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SUPPLEMENTARY MATERIAL TO

Synthesis and antiproliferative activity of new thiazole hybrids with [3.3.0]furofuranone or tetrahydrofuran scaffolds

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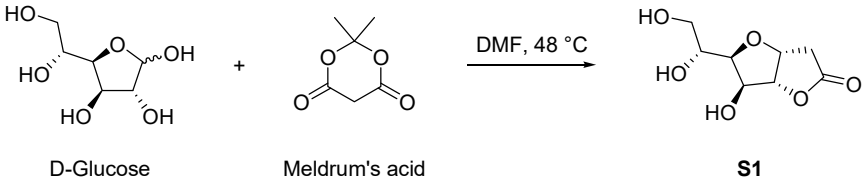
PREPARATION OF STARTING INTERMEDIATES

*3,6-Anhydro-2-deoxy-D-glycero-D-ido-octono-l,4-lactone (**S1**)*



Scheme S-1. Preparation of **S1**.

To a suspension of D-Glucose (0.180 g, 1.00 mmol in anhydrous DMF (5 mL) was added anhydrous Et_3N (1.68 mL, 12.00 mmol) and Meldrum's acid (0.290 g, 2.00 mmol). The reaction mixture was stirred at 40 °C for 4 days and then evaporated. The residue was purified on a column of flash silica (19:1 EtOAc/MeOH) whereby pure **S1** (0.102 g, 50%) was obtained as a white powder. Recrystallization from a mixture of Me_2CO/light petroleum gave colourless needles, mp 119 °C, $[\alpha]_D$ = +32.2 (*c* 0.5, H_2O), lit.[1] $[\alpha]_D$ = +29.0 (*c* 0.5, H_2O), R_f = 0.27 (19:1 EtOAc/MeOH). Spectral data (IR, ^{1}H-NMR, ^{13}C-NMR and MS) were in good agreement with reported values.[1]

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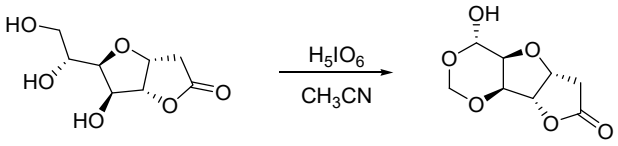
*(7S)-3,6-Anhydro-2-deoxy-7-C-hydroxy-5,7-O-methylidene-D-ido-heptono-1,4-lactone (**S2**)*



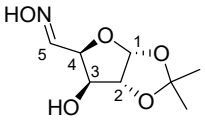
S1 **S2**

Scheme S-2. Preparation of **S2**

To a stirred solution of compound **S1** (0.145 g, 0.71 mmol) in anhydrous MeCN (15 mL) was added H_5IO_6 (0.146 g, 0.64 mmol). After stirring at room temperature for 22 h, the reaction mixture was evaporated with silica gel and purified by flash chromatography (9:1 CH_2Cl_2/Me_2CO). This gives a mixture of pure **S2** (0.108 g, 75 %) which crystallizes from Me_2CO/hexane in the form of cloudy needles, mp 152–153 °C, $[\alpha]_D$ = +130 (*c* 0.25, Me_2CO), R_f = 0.31 (9:1 CH_2Cl_2/Me_2CO). IR, NMR (^{1}H and ^{13}C) and MS data were in good agreement with previously recorded values.[2]

SPECTROSCOPIC DATA OF SYNTHESIZED COMPOUNDS

*(E,Z)-1,2-O-Isopropylidene-α-D-xylo-pentodialdo-1,4-furanose-5-oxime (**10**)*



10

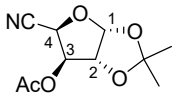
IR (film): ν_{max} 3390, 1637 cm^{-1}.

^{1}H NMR (250 MHz, DMSO-d_6, δ): 11.27 and 11.13 (2 × *s*, 1 H each, NOH both isomers), 7.26 (*d*, 1 H, $J_{4,5}$ = 7.2 Hz, H-5, *E* isomer), 6.67 (*d*, 0.8 H, $J_{4,5}$ = 4.6 Hz, H-5, *Z*-isomer), 5.88 (*m*, H-1 both isomers), 5.57 (*d*, 1 H, $J_{3,OH}$ = 4.3 Hz, OH, *E*-isomer), 5.43 (*d*, 0.8 H, $J_{3,OH}$ = 4.7 Hz, OH, *Z*-isomer), 4.50 (*m*, 0.8 H, H-4, *Z* isomer), 4.21–4.44 (*m*, H-2, both isomers, H-4, *E*-isomer), 4.21 (*br s*, 0.8 H, H-3, *Z*-isomer), 4.03 (*br s*, 1 H, H-3, *E*-isomer), 1.39 and 1.23 (2 × *s*, 3 H each, C*Me*$_2$). The ratio of isomers: *E*/*Z* = 1:0.8

^{13}C NMR (62.9 MHz, DMSO-d_6, δ): 147.38 (C-5, *Z*-isomer), 146.00 (C-5, *E*-isomer), 110.83 and 110.73 (Me$_2$*C*, both isomers), 104.55 (C-1, *E*-isomer), 104.15 (C-1, *Z*-isomer), 85.14, 78.18, 74. 98, (C-2 and C-4, both isomers), 75.50 and 74.24 (C-3, both isomers), 26.70, 26.07 and 26.04, (*Me*$_2$C, both isomers).

(+)ESI-HRMS (*m/z*): calculated for [$C_8H_{13}NO_5$ + Na^+] 226.06859, observed 226.06817.

*3-O-Acetyl-1,2-O-isopropylidene-α-D-xylo-furanoseurononitrile (**11**)*



11

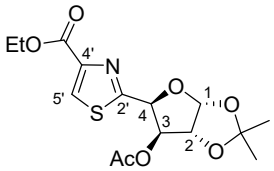
IR (film): ν_{max} 1754, 2260 cm^{-1}.

^{1}H NMR (250 MHz, $CDCl_3$, δ): 5.95 (*d*, 1 H, $J_{1,2}$ = 3.5 Hz, H-1), 5.40 (*d*, 1 H, $J_{3,4}$ = 3.4 Hz, H-3), 4.95 (*d*, 1 H, $J_{3,4}$ = 3.4 Hz, H-4), 4.55 (*d*, 1 H, $J_{1,2}$ = 3.5 Hz, H-2), 2.13 (*s*, 3 H, $COCH_3$), 1.45 and 1.27 (2 × *s*, 3 H each, CMe_2).

^{13}C NMR (62.9 MHz, $CDCl_3$, *δ*): 168.51 ($COCH_3$), 113.31 (CN), 112.93 (Me_2C), 104.94 (C-1), 81.89 (C-2), 75.06 (C-3), 68.03 (C-4), 26.23 and 25.52 (Me_2C), 19.91 ($COCH_3$).

(+)ESI-HRMS (*m/z*): calculated for [$C_{10}H_{13}NO_5$ + NH_4^+] 245.11229, observed 245.11320.

*3-O-Acetyl-4-C-(4'-(ethoxycarbonyl)thiazol-2'-yl)-1,2-O-isopropylidene-α-D-xylo-tetrofuranose (**12**)*



12

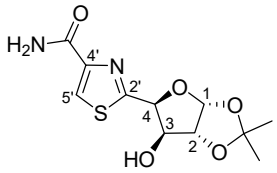
IR (KBr): ν_{max} 1755 and 1731 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$, δ): 8.20 (*s*, 1 H, H-5′), 6.09 (*d*, 1 H, $J_{1,2}$ = 3.6 Hz, H-1), 5.80 (*d*, 1 H, $J_{3,4}$ = 3.1 Hz, H-4), 5.52 (*d*, 1 H, $J_{3,4}$ = 3.1 Hz, H-3), 4.67 (*d*, 1 H, $J_{1,2}$ = 3.6 Hz, H-2), 4.43 (*q*, 2 H, J = 7.1 Hz, CH_2CH_3), 1.92 (*s*, 3 H, $COCH_3$), 1.42 (*t*, 3 H, CH_2CH_3), 1.58 and 1.37 (2 × *s*, 3 H each, CMe_2).

^{13}C NMR (100 MHz, $CDCl_3$, δ): 168.89 ($OCOCH_3$), 165.96 (CO_2Et), 161.28 (C-2′), 147.00 (C-4′), 133.41 129.48 128.32, and 127.99, (Ph), 128.32 (C-5′), 113.08 (Me_2C), 104.99 (C-1), 83.40 (C-2), 78.91 (C-4), 77.06 (C-3), 61.60 (CH_2CH_3), 26.78 and 26.34 (Me_2C), 20.60 ($OCOCH_3$), 14.39 (CH_2CH_3).

(+)ESI-HRMS (*m/z*): calculated for [$C_{15}H_{19}NO_7$ + H^+] 358.09482, observed 358.09550.

*4-C-(4′-(Carbamoyl)thiazol-2′-yl)-1,2-O-isopropylidene-α-D-xylo-tetrofuranose (**3**)*



3

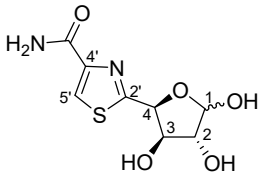
IR (film): ν_{max} 3348, 1668, 1590 cm^{-1}.

^{1}H NMR (250 MHz, acetone-d_6, δ): 8.16 (*s*, 1 H, H-5′), 7.46 and 6.89 (2 × *br s*, 1 H each, NH_2), 6.09 (*d*, 1 H, $J_{1,2}$ = 3.4 Hz, H-1), 5.43 (*d*, 1 H, $J_{3,4}$ = 2.7 Hz, H-4), 4.70 (*d*, 1 H, $J_{1,2}$ = 3.4 Hz, H-2), 4.64 (*d*, 1 H, $J_{3,4}$ = 2.4 Hz, H-3), 4.44 (*br s*, 1 H, OH), 1.50 and 1.33 (2 × *s*, 3 H each, CMe_2).

^{13}C NMR (62.9 MHz, acetone-d_6, δ): 167.94 (***C***ONH$_2$), 163.35 (C-2′), 150.78 (C-4′), 125.18 (C-5′), 112.57 (Me$_2$*C*), 106.12 (C-1), 86.27 (C-2), 81.76 (C-4), 76.59 (C-3), 27.17 and 26.37 (*Me*$_2$C).

(+)ESI-HRMS (*m/z*): calculated for [$C_{11}H_{13}N_2O_5S$ + H^+] 287.06962, observed 287.06946.

*4-C-(4′-(Carbamoyl)thiazol-2′-yl)-D-xylo-tetrofuranose (**4**)*



4

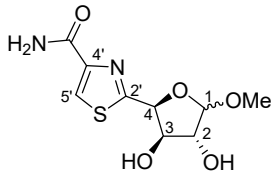
IR (film): ν_{max} 3354, 1674 cm^{-1}.

^{1}H NMR (400 MHz, methanol-d_4, δ): 8.22 and 8.19 (2 × *s*, 1 H, H-5′ both anomers), 5.63 (*d*, 1 H, $J_{1,2}$ = 3.6 Hz, H-1α), 5.49–5.55 (*m*, 2 H, H-4α and H-4β), 5.27 (*s*, 1 H, H-1β), 3.57–4.44 (*m*, H-2 and H-3, both anomers). Ratio of anomers: α/β = 1:1.

^{13}C NMR (100 MHz, methanol-d_4, δ): 172.07 and 171.49 (*C*ONH$_2$, both anomers), 166.16 and 160.01 (C-4′, both anomers), 150.40 and 150.24 (C-2′, both anomers), 126.13 and 125.32 (C-5′, both anomers), 105.01 (C-1β), 99.25 (C-1α).

(+)ESI-HRMS (*m/z*): calculated for [$C_8H_{10}N_2O_5S$ + H^+] 247.03832, observed 247.03747.

*Methyl 4-C-(4′-(carbamoyl)thiazol-2′-yl)-D-xylo-tetrofuranoside (**5**)*



5

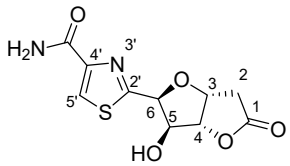
IR (film): ν_{max} 3340, 1668 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6 + D_2O, δ): 8.17 (*s*, 1.5 H, H-5′ both anomers), 7.78 and 7.42 (residual signals from CONH_2), 5.43 (*d*, 0.5 H, $J_{3,4}$ = 4.9 Hz, H-4β), 5.32 (*d*, 1 H, $J_{3,4}$ = 5.5 Hz, H-4α), 5.04 (*d*, 1 H, $J_{1,2}$ = 4.0 Hz, H-1α), 4.83 (*s*, 0.5 H, H-1β), 4.21 (*t*, 1 H, *J*=5.1 Hz, H-3α), 4.13 (*dd*, 0.5 H, $J_{2,3}$=1.1, $J_{3,4}$=4.7 Hz, H-3β), 3.97–4.02 (*m*, 1.5 H, H-2β,α), 3.37 and 3.35 (2 × *s*, OCH_3 β and α).

^{13}C NMR (62.9 MHz, DMSO-d_6 + D_2O, *δ*): 169.49 and 168.87 (CONH$_2$ β and α), 162.45 and 162.41 (C-2′ β and α), 149.68 and 149.59 (C-4′ β and α), 124.68 and 124.53 (C-5′ β and α), 110.30 (C-1β), 103.59 (C-1α), 82.22 (C-4 β), 80.41 (C-2 β), 78.59 (C-4 α), 76.67 (C-2 α), 76.20 (C-3 β and α), 55.63 and 55.13 (O*C*H$_3$ β and α).

(+)ESI-HRMS (*m/z*): calculated for [$C_9H_{12}N_2O_5S$ + H^+] 261.05397, observed 261.05441.

*3,6-Anhydro-6-C-(4′-(carbamoyl)thiazol-2′-yl)-2-deoxy-D-ido-hexono-1,4-lactone (**6**)*



6

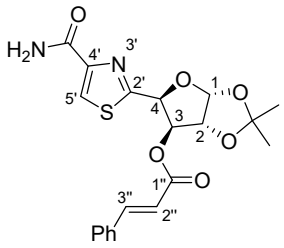
IR (KBr): ν_{max} 1781 cm^{-1}.

^{1}H NMR (250 MHz, DMSO-d_6, δ): 8.30 (*s*, 1 H, H-5′), 7.69 and 7.54 (2 × *br s*, 2 H, NH_2), 5.93 (*d*, 1 H, $J_{5,OH}$ = 5.1 Hz, OH), 5.26 (*d*, 1 H, $J_{5,6}$ = 3.0 Hz, H-6), 5.05 (*m*, 1 H, H-3), 5.00 (*d*, 1 H, $J_{3,4}$ = 4.2 Hz, H-4), 4.48 (*br s*, 1 H, H-5), 2.93 (*dd*, 1 H, $J_{2a,2b}$ = 18.7 Hz, $J_{2b,3}$ = 6.2 Hz, H-2b), 2.60 (*d*, 1 H, $J_{2a,2b}$ = 18.7 Hz, H-2a).

^{13}C NMR (62.9 MHz, DMSO-d_6, δ): 175.63 (C-1), 166.74 (*C*CONH$_2$), 162.37 (C-2′), 149.66 (C-4′), 124.97 (C-5′), 87.60 (C-4), 80.71 (C-6), 77.65 (C-3), 74.00 (C-5), 35.53 (C-2).

(+)ESI-HRMS (*m/z*): calculated for [$C_{10}H_{10}N_2O_5S$ + H^+] 271.03832, observed 271.03832.

*4-C-(4'-(Carbamoyl)thiazol-2'-yl)-3-O-cinnamoyl-1,2-O-isopropylidene-α-D-xylo-tetrofuranose (**7**)*



7

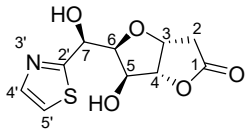
IR (KBr): ν_{max} 3466, 1725, 1690, 1634, 1578, 1524 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$, δ): 8.15 (*s*, 1 H, H-5′), 7.53 (*d*, 1 H, $J_{2'',3''}$ = 16.0 Hz, H-3″), 7.34–7.48 (*m*, 5 H, Ph), 6.22 (*d*, 1 H, $J_{2'',3''}$ = 16.0 Hz, H-2″), 6.18 (*d*, 1 H, $J_{1,2}$ = 3.6 Hz, H-1), 5.99 and 7.12 (2 × *br s*, 1 H each, NH_2), 5.73 (*d*, 1 H, $J_{3,4}$ = 3.1 Hz, H-4), 5.71 (*d*, 1 H, $J_{3,4}$ = 3.1 Hz, H-3), 4.78 (*d*, 1 H, $J_{1,2}$ = 3.6 Hz, H-2), 1.63 and 1.40 (2 × *s*, 3 H each, C*Me*$_2$).

^{13}C NMR (100 MHz, $CDCl_3$, δ): 165.32 and 164.87 ($CONH_2$ and CO from cinnamoyl), 162.81 (C-2′), 149.30 (C-4′), 146.53 (C-3″), 133.71 130.79, 128.90, 128.19, (Ph), 124.94 (C-5′), 116.16 (C-2″), 113.01 (Me$_2$*C*), 105.13 (C-1), 83.48 (C-2), 79.12 (C-4), 76.68 (C-3), 26.82 and 26.23 (*Me*$_2$C).

(+)ESI-HRMS (*m/z*): calculated for [$C_{20}H_{20}N_2O_6S$ + H^+] 417.11148, observed 417.11006.

*3,6-Anhydro-2-deoxy-7-C-(thiazol-2'-yl)-D-glycero-D-ido-heptono-1,4-lactone (**8**)*



8

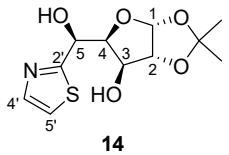
IR (film): ν_{max} 3451, 1789 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.82 (*d*, 1 H, $J_{4',5'}$ = 3.3 Hz, H-4′), 7.43 (*d*, 1 H, $J_{4',5'}$ = 3.3 Hz, H-5′), 5.35 (*t*, 1 H, *J* = 5.0 Hz, H-7), 4.90–4.99 (*br s*, 3 H, H-3, H-4 and OH), 4.72 (*br s*, 1 H, H-5), 4.48 (*t*, 1 H, *J* = 4.4 Hz, H-6), 3.75 (*br s*, 1 H, OH), 2.65–2.85 (*m*, 2 H, H-2).

^{13}C NMR (100 MHz, $CDCl_3$, δ): 174.84 (C-1), 170.52 (C-2′), 142.26 (C-4′), 120.24 (C-5′), 88.32 (C-4), 83.56 (C-6), 77.84 (C-3), 75.55 (C-5), 71.29 (C-7), 36.25 (C-2).

(+)ESI-HRMS (*m/z*): calculated for [$C_{10}H_{11}NO_5S + H^+$] 258.04364, observed 258.04362.

*1,2-O-Isopropylidene-5-C-(thiazol-2'-yl)-α-D-gluco-pentofuranose (**14**)*



14

IR (film): ν_{max} 3340 cm^{-1}.

^{1}H NMR (500 MHz, methanol-d_4, δ): 7.75 (*d*, 1 H, $J_{4',5'}$ = 3.3 Hz, H-4′), 7.57 (*d*, 1 H, $J_{4',5'}$ = 3.3 Hz, H-5′), 5.88 (*d*, 1 H, $J_{1,2}$ = 3.6 Hz, H-1), 5.21 (*d*, 1 H, $J_{4,5}$ = 7.9 Hz, H-5), 4.51 (*d*, 1 H, $J_{1,2}$ = 3.6 Hz, H-2), 4.32 (*dd*, 1 H, $J_{3,4}$ = 2.8, $J_{4,5}$ = 7.9 Hz, H-4), 4.27 (*d*, 1 H, $J_{3,4}$ = 2.7 Hz, H-3), 1.43 and 1.28 (2 × *s*, 3 H each, C*Me*$_2$).

^{13}C NMR (125 MHz, methanol-d_4, δ): 175.51 (C-2′), 142.99 (C-4′), 121.18 (C-5′), 112.99 (Me$_2$*C*), 106.54 (C-1), 86.60 (C-2), 84.39 (C-4), 75.56 (C-3), 70.06 (C-5), 27.23 and 26.58 (*Me*$_2$C).

SAR ANALYSIS

TABLE S-I. Cytotoxicity data for SAR analysis.

Compounds	IC_{50} / μM[a], 72 h						
	K562	HL-60	Jurkat	Raji	MCF-7	HeLa	A549
(+)-Goniofufurone (**1**)	0.41	201.32	32.45	18.45	16.59	8.32	35.21
Tiazofurin (**2**)	2.06	0.67	0.09	5.28	2.03	3.26	5.92
3	21.01	7.64	7.09	15.64	10.52	4.36	18.21
4	2.55	8.51	11.36	14.32	8.65	8.31	24.64
5	17.50	7.79	11.36	7.63	18.36	8.64	5.46
6	1.63	1.02	18.52	9.02	2.61	0.75	4.64
7	3.54	12.63	4.32	12.64	10.02	1.25	3.45
8	3.05	3.54	25.02	25.41	7.62	9.06	11.59
12	3.47	9.10	7.52	1.58	15.20	3.70	10.35
DOX	0.25	0.92	0.03	2.98	0.20	0.07	4.91

[a]IC_{50} is the concentration of compound required to inhibit the cell growth by 50 % compared to an untreated control. Values are means of three independent experiments. Coefficients of variation were less than 10 %.

The structure-activity relationships were accessed as follows: the IC_{50} values of two compounds were compared, and the Δ log IC_{50} was calculated (Δ log IC_{50} is a difference between the log IC_{50} values of an analogue and the corresponding control compound). Positive Δ log IC_{50} values show a decrease of antiproliferative activity, whereas negative values indicate an increase in the activity upon the structural modification being considered. The results are presented in Fig. S-1.

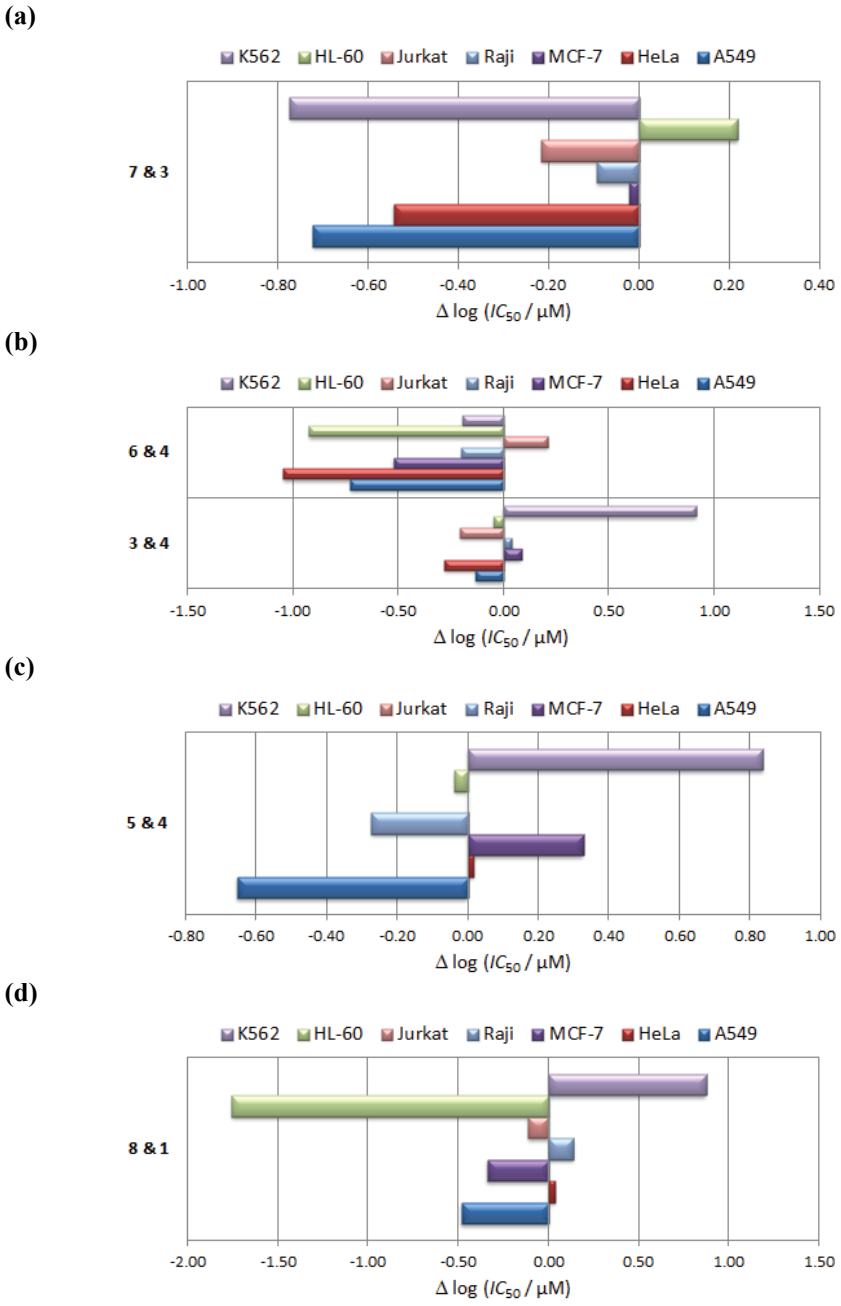
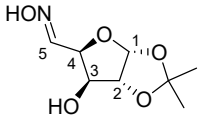
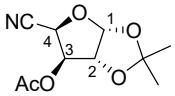
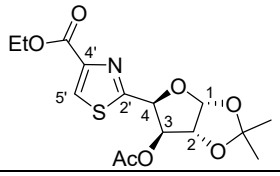
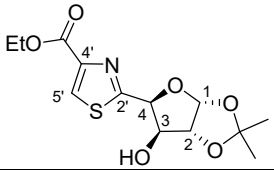
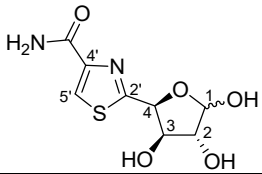
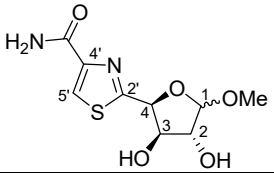
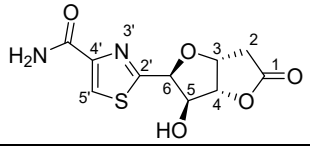
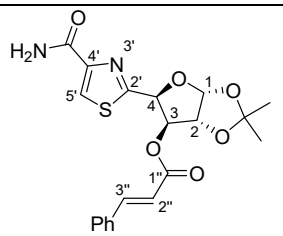
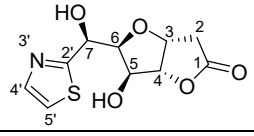
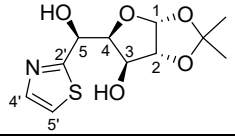


Fig. S-1. Influence of selected structural features on antitumour activities: (a) presence of cinnamoyl ester group; (b) presence of lactone/isopropyledene ring; (c) influence of methoxy group at C-1; (d) influence of thiazol *vs.* phenyl ring.

TABLE OF SYNTHESIZED COMPOUNDS

Table S-II. Chemical structures, numbering schemes and names (labels) of synthesised compounds

Entry	Structure	Name (label)
1		(*E,Z*)-1,2-*O*-Isopropylidene-α-D-*xylo*-pentodialdo-1,4-furanose-5-oxime (**10**)
2		3-*O*-Acetyl-1,2-*O*-isopropylidene-α-D-*xylo*-furanoseurononitrile (**11**)
3		3-*O*-Acetyl-4-*C*-(4′-(ethoxycarbonyl)thiazol-2′-yl)-1,2-*O*-isopropilidene-α-D-*xylo*-tetrofuranose (**12**)
4		4-*C*-(4′-(Carbamoyl)thiazol-2′-yl)-1,2-*O*-isopropylidene-α-D-*xylo*-tetrofuranose (**3**)
5		4-*C*-(4′-(Carbamoyl)thiazol-2′-yl)-D-*xylo*-tetrofuranose (**4**)
6		Methyl 4-*C*-(4′-(carbamoyl)thiazol-2′-yl)-D-*xylo*-tetrofuranoside (**5**)
7		3,6-Anhydro-6-*C*-(4′-(carbamoyl)thiazol-2′-yl)-2-deoxy-D-*ido*-hexono-1,4-lactone (**6**)

Entry	Structure	Name (label)
8		4-*C*-(4′-(Carbamoyl)thiazol-2′-yl)-3-*O*-cinnamoyl-1,2-*O*-isopropylidene-α-D-*xylo*-tetrofuranose (**7**)
9		3,6-Anhydro-2-deoxy-7-*C*-(thiazol-2′-yl)-D-*glycero*-D-*ido*-heptono-1,4-lactone (**8**)
10		1,2-*O*-Isopropylidene-5-*C*-(thiazol-2′-yl)-α-D-*gluco*-pentofuranose (**14**)

X-RAY ANALYSIS

TABLE S-III. Crystallographic and refinement details of **6** and **14**

	6	**14**
Crystal data		
Chemical formula	$C_{10}H_{10}N_2O_5S$	$C_{11}H_{15}NO_5S$
M_r	270.26	273.30
Crystal system	Orthorhombic	Monoclinic
Space group	$P2_12_12_1$	$P2_1$
Temperature, K	295	295
a / Å	5.24495 (15)	9.3233 (3)
b / Å	9.6990 (3)	6.5430 (2)
c / Å	22.4217 (6)	11.4925 (4)
β / °	90	91.526 (3)
V / Å^3	1140.61 (5)	700.81 (4)
Z	4	2
Radiation type	Mo $K\alpha$	Mo $K\alpha$
μ / mm^{-1}	0.30	0.24
Crystal size, mm	0.67×0.15×0.09	0.67×0.56×0.33
Data collection		
Absorption correction type	Analytical	Analytical
T_{min}	0.892	0.743
T_{max}	0.978	0.937
Measured reflections	18935	10936
Independent reflections	2810	3288
Observed reflections [$I > 2\sigma(I)$]	2649	3030
R_{int}	0.024	0.018
$(\sin \theta/\lambda)_{max}$ / Å^{-1}	0.682	0.681
Refinement		
R [$F^2 > 2\sigma(F^2)$]	0.034	0.037
wR [F^2]	0.081	0.089
S	1.14	1.09
Reflections	2810	3288
Parameters	175	173

	6	**14**
Restraints	0	1
H-atom treatment	Mixed	Mixed
$\Delta\rho_{max}$ / e Å^{-3}	0.27	0.15
$\Delta\rho_{min}$ / e Å^{-3}	−0.26	−0.23
No. of $(I^+-I^-)/(I^++I^-)$ quotients[5]	980	1212
Absolute structure parameter[5]	0.04 (2)	−0.05 (2)

TABLE S-IV. Conformational analysis of tiazofurin derivatives and **6**. Cremer-Pople puckering parameters for furanose ring in tiazofurin derivatives and **6** are calculated for furanose ring atoms enumerated O→C1′→C2′→C3′→C4′, counting clockwise. Thiazole ring is coupled to C1′ atom.

CSD refcode	φ_2 / °	q_2 / Å	closest descriptor	$\lvert\chi\rvert$ / °	Reference
GAPCUV	53.5	0.401	C2'-*exo* – C1'-*endo*	55.5	[4]
FAFMOP	58.1	0.345	C2'-*exo* – C1'-*endo*	21.6	5
FAFMUV	59.7	0.307	major C2'-*exo* – minor C1'-*endo*	23.0	5
BOBNEL10	67.0	0.423	major C2'-*exo* – minor C1'-*endo*	30.7	6
VUNNUN	82.5	0.309	major C2'-*exo* – minor C3'-*endo*	34.5	7
BETKOA10	83.5	0.369	major C2'-*exo* – minor C3'-*endo*	40.8	6
FAFNAC	88.9	0.358	C2'-*exo* – C3'-*endo*	32.5	5
6	255.0 (4)	0.353 (2)	C2'-*endo*	24.3(2)	This work
BOBNOV10	269.2	0.443	major C3'-*exo* – minor C2'-*endo*	20.8	6
VUNPAV	310.2	0.374	C3'-*exo* – C4'-*endo*	27.2	7
YIHCAT	349.9	0.329	major *O*-*exo* – minor C4'-*endo*	16.2	8

TABLE S-V Parameters of hydrogen bonding in **6**

D—H···*A*	*d*(*D*—H) / Å	*d*(H···*A*) / Å	*d*(*D*···*A*) / Å	∠(*D*—H···*A*) / °
N6′—H6′*A*···O1 ^{i}	0.86 (4)	2.08 (4)	2.935 (3)	171 (3)
O5—H5···O6′ ^{ii}	0.92 (4)	1.78 (4)	2.696 (3)	176 (3)

Symmetry codes: (i) −*x*+1/2, −*y*+1, *z*+1/2; (ii) −*x*+2, *y*−1/2, −*z*+3/2.

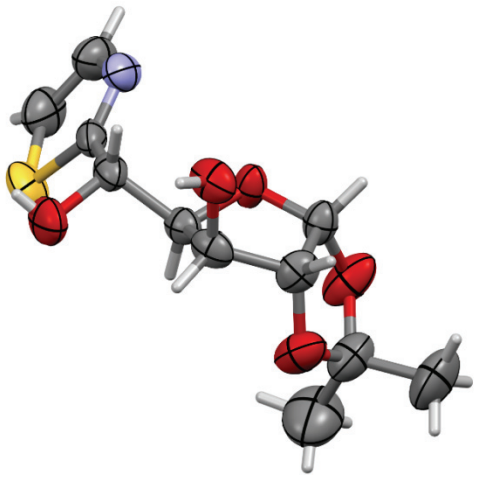


Fig. S-2. Molecular structure of compound **14** (CCDC 2218112)

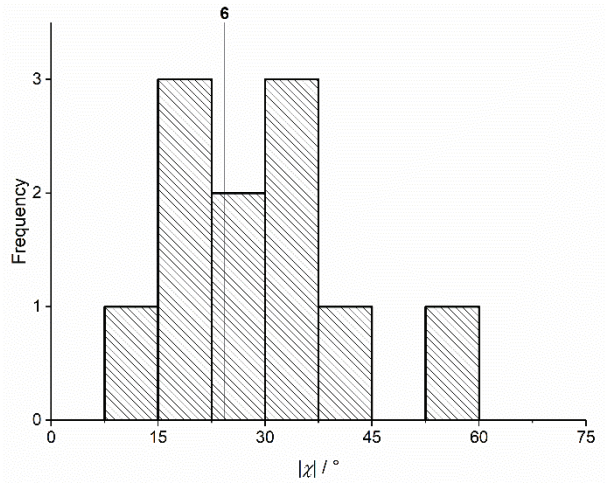


Fig. S-3. Distribution of torsion angle χ (O–C1′–C–S) for analyzed tiazofurin analogues

REFERENCES

1. P. Köll, A. Wernicke, J. Kovács, A. Lützen, *J. Carbohydr. Chem*. **19** (2000) 1019 (http://dx.doi.org/10.1080/07328300008544132)
2. G. Benedeković, J. Francuz, I. Kovačević, M. Popsavin, B. Srećo Zelenović, V. Kojić, G. Bogdanović, V. Divjaković, V. Popsavin, *Eur. J. Med. Chem*. **82** (2014) 449 (http://dx.doi.org/10.1016/j.ejmech.2014.05.081)
3. S. Parsons, H. Flack, T. Wagner, *Acta Crystallogr. Sect B* **69** (2013) 249 (https://doi.org/10.1107/S2052519213010014)
4. B. M. Goldstein, D. T. Mao, V. E. Marquez, *J. Med. Chem*. **31** (1988) 1026 (https://doi.org/10.1021/jm00400a024)
5. T. J. Miller, H. D. Farquar, A. Sheybani, C. E. Tallini, A. S. Saurage, F. R. Fronczek, R. P. Hammer, *Org. Lett*. **4** (2002) 877 (https://doi.org/10.1021/ol017003g)
6. B. M. Goldstein, F. Takusagawa, H. M. Berman, P. C. Srivastava, R. K. Robins, *J. Am. Chem. Soc*. **105** (1983) 7416 (https://doi.org/10.1021/ja00363a035)
7. F. T. Burling, W. H. Hallows, M. J. Phelan, B. Gabrielsen, B. M. Goldstein, *Acta Crystallogr. Sect. B* **48** (1992) 677 (https://doi.org/10.1107/S0108768192001101)
8. A. Dondoni, M.-C. Scherrmann, *J. Org. Chem*. **59** (1994) 6404 (https://doi.org/10.1021/jo00100a050).