Synthesis of some new disubstituted- and deoxytrisubstituted-α-D-allofuranoses

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Dedicated to Dr. A. V. Rama Rao on the occasion of his 70th birthday
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Abstract
1,2:5,6-Di-*O*-isopropylidene-3-*C*-undecyl-3-*O*-(substituted)-α-D-allofuranoses (**4a-e**), 1,2-*O*-isopropylidene-3-*C*-undecyl-3-*O*-(substituted)-α-D-allofuranoses (**5a-e**) and 1,2-*O*-isopropylidene-3-*C*-undecyl-3-*O*-methyl-6-deoxy-6-(substituted)-α-D-allofuranoses (**9a-d**) have been synthesized and evaluated for various *in vitro* cancer cell lines. In primary *in vitro* screening, some of them show little anti-cancer activity.

Keywords: Synthesis, aminoalkyl derivative, allofuranose, anti-cancer activity

Introduction

Carbohydrates play an important role in the interaction of cell with their environment. It is now well documented that glycoproteins and glycolipids mediate the attachment of pathogenic organisms to cells. These molecules are also involved in the process of oncogenesis[1–4] (i.e. the transformation of normal cell into cancer cell), metastasis[5–7] (i.e. the spread of cancer through the body) and the targeting of leukocyte to the areas of infection. Carbohydrate groups also influence protein structure and are involved in protein folding and in stabilizing protein that comes in to the contact with the external environment of the cell. The importance of glycoconjugates in biological process has triggered a massive effort to synthesize "substituted carbohydrates."

Several branched-chain sugar derivatives have been synthesized and evaluated as anti-cancer agents. Low molecular weight sugar derivatives[8–11] with aminoalkyl appendages are known as anti-cancer agents (Figure 1). In continuation of our work[11,12] on aminoalkyl derivatives of sugars, we have synthesized disubstituted and deoxytrisubstituted derivatives of 3-*C*-substituted-α-D-allofuranose (**4**, **5** and **9**) and evaluated them for anti-cancer activity, which are reported in this paper.

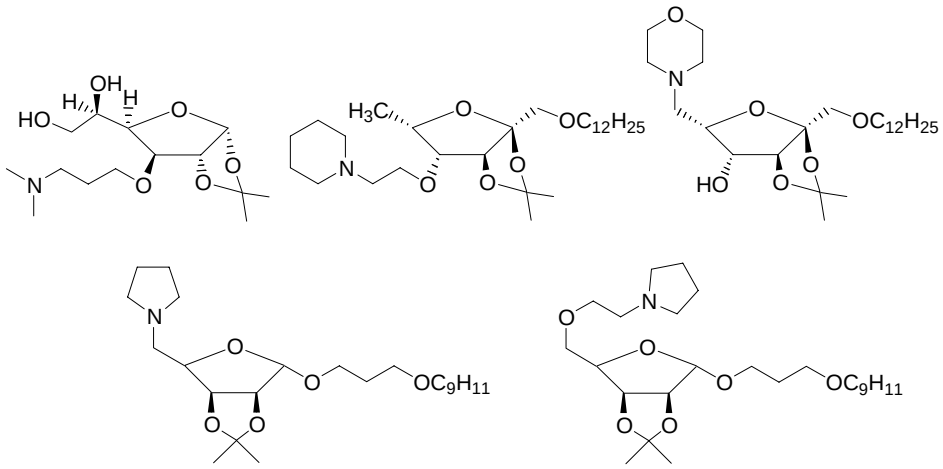
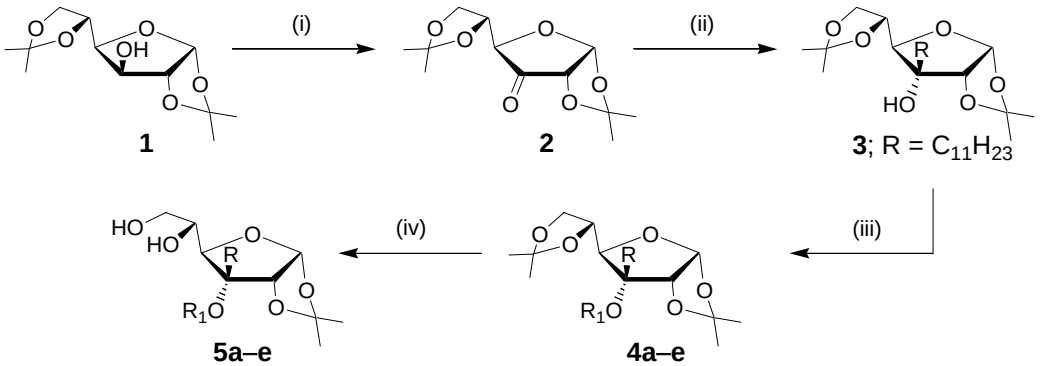


Figure 1. Structures of some aminoalkyl sugar derivatives having anti-cancer activity.

Results and Discussion

Chemistry

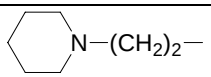
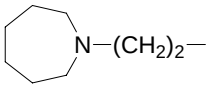
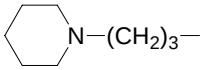
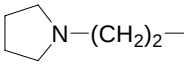
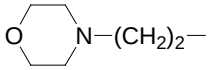
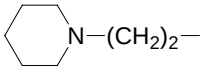
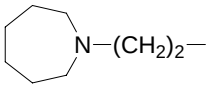
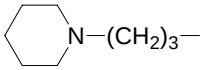
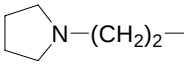
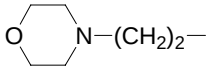
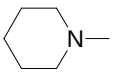
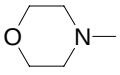
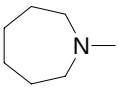
Compounds **4a–e** and **5a–e** were prepared as described in Scheme 1 starting from 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (**1**), which in turn was prepared from α-D-glucose as described in literature.[13] The compound **1** was then subjected to Swern oxidation at C–3 position to give the 1,2:5,6-di-*O*-isopropylidene-α-D-ribohexofuranos-3-ulose (**2**)[14] in 67% yield. The Grignard reaction[15,16] on compound **2** with 1-undecyl magnesium bromide afforded 1,2:5,6-di-*O*-isopropylidene-3-*C*-undecyl-α-D-allofuranose **(3)**. The compound **3** on condensation with various 1-(ω-haloalkyl)-piperidine/pyrrolidines/morpholine/hexamethyleneimine in the presence of NaOH at 110 ^{o}C gave 1,2:5,6-di-*O*-isopropylidene-3-*C*-undecyl-3-*O*-substituted-α-D-allofuranose (**4a–e**) in good yields. The selective deprotection of 5,6-*O*-isopropylidine group of 1,2:5,6-di-*O*-isopropylidene-3-*C*-undecyl-3-*O*-substituted-α-D-allofuranose (**4a–e**) led to the formation of 1,2-*O*-isopropylidene-3-*C*-undecyl-3-*O*-substituted-α-D-allofuranose (**5a–e**) (Scheme 1, Table 1).



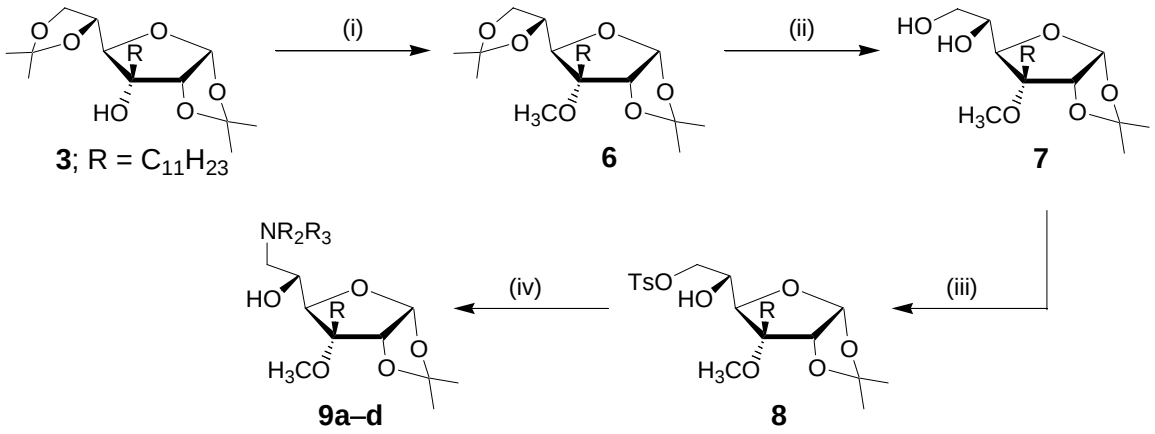
(i) DMSO, Ac_2O, 60 ^{o}C, 8 h; (ii) $C_{11}H_{23}MgBr$, Et_2O, 0→30 ^{o}C, 6 h; (iii) R_1Cl, NaOH, 110 ^{o}C, 7-8 h; (iv) 30% $HClO_4$, THF, 0→5 ^{o}C, 6-8 h.

Scheme 1. Synthesis of compounds **4**–**5**.

Table 1. Compounds **4**, **5** and **9**

Compds	R_1	NR_2R_3	Mol. Formula (Mol. Wt.)	Analysis (%)	
				Calcd	Found
4a		-	$C_{30}H_{55}NO_6$ (525)	C: 68.53 H: 10.54 N: 2.66	C: 68.21 H: 10.39 N: 2.59
4b		-	$C_{31}H_{57}NO_6$ (539)	C: 68.98 H: 10.64 N: 2.59	C: 68.63 H: 10.52 N: 2.28
4c		-	$C_{31}H_{57}NO_6$ (539)	C: 68.98 H: 10.64 N: 2.59	C: 69.11 H: 10.88 N: 2.74
4d		-	$C_{29}H_{53}NO_6$ (511)	C: 68.06 H: 10.44 N: 2.74	C: 67.95 H: 10.19 N: 2.56
4e		-	$C_{29}H_{53}NO_7$ (527)	C: 66.00 H: 10.12 N: 2.65	C: 66.17 H: 10.35 N: 2.84
5a		-	$C_{27}H_{51}NO_6$ (485)	C: 66.77 H: 10.58 N: 2.88	C: 67.01 H: 10.83 N: 3.07
5b		-	$C_{28}H_{53}NO_6$ (499)	C: 67.30 H: 10.69 N: 2.80	C: 67.02 H: 10.38 N: 2.51
5c		-	$C_{28}H_{53}NO_6$ (499)	C: 67.30 H: 10.69 N: 2.80	C: 66.96 H: 10.37 N: 2.44
5d		-	$C_{26}H_{49}NO_6$ (471)	C: 66.21 H: 10.47 N: 2.97	C: 66.53 H: 10.79 N: 3.22
5e		-	$C_{26}H_{49}NO_7$ (487)	C: 64.03 H: 10.13 N: 2.87	C: 64.38 H: 10.29 N: 3.08
9a	-		$C_{26}H_{49}NO_5$ (455)	C: 68.53 H: 10.84 N: 3.07	C: 68.24 H: 10.55 N: 2.89
9b	-		$C_{25}H_{47}NO_6$ (457)	C: 65.61 H: 10.35 N: 3.06	C: 65.73 H: 10.41 N: 3.20
9c	-		$C_{25}H_{47}NO_5$ (441)	C: 67.99 H: 10.73 N: 3.17	C: 68.33 H: 11.03 N: 3.39
9d	-		$C_{27}H_{51}NO_5$ (469)	C: 69.04 H: 10.94 N: 2.98	C: 68.81 H: 10.69 N: 2.77

In the 6-deoxy-6-substituted series, the compounds **9a–d** (Scheme 2, Table 1) were prepared from key intermediate 1,2:5,6-di-*O*-isopropylidene-3-*C*-undecyl-3-*O*-methyl-α-D-allofuranose (**6**), which was obtained by the reaction of methyl iodide in presence of NaOH with compound **3**. The selective deprotection of 5,6-*O*-isopropylidene group, tosylation of primary alcohol (6–OH) by *p*-toluenesulphonyl chloride followed by displacement of tosylate group with cyclic amines like piperidine, pyrrolidine, morpholine and hexamethyleneimine *via*. S_N2 mechanism afforded 1,2-*O*-isopropylidene-3-*C*-undecyl-3-*O*-methyl-6-deoxy-6-substituted-α-D-allofuranose (**9a-d**) in good yields. The structures of all the new compounds were determined on the basis of complementary spectroscopic (^{1}H NMR and MS) and analytical data.



(i) CH_3I, NaOH, 50 °C, 12 h; (ii) 30% $HClO_4$, THF, 0→5 °C, 6-8 h; (iii) Tosyl chloride, pyridine, 0→5 °C, 6-7 h; (iv) R_2R_3NH, 70 °C, 6-8 h.

Scheme 2. Synthesis of compounds **9**.

Pharmacological evaluation

These compounds were submitted to the National Cancer Institute (Bethesda, MD) for screening. For primary *in vitro* screening, all compounds **4a–e**, **5a–e** and **9a–d** were evaluated for their cytotoxic potency on three human cell lines (NCI-H460 lung cancer, MCF7 breast cancer and SF-268 CNS cancer). A compound is considered to be active when it reduces the growth of any of the cell lines to 32% or less. Among them, compounds **4a**, **5a**, **9a** and **9d** were found active (concentration 10^{-4} M) in primary screening. Further investigation is in progress.

In conclusion, a series of disubstituted- and deoxytrisubstituted-α-D-allofuranoses was synthesized and evaluated for anti-cancer activity. These results confirm the validity of our approach providing an easy and practical access to α-D-allofuranose based derivatives possessing *in vitro* antiproliferative activity against human tumor cells. The further investigation of compounds **4a**, **5a**, **9a** and **9d** on a full panel of 60 human cancer lines is in progress and results will be published in due course.

Experimental Section

General Procedures. Melting points were determined in open capillaries on a Büchi B-545 melting point apparatus. Compounds were routinely checked for their purity on silica gel 60 F_{254} TLC plates and their spots were visualized by exposing them to iodine vapors or by charring the plates with 5% H_2SO_4-EtOH reagent. ^{1}H NMR spectra were recorded on Bruker Advance DRX 200 MHz instrument as solutions (in $CDCl_3$) using TMS as internal reference, and chemical shifts values are expressed in δ units. Mass spectra were run on Applied Biosystems API 3000 instrument using direct inlet system under positive ion electrospray ionization source. Elemental analyses were carried out with a Perkin Elmer 2400 analyzer and the values found were within ±0.4% of theoretical values.

1,2:5,6-Di-*O*-isopropylidene-α-D-glucofuranose (1). This was prepared according to literature method[18] in 41% yield; mp 108–109 °C (lit.[18] mp 109–110 °C). ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.38 (s, 6H), 1.42 (s, 6H), 2.59 (br s, 1H), 3.80–4.62 (m, 6H), 5.94 (d, *J* = 4.0 Hz, 1H). MS: *m/z* (%) 261 (100) [M+1].

1,2:5,6-Di-*O*-isopropylidene-α-D-ribohexofuranos-3-ulose (2). A mixture of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (**1**, 75.0 g, 288.0 mmol), DMSO (300 mL) and acetic anhydride (150 mL) were stirred at 60 °C for 8 h. TLC monitored the progress of reaction. After completion of reaction, solvents were removed under reduced pressure and the residue was stirred with mixture of water (7.5 mL), hexane (75 mL) and Et_2O (30 mL) for 15 min. The solid thus separated out was filtered, washed with hexane-Et_2O mixture (3:1) and dried under reduced pressure to give compound **2** as a monohydrate. The monohydrated compound was dissolved in benzene (500 mL) and refluxed using Dean–Stark apparatus for 1 h to remove water. The reaction mixture was then cooled to ambient temperature and the solvent was removed at reduced pressure to give compound **2** as colorless oil, yield 50.0 g (67%). ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.37 (s, 6H), 1.42 (s, 6H), 3.80–4.62 (m, 5H), 5.95 (d, *J* = 4.0 Hz, 1H). MS: *m/z* (%) 259 (100) [M+1].

1,2:5,6-Di-*O*-isopropylidene-3-*C*-undecyl-α-D-allofuranose (3). To a well-stirred suspension of magnesium powder (6.94 g, 298.5 mmol) in anhydrous Et_2O (150 mL) was added a solution of 1-bromoundecane (1.6 mL, 7.2 mmol) in anhydrous Et_2O (2.0 mL), drop wise manner. After the reaction had initiated, 1-bromoundecane (50 mL, 224.2 mmol) in 50 mL of anhydrous Et_2O was added drop wise over a period of 30 min. The reaction mixture was cooled to 0 °C, and to this a solution of ketose **2** (15.0 g, 57.9 mmol) in 30 mL of anhydrous Et_2O was added drop wise at the same temperature. The resulting reaction mixture was stirred for 6 h at 30 °C. TLC monitored the progress of reaction. After the completion of reaction, the reaction mixture was poured into ice-cold water. The organic layer was separated out and the aqueous layer was extracted with Et_2O (2×50 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and filtered. Filtrate was concentrated at reduced pressure to yield the crude product which was purified by column chromatography over silica gel (100-200 mesh) using EtOAc/hexane (5:95)

as eluent to give **3** as colorless oil, yield 15.0 g (63%). ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.90 (s, 3H), 1.28–1.31 (m, 18H), 1.34 (s, 6H), 1.39 (s, 6H), 1.74-1.88 (m, 2H), 3.70-4.54 (m, 6H), 5.47 (d, *J* = 4.0 Hz, 1H). MS: *m/z* (%) 415 (100) [M+1].

1,2:5,6-Di-*O*-isopropylidene-3-*C*-undecyl-3-*O*-{2′-(piperidin-1-yl)ethyl}-α-D-allofuranose (4a). General procedure for the preparation of 4.

A mixture of compound **3** (1.2 g, 2.89 mmol), 1-(2-chloroethyl)-piperidine hydrochloride (0.58 g, 3.18 mmol) and sodium hydroxide (0.46 g, 11.5 mmol) was stirred at 110 ^{o}C for 6 h. The reaction mixture was cooled and extracted with EtOAc (2×25 mL). The combined EtOAc layers were washed with water (1×25 mL), brine (1×25 mL), dried over anhydrous Na_2SO_4 and filtered. The solvent was removed at reduced pressure to give **4a** as an oil, which was purified by column chromatography over silica gel (100–200 mesh) using EtOAc/hexane (7:3) as eluent, yield 0.91 g (60%). ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.90 (t, *J* = 6.5 Hz, 3H), 1.28–1.44 (m, 36H), 1.80–1.95 (m, 2H), 2.23–2.31 (m, 4H), 2.55–2.60 (m, 2H), 3.30–3.34 (m, 2H), 3.90–4.31 (m, 5H), 5.79 (d, *J* = 4.0 Hz, 1H). MS: *m/z* (%) 526 (100) [M+1].

1,2:5,6-Di-*O*-isopropylidene-3-*C*-undecyl-3-*O*-{2′-(hexamethyleneimino)ethyl}-α-D-allofuranose (4b). Colorless thick oil (65%). ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.90 (t, *J* = 6.5 Hz, 3H), 1.27–1.46 (m, 30H), 1.60–1.70 (m, 8H), 1.80–1.94 (m, 2H), 2.25–2.31 (m, 4H), 2.55–2.59 (m, 2H), 3.30–3.33 (m, 2H), 3.86–4.32 (m, 5H), 5.78 (d, *J* = 4.0 Hz, 1H). MS: *m/z* (%) 540 (100) [M+1].

1,2:5,6-Di-*O*-isopropylidene-3-*C*-undecyl-3-*O*-{3′-(piperidin-1-yl)propyl}-α-D-allofuranose (4c). Colorless thick oil (63%). ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.90 (t, *J* = 6.5 Hz, 3H), 1.28-1.46 (m, 36H), 1.52-1.56 (m, 2H), 1.80-1.95 (m, 2H), 2.25-2.30 (m, 4H), 2.57-2.60 (m, 2H), 3.30–3.34 (m, 2H), 3.39-4.30 (m, 5H), 5.78 (d, *J* = 4.0 Hz, 1H). MS: *m/z* (%) 540 (100) [M+1].

1,2:5,6-Di-*O*-isopropylidene-3-*C*-undecyl-3-*O*-{2′-(pyrrolidin-1-yl)ethyl}-α-D-allofuranose (4d). Colorless thick oil (68%). ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.10 (t, *J* = 6.5 Hz, 3H), 1.26-1.47 (m, 30H), 1.72-1.79 (m, 4H), 1.80-1.92 (m, 2H), 2.53-2.61 (m, 6H), 3.33-3.36 (m, 2H), 3.87-4.30 (m, 5H), 5.79 (d, *J* = 4.0 Hz, 1H). MS: *m/z* (%) 512 (100) [M+1].

1,2:5,6-Di-*O*-isopropylidene-3-*C*-undecyl-3-*O*-{2′-(morpholin-1-yl)ethyl}-α-D-allofuranose (4e). Colorless thick oil (60%). ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.90 (t, *J* = 6.5 Hz, 3H), 1.28-1.44 (m, 30H), 1.80-1.95 (m, 2H), 2.28-2.62 (m, 6H), 3.35-3.58 (m, 6H), 3.89-4.31 (m, 5H), 5.79 (d, *J* = 4.0 Hz, 1H). MS: *m/z* (%) 528 (100) [M+1]

General procedure for the preparation of 5

1,2-*O*-Isopropylidene-3-*C*-undecyl-3-*O*-{2′-(piperidin-1-yl)ethyl}-α-D-allofuranose (5a). To a stirred solution of **4a** (0.5 g) in THF (5 mL) was added 30% aqueous perchloric acid (0.5 mL) at 0 ^{o}C in drop wise manner and resulting reaction mixture was stirred for 6 h at the same temperature. The reaction mixture was neutralized with saturated aqueous sodium carbonate solution (pH 9.0) and the compound was extracted with EtOAc (2×20 mL). The combined EtOAc extracts were washed with water (1×10 mL), brine (1×10 mL), dried over anhydrous

Na_2SO_4 and filtered. The filtrate was concentrated at reduced pressure to give crude product, which was purified by column chromatography over silica gel (100-200 mesh) using EtOAc/hexane (8:2) as eluent to give **5a** as colorless thick oil, yield 0.32 g (71%). ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.10 (t, *J* = 6.5 Hz, 3H), 1.26-1.40 (m, 30H), 1.81-1.90 (m, 2H), 2.23-2.31 (m, 4H), 2.59-2.63 (m, 2H), 3.32-3.38 (m, 2H), 3.60-4.65 (m, 5H), 4.70 (br s, 2H), 5.90 (d, *J* = 4.0 Hz, 1H). MS: *m/z* (%) 486 (100) [M+1].

1,2-*O*-Isopropylidene-3-*C*-undecyl-3-*O*-{2′-(hexamethyleneimino)ethyl}-α-D-allofuranose (5b). Colorless thick oil (69%). ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.00 (t, *J* = 6.5 Hz, 3H), 1.21-1.42 (m, 24H), 1.61-1.72 (m, 8H), 1.80-1.90 (m, 2H), 2.26-2.32 (m, 4H), 2.56-2.59 (m, 2H), 3.31-3.34 (m, 2H), 3.61-4.66 (m, 5H), 4.70 (br s, 2H), 6.00 (d, *J* = 4.0 Hz, 1H). MS: *m/z* (%) 500 (100) [M+1].

1,2-*O*-Isopropylidene-3-*C*-undecyl-3-*O*-{3′-(piperidin-1-yl)propyl}-α-D-allofuranose (5c). Colorless thick oil (67%). ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.00 (t, *J* = 6.5 Hz, 3H), 1.21-1.41 (m, 30H), 1.66-1.90 (m, 4H), 2.28-2.31 (m, 4H), 2.58-2.61 (m, 2H), 3.32-3.36 (m, 2H), 3.65-4.65 (m, 5H), 4.70 (br s, 2H), 5.90 (d, *J* = 4.0 Hz, 1H). MS: *m/z* (%) 500 (100) [M+1].

1,2-*O*-Isopropylidene-3-*C*-undecyl-3-*O*-{2′-(pyrrolidin-1-yl)ethyl}-α-D-allofuranose (5d). Colorless thick oil (66%). ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.95 (t, *J* = 6.5 Hz, 3H), 1.24-1.41 (m, 24H), 1.72-1.92 (m, 6H), 2.53-2.62 (m, 6H), 3.33-3.37 (m, 2H), 3.65-4.66 (m, 5H), 4.70 (br s, 2H), 5.91 (d, *J* = 4.0 Hz, 1H). MS: *m/z* (%) 472 (100) [M+1].

1,2-*O*-Isopropylidene-3-*C*-undecyl-3-*O*-{2′-(morpholin-1-yl)ethyl}-α-D-allofuranose (5e). Colorless thick oil (66%). ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.90 (t, *J* = 6.5 Hz, 3H), 1.20-1.40 (m, 24H), 1.70-1.95 (m, 2H), 2.30-2.45 (m, 6H), 3.30-3.45 (m, 6H), 3.65-4.66 (m, 5H), 4.70 (br s, 2H), 5.91 (d, *J* = 4.0 Hz, 1H). MS: *m/z* (%) 488 (100) [M+1].

1,2:5,6-Di-*O*-isopropylidene-3-*C*-undecyl-3-*O*-methyl-α-D-allofuranose (6). A mixture of compound **3** (6.0 g, 14.5 mmol), methyl iodide (1.44 mL, 23.1 mmol), and sodium hydroxide (2.31 g, 57.9 mmol) was refluxed at 50 ^{o}C for 12 h. After completion of reaction, the reaction mixture was cooled to ambient temperature and suspended in EtOAc (100 mL), washed with water (1×50 mL), brine (1×50 mL), dried over anhydrous Na_2SO_4 and filtered. The filtrate was concentrated at reduced pressure to give crude product, which was purified by column chromatography over silica gel (100-200 mesh) using EtOAc/hexane (5:95) as eluent to give **6** as colorless thick oil, yield 5.1 g (82%). ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.00 (t, *J* = 6.5 Hz, 3H), 1.28-1.40 (m, 30H), 1.75-1.89 (m, 2H), 3.29 (s, 3H), 3.89-4.32 (m, 5H), 5.25 (d, *J* = 4.0 Hz 1H). MS: *m/z* (%) 429 (100) [M+1].

1,2-*O*-Isopropylidene-3-*C*-undecyl-3-*O*-methyl-α-D-allofuranose (7). To a stirred solution of compound **6** (5.0 g, 11.6 mmol) in THF (25 mL) was added 30% aqueous perchloric acid (5 mL) at 0 ^{o}C. After completion of addition the stirring was continued at the same temperature for 6 h. The reaction mixture was neutralized with saturated aqueous sodium carbonate solution (pH 9.0) and the compound was extracted with EtOAc (2×50 mL). The combined EtOAc extracts were washed with water (2×25 mL), brine (1×25 mL), dried over anhydrous Na_2SO_4 and filtered. The

filtrate was concentrated at reduced pressure to give **7** as thick oil, which was purified by column chromatography over silica gel (100-200 mesh) using EtOAc/hexane (6:4) as eluent, yield 3.5 g (77%). ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.88 (t, *J* = 6.5 Hz, 3H), 1.31-1.50 (m, 24H), 1.75-1.89 (m, 2H), 3.25 (s, 3H), 3.58 (br s, 2H), 3.62-4.39 (m, 5H), 5.42 (d, *J* = 4.0 Hz, 1H). MS: *m/z* (%) 389 (100) [M+1].

1,2-*O*-Isopropylidene-3-*C*-undecyl-3-*O*-methyl-6-*p*-tosyl-α-D-allofuranose (8). To a solution of diol **7** (3.5 g, 9.0 mmol) in pyridine (20 mL), was added a solution of *p*-toluenesulphonyl chloride (1.8 g, 9.9 mmol) in pyridine (20 mL) drop wise at 0 ^{o}C under stirring. After complete addition the reaction mixture was stirred for 6 h at the same temperature. After the completion of reaction, the solvent was removed under reduced pressure and residue was dissolved in EtOAc (50 mL), washed with water (2×20 mL) and saturated solution of sodium bicarbonate (2×20 mL). The organic layer was dried over anhydrous Na_2SO_4 and filtered. The filtrate was concentrated at reduced pressure to give **8** as viscous oil, yield 4.0 g (82%). ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.86 (t, *J* = 6.5 Hz, 3H), 1.30-1.52 (m, 24H), 1.73-1.88 (m, 2H), 2.35 (s, 3H), 3.26 (s, 3H), 3.61 (br s, 1H), 3.80-4.41 (m, 5H), 5.45 (d, *J* = 3.9 Hz, 1H), 7.25-7.60 (m, 4H). MS: *m/z* (%) 543 (100) [M+1].

General procedure for the preparation of 9

1,2-*O*-Isopropylidene-3-*C*-undecyl-3-*O*-methyl-6-deoxy-6-(piperidin-1-yl)-α-D-allofuranose (9a)

A mixture of compound **8** (1.2 g, 2.2 mmol) and piperidine (1.2 mL) was heated at 70 ^{o}C for 6 h under stirring. The excess piperidine was removed at reduced pressure and residue was dissolved in EtOAc (25 mL). The EtOAc layer was washed with a saturated solution of $NaHCO_3$ (1×20 mL) and brine (1×20 mL) and dried over anhydrous Na_2SO_4, filtered. The solvent was removed at reduced pressure to yield crude product, which was purified by column chromatography over silica gel (100-200 mesh) using EtOAc/hexane (7:3) as eluent to give **9a** as colorless thick oil, yield 0.69 g (69%). ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.97 (t, *J* = 6.5 Hz, 3H), 1.30-1.45 (m, 24H), 1.55-1.85 (m, 8H), 2.20-2.55 (m, 7H), 3.42 (s, 3H) 3.65-4.20 (m, 3H), 5.52 (d, *J* = 4.0 Hz, 1H). MS: *m/z* (%) 456 (100) [M+1].

1,2-*O*-Isopropylidene-3-*C*-undecyl-3-*O*-methyl-6-deoxy-6-(morpholin-1-yl)-α-D-allofuran- ose (9b). Colorless thick oil (63%). ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.00 (t, *J* = 6.5 Hz, 3H), 1.30-1.50 (m, 24H), 1.73-1.89 (m, 2H), 2.30-2.37 (m, 5H), 2.45–2.66 (m, 2H), 3.44 (s, 3H), 3.53-3.66 (m, 4H), 3.70-4.20 (m, 3H), 5.53 (d, *J* = 3.9 Hz, 1H). MS: *m/z* (%) 458 (100) [M+1].

1,2-*O*-Isopropylidene-3-*C*-undecyl-3-*O*-methyl-6-deoxy-6-(pyrrolidin-1-yl)-α-D-allofuran- ose (9c). Colorless thick oil (69%). ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.95 (t, *J* = 6.5 Hz, 3H), 1.28-1.40 (m, 24H), 1.55-1.80 (m, 6H), 2.20-2.50 (m, 7H), 3.45 (s, 3H) 3.60-4.22 (m, 3H), 5.50 (d, *J* = 4.0 Hz, 1H). MS: *m/z* (%) 442 (100) [M+1].

1,2-*O*-Isopropylidene-3-*C*-undecyl-3-*O*-methyl-6-deoxy-6-hexamethyleneimino-α-D-allofur- anose (9d). Colorless thick oil (64%). ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.00 (t, *J* = 6.5 Hz, 3H),

1.31-1.45 (m, 24H), 1.61-1.87 (m, 10H), 2.25-2.58 (m, 7H), 3.40 (s, 3H) 3.62-4.20 (m, 3H), 5.55 (d, *J* = 4.0 Hz, 1H). MS: *m/z* (%) 470 (100) [M+1].

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