Electronic Supplementary Material (ESI) for RSC Medicinal Chemistry.

Colorectal anti-cancer activity of a novel class of triazolic triarylmethanes derivatives

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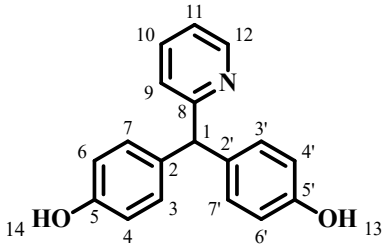
I. Chemistry

I.1. Materials and Methods

All reagents were obtained from commercial sources unless otherwise noted and used as received. Heated experiments were conducted using thermostatically controlled heating mantles and were performed under an atmosphere oxygen-free in oven-dried glassware when necessary. The reactions were monitored by analytical Thin Layer Chromatography (TLC). TLC was performed on aluminum sheets precoated silica gel plates (60 F254, Merck). TLC plates were visualized using irradiation with light at 254 nm. Flash column chromatography (FCC) was carried out when necessary using silica gel 60 (particle size 0.040-0.063 mm, Merck).

Melting points were recorder on a Kofler hot block Heizbank type 7841 and were uncorrected. The structures of the products were checked by comparison of NMR, IR and MS data and by the TLC behavior. ^{1}H and ^{13}C-NMR spectra were recorded on a Bruker BioSpin GmbH spectrometer 400 MHz, at room temperature. Chemical shifts are reported in δ units, parts per million (ppm). Coupling constants (J) are measured in hertz (Hz). Splitting patterns are designed as followed: s, singlet; d, doublet; dd, doublet of doublets; m, multiplet; t, triplet; td, trilet of doublet; ddd: doublet of doublet of doublet. DEPT experiments and various 2D techniques such as COSY, HSQC and HMBC were used to establish the structures and to assign the signals. GC-MS analysis were performed with an Agilent 689 0N instrument equipped with a dimethyl polysiloxane capillary column (12 m x 0.20 mm) and an Agilent 5973N MS detector-column temperature gradient 80-300 °C (method 80): 80 °C (1 min); 80 °C to 300 °C (12.05 °C/min); 300 °C (2 min). Low resolution mass spectra (ESI-LRMS) were performed from ionization by electrospray on a Waters Micromass ZQ2000. Infrared spectra were recorded over the 400-4000 cm^{-1} range with an Agilent Technologies Cary 630 FTIR/ ATR/ ZnSe spectrometer. High-resolution mass spectra (HRMS) analyses were acquired on a Thermo Scientific LTQ Orbitrap mass spectrometer.

4,4'-(pyridin-2-ylmethylene)diphenol 2



$C_{18}H_{15}NO_2$
277.32 g/mol

CAS RN 603-41-8

To a aqueous solution of KOH (62.25 mmol, 3.492 g, 3 eq,) containing 10% of EtOH was added the 4,4'-(pyridin-2-ylmethylene)bis(4,1-phenylene) diacetate **1** (20.75 mmol, 7.5 g). The reaction was stirred at room temperature during 48 h. After reaction completion, HCl was added to the mixture until pH = 1-2 then alkalized with Na_2CO_3 until pH = 8-9. The mixture was extracted with EtOAc, and then organic phase was washed with water. The combined organic phase was dried over anhydrous $MgSO_4$, filtered and concentrated to afford 4,4'-(pyridin-2-ylmethylene)diphenol **2** as a white solid with a yield of 97%.

TLC: CyHex/EtOAc: 60/40, R_f= 0.4

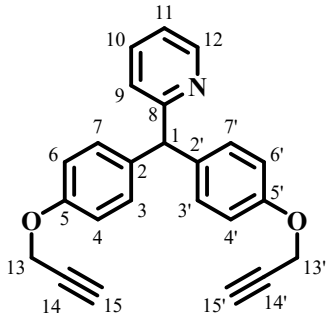
^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) : 9.27 (s, 1H, OH), 8.45 (dd, $J_{12\text{-}11}$= 4.8 Hz, $J_{12\text{-}10}$= 1.8 Hz, 1H, H12), 7.69 (td, $J_{10\text{-}11,\ 10\text{-}9}$ = 7.68 Hz, $J_{10\text{-}12}$ = 1.8 Hz 1H, H10), 7.18 (m, 2H, H9, H11), 6.91(d, $J_{3\text{-}4,\ 3'\text{-}4',\ 7\text{-}6,\ 7'\text{-}6'}$ = 8.56 Hz, 4H, H3, H7, H3', H7'), 6.62 (d,$J_{4\text{-}3,\ 4'\text{-}3',\ 6\text{-}7,\ 6'\text{-}7'}$ = 8.56 Hz, 4H, H4, H6, H4', H6'), 5.41(s,1H, H1). (Similar to literature [1]

^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm) : 163.6 (C_8), 155.6 (C_5), 149.0 (C_{12}), 136.5 (C_{10}), 133.8 (C_2), 129.8 (C_3, C_7), 123.2 (C_9), 121.3 (C_{11}), 114.9 (C_4, C_6), 56.7 (C_1).

IR ν (cm^{-1}) : 3302($\nu_{O\text{-}H}$), 3030($\nu_{Csp2\text{-}H}$), 2977, 2924 and 2890($\nu_{Csp3\text{-}H}$), 1611, 1593, 1510 and 1469($\nu_{C=C}$); 1238($\nu_{asym\ C\ N}$); 1174 ($\nu_{C\ O}$). (Similar to literature [1]

LRMS (ESI, CV = 30) : 300.17 $[M+Na]^+$, 278.19 $[M+H]^+$.

2-(bis(4-(prop-2-ynyloxy)phenyl)methyl)pyridine 3



$C_{24}H_{19}NO_2$
353.41 g/mol

CAS RN 896732-94-8

(Experimental protocol modified from the literature [2])

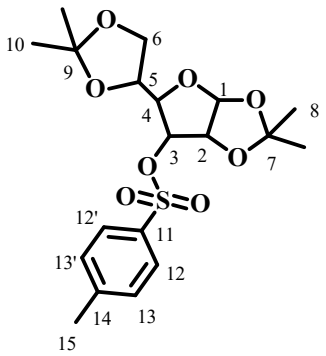
To a solution of 4,4'-(pyridin-2-ylmethylene)diphenol **2** (2.77 mmol, 770 mg), K_2CO_3 (13.85 mmol, 1914 mg, 5 eq) in anhydrous acetone (30 mL), was added 2-propargyl bromide (2.16 mmol, 0.24 mL, 6 eq,) under argon. The reaction mixture was stirred at 60 °C during 4 h. After reaction completion, the mixture was warmed to room temperature, concentrated, washed with water and then extracted with DCM. The organic phase was dried over anhydrous $MgSO_4$, filtered and concentrated. The 2-(bis(4-(prop-2-ynyloxy)phenyl)methyl)pyridine **3** was afforded without purification as an orange oil in 99% yield (970 mg).

TLC: (CyHex/EtOAc: 80/20), R_f= 0.5

^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) : 8.52 (dd, $J_{12\text{-}11}$= 4.8 Hz, $J_{12\text{-}10}$= 1.8 Hz, 1H, H12), 7.71 (td, $J_{10\text{-}11,\ 10\text{-}9}$= 7.68 Hz, $J_{10\text{-}12}$= 1.8 Hz 1H, H10), 7.46-7.45 (m, 1H, H9), 7.23-7.22 (m, 1H, H11), 7.14-7.13 (m, 4H, H3,H7,H3',H7'), 6.92-6.88 (m, 4H, H4, H6, H4', H6'), 5.55 (s, 1H, H1), 4.74 (d, $J_{13\text{-}15,\ 13'\text{-}15'}$= 2.4 Hz, 4H, H13, H13'), 3.54 (t, $J_{15\text{-}13,\ 15'\text{-}13'}$= 2.3 Hz, 2H, H15, H15'). (similar to literature[3]);

^{13}C NMR (400 MHz, DMSO-d_6) δ (ppm) : 163.34 (C8), 156.07 (C5, C5'), 149.63 (C12), 137.19 (C10), 136.57 (C2, C2'), 130.36 (C3, C7, C3, C7'), 123.96 (C9), 122.00 (C11), 115.00 (C4, C6, C4, C6'), 79.82 (C14, C14'), 78.61 (C15, C15'), 56.89 (C1), 55.38 (C13, C13'). (similar to literature[3]);

5-(2,2-dimethyl-1,3-dioxolan-4-yl)-2,2-dimethyltetrahydrofuro[2,3-d][1,3]dioxol-6-yl-4-methylbenzenesulfonate



$C_{19}H_{26}O_8S$
414.46 g/mol

CAS RN 3253-75-6

(Experimental protocol modified from the literature[4])

p-Toluenesulfonyl chloride (14.2 mmol, 2.78 g, 2 eq) was added dropwise to a solution of 1,2:5,6-Di-O-isopropylidene-α-D-glucofuranose (7.6 mmol, 2 g) in anhydrous pyridine (15 mL). The mixture was stirred at room temperature during 48 h. The crude mixture was concentrated, washed with water and then extracted with DCM. The organic phase was dried over anhydrous $MgSO_4$, filtered and concentrated. After purification by FCC on silica gel (CyHex/EtOAc, 80:20), the 5-(2,2-dimethyl-1,3-dioxolan-4-yl) -2,2-dimethyltetrahydrofuro [2,3-d][1,3]dioxol-6-yl 4-methylbenzenesulfonate was obtained as a yellow amorphous solid (2.9 g) in 94% yield.

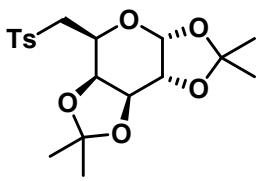
TLC: CyHex/EtOAc 60:40, R_f = 0.4

^{1}H NMR (400 MHz, DMSO-d$_6$) δ (ppm) : 7.84 (d, $J_{12\text{-}13}$ = 8.4 Hz, 2H, H12, H12'), 7.50 (d, $J_{13\text{-}12}$ = 8.0 Hz, 2H, H13, H13'), 5.99 (d, $J_{1\text{-}2}$ = 3.8 Hz, 1H, H1), 4.74 (d, $J_{2\text{-}1}$ = 3.8 Hz, 1H, H2), 4.68 (d, $J_{3\text{-}4}$ = 2.9 Hz, 1H, H3), 4.00 (dd, $J_{4\text{-}5}$ = 6.3 Hz, $J_{4\text{-}3}$ = 3.0 Hz, 1H, H4), 3.93 – 3.87 (m, 2H, H5, H6a), 3.74-3.69 (m, 1H, H6b), 2.43 (s, 3H, H15, CH_3), 1.39 (s, 3H, H8, CH_3), 1.26 (s, 3H, H8, CH_3), 1.10 (s, 3H, H10, CH_3), 1.07 (s, 3H, H10, CH_3). similar to literature[5];

^{13}C NMR (100 MHz, DMSO-d$_6$) δ (ppm) : 145.44 (C11), 131.82 (C14), 130.13 (C13, C13'), 128.12 (C12, C12'), 111.72 (C7), 108.30 (C9), 104.56 (C1), 82.79 (C2), 82.06 (C3), 78.96 (C4), 71.33 (C5), 65.91 (C6), 24.60 (C8, C10), 21.12 (C15). similar to literature[5];

IR ν (cm^{-1}) : 2988, 2945 ($\nu_{Csp3\text{-}H}$); 1673, 1600, 1510 and 1459 ($\nu_{C=C}$); 1225 ($\nu_{asym\ O\text{-}C\text{-}O}$); 1073 ($\nu_{sym\ O\text{-}C\text{-}O}$); 841 ($\delta_{Csp2\text{-}H\ p\text{-}substitution}$).

(3aR,5R,5aS,8aS,8bR)-2,2,7,7-tetramethyltetrahydro-3aH-bis([1,3]dioxolo)[4,5-b:4',5'-d]pyran-5-yl)methyl 4-methylbenzenesulfonate ,



$C_{19}H_{26}O_8S$
414.46 g/mol

CAS RN: 4478-43-7

p-Toluenesulfonyl chloride (8.36 mmol, 1.6 g, 2 eq) was added dropwise to a solution of 1,2:3,4-Di-O-isopropylidene-α-*D*-galactopyranose (4.18 mmol, 1.088 g) in anhydrous pyridine (15 mL). The mixture was stirred at room temperature during 48 h. The crude mixture was concentrated, washed with water and then extracted with DCM. The organic phase was dried over anhydrous $MgSO_4$, filtered and concentrated. After purification by FCC on silica gel (CyHex/EtOAc, 80:20), the desired compound was obtained as a white solid (1.74 g) in 98% yield.

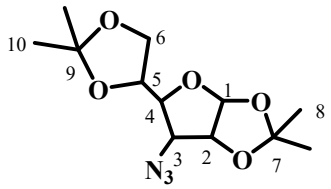
TLC: CyHex/EtOAc 60:40, R_f = 0.6

^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) : 7.80 (d, $J_{12\text{-}13}$ = 8.3 Hz, 2H, H12), 7.49 (d, $J_{13\text{-}12}$ = 8.0 Hz, 2H, H13) , 5.42 (d, $J_{1\text{-}2}$ = 5.0 Hz, 1H, H1), 4.61 – 4.53 (m, 1H, H3), 4.35 (dd, $J_{2\text{-}1}$ = 5.0 Hz, $J_{2\text{-}3}$ = 2.5 Hz, 1H, H2), 4.24 – 4.19 (m, 1H, H4), 4.15 (dd, $J_{6a\text{-}6b}$ = 10.3, $J_{6a\text{-}5}$ = 3.5 Hz, 1H, H6a), 3.94 (dd, $J_{6b\text{-}6a}$ = 10.3 Hz, $J_{6b\text{-}5}$ = 8.1 Hz, 1H, H6b), 3.87 (ddd, $J_{5\text{-}6b}$ = 8.0 Hz, $J_{5\text{-}6a}$ = 3.2 Hz, $J_{5\text{-}4}$ = 1.9 Hz, 1H, H5), 2.42 (s, 3H, H15), 1.38 (s, 3H, CH_3), 1.27 (s, 9H, $2CH_3$), 1.23 (s, 3H, CH_3). (similar to literature[6]);

^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm) : 145.11 (C11), 132.07 (C14), 130.22 (C13, C13'), 127.75 (C12, C12'), 108.73 (C7), 108.08 (C9), 95.48 (C1), 69.97 (C3), 69.89 (C4), 69.47 (C2), 69.17 (C6), 65.63 (C5), 25.70 (C8) 24.20 (C10), 21.11 (C15). (similar to literature[6]);

IR ν (cm^{-1}) : 2994, 2916 ($\nu_{Csp3\text{-}H}$); 1670, 1598, 1510 and 1455 ($\nu_{C=C}$); 1223 ($\nu_{asym\ O\text{-}C\text{-}O}$); 1068 ($\nu_{sym\ O\text{-}C\text{-}O}$); 841 ($\delta_{Csp2\text{-}H\ p\text{-}substitution}$).

6-azido-5-(2,2-dimethyl-1,3-dioxolan-4-yl)-2,2-dimethyltetrahydrofuro[2,3-d][1,3]dioxole 7



$C_{12}H_{19}N_3O_5$
285.29 g/mol

CAS RN 13964-23-3

To a solution of tosylated diacetone glucofuranose (6.5 mmol, 2.7 g) in anhydrous DMF (50 mL), was added dropwise the sodium azide (32.5 mmol, 4.9 g, 5 eq) and the TBAHS (0.027 mmol, 9.2 mg, 0.0042 eq). The mixture was stirred during 72 h at 120 °C. After reaction completion, the mixture was concentrated, washed with water and then extracted with DCM. The organic phase was dried over anhydrous $MgSO_4$, filtered and concentrated. After purification by FCC on silica gel (CyHex/EtOAc, 90:10), the 6-azido-5-(2,2-dimethyl-1,3-dioxolan-4-yl)-2,2-dimethyltetrahydrofuro[2,3-d][1,3]dioxole **7** was obtained as a yellow oil (258.2 mg) in 61% yield.

TLC: CyHex/EtOAc 60:40, R_f = 0.6

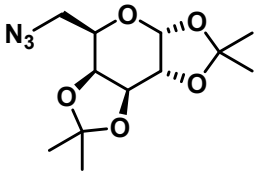
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) : 5.78 (d, J_{1-2} = 5.0 Hz, 1H, H1), 4.73 (dd, J_{2-3} = 9.1 Hz, J_{2-1} = 4.8 Hz, 1H, H2), 4.21-4.12 (m, 2H, H6a, H5), 4.04-3.97 (m, 2H, H4, H6b), 3.52 (dd, J_{3-2} = 9.1 Hz, J_{3-4} = 4.5 Hz, H3), 1.58 (s, 3H, H8, CH_3), 1.48 (s, 3H, H8, CH_3), 1.36 (s, 3H, H10, CH_3), 1.38 (s, 3H, H10, CH_3). (similar to literature[7–10]);

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) : 113.40 (C7), 110.24 (C9), 104.07 (C1), 80.70 (C2), 78.19 (C4), 75.90 (C5), 66.89 (C6), 62.73 (C3), 26.63 (C8), 26.41 (C10). (similar to literature[7–10]);

LRMS: (ES+, CV=30) m/z: 308.24 $[M+Na]^+$; 243.23 $[M-N_3]^+$; 207.19 $[M-C_5H_9O_2+Na]^+$.

IR ν (cm^{-1}) : 2989, 2939 (ν_{Csp3-H}); 2108 (ν_{N3}); 1251 (ν_{C-N}), 1212 ($\nu_{asym\ C-O-C}$); 1065 ($\nu_{sym\ C-O-C}$).

(3aR,5R,5aS,8aS,8bR)-5-(azidomethyl)-2,2,7,7-tetramethyltetrahydro-5H-bis([1,3]dioxolo)[4,5-b:4',5'-d]pyran (5)



$C_{12}H_{19}N_3O_5$
285.30 g/mol

CAS RN 4711-00-6

To a solution of tosylated diacetone galactopyranose (3.86 mmol, 1.6 g) in anhydrous DMF (32 mL), was added dropwise the sodium azide (19.3 mmol, 2.9 g, 5 eq) and the TBAHS (0.016 mmol, 5.5 mg, 0.0042 eq). The mixture was stirred during 16 h at 120 °C. After reaction completion, the mixture was concentrated, washed with water and then extracted with DCM. The organic phase was dried over anhydrous $MgSO_4$, filtered and concentrated. After purification by FCC on silica gel (CyHex/EtOAc, 80:20), the desired compound **5** was obtained as a yellow oil (1.07 g) in 97% yield.

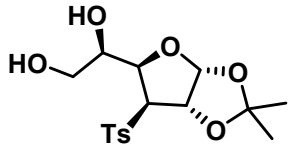
TLC: CyHex/EtOAc 70:30, R_f = 0.7

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) : 5.55 (d, $J_{1\text{-}2}$ = 5.0 Hz, 1H, H1), 4.63 (dd, $J_{3\text{-}4}$ = 7.9 Hz, $J_{3\text{-}2}$ = 2.5 Hz, 1H, H3), 4.34 (dd, $J_{2\text{-}1}$ = 5.0 Hz, $J_{2\text{-}3}$ = 2.5 Hz, 1H, H2), 4.19 (dd, $J_{4\text{-}3}$ = 7.9, $J_{4\text{-}5}$ = 1.9 Hz, 1H, H4), 3.91 (ddd, $J_{5\text{-}6a}$ = 7.5 Hz, $J_{5\text{-}6b}$ = 5.3 Hz, $J_{5\text{-}4}$ = 1.9 Hz, 1H, H5), 3.51 (dd, $J_{6a\text{-}6b}$ = 12.7, $J_{6a\text{-}5}$ = 7.9 Hz, 1H, H6a), 3.36 (dd, $J_{6b\text{-}6a}$ = 12.7 Hz, $J_{6b\text{-}5}$ = 5.3 Hz, 1H, H6b), 1.55 (s, 3H, H10, CH_3), 1.46 (s, 3H, CH_3, H10), 1.33 (s, 3H, CH_3, H8), 1.35 (s, 3H, CH_3, H8).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) : 109.77 (C7), 108.96 (C9), 96.49 (C1), 71.29 (C4), 70.94 (C3), 70.52 (C2), 67.13 (C5), 50.80 (C6), 26.17 (C10), 26.08 (C10), 25.02 (C8), 24.57 (C8).

IR ν (cm^{-1}) : 2989, 2937 ($\nu_{Csp3\text{-}H}$); 2099 (ν_{N3}); 1254 ($\nu_{C\text{-}N}$), 1210 ($\nu_{sym\ C\text{-}O\text{-}C}$); 1065 ($\nu_{sym\ C\text{-}O\text{-}C}$).

(R)-1-((3aR,5R,6S,6aS)-2,2-dimethyl-6-tosyltetrahydrofuro[2,3-d][1,3]dioxol-5-yl)ethane-1,2-diol



$C_{16}H_{22}O_7S$
358.40 g/mol

p-Toluenesulfonyl chloride (14.2 mmol, 2.78 g, 2 eq) was added dropwise to a solution of 1,2:5,6-Di-O-isopropylidene-α-D-glucofuranose (7.6 mmol, 2 g) in anhydrous pyridine (15 mL). The mixture was stirred at room temperature during 48 h. The crude mixture was concentrated, washed with water and then extracted with DCM. The organic phase was dried over anhydrous $MgSO_4$, filtered and concentrated. After purification by FCC on silica gel (CyHex/EtOAc, 80:20), the 5-(2,2-dimethyl-1,3-dioxolan-4-yl) -2,2-dimethyltetrahydrofuro [2,3-d][1,3]dioxol-6-yl 4-methylbenzenesulfonate was obtained as a yellow amorphous solid (2.9 g) in 94% yield.

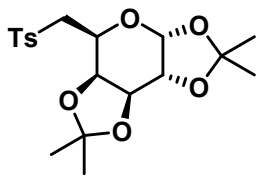
TLC: CyHex/EtOAc 60:40, R_f = 0.4

^{1}H NMR (400 MHz, DMSO-d$_6$) δ (ppm) : 7.84 (d, $J_{12\text{-}13}$ = 8.4 Hz, 2H, H12, H12'), 7.50 (d, $J_{13\text{-}12}$ = 8.0 Hz, 2H, H13, H13'), 5.99 (d, $J_{1\text{-}2}$ = 3.8 Hz, 1H, H1), 4.74 (d, $J_{2\text{-}1}$ = 3.8 Hz, 1H, H2), 4.68 (d, $J_{3\text{-}4}$ = 2.9 Hz, 1H, H3), 4.00 (dd, $J_{4\text{-}5}$ = 6.3 Hz, $J_{4\text{-}3}$ = 3.0 Hz, 1H, H4), 3.93 – 3.87 (m, 2H, H5, H6a), 3.74-3.69 (m, 1H, H6b), 2.43 (s, 3H, H15, CH_3), 1.39 (s, 3H, H8, CH_3), 1.26 (s, 3H, H8, CH_3), 1.10 (s, 3H, H10, CH_3), 1.07 (s, 3H, H10, CH_3).

^{13}C NMR (100 MHz, DMSO-d$_6$) δ (ppm) : 145.44 (C11), 131.82 (C14), 130.13 (C13, C13'), 128.12 (C12, C12'), 111.72 (C7), 108.30 (C9), 104.56 (C1), 82.79 (C2), 82.06 (C3), 78.96 (C4), 71.33 (C5), 65.91 (C6), 24.60 (C8, C10), 21.12 (C15).

IR ν (cm^{-1}) : 2988, 2945 ($\nu_{Csp3\text{-}H}$); 1673, 1600, 1510 and 1459 ($\nu_{C=C}$); 1225 ($\nu_{asym\ O\text{-}C\text{-}O}$); 1073 ($\nu_{sym\ O\text{-}C\text{-}O}$); 841 ($\delta_{Csp2\text{-}H\ p\text{-}substitution}$).

(3aR,5R,5aS,8aS,8bR)-2,2,7,7-tetramethyltetrahydro-3aH-bis([1,3]dioxolo)[4,5-b:4',5'-d]pyran-5-yl)methyl 4-methylbenzenesulfonate , 7



$C_{19}H_{26}O_8S$
414.46 g/mol

CAS RN : 4478-43-

p-Toluenesulfonyl chloride (8.36 mmol, 1.6 g, 2 eq) was added dropwise to a solution of 1,2:3,4-Di-O-isopropylidene-α-*D*-galactopyranose (4.18 mmol, 1.088 g) in anhydrous pyridine (15 mL). The mixture was stirred at room temperature during 48 h. The crude mixture was concentrated, washed with water and then extracted with DCM. The organic phase was dried over anhydrous $MgSO_4$, filtered and concentrated. After purification by FCC on silica gel (CyHex/EtOAc, 80:20), the desired compound was obtained as a white solid (1.74 g) in 98% yield.

TLC: CyHex/EtOAc 60:40, R_f = 0.6

^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) : 7.80 (d, $J_{12\text{-}13}$ = 8.3 Hz, 2H, H12), 7.49 (d, $J_{13\text{-}12}$ = 8.0 Hz, 2H, H13) , 5.42 (d, $J_{1\text{-}2}$ = 5.0 Hz, 1H, H1), 4.61 – 4.53 (m, 1H, H3), 4.35 (dd, $J_{2\text{-}1}$ = 5.0 Hz, $J_{2\text{-}3}$ = 2.5 Hz, 1H, H2), 4.24 – 4.19 (m, 1H, H4), 4.15 (dd, $J_{6a\text{-}6b}$ = 10.3, $J_{6a\text{-}5}$ = 3.5 Hz, 1H, H6a), 3.94 (dd, $J_{6b\text{-}6a}$ = 10.3 Hz, $J_{6b\text{-}5}$ = 8.1 Hz, 1H, H6b), 3.87 (ddd, $J_{5\text{-}6b}$ = 8.0 Hz, $J_{5\text{-}6a}$ = 3.2 Hz, $J_{5\text{-}4}$ = 1.9 Hz, 1H, H5), 2.42 (s, 3H, H15), 1.38 (s, 3H, CH_3), 1.27 (s, 9H, $2CH_3$), 1.23 (s, 3H, CH_3).

^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm) : 145.11 (C11), 132.07 (C14), 130.22 (C13, C13'), 127.75 (C12, C12'), 108.73 (C7), 108.08 (C9), 95.48 (C1), 69.97 (C3), 69.89 (C4), 69.47 (C2), 69.17 (C6), 65.63 (C5), 25.70 (C8) 24.20 (C10), 21.11 (C15).

IR ν (cm^{-1}) : 2994, 2916 ($\nu_{Csp3\text{-}H}$); 1670, 1598, 1510 and 1455 ($\nu_{C=C}$); 1223 ($\nu_{asym\ O\text{-}C\text{-}O}$); 1068 ($\nu_{sym\ O\text{-}C\text{-}O}$); 841 ($\delta_{Csp2\text{-}H\ p\text{-}substitution}$).

References

[1] C. Ricco, F. Abdmouleh, C. Riccobono, L. Guenineche, F. Martin, E. Goya-Jorge, N. Lagarde, B. Liagre, M. Ben Ali, C. Ferroud, M. El Arbi, M.S.I. Veitía, Pegylated triarylmethanes: Synthesis, antimicrobial activity, anti-proliferative behavior and in silico studies, Bioorg. Chem. 96 (2020) 103591. https://doi.org/10.1016/j.bioorg.2020.103591.

[2] R. Berscheid, F. Vögtle, Z. Nieger, Mehrfach verbrückte Triphenylmethane, Chem. Ber. 125 (1992) 1687–1695. https://doi.org/10.1002/cber.19921250726.

[3] N.C. Habermehl, F. Mohr, D.J. Eisler, M.C. Jennings, R.J. Puddephatt, Organogold(I) macrocycles and [2]catenanes containing pyridyl and bipyridyl substituents - Organometallic catenanes as ligands, Can. J. Chem. 84 (2006) 111–123. https://doi.org/10.1139/V05-229.

[4] A. Nagy, B. Csordás, V. Zsoldos-Mády, I. Pintér, V. Farkas, A. Perczel, C-3 epimers of sugar amino acids as foldameric building blocks: improved synthesis, useful derivatives, coupling strategies, Amino Acids. 49 (2017) 223–240. https://doi.org/10.1007/s00726-016-2346-5.

[5] A. Mukherji, R.B. Addanki, S. Halder, P.K. Kancharla, Sterically Strained Brønsted Pair Catalysis by Bulky Pyridinium Salts: Direct Stereoselective Synthesis of 2-Deoxy and 2,6-Dideoxy-β-thioglycosides from Glycals, J. Org. Chem. 86 (2021) 17226–17243. https://doi.org/10.1021/acs.joc.1c02305.

[6] S. Ferreira, A.C.R. Sodero, M.F.C. Cardoso, E.S. Lima, C.R. Kaiser, F.P. Silva, V.F. Ferreira, Synthesis, Biological Activity, and Molecular Modeling Studies of 1H-1,2,3-Triazole Derivatives of Carbohydrates as a-Glucosidases Inhibitors, J. Med. Chem. 53 (2010) 2364–2375. https://doi.org/10.1021/jm901265h.

[7] A.P. Wang, C. Liu, S. Yang, Z. Zhao, P. Lei, An efficient method to synthesize novel 5-O-(6′-modified)-mycaminose 14-membered ketolides, Tetrahedron. 72 (2016) 285–297. https://doi.org/10.1016/j.tet.2015.11.029.

[8] Z.-G. Gao, H.T. Duong, T. Sonina, S.-K. Kim, P. Van Rompaey, S. Van Calenbergh, L. Mamedova, H.O. Kim, M.J. Kim, A.Y. Kim, B.T. Liang, L.S. Jeong, K.A. Jacobson, Orthogonal Activation of the Reengineered A3 Adenosine Receptor (Neoceptor) Using Tailored Nucleoside Agonists, J. Med. Chem. 49 (2006) 2689–2702. https://doi.org/10.1021/jm050968b.

[9] L.R. Comstock, J.M. Denu, Synthesis and biochemical evaluation of O-acetyl-ADP-ribose and N-acetyl analogs, Org. Biomol. Chem. 5 (2007) 3087–3091. https://doi.org/10.1039/b710231c.

[10] X.P. He, Y.L. Zeng, Y. Zang, J. Li, R.A. Field, G.R. Chen, Carbohydrate CuAAC click chemistry for therapy and diagnosis, Carbohydr. Res. 429 (2016) 1–22. https://doi.org/10.1016/j.carres.2016.03.022.