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A stereo- and regio-controlled synthesis of bromothiophenyl C-nucleosides. Tandem bromination-ribosylation via halogen dance process

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ABSTRACT

Metallation–ribosylation of 2-bromothiophene **1** when conducted at room temperature afforded the original glycosylated dibromothiophene **3b** following a regiocontrolled halogen transfer-based halogen-dance process. Then, stereocontrolled reduction-cyclization of hemiacetals **3a–c** allowed straightforward access to the halogenated thiophenyl-C-nucleosides **6a–c**.

C-Nucleosides are important targets in modern organic chemistry due to their high potential value as bioactive molecules and biochemical probes.[1] Recently, several synthetic C-nucleosides have been studied as building blocks in artificial DNA and RNA for different biochemical applications.[2] They have been found in a lot of naturally occurring and synthetic products with potent antiviral or antitumor activities. Among them, tiazofurin has recently been approved as an orphan drug for treatment of chronic myelogenous leukemia in accelerated phase or blast crisis.[3] The benzamide riboside is another tiazofurin analog with improved biological properties.[4] Therefore, stereospecific methods which allow access to suitable precursors are of great interest.

In connection with our ongoing project aimed at using 2-bromothiophene **1** as starting material for post-synthetic transformations and to prepare various probe-like C-nucleosides by their incorporation into oligonucleotides,[5] we envisioned the preparation of new brominated thiophene C-nucleosides as candidates to advanced procursors.

We have recently reported that metallation–alkylation of 2-bromothiophene conducted at low temperature led to the side α-alkylation, while, when conducted at room temperature the formation of dibromothiophenes occured following an original alkylation/halogen-dance tandem process.[6] To further explore the scope of this reaction, we report herein a straightforward synthesis of bromothiophenyl C-nucleosides with a total regio- and stereocontrol. The synthesis involves three key steps (Fig. 1): (1) regiocontrolled halogen dance/glygosylation tandem reaction, (2) stereoselective hemiacetal reduction and (3) stereocontrolled intramolecular cycloetherification leading to novel brominated thiophenyl-C-nucleosides.

Thus, regioselective *ortho*-lithiation of **1**, using LDA in THF at −78 °C, followed by addition of the protected ribonolactone **2**

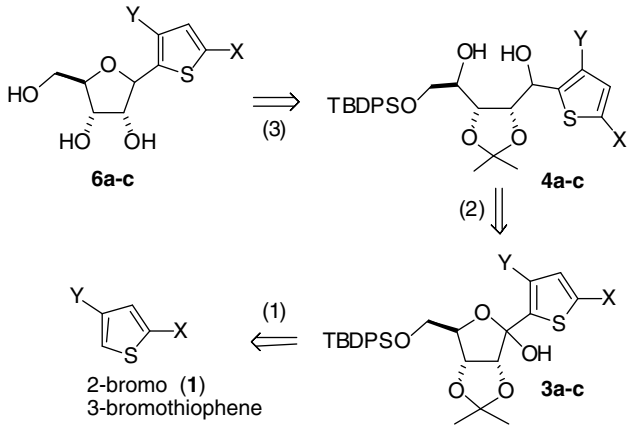

Figure 1. Retrosynthetic pathway (1) regio-controlled glycosylation, (2) stereocontrolled reduction, and (3) intramolecular ring closure and deprotection.

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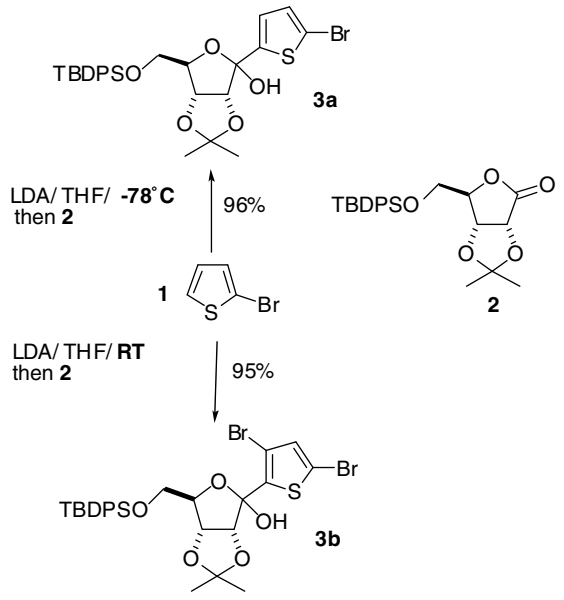
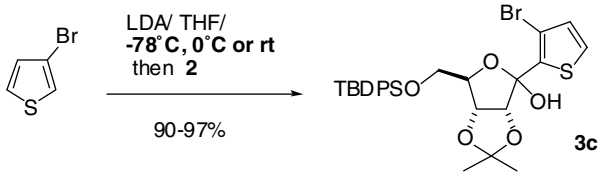
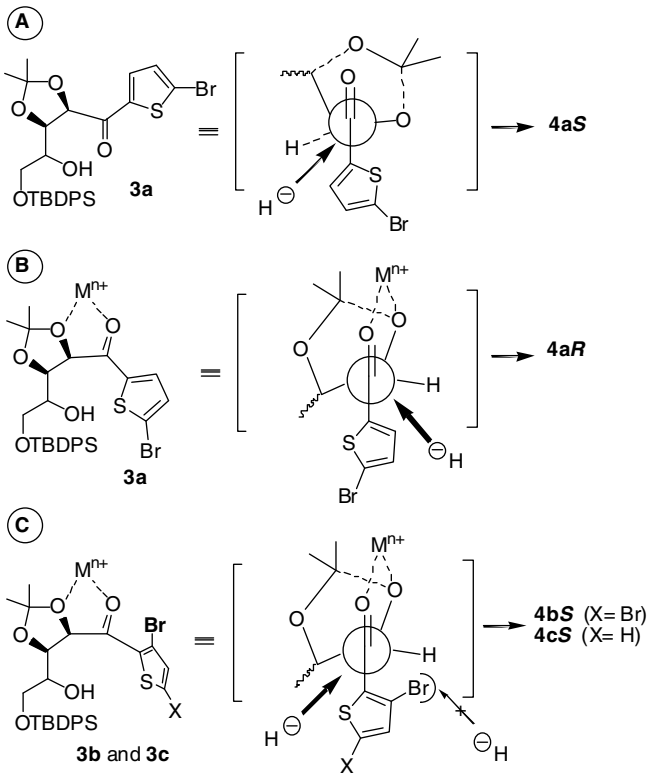


Scheme 1. **1** (2.2 equiv), LDA (2.2 equiv), **2** (1 mmol).

afforded the hemiacetal product **3a** in 96% yield (Scheme 1). Interestingly, the same reaction sequences when performed at room temperature afforded the 3,5-dibromo hemiacetal adduct **3b** as the sole product of the reaction (95% yield). The structures of **3a** and **3b** were unambiguously confirmed by MS and NMR spectroscopy.[7] As expected, **3a** results from a lithiation/glycosylation sequence while **3b** is produced following tandem halogen dance/ribosylation process involving a cascade of bromide transfer.[6] In

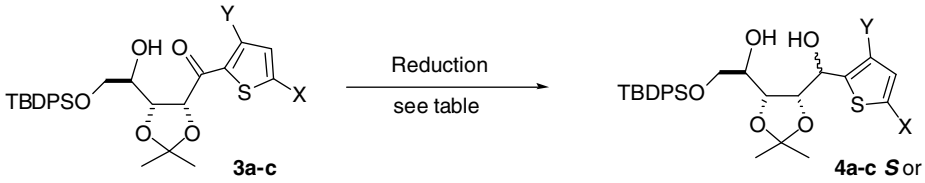


Scheme 2. Bromine and sulfur atoms directed and stabilized metallation (no halogen dance).



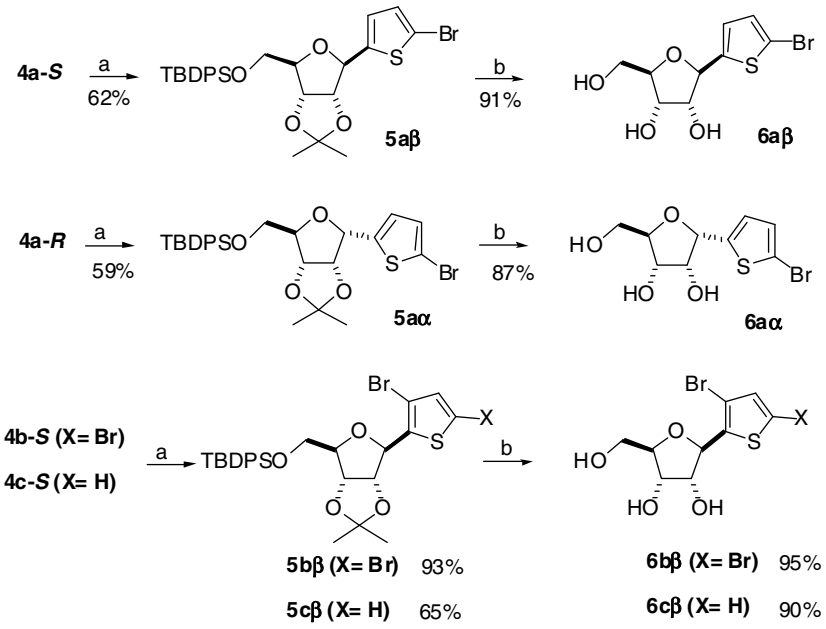
Scheme 3. Felkin-Ahn (A) and chelated model (B and C).

Table 1



Entry[a]	Substrat	Reducing agent	T (°C)/ Time (h)	Yield[b] (%)		S/R ratio[c]
1	**3a** X = Br, Y = H	$NaBH_4$	rt/0.5	**4a**	85	50/50
2	**3a**	$NaBH_4$	0/1	**4a**	80	45/55
3	**3a**	$NaBH_4$	−78/1	**4a**	79	50/50
4	**3a**	$LiAlH_4$	0/1	**4a**	90	70/30
5	**3a**	DIBAL-H	0/1	**4a**	90	75/25
6	**3a**	L-Selectride	0/1	**4a**	85	95/5
7	**3a**	L-Selectride	−78/1	**4a**	82	>98/2
8	**3a**		0/1	**4a**	92	30/70
9	**3a**	L-Selectride/$ZnCl_2$	−78/1	**4a**	87	5/95
10	**3b** X = Y = Br	$NaBH_4$	0/0.5	**4b**	86	50/50
11	**3b**	L-Selectride	−78 or rt/ 4	**4b**	0	0
12	**3b**	L-Selectride/$ZnCl_2$	−78/1.5	**4b**	80	>98/2
13	**3c** X = H, Y = Br	$NaBH_4$	0/0.5	**4c**	85	50/50
14	**3c**	L-Selectride	−78 or rt/4	**4c**	0	0
15	**3c**	L-Selectride/ $ZnCl_2$	−78/1.5	**4c**	86	>98/2

Conditions:
[a] Reducing agent (1.5 equiv), THF. $ZnCl_2$ (1 equiv).
[b] Yield of pure isolated products.
[c] S/R ratio based on ^1H NMR and HPLC analysis.



Scheme 4. Reagents and condition: (a) DEAD, PPh_3, THF, 70 °C. (b) aq H_2SO_4, dioxane.

contrast to 2-bromothiophene, when 3-bromothiophene was subjected to lithiation–glycosylation with ribonolactone, the halogen-dance reaction did not occur and only the 5-ribosylated product **3c** was isolated.[7] Moreover, as shown in Scheme 2, the temperature had no effect on the regioselectivity of the reaction. In this case, the 2-lithiated intermediate is highly stabilized by both 'Br' and 'S' atoms, thus hampering the halogen transfer.[8]

With hemiacetals **3a**, **3b** and **3c** in hand, the synthesis of bromothiophenyl-C-nucleosides was next investigated, following ketone reduction and C4′–C1′ cycloetherification sequence. Thus, treatment of **3a**, **3b** and **3c** with $NaBH_4$ gave good yield of the corresponding diols **4a**, **4b** and **4c**, respectively (Table 1, entries 1–3, 10 and 13). No stereoselectivity was observed in this reaction even at low temperatures for example, the diols were obtained as an equimolar mixture of *R*/*S* diastereomers. When $LiAlH_4$ or DIBAL-H was used for the reduction of **3a**, a low stereoselectivity was noticed (*R*/*S* = 70/30, entries 4 and 5). Interestingly, reduction of **3a** using L-selectride (Felkin-Ahn model, Scheme 3A) or a couple of L-selectride/$ZnCl_2$ (chelation control, Scheme 3B)[9,10] provided high yield and high diastereomeric ratio of the corresponding diols **4a*R*** and **4a*S***, respectively (entries 6–9).[11] The stereochemistry of each diol was unambiguously assigned by correlation with the stereochemistry of their cyclized product taking into account an inversion of the configuration at C1′ stereocenter (vide infra). Unfortunately, in contrast to **3a**, reduction of derivatives **3b** and **3c** with L-selectride alone (entries 11 and 14) did not work even under forced conditions (excess of the reducing agent and high temperature). In these cases, the hydride delivery from the bulky L-selectride reagent was probably hampered by the bromine atom in position 3 of the thiophene ring. Indeed, we expected that this halogen in proximity of the ketone induced a conformation change to minimize the electrostatic repulsion with the carbonyl group which resulted in a twisted, non-planar thiophene–ketone conformation. In this case both faces are protected from the bulky L-selectride approach. Surprisingly, while the reduction of **3a** with L-selectride/$ZnCl_2$ gave the expected **4a*R*** diol according to a chelation control model (Scheme 3B), the reduction of **3b** and **3c** under the same conditions led to the opposite stereochemical outcome:**4b*S*** and **4c*S***, respectively (entries 12 and 15).[12] These unexpected results could also be ascribed to the bromine atom effect in position 3 thus, allowing the hydride delivery from the less bulky face (Scheme 3C).

The ring-closing step was then achieved using intramolecular Mitsunobu reaction on diols **4a*R***, **4a*S***, **4b*S*** and **4c*S*,** to give the protected C-nucleosides **5aα**, **5aβ**, **5bβ** and **5cβ**, respectively, in moderate to high yields (Scheme 4). In all cases, selective C4′–C1′ cycloetherification was observed according to a more reactive benzylic hydroxy at C1′ versus C4′. In line with this result, we found that the dibromothiophene diol **4b*S*** undergoes clean and high yielding cyclization (95% yield) compared to the monobrominated analogs **4a*S***, **4a*R***, and **4c*S*** (59–65% yield). This is probably due to the halogen withdrawing effect thus activating the benzylic hydroxy position for an easy intramolecular C4′–C1′ ring closure. Finally, the stereochemistry of each cyclized product was determined on the basis of ^{1}H 2D NOESY experiments. Indeed, the β configuration (**5a–cβ**) was clearly evidenced by a NOE correlation between H1′ and H4′. In the same way, we observed for the other anomer (**5aα**) clear NOE correlations between H1′–H3′ and H1′–H5′ in accordance with an α configuration.

The last step consists on the cleavage of the isopropylidene and TBDPS protecting groups. Thus, treatment of protected precursors **5aα**, **5aβ**, **5bβ**, and **5cβ**, with aq H_2SO_4 in dioxane afforded good yields (87–95%) of the corresponding free nucleosides **6aα**, **6aβ**, **6bβ**, and **6cβ**, respectively (87–95%) (Scheme 4).[13]

In conclusion, we discovered a new halogenation/glycosylation tandem reaction that allows access to bromothiophenyl C-nucleosides from 2-bromothiophene. The process most probably involves an original halogen transfer cascade in highly regiocontrolled and ordered fashion. The reduction and ring-closing steps were efficiently achieved with a full stereocontrol leading to C-nucleosides with fixed anomeric configuration. The presence of bromine(s) would provide useful post-synthetic transformations for the preparation of original functionnalized thiophenyl C-nucleosides.

Acknowledgments

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References and notes

1. For recent reviews on the chemistry of C-glycoside analogues, see: (a) Wu, Qinpei; Simons, C. *Synthesis* **2004**, 1533; (b) Bililign, T.; Griffith, B. R.; Thorson, J. S. *Nat. Prod. Rep.* **2005**, *22*, 742; (c) Lee, D. Y. W.; He, M. S. *Curr. Top. Med. Chem.* **2005**, *5*, 1333.
2. (a) Kool, E. T. *Acc. Chem. Res.* **2002**, *35*, 936; (b) Sismour, A. M.; Benner, S. A. *Nucleic Acids Res.* **2005**, *33*, 5640; (c) Leconte, A. M.; Matsuda, S.; Hwang, G. T.; Romesberg, F. E. *Angew. Chem., Int. Ed.* **2006**, *45*, 4326.
3. For a brief overview of the biological and clinical impact of Tiazofurin, see: Grifantini, M. *Curr. Opin. Invest. Drugs* **2000**, *1*, 257.
4. Novotny, L.; Rauko, P.; Yalowitz, J. A.; Szekeres, T. *Curr. Med. Chem.* **2002**, *9*, 773.
5. (a) Guianvarc'h, D.; Fourrey, J.-L.; Sun, J.-S.; Maurisse, R.; Benhida, R. . *Bioorg. Med. Chem.* **2003**, *11*, 2751; (b) Guianvarc'h, D.; Fourrey, J.-L.; Maurisse, R.; Sun, J.-S. ; Benhida, R. *Org. Lett.* **2002**, *4*, 4209; (c) Guianvarc'h, D.; Fourrey, J.-L.; Tran Huu Dau, M.-E.; Guérineau, V.; Benhida, R. *J. Org. Chem.* **2002**, *67*, 3724; For post-synthetic transformation of halogenated C-nucleosides see: (d) Spadafora, M.; Mehiri, M.; Burger, A.; Benhida, R. *Tetrahedron Lett.* **2008**, *49*, 3967; (e) Stefko, M.; Pohl, R.; Kepetárová, B.; Hocek, M. *Eur. J. Org. Chem.* **2008**, 1689; (f) Barta, J.; Pohl, R.; Kepetárová, B.; Ernsting, N. P.; Hocek, M. *J. Org. Chem.* **2008**, *72*, 6797; (g) Joubert, N.; Pohl, R.; Klepetárová; Hocek, M. *J. Org. Chem.* **2007**, *72*, 6797.
6. Peyron, C.; Navarre, J.-M.; Van Craynest, N.; Benhida, R. *Tetrahedron Lett.* **2005**, *46*, 3315.
7. *Hemiacetal* **3a**: TLC (cyclohexane/AcOEt: 8/2): R_f = 0.63. ^{1}H NMR (CD_3OD, 200 MHz) δ ppm 1.04–1.08 (2s, 9H, tBu), 1.24 (s, 3H, CH_3), 1.42 (s, 3H, CH_3), 3.71–3.94 (m, 2H, $H_{5'}$), 4.17–4.27 (m, 1H, $H_{4'}$), 4.47 (d, 1H, J = 5.7 Hz, $H_{3'}$), 4.84 (d, 1H, J = 3.9 Hz, $H_{2'}$), 6.83 (d, 1H, J = 3.9 Hz, H_3 thiophene), 6.92 (d, 1H, J = 3.8 Hz, H_4 thiophene), 7.35–7.46 (m, 6H, Ph), 7.64–7.72 (m, 4H, Ph). ^{13}C NMR (CD_3OD, 50 MHz) δ ppm 19.79 (C(CH_3)$_3$), 24.44 (CH_3), 26.26 (CH_3), 26.51 (C(CH_3)$_3$), 66.35 ($C_{5'}$), 84.63 ($C_{2'}$), 87.19 ($C_{4'}$or $C_{3'}$), 88.07 ($C_{3'}$ or $C_{4'}$), 106.85 (C(CH_3)$_2$), 113.40 ($C_{1'}$), 113.80 (C_2), 126.15 (C_4), 127.60 (C_{Ph}), 127.93 (C_{Ph}), 129.28 (C_3), 130.05 (C_{Ph}), 133.41 (C_{Ph}), 134.95 (C_{Ph}), 135.71 (C_{Ph}), 145.66 (C_5). MS (ESI$^-$) m/z (rel intensity): 587.0–589.0 (100, 69, MH$^-$). MS (ESI$^+$): 610,8–612,8 [100, 83, (MNa)$^+$]. Anal. Calcd for $C_{28}H_{33}BrO_5SSi$: C, 57.04; H, 5.64. Found: C, 57.29; H, 5.87. Hemiacetal **3b** TLC (cyclohexane/AcOEt: 8/2): R_f = 0.70. ^{1}H NMR (200 MHz, CD_3OD) δ 1.07 (2s, 9H, tBu), 1.27 (s, 3H, CH_3), 1.32 (s, 3H, CH_3), 3.80 (m, 2H, $H_{5'}$), 4.23 (m, 1H, $H_{4'}$), 4.85 (m, 1H, $H_{3'}$), 4.90 (br s, 1H, $H_{2'}$), 6.95 (s, 1H, H thiophene), 7.42 (m, 6H, Ph), 7.67 (m, 4H, Ph). ^{13}C NMR (50 MHz, CD_3OD)δ 20.04 (C tBu), 25.37 (CH_3), 26.91 (CH_3), 27.36 (CH_3 tBu), 66.25 ($C_{5'}$), 84.82 ($C_{3'}$), 86.95 ($C_{4'}$), 87.30 ($C_{2'}$), 107.13 (C_{isop}), 108.08 ($C_{1'}$), 112.88 (CBr–S), 113.87 (*CBr–C–S*), 128.91 (C_{Ph}), 131.04 (C_{Ph}), 134.44 (CH), 134.52 (C_{Ph}), 136.71 (C_{Ph}), 141.78 (C–S). MS (ESI$^+$) m/z (rel intensity): 688.7–690.7–692.7 (47, 100, 50, MNa$^+$), 704.6–706.6–708.6 (36, 100, 64, MK$^+$). Hemiacetal **3c** ^{1}H NMR (200 MHz, CD_3OD) δ ppm 1.08 (s, 9H, tBu), 1.27 (s, 3H, CH_3), 1.29 (s, 3H, CH_3), 3.71–3.96 (m, 2H, $H_{5'}$), 4.18–4.29 (m, 1H, $H_{4'}$), 4.90 (br s, $H_{2'}$ and $H_{3'}$), 6.92 (d, 1H, J = 5.3 Hz, H_5 or H_4), 7.27 (d, 1H, J = 5.3 Hz, H_4 or H_5), 7.36–7.46 (m, 6H, Ph), 7.64–7.72 (m, 4H, Ph). ^{13}C NMR (50 MHz, CD_3OD) δ ppm 20.45 (C(CH_3)$_3$), 25.88 (CH_3), 27.33 (CH_3), 27.78 (C(CH_3)$_3$), 66.82 ($C_{5'}$), 85.33 ($C_{3'}$), 87.48 ($C_{4'}$), 87.58 ($C_{2'}$), 107.75 ($C_{1'}$ or C_3), 109.18 (C(CH_3)$_2$), 114.17 (C_3 or $C_{1'}$), 126.73 (C_5), 128.98 (C_4), 129.31 (C_{Ph}), 131.43 (C_{Ph}), 132.59 (C_2), 134.99 (C_{Ph}), 137.13 (C_{Ph}). (ESI$^+$) m/z (rel intensity): 611.3–613.3 (91, 100, MNa$^+$). Anal. Calcd for $C_{28}H_{33}BrO_5SSi$: C, 57.04; H, 5.64. Found: C, 57.17; H, 5.73.
8. For the use of a bromine atom as *ortho*-directing group, see: (a) Lulinski, S.; Serwatowski, J. *J. Org. Chem.* **2003**, *68*, 5384; (b) Lulinski, S.; Serwatowski, J. *J. Org. Chem.* **2003**, *68*, 9384; (c) Gohier, F.; Mortier, J. *J. Org. Chem.* **2003**, *68*, 2030.
9. Navarre, J.-M.; Guianvarc'h, D.; Farese Di Giorgio, A.; Condom, R.; Benhida, R. *Tetrahedron Lett.* **2003**, *44*, 2199.
10. Hanessian, S.; Machaalani, R. . *Tetrahedron Lett.* **2003**, *44*, 8321.
11. *Diol* **4aS**: TLC (cyclohexane/AcOEt: 8/2): R_f = 0.52. ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.07 (s, 9H, tBu), 1.36 (s, 3H, CH_3), 1.46 (s, 3H, CH_3), 2.88 (d, 1H, J = 5.5 Hz, OH), 3.23 (d, 1H, J = 7.6 Hz, OH), 3.72–3.95 (m, 2H, $H_{5'}$), 4.12–4.20 (m, 1H, $H_{4'}$), 4.20–4.30 (m, 1H, $H_{3'}$), 4.43 (dd, 1H, J = 2.1 and 6.3 Hz, $H_{2'}$), 5.30 (dd, 1H, J = 1.9 and 6.3 Hz, $H_{1'}$), 6.81 (d, 1H, J = 3.6 Hz, H_4), 6.90 (d, 1H, J = 3.8 Hz, H_3), 7.35–7.50 (m, 6H, Ph), 7.62–7.72 (m, 4H, Ph). ^{13}C NMR (50 MHz, $CDCl_3$) δ 19.46 (C(CH_3)$_3$), 24.72 (CH_3), 24.82 (CH_3), 27.0 (C(CH_3)$_3$), 65.41 ($C_{5'}$), 68.08 ($C_{1'}$), 69.76 ($C_{3'}$), 77.35 ($C_{4'}$), 79.79 ($C_{2'}$), 109.11 (C(CH_3)$_2$), 112.19 (C_2), 124.88 (C_4), 127.9 (C_{Ph}), 129.31 (C_3), 130.04 (C_{Ph}), 132.96 (C_{Ph}), 135.66 (C_{Ph}), 147.59 (C_5). (ESI$^+$) m/z (rel intensity): 613.5–615.6 (91, 100, MNa$^+$). Diol **4aR**: TLC (cyclohexane/AcOEt: 8/2): R_f = 0.43. ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.04 ppm (s, 9H, tBu), 1.32 (s, 3H, CH_3), 1.37 (s, 3H, CH_3), 2.94 (d, 1H, J = 4.8 Hz, OH), 3.60–3.85 (m, 4H, OH, $H_{4'}$, $H_{5'}$), 4.01–4.17 (m, 1H, $H_{3'}$), 4.24 (dd, 1H, J = 3.2 and 7.4 Hz, $H_{2'}$), 5.07 (dd, 1H, J = 2.7 and 8.7 Hz, $H_{1'}$), 6.81 (dd, 1H, J = 1.0 and 3.8 Hz, H_4), 6.91 (d, 1H, J = 3.8 Hz, H_3), 7.35–7.45 (m, 6H, Ph), 7.58–7.70 (m, 4H, Ph). ^{13}C NMR (50 MHz, $CDCl_3$) δ 19.46 (C(CH_3)$_3$), 24.72 (CH_3), 24.82 (CH_3), 27.0 (C(CH_3)$_3$), 65.41 ($C_{5'}$), 68.08 ($C_{1'}$), 69.76 ($C_{3'}$), 77.35 ($C_{4'}$), 79.79 ($C_{2'}$), 109.11 (C(CH_3)$_2$), 112.19 (C_2), 124.88 (C_4), 127.9 (C_{Ph}), 129.31 (C_3), 130.04 (C_{Ph}), 132.96 (C_{Ph}), 135.66 (C_{Ph}), 147.59 (C_5). (ESI$^+$) m/z: (rel intensity): 613.5– 615.5 (93, 100, MNa$^+$).
12. *Diol* **4bS**: TLC (cyclohexane/AcOEt: 8/2): R_f = 0.58. ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.08 (s, 9H, tBu), 1.35 (s, 3H, CH_3), 1.53 (s, 3H, CH_3), 2.89 (d, 1H, J = 5.3 Hz, OH), 3.16 (d, 1H, J = 6.3 Hz, OH), 3.75–3.96 (m, 2H, $H_{5'}$), 4.21–4.28 (m, 2H, $H_{3'}$and $H_{4'}$), 4.34–4.42 (m, 1H, $H_{2'}$), 5.46 (dd, 1H, J = 1.3 and 6.2 Hz, $H_{1'}$), 6.89 (s, 1H, H_3), 7.33–7.48 (m, 6H, Ph), 7.62–7.72 (m, 4H, Ph). ^{13}C NMR (50 MHz, $CDCl_3$) δ 19.34 (C(CH_3)$_3$), 24.84 (CH_3), 26.66 (CH_3), 26.88 (C(CH_3)$_3$), 65.18 ($C_{5'}$), 67.92–69.75–76.22 ($C_{1'}$, $C_{3'}$ and $C_{4'}$), 78.59 ($C_{2'}$), 106.38 (C(CH_3)$_2$), 109.20 (C_4), 112.60 (C_2), 127.85–127.90 (C_{Ph}), 130.1 (C_3), 131.4–131.8 (C_{Ph}), 131.39–32.77 (C_{Ph}), 135.54–135.58 (C_{Ph}), 142.19 (C_5). (ESI$^+$) m/z (rel intensity): 691.1–693.1–695.0 (93, 100, 47, MNa$^+$). Diol **4cS**: TLC (cyclohexane/AcOEt: 8/2): R_f = 0.56. ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.08 (s, 9H, tBu), 1.35 (s, 3H, CH_3), 1.52 (s, 3H, CH_3), 2.86 (d, 1H, J = 5.4 Hz, OH), 3.17 (d, 1H, J = 6.4 Hz, OH), 3.78–3.98 (m, 2H, $H_{5'}$), 4.22–4.28 (m, 2H, $H_{3'}$ and $H_{4'}$), 4.40–4.46 (m, 1H, $H_{2'}$), 5.52 (dd, 1H, J = 1.6 and 6.3 Hz, $H_{1'}$), 6.93 (d, 1H, J = 5.3 Hz, H_4), 7.26 (d, 1H, J = 5.3 Hz, H_5), 7.35–7.45 (m, 6H, Ph), 7.63–7.70 (m, 4H, Ph). ^{13}C NMR(50 MHz, $CDCl_3$) δ 19.45 (C(CH_3)$_3$), 24.98 (CH_3), 26.98 (C(CH_3)$_3$), 31.08 (CH_3), 65.34 ($C_{5'}$), 67.60 ($C_{1'}$), 69.82 ($C_{4'}$), 77.36 ($C_{3'}$), 79.05 ($C_{2'}$), 107.59 (C(CH_3)$_2$), 109.15 (C_3), 125.60 (C_5), 127.9 (C_{Ph}), 129.57 (C_4), 130.08 (C_{Ph}), 132.9 (C_{Ph}), 135.7 (C_{Ph}), 140.38 (C_2). (ESI$^+$) m/z (rel intensity): 613.2–615.1 (93, 100, MNa$^+$).
13. *Compound* **5bβ**: TLC (cyclohexane/AcOEt: 8/2): R_f = 0.62. ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.07 (s, 9H, tBu), 1.33 (s, 3H, CH_3), 1.54 (s, 3H, CH_3), 3.90 (dd, 1H, J = 4.9 and 10.5 Hz, $H_{5'}$), 3.94 (dd, 1H, J = 3.3 and 10.3 Hz, $H_{5'}$), 4.30 (d, 1H, J = 6.5 Hz, $H_{3'}$), 4.36 (m, 1H, $H_{4'}$), 4.70 (d, 1H, J = 5.1 Hz, $H_{2'}$), 5.49 (dd, 1H, J = 1.2 and 5.1 Hz, $H_{1'}$), 7.03 (s, 1H, H_3), 7.41–7.48 (m, 6H, Ph), 7.74–7.79 (m, 4H, Ph). ^{13}C NMR (125 MHz, $CDCl_3$) δ 19.46 (C(CH_3)$_3$), 24.97 (CH_3), 26.78 (CH_3), 27.00 (C(CH_3)$_3$), 65.30 ($C_{5'}$), 68.04 ($C_{1'}$), 69.86 ($C_{2'}$), 76.33 ($C_{3'}$), 78.70 ($C_{4'}$), 106.49 (C_4), 109.31 (C(CH_3)$_2$), 112.72 (C_2), 128.02 (C_{Ph}), 130.09 (C_{Ph}), 131.50 (C_3), 132.89 (C_{Ph}), 135.67 (C_{Ph}), 142.31 (C_5). MS (ESI$^+$) m/z (rel intensity): 673.4–675.7–677.5 (51, 100, 51, MNa$^+$). *Compound* **6bβ**: TLC (CH_2Cl_2/MeOH: 8/2): R_f = 0.33. ^{1}H NMR (200 MHz, CD_3OD) δ 3.07 (m, 2H, $H_{5'}$), 3.95–4.58 (m, 2H, $H_{3'}$ and $H_{4'}$), 4.42–4.49 (m, 1H, $H_{2'}$), 5.32 (d, 1H, J = 3.6 Hz, $H_{1'}$), 6.95 (s, 1H, H_4). ^{13}C NMR (50 MHz, CD_3OD)δ 58.77 ($C_{5'}$), 75.98–77.01–78.82–79.43 ($C_{1'}$, $C_{2'}$, $C_{3'}$ and $C_{4'}$), 107.88 (C_3), 114.23 (C_5), 126.78 (C_4). MS (ESI$^+$) m/z (rel intensity): 394.5–396.8–398.4 [51, 100, 50, (MNa)$^+$]. Anal. Calcd for $C_9H_{10}Br_2O_4S$: C, 28.90; H, 2.69. Found: C, 29.11; H, 2.54. *Compound* **6cβ**: TLC (MeOH/H_2O: 8/2): R_f = 0.6. ^{1}H NMR (200 MHz, $CDCl_3$+ CD_3OD) δ 3.74 (dd, 1H, J = 4.3 and 12.1 Hz, $H_{5'}$), 3.86 (dd, 1H, J = 3.5 and 12.1 Hz, $H_{5'}$), 3.93–4.03 (m, 1H, $H_{4'}$), 4.05–4.18 (m, 2H, $H_{2'}$ and $H_{3'}$), 5.15 (d, 1H, J = 4.4 Hz, $H_{1'}$), 6.93 (d, 1H, J = 5.3 Hz, H_4), 7.24 (d, 1H, J = 5.3 Hz, H_5). ^{13}C NMR (50 MHz, $CDCl_3$ + CD_3OD) δ 62.49 ($C_{5'}$), 71.05 ($C_{3'}$), 77.37 ($C_{2'}$), 80.83 ($C_{1'}$), 84.04 ($C_{4'}$), 125.36 (C_5), 130.51 (C_4), 138.00 (C_2). MS (ESI$^+$) m/z (rel intensity): 316.7–318.7 [100, 98 (MNa)$^+$]. Anal. Calcd for $C_9H_{11}BrO_4S$: C, 36.62; H, 3.76. Found: C, 36.76; H, 3.83.