamine hydrobromide, the filtrate was concentrated under reduced pressure. The residue was recrystallized from ethanol to give **5a–5f** in 80–84% yields.

(Z)-1-[5-C-(2,3-O-Isopropylidene-1,4-anhydro-β-D-erythro-furanosyl)-2-methylfuran]-2-bromo-3-phenylprop-2-en-1-one (**5a**, $C_{21}H_{21}BrO_5$)
Yellow foam (80%); ^{1}H NMR ($CDCl_3$, 250 MHz): $\delta = 1.26$ (s, CH_3), 1.59 (s, CH_3), 2.24 (s, CH_3), 3.60 (m, H-4′$_a$), 4.11 (m, H-4′$_b$), 4.25 (m, H-3′), 4.56 (d, $J = 6.4$ Hz, H-2′), 4.69 (d, $J =$

6.4 Hz, H-l′), 6.46 (s, H-4), 7.39–7.59 (m, *Ar*–H), 8.45 (s, CH) ppm; MS (ESI): $m/z = 455/457$ [$M^+ + Na$].

(Z)-1-[5-C-(2,3-O-Isopropylidene-1,4-anhydro-β-D-erythrofuranosyl)-2-methylfuran]-2-bromo-3-(2-bromophenyl)-prop-2-en-1-one (**5b**, $C_{21}H_{20}Br_2O_5$)
Yellow foam (82%); ^{1}H NMR ($CDCl_3$, 250 MHz): $\delta = 1.23$ (s, CH_3), 1.52 (s, CH_3), 2.22 (s, CH_3), 3.61 (m, H-4′$_a$), 4.10 (m, H-4′$_b$), 4.22 (m, H-3′), 4.54 (d, $J = 6.4$ Hz, H-2′), 4.65 (d, $J =$ 6.4 Hz, H-l′), 6.49 (s, H-4), 7.38–7.49 (m, *Ar*–H), 8.40 (s, CH) ppm; MS (ESI): $m/z = 533/535$ [$M^+ + Na$].

(Z)-1-[5-C-(2,3-O-Isopropylidene-1,4-anhydro-β-D-erythrofuranosyl)-2-methylfuran]-2-bromo-3-(4-bromophenyl)-prop-2-en-1-one (**5c**, $C_{21}H_{20}Br_2O_5$)
Yellow foam (84%); ^{1}H NMR ($CDCl_3$, 250 MHz): $\delta = 1.26$ (s, CH_3), 1.56 (s, CH_3), 2.23 (s, CH_3), 3.54 (m, H-4′$_a$), 4.10 (m, H-4′$_b$), 4.22 (m, H-3′), 4.59 (d, $J = 6.4$ Hz, H-2′), 4.53 (d, $J = 6.4$ Hz, H-l′), 6.49 (s, H-4), 7.59–7.77 (m, *Ar*–H), 8.35 (s, CH) ppm; MS (ESI): $m/z = 533/535$ [$M^+ + Na$].

(Z)-1-[5-C-(2,3-O-Isopropylidene-1,4-anhydro-β-D-erythrofuranosyl)-2-methylfuran]-2-bromo-3-(2,4-dibromophenyl)prop-2-en-1-one (**5d**, $C_{21}H_{19}Br_3O_5$)
Yellow foam (83%); ^{1}H NMR ($CDCl_3$, 250 MHz): $\delta = 1.25$ (s, CH_3), 1.52 (s, CH_3), 2.26 (s, CH_3), 3.56 (m, H-4′$_a$), 4.11 (m, H-4′$_b$), 4.29 (m, H-3′), 4.63 (d, $J = 6.4$ Hz, H-2′), 4.58 (d, $J = 6.4$ Hz, H-l′), 6.51 (s, H-4), 7.49–7.57 (m, *Ar*–H), 7.62 (s, *Ar*–H), 8.47 (s, CH) ppm; MS (ESI): $m/z = 613/615$ [$M^+ + Na$].

(Z)-1-[5-C-(2,3-O-Isopropylidene-1,4-anhydro-β-D-erythrofuranosyl)-2-methylfuran]-2-bromo-3-(2-fluorophenyl)-prop-2-en-1-one (**5e**, $C_{21}H_{20}BrFO_5$)
Yellow foam (81%); ^{1}H NMR ($CDCl_3$, 250 MHz): $\delta = 1.22$ (s, CH_3), 1.48 (s, CH_3), 2.20 (s, CH_3), 3.50 (m, H-4′$_a$), 4.10 (m, H-4′$_b$), 4.20 (m, H-3′), 4.57 (d, $J = 6.4$ Hz, H-2′), 4.48 (d, $J = 6.4$ Hz, H-l′), 6.47 (s, H-4), 7.29–7.36 (m, *Ar*–H), 8.33 (s, CH) ppm; MS (ESI): $m/z = 473/475$ [$M^+ + Na$].

(Z)-1-[5-C-(2,3-O-Isopropylidene-1,4-anhydro-β-D-erythrofuranosyl)-2-methylfuran]-2-bromo-3-(3-nitrophenyl)-prop-2-en-1-one (**5f**, $C_{21}H_{20}BrNO_7$)
Yellow foam (82%); ^{1}H NMR ($CDCl_3$, 250 MHz): $\delta = 1.26$ (s, CH_3), 1.54 (s, CH_3), 2.24 (s, CH_3), 3.57 (m, H-4′$_a$), 4.14 (m, H-4′$_b$), 4.27 (m, H-3′), 4.61 (d, $J = 6.4$ Hz, H-2′), 4.57 (d, $J = 6.4$ Hz, H-l′), 6.52 (s, H-4), 7.79–7.89 (m, *Ar*–H), 8.31 (s, *Ar*–H), 8.45 (s, CH) ppm; MS (ESI): $m/z = 500/502$ [$M^+ + Na$].

General procedure for the preparation of ***6–8***
Compounds **3**–**5** (0.25 g) were refluxed in 10 cm^3 70% aqueous *Ac*OH for 2 h. The solvents were removed under reduced pressure. Water (4×5 cm^3) and then *Et*OH (3×5 cm^3) were coevaporated from the remaining residue. The residue was purified by column chromatography using 5% *Me*OH in $CHCl_3$ to give **6a**–**6f** (75–82%), **7a**–**7f** (68–75%), and **8a**–**8f** (72–78%) yields.

(E)-1-[5-C-(1,4-Anhydro-β-D-erythrofuranosyl)-2-methylfuran]-3-phenylprop-2-en-1-one (**6a**, $C_{18}H_{18}O_5$)
White powder (82%); mp 111–113°C; ^{1}H NMR ($CDCl_3$, 250 MHz): $\delta = 2.25$ (s, CH_3), 3.65 (m, H-3′), 3.78 (m, H-4′$_a$), 4.03 (m, H-4′$_b$), 4.15 (m, H-2′), 4.85 (br, s, $2 \times$OH), 5.30 (d, $J = 6.4$ Hz, H-l′), 6.45 (s, H-4), 7.50 (d, $J = 15.5$ Hz, COC*H*=CH), 7.70–7.80 (m, *Ar*–H), 7.90 (d, $J = 15.5$ Hz, COCH=C*H*) ppm; MS (ESI): $m/z = 337$ [$M^+ + Na$].

(E)-1-[5-C-(1,4-Anhydro-β-D-erythrofuranosyl)-2-methylfuran]-3-(2-bromophenyl)prop-2-en-1-one
(**6b**, $C_{18}H_{17}BrO_5$)
Pale yellow powder (81%); mp 117–119°C; ^{1}H NMR ($CDCl_3$, 250 MHz): $\delta = 2.19$ (s, CH_3), 3.69 (m, H-3′), 3.79 (m, H-4′$_a$), 4.07 (m, H-4′$_b$), 4.17 (m, H-2′), 4.81 (br, s, $2 \times$OH), 5.36 (d, $J = 6.4$ Hz, H-l′), 6.49 (s, H-4), 7.51 (d, $J = 15.5$ Hz, COC*H*=CH), 7.66–7.73 (m, *Ar*–H), 7.88 (d, $J = 15.5$ Hz, COCH=C*H*) ppm; MS (ESI): $m/z = 415/417$ [$M^+ + Na$].

(E)-1-[5-C-(1,4-Anhydro-β-D-erythrofuranosyl)-2-methylfuran]-3-(4-bromophenyl)prop-2-en-1-one
(**6c**, $C_{18}H_{17}BrO_5$)
Pale yellow powder (82%); mp 133–135°C; ^{1}H NMR ($CDCl_3$, 250 MHz): $\delta = 2.17$ (s, CH_3), 3.60 (m, H-3′), 3.69 (m, H-4′$_a$), 4.04 (m, H-4′$_b$), 4.18 (m, H-2′), 4.77 (br, s, $2 \times$OH), 5.34 (d, $J = 6.4$ Hz, H-l′), 6.47 (s, H-4), 7.50 (d, $J = 15.5$ Hz, COC*H*=CH), 7.76–7.80 (m, *Ar*–H), 7.93 (d, $J = 15.5$ Hz, COCH=C*H*) ppm; MS (ESI): $m/z = 415/417$ [$M^+ + Na$].

(E)-1-[5-C-(1,4-Anhydro-β-D-erythrofuranosyl)-2-methylfuran]-3-(2,4-dibromophenyl)prop-2-en-1-one
(**6d**, $C_{18}H_{16}Br_2O_5$)
Yellow powder (80%); mp 149–151°C; ^{1}H NMR ($CDCl_3$, 250 MHz): $\delta = 2.15$ (s, CH_3), 3.57 (m, H-3′), 3.70 (m, H-4′$_a$), 4.02 (m, H-4′$_b$), 4.16 (m, H-2′), 4.79 (br, s, $2 \times$OH), 5.30 (d, $J = 6.4$ Hz, H-l′), 6.48 (s, H-4), 7.36–7.44 (m, *Ar*–H), 7.48 (d, $J = 15.5$ Hz, COC*H*=CH), 7.58 (s, *Ar*–H), 7.88 (d, $J = 15.5$ Hz, COCH=C*H*) ppm; MS (ESI): $m/z = 493/495$ [$M^+ + Na$].

(E)-1-[5-C-(1,4-Anhydro-β-D-erythrofuranosyl)-2-methylfuran]-3-(2-fluorophenyl)prop-2-en-1-one
(**6e**, $C_{18}H_{17}FO_5$)
White powder (77%); mp 121–123°C; ^{1}H NMR ($CDCl_3$, 250 MHz): $\delta = 2.17$ (s, CH_3), 3.59 (m, H-3′), 3.76 (m, H-4′$_a$), 4.07 (m, H-4′$_b$), 4.18 (m, H-2′), 4.87 (br, s, $2 \times$OH), 5.38 (d, $J = 6.4$ Hz, H-l′), 6.52 (s, H-4), 7.22–7.33 (m, *Ar*–H), 7.45 (d, $J = 15.5$ Hz, COC*H*=CH), 7.82 (d, $J = 15.5$ Hz, COCH=C*H*) ppm; MS (ESI): $m/z = 355$ [$M^+ + Na$].

(E)-1-[5-C-(1,4-Anhydro-β-D-erythrofuranosyl)-2-methylfuran]-3-(3-nitrophenyl)prop-2-en-1-one
(**6f**, $C_{18}H_{17}NO_5$)
Pale yellow powder (75%); mp 170–172°C; ^{1}H NMR ($CDCl_3$, 250 MHz): $\delta = 2.17$ (s, CH_3), 3.68 (m, H-3′), 3.79 (m, H-4′$_a$), 4.09 (m, H-4′$_b$), 4.13 (m, H-2′), 4.80 (br, s, $2 \times$OH), 5.34 (d, $J = 6.4$ Hz, H-l′), 6.47 (s, H-4), 7.47 (d, $J = 15.5$ Hz, COC*H*=CH), 7.62–7.78 (m, *Ar*–H), 7.82–7.95 (m, COCH=C*H*, *Ar*–H) ppm; MS (ESI): $m/z = 382$ [$M^+ + Na$].

1-[5-C-(1,4-Anhydro-β-D-erythrofuranosyl)-2-methylfuran]-2,3-dibromo-3-phenylpropan-1-one (**7a**, $C_{18}H_{18}Br_2O_5$)
Yellow powder (75%); mp 166–168°C; ^{1}H NMR ($CDCl_3$, 250 MHz): $\delta = 2.13$ (s, CH_3), 3.55 (m, H-3′), 3.70 (m, H-4′$_a$), 4.03 (m, H-4′$_b$), 4.14 (m, H-2′), 4.80 (br, s, 2 × OH), 5.35 (d, $J = 6.4$ Hz, H-l′), 5.60 (d, $J = 2.5$ Hz, CH), 5.70 (d, $J = 2.5$ Hz, CH), 6.50 (s, H-4), 7.22–7.37 (m, *Ar*–H) ppm; MS (ESI): $m/z = 495/497$ [$M^+ + Na$].

1-[5-C-(1,4-Anhydro-β-D-erythrofuranosyl)-2-methylfuran]-2,3-dibromo-3-(2-bromophenyl)propan-1-one
(**7b**, $C_{18}H_{17}Br_3O_5$)
Yellow powder (75%); mp 173–175°C; ^{1}H NMR ($CDCl_3$, 250 MHz): $\delta = 2.16$ (s, CH_3), 3.60 (m, H-3′), 3.74 (m, H-4′$_a$), 4.03 (m, H-4′$_b$), 4.19 (m, H-2′), 4.79 (br, s, 2 × OH), 5.40 (d, $J = 6.4$ Hz, H-l′), 5.65 (d, $J = 2.5$ Hz, CH), 5.72 (d, $J = 2.5$ Hz, CH), 6.54 (s, H-4), 7.12–7.35 (m, *Ar*–H) ppm; MS (ESI): $m/z = 575/577$ [$M^+ + Na$].

1-[5-C-(1,4-Anhydro-β-D-erythrofuranosyl)-2-methylfuran]-2,3-dibromo-3-(4-bromophenyl)propan-1-one
(**7c**, $C_{18}H_{17}Br_3O_5$)
Yellow powder (73%); mp 190–192°C; ^{1}H NMR ($CDCl_3$, 250 MHz): $\delta = 2.18$ (s, CH_3), 3.60 (m, H-3′), 3.70 (m, H-4′$_a$), 4.06 (m, H-4′$_b$), 4.23 (m, H-2′), 4.88 (br, s, 2 × OH), 5.47 (d, $J = 6.4$ Hz, H-l′), 5.64 (d, $J = 2.5$ Hz, CH), 5.79 (d, $J = 2.5$ Hz, CH), 6.59 (s, H-4), 7.19–7.38 (m, *Ar*–H) ppm; MS (ESI): $m/z = 575/577$ [$M^+ + Na$].

1-[5-C-(1,4-Anhydro-β-D-erythrofuranosyl)-2-methylfuran]-2,3-dibromo-3-(2,4-dibromophenyl)propan-1-one
(**7d**, $C_{18}H_{16}Br_4O_5$)
Yellow powder (71%); mp 201–203°C; ^{1}H NMR ($CDCl_3$, 250 MHz): $\delta = 2.15$ (s, CH_3), 3.57 (m, H-3′), 3.78 (m, H-4′$_a$), 4.09 (m, H-4′$_b$), 4.22 (m, H-2′), 4.85 (br, s, 2 × OH), 5.45 (d, $J = 6.4$ Hz, H-l′), 5.66 (d, $J = 2.5$ Hz, CH), 5.76 (d, $J = 2.5$ Hz, CH), 6.50 (s, H-4), 7.19–7.30 (m, *Ar*–H), 7.60 (s, *Ar*–H) ppm; MS (ESI): $m/z = 653/655$ [$M^+ + Na$].

1-[5-C-(1,4-Anhydro-β-D-erythrofuranosyl)-2-methylfuran]-2,3-dibromo-3-(2-fluorophenyl)propan-1-one
(**7e**, $C_{18}H_{17}Br_2FO_5$)
Yellow powder (69%); mp 216–218°C; ^{1}H NMR ($CDCl_3$, 250 MHz): $\delta = 2.17$ (s, CH_3), 3.60 (m, H-3′), 3.70 (m, H-4′$_a$), 4.03 (m, H-4′$_b$), 4.17 (m, H-2′), 4.78 (br, s, 2 × OH), 5.41 (d, $J = 6.4$ Hz, H-l′), 5.64 (d, $J = 2.5$ Hz, CH), 5.70 (d, $J = 2.5$ Hz, CH), 6.50 (s, H-4), 7.10–7.29 (m, *Ar*–H) ppm; MS (ESI): $m/z = 513/515$ [$M^+ + Na$].

1-[5-C-(1,4-Anhydro-β-D-erythrofuranosyl)-2-methylfuran]-2,3-dibromo-3-(3-nitrophenyl)propan-l-one
(**7f**, $C_{18}H_{17}Br_2NO_7$)
Yellow powder (68%); mp 207–209°C; ^{1}H NMR ($CDCl_3$, 250 MHz): $\delta = 2.19$ (s, CH_3), 3.63 (m, H-3′), 3.76 (m, H-4′$_a$), 4.05 (m, H-4′$_b$), 4.17 (m, H-2′), 4.75 (br, s, 2 × OH), 5.42 (d, $J = 6.4$ Hz, H-l′), 5.62 (d, $J = 2.5$ Hz, CH), 5.71 (d, $J = 2.5$ Hz, CH), 6.51 (s, H-4), 7.72–7.85 (m, *Ar*–H), 8.06 (s, *Ar*–H) ppm; MS (ESI): $m/z = 540/542$ [$M^+ + Na$].

(Z)-1-[5-C-(1,4-Anhydro-β-D-erythrofuranosyl)-2-methylfuran]-2-bromo-3-phenylprop-2-en-1-one (**8a**, $C_{18}H_{17}BrO_5$)
Yellow powder (78%); mp 201–203°C; ^{1}H NMR ($CDCl_3$, 250 MHz): $\delta = 2.19$ (s, CH_3), 3.69 (m, H-3′), 3.79 (m, H-4′$_a$), 4.00 (m, H-4′$_b$), 4.16 (m, H-2′), 4.82 (br, s, 2 × OH), 5.49 (d, $J = 6.4$ Hz, H-l′), 6.46 (s, H-4), 7.39–7.50 (m, *Ar*–H), 8.40 (s, CH) ppm; MS (ESI): $m/z = 415/417$ [$M^+ + Na$].

(Z)-1-[5-C-(1,4-Anhydro-β-D-erythrofuranosyl)-2-methylfuran]-2-bromo-3-(2-bromophenyl)prop-2-en-1-one
(**8b**, $C_{18}H_{16}Br_2O_5$)
Yellow powder (76%); mp 188–190°C; ^{1}H NMR ($CDCl_3$, 250 MHz): $\delta = 2.15$ (s, CH_3), 3.65 (m, H-3′), 3.75 (m, H-4′$_a$), 4.06 (m, H-4′$_b$), 4.14 (m, H-2′), 4.80 (br, s, 2 × OH), 5.51 (d, $J = 6.4$ Hz, H-l′), 6.44 (s, H-4), 7.19–7.39 (m, *Ar*–H), 8.37 (s, CH) ppm; MS (ESI): $m/z = 493/495$ [$M^+ + Na$].

(Z)-1-[5-C-(1,4-Anhydro-β-D-erythrofuranosyl)-2-methylfuran]-2-bromo-3-(4-bromophenyl)prop-2-en-1-one
(**8c**, $C_{18}H_{16}Br_2O_5$)
Yellow powder (77%); mp 199–201°C; ^{1}H NMR ($CDCl_3$, 250 MHz): $\delta = 2.18$ (s, CH_3), 3.60 (m, H-3′), 3.70 (m, H-4′$_a$), 4.03 (m, H-4′$_b$), 4.12 (m, H-2′), 4.81 (br, s, 2 × OH), 5.50 (d, $J = 6.4$ Hz, H-l′), 6.40 (s, H-4), 7.42–7.69 (m, *Ar*–H), 8.17 (s, CH) ppm; MS (ESI): $m/z = 493/495$ [$M^+ + Na$].

(Z)-1-[5-C-(1,4-Anhydro-β-D-erythrofuranosyl)-2-methylfuran]-2-bromo-3-(2,4-dibromophenyl)prop-2-en-1-one
(**8d**, $C_{18}H_{15}Br_3O_5$)
Yellow powder (74%); mp 215–217°C; ^{1}H NMR ($CDCl_3$, 250 MHz): $\delta = 2.19$ (s, CH_3), 3.67 (m, H-3′), 3.79 (m, H-4′$_a$), 4.08 (m, H-4′$_b$), 4.17 (m, H-2′), 4.83 (br, s, 2 × OH), 5.54 (d, $J = 6.4$ Hz, H-l′), 6.43 (s, H-4), 7.39–7.44 (m, *Ar*–H), 7.60 (s, *Ar*–H), 8.35 (s, CH) ppm; MS (ESI): $m/z = 573/575$ [$M^+ + Na$].

(Z)-1-[5-C-(1,4-Anhydro-β-D-erythrofuranosyl)-2-methylfuran]-2-bromo-3-(2-fluorophenyl)prop-2-en-1-one
(**8e**, $C_{18}H_{16}BrFO_5$)
Yellow powder (72%); mp 210–212°C; ^{1}H NMR ($CDCl_3$, 250 MHz): $\delta = 2.13$ (s, CH_3), 3.62 (m, H-3′), 3.69 (m, H-4′$_a$), 4.01 (m, H-4′$_b$), 4.12 (m, H-2′), 4.77 (br, s, 2 × OH), 5.50 (d, $J = 6.4$ Hz, H-l′), 6.40 (s, H-4), 7.10–7.29 (m, *Ar*–H), 8.39 (s, CH) ppm; MS (ESI): $m/z = 433/435$ [$M^+ + Na$].

(Z)-1-[5-C-(1,4-Anhydro-β-D-erythrofuranosyl)-2-methylfuran]-2-bromo-3-(3-nitrophenyl)prop-2-en-1-one
(**8f**, $C_{18}H_{16}BrNO_7$)
Yellow powder (72%); mp 233–235°C; ^{1}H NMR ($CDCl_3$, 250 MHz): $\delta = 2.19$ (s, CH_3), 3.69 (m, H-3′), 3.79 (m, H-4′$_a$), 4.07 (m, H-4′$_b$), 4.19 (m, H-2′), 4.84 (br, s, 2 × OH), 5.57 (d, $J = 6.4$ Hz, H-l′), 6.48 (s, H-4), 7.69–7.89 (m, *Ar*–

H), 8.31 (s, *Ar*–H), 8.43 (s, CH) ppm; MS (ESI): $m/z =$ 460/462 [$M^+ + Na$].

Antimicrobial testing

The hole plate method was used to investigate the antibacterial activities of the different compounds. Nutritive agar plates seeded with the test organisms (three plates for each organism) were allowed to solidify, and then 5 mm diameter holes were formed in the plates using a cork borer. Each hole was filled with one drop of the ethanolic solution of the tested compound, while the hole in the center of the plate was filled with one drop of ethanol. Plates were separately incubated at 30°C for 24 h. Inhibition zones (zones with no growth) around the holes were measured.

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