Synthesis A. Wiegand et al. THIEME OPEN ACCESS Feature

GlucoSiFA and LactoSiFA: New Types of Carbohydrate-Tagged Silicon-Based Fluoride Acceptors for ^{18}F-Positron Emission Tomography (PET)

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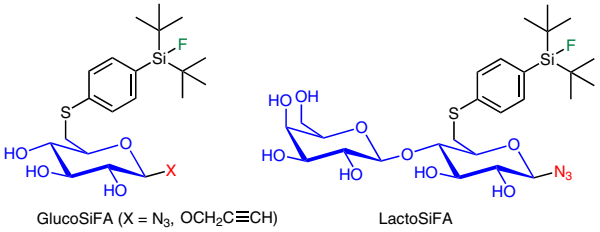
Published as part of the *50 Years SYNTHESIS – Golden Anniversary Issue*



GlucoSiFA (X = N_3, $OCH_2C{\equiv}CH$) LactoSiFA

Received: 11.12.2018
Accepted: 17.12.2018
Published online: 24.01.2019
DOI: 10.1055/s-0037-1611656; Art ID: ss-2018-z0819-fa

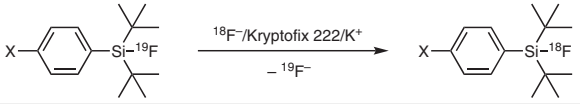
Abstract GlucoSiFA derivatives bearing an azide or alkynyl side chain were obtained from peracetyl-D-glucose using as key step a tosylate substitution by a SiFA thiolate obtained from 4-(di-*tert*-butylfluorsilyl)benzenethiol. In analogy, two-fold SiFA-substituted maltose and lactose derivatives were synthesized via bistosylates. Introduction of an acetal-protecting group in β-D-azidolactose allowed the synthesis of a LactoSiFA derivative bearing only one SiFA moiety.

Key words carbohydrates, silicon-based fluoride acceptors, nucleophilic substitution, tosylation, regioselectivity

The introduction of positron emission tomography (PET) as a non-invasive method for medical diagnostic in vivo imaging has become an indispensable tool in precision medicine development.[1] PET not only helps to understand the complex interplay between biological targets such as receptors and enzymes and their cognate ligands but furthermore assists devising new therapeutic regimens based on non-invasive biological target validation. Besides PET, a straightforward example for diagnostic imaging is the use of X-rays that has revolutionized medicine. However, this method only yields anatomic/structural information whereas PET and related radioisotope-based imaging methodologies look directly at dynamic biological processes without interference. PET, in addition to magnetic resonance imaging (MRI) and computed tomography (CT), has proved to be an elegant and non-invasive method to elucidate in vivo biochemistry. It allows metabolic tracking of bioactive compounds and quantification of biochemical and/or enzymatic processes in living organisms. Among commonly used radioactive isotopes such as ^{11}C, ^{13}N, ^{15}O, ^{18}F, ^{64}Cu, and ^{68}Ga,[2] the use of fluorine-18 has become rather popular due to its favorable physical properties such as a half-life of 109.7 minutes that allows for longer synthesis times and remote shipment to local imaging facilities and a low positron energy leading to PET images of highest resolution.

There are different strategies for incorporating ^{18}F into radiopharmaceuticals. On the one hand, fluorination at carbon atoms in both aromatic and aliphatic compounds can be achieved by electrophilic as well as nucleophilic reactions and a variety of appropriate reagents has been developed for this purpose.[2,3] Alternatively, ^{18}F can also be bound via isotopic exchange to non-carbon elements such as boron, aluminum, silicon, and phosphorus.[3a] These non-canonical labeling concepts got momentum in the last two decades although some of the labeling principles have already been introduced to the literature as early as 1958[4] but remained dormant for many years. The progress achieved in these types of chemistry was regularly summarized in review articles.[3a,5] Aryldialkylsilicon fluorides, ArR_2SiF, in which the silicon atom is sufficiently protected with R = isopropyl[6] or *tert*-butyl[7a] substituents are stable under physiological conditions and undergo ^{19}F to ^{18}F isotopic exchange with good radiochemical yields. The *tert*-butyl-

substituted variant is now widely known as SiFA methodology and has become popular in several research groups (Equation 1).[7b–e]



Equation 1 Isotope exchange in silicon-based fluoride acceptors (SiFA)

One last problem when using SiFA-substituted biomolecules for PET applications is the high lipophilicity caused by the organosilicon moiety. Sugars such as glucose are water-soluble and carbon-bound ^{18}F-derivatives such a 2-[^{18}F]fluorodeoxyglucose ([^{18}F]FDG) are applied as PET radiotracers.[7e,f] With this in mind and the intention to increase the water-solubility of the SiFA moiety, herein we report the synthesis and characterization of SiFA-substituted sugar de-

Biographical Sketches

Anja Wiegand studied chemistry at the Faculty of Chemistry and Chemical Biology of TU Dortmund. She obtained her B.Sc. in 2012 and her M.Sc. in 2014. In 2018, she finished her Ph.D. work on carbohydrate-based NHC-gold complexes and SiFA compounds under the supervision of Prof. Dr. Norbert Krause.

Vera Wiese studied chemical biology at the Faculty of Chemistry and Chemical Biology of TU Dortmund. She obtained her B.Sc. in 2015 and her M.Sc. in 2018. For her Master's thesis, she worked on the synthesis of disccharaide-based SiFA compounds under the supervision of Prof. Dr. Norbert Krause.

Britta Glowacki studied chemistry at the Faculty of Chemistry and Chemical Biology of TU Dortmund. She obtained her B.Sc. in 2011 and her M.Sc. in 2013. In 2018, she finished her Ph.D. work on amino alcoholate derivatives of group XIV elements under the supervision of Prof. Dr. Klaus Jurkschat.

Ljuba Iovkova was born in Sofia, Bulgaria and moved to Germany to study pharmacy and chemistry. In 2006, she obtained her Diploma from the TU Dortmund. She carried out graduate work at the same university under the supervision of Prof. Dr. Klaus Jurkschat, earning a Ph.D. in chemistry in 2010. After researcher positions in the academic and industrial field she joined again the Faculty of Chemistry and Chemical Biology at the TU Dortmund in 2014 as Akademische Rätin.

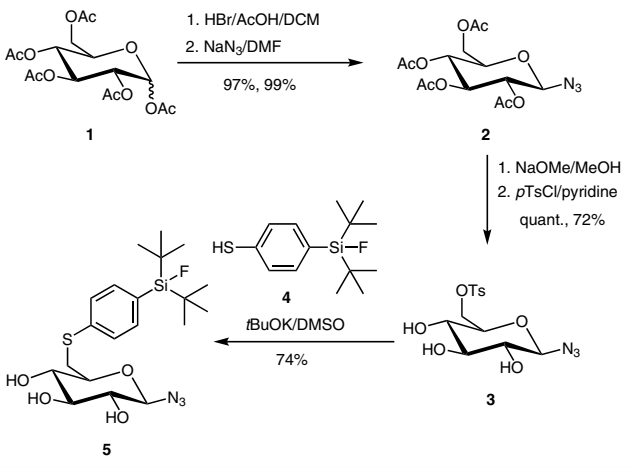
Ralf Schirrmacher obtained his Ph.D. in nuclear chemistry from the University of Mainz in 1999. After a brief postdoctoral stay at the University of Pennsylvania, he continued research at the University of Mainz as a civil servant until 2007. In 2008 he was appointed Head of Radiochemistry and Director of Cyclotron at the McConnell Brain Imaging Center at the Montreal Neurological Institute (MNI) of McGill University. During his time at McGill University he held a Canada Research Chair in Molecular Imaging and Radiochemistry. He is currently a Full Professor in Oncologic Imaging at the Faculty of Medicine at the MICF and Cross Cancer Center at the University of Alberta at Edmonton. His research group develops new imaging agents for Positron Emission Tomography (PET) imaging in the field of oncology and neurology using a variety of different radionuclides such as carbon-11, fluorine-18, gallium-68, different radioisotopes of iodine and copper-64.

Klaus Jurkschat received his Ph.D. from Martin Luther University Halle-Wittenberg, Germany, in 1980 and habilitated in 1987 at the same university. After postdoctoral work with Jean-Bernard Robert at CENG Grenoble, France, and Marcel Gielen/Rudolph Willem at VUB Brussels, Belgium, and staying as visiting researcher at SUNY Albany (with Henry G. Kuivila), N.Y., USA, and Deakin University Geelong (with Dainis Dakternieks), Vic. Australia, he went to Dortmund, Germany, where from 1994 to 2018 he was employed as a Full Professor for Inorganic Chemistry at the Technische Universität. He was a Guest Professor at Universite Bordeaux 1 (2000) and Universite Rennes 1 (2012). He is Editor-in-Chief of the journal 'Main Group Metal Chemistry' and author of approximately 320 publications. The chemistry of hypercoordinate main group element compounds in all its facets is in the center of his research interests.

Norbert Krause graduated from TU Braunschweig in 1984 and received his Ph.D. in 1986. After postdoctoral stays at the ETH Zürich and Yale University, he joined TU Darmstadt and obtained his Habilitation in 1993. In 1994, he moved to the University of Bonn as Associate Professor, before being appointed to his present position as Full Professor at TU Dortmund in 1998. He was a Fellow of the Japan Society for the Promotion of Science (JSPS) in 2003, 2009, and 2015, and Guest Professor at the Université Catholique de Louvain (2007), at the University of California, Santa Barbara, U.S.A. (2009), and at the École Supérieure de Physique et de Chimie Industrielles de la Ville de Paris (ESPCI), France (2009). He was a member of the Editorial Board of the European Journal of Organic Chemistry (2006–2013). His research focuses on sustainable coinage metal (copper, silver, and gold) catalysis, in particular with water as bulk solvent.

rivatives that also contain a variety of functional groups that hold potential for subsequent protein conjugation by click-type chemistry.

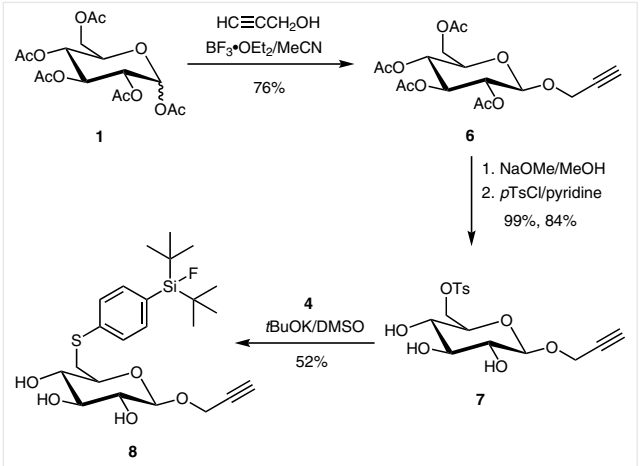
Our synthesis of the β-D-azido-substituted GlucoSiFA derivative **5** (Scheme 1) started with peracetyl-D-glucose (**1**; mixture of anomers), which was first brominated at the anomeric center with HBr/AcOH. The resulting α-D-glycosyl bromide underwent clean substitution with sodium azide to afford β-D-glycosyl azide **2**. Both steps proceeded in excellent yield, as did the subsequent deprotection with sodium methoxide. A selective monotosylation at the primary hydroxy group of the unprotected β-D-azidoglucose gave the difunctionalized monosaccharide **3** in 72% yield. Finally, the desired GlucoSiFA derivative **5** was obtained in 74% yield (51% over 5 steps) by nucleophilic substitution of the tosylate with deprotonated 4-(di-*tert*-butylfluorsilyl)benzenethiol (**4**).[8] Due to the pronounced base sensitivity of SiFA derivatives, this step has to be carried out with bulky, less nucleophilic bases. In the event, potassium *tert*-butoxide in DMSO gave the best results.



Scheme 1 Synthesis of β-D-azido-substituted GlucoSiFA derivative **5**

Starting point of the synthesis of the β-D-alkynyl-substituted GlucoSiFA derivative **8** (Scheme 2) was the Lewis acid catalyzed substitution of the anomeric acetyl group of peracetyl-D-glucose (**1**) with propargyl alcohol, which provided β-D-glycoside **6** in 76% yield. The following steps via monotosylate **7** proceeded as before and gave target molecule **8** in 33% yield over four steps.

In order to further increase the hydrophilicity of carbohydrate-tagged SiFA derivatives, we next used disaccharides as starting material. Here, serious reactivity and selectivity issues were encountered. For example, even though β-D-azidogalactose can be monotosylated selectively at the primary hydroxy group, all attempts of a monotosylation of β-D-azidomelibiose (which also contains only one primary hydroxy group) failed and provided either mixtures of bistosylated products at low yield, or no product at all. We then shifted our attention to maltose and lactose as starting disaccharides and first prepared two-fold SiFA-substituted derivatives (Scheme 3).



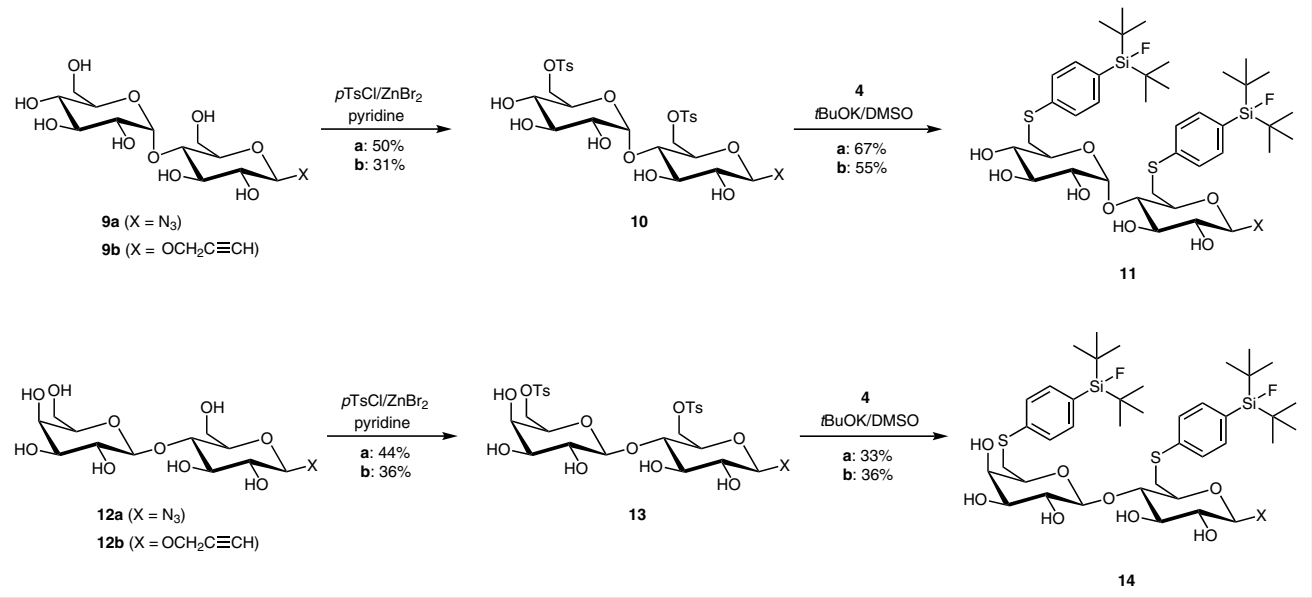
Scheme 2 Synthesis of β-D-alkynyl-substituted GlucoSiFA derivative **8**

Whereas the tosylation of β-azido-D-maltose (**9a**) with *p*TsCl in pyridine proceeded rather sluggishly, the reactivity was strongly increased in the presence of zinc bromide.[9] Under these conditions, complete conversion was observed after 1 hour at –20 °C, and the bistosylate **10a** was isolated in 50% yield. Both leaving groups could be replaced with SiFA moieties under standard conditions using **4** and *t*BuOK to afford the target molecule **11a** in 67% yield. The corresponding SiFA-tagged β-alkynyl-D-maltose **11b** was obtained in the same manner from **9b** via bistosylate **10b** in 31% and 55% yield, respectively.

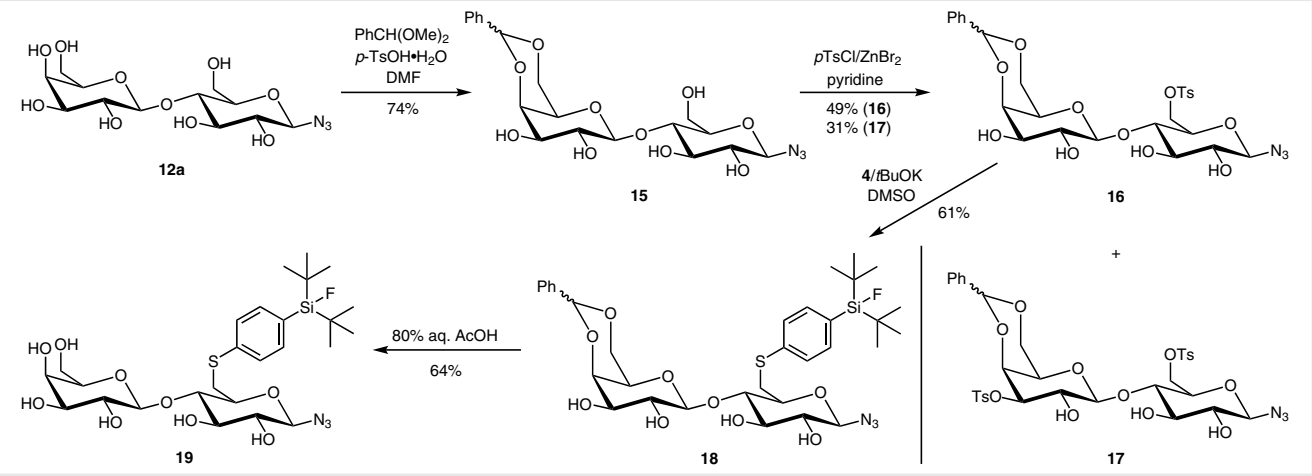
Similar to the maltose derivatives, the corresponding β-azido- and alkynyl-substituted D-lactoses **12a**/**b** could not be selectively monotosylated at one of the two primary hydroxy groups. Rather, the bistosylates **13a**/**b** were obtained in 44% and 36% yield, which were converted into the two-fold SiFA-modified lactoses **14a**/**b** in moderate yields (33/36%).

It is evident from these results that a protection of one of the two primary hydroxy groups is required for the synthesis of a disaccharide bearing only one SiFA unit. Gratifyingly, the presence of an axial OH group in the galactose ring of β-D-azidolactose **12a** allows a selective acetalization to afford product **15** in 74% yield (Scheme 4).[10] For this substrate, the selectivity of the tosylation was examined in detail (Table 1).

With 4 equivalents of zinc bromide and 5 equivalents of tosyl chloride in pyridine at –20 °C, a mixture of the desired monotosylate **16** (41% yield) and the bistosylate **17** (21% yield) was obtained after 10 minutes (Table 1, entry 1). Thus, not only the primary, but also the secondary hydroxy group at C-4′ are reactive under these conditions. As expected, increasing the reaction time up to 40 minutes fa-



Scheme 3 Synthesis of two-fold SiFA-substituted maltose and lactose derivatives **11** and **14**



Scheme 4 Synthesis of β-D-azido-substituted LactoSiFA derivative **19**

vored the formation of the bistosylate **17** (entries 2–4); the best yield of the monotosylate **16** (49%) was obtained after 30 minutes and decreased to 30% after 40 minutes. Smaller amounts of *p*TsCl afforded a higher selectivity in favor of the monotosylate **16** (entries 5 and 6), which was isolated as the sole product in the presence of 1.3 equivalents of *p*TsCl (entry 6), albeit in a low yield of 30%. Interestingly, the tosylation of the corresponding lactose derivative bearing a propargyl glycoside instead of the azido group gave only a bistosylate bearing the tosyl groups at the 2-CH_2 group and C-4. At this point, it is not clear which factors govern the regioselectivity of these transformations. Unfortunately, attempts to introduce other leaving groups (mesylate, 4-bromophenylsulfonate, bromide) failed.

The structural assignment of tosylation products **16** and **17** is based on extensive NMR studies. Moreover, both products were isolated in crystalline form and characterized by single crystal X-ray diffraction analysis. The quality of the crystals of monotosylate **16** was rather low and allowed only the structural assignment of the constitution, but not of the absolute stereochemistry of the acetal stereocenter. In contrast to this, the acetal stereocenter of the major isomer (87%) of bistosylate **17** (Figure 1) shows *S*-configuration as estimated by the twin law of the measured crystal.[11] The X-ray diffraction analysis also proved the presence of the two tosyl groups at the 2-CH_2 and 4′ positions.

The protected monotosylated β-azido-D-lactose derivative **16** obtained in 49% yield under the conditions of Table

Table 1 Tosylation of Disaccharide **15**[a]

Entry	$ZnBr_2 \cdot 2\ H_2O$ (equiv)	*p*TsCl (equiv)	Time (min)	**16** (Yield %)	**17** (Yield %)
1	4	5	10	41	21
2	4	5	20	38	30
3	4	5	30	49	31
4	4	5	40	30	34
5	1.5	2	40	39	24
6	4	1.3	40	30	0

[a] In pyridine at –20 °C.

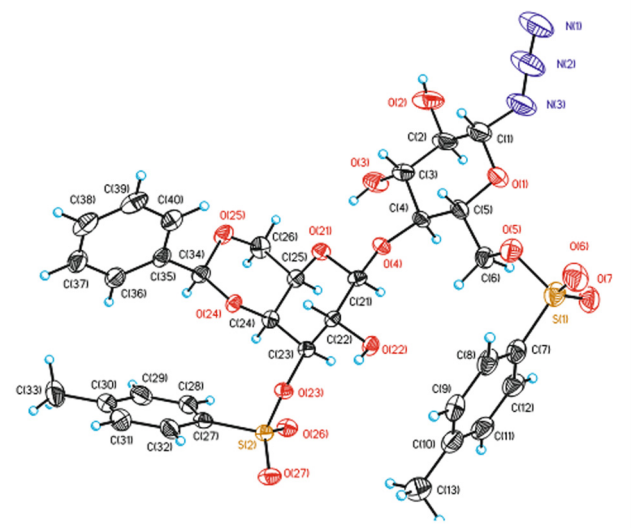


Figure 1 X-ray crystal structure of bistosylate **17**

1, entry 3, was treated with the thiolate formed by deprotonation of 4-(di-*tert*-butylfluorsilyl)benzenethiol (**4**) with *t*BuOK. The SiFA-tagged lactose derivative **18** was isolated in 61% yield. Finally, acetal cleavage was achieved by heating **18** with 80% aqueous acetic acid to 70 °C for 4 hours. This afforded the desired β-D-azido-substituted LactoSiFA derivative **19** in 64% yield (14% over 4 steps from **12a**) (Scheme 4).

In conclusion, this work demonstrates the utility of carbohydrates for the synthesis of hydrophilic SiFA derivatives. The GlucoSiFA derivatives **5** and **8** bearing an azide or alkynyl handle for peptide and protein conjugation via 1,3-dipolar cycloaddition were obtained in a straightforward manner from peracetyl-D-glucose in 51% and 36% overall yield, respectively. The key step is the substitution of a tosylate by a SiFA thiolate obtained from 4-(di-*tert*-butylfluorsilyl)benzenethiol (**4**). In analogy, the two-fold SiFA-substituted maltose and lactose derivatives **11** and **14** are readily accessible in overall yields between 13% and 34%. Introduction of an acetal protecting group in β-D-azidolactose **12a** allowed the synthesis of the LactoSiFA derivative **19** in 14% overall yield. Further work is devoted to improved procedures for the monofunctionalization of suitable carbohydrates, as well as, the synthesis of carbohydrate-tagged SiFA derivatives bearing different handles for protein conjugation.

Reactions were carried out under argon atmosphere using oven- or flame-dried glassware. Air- and moisture-sensitive reagents were transferred via syringe. All reagents were obtained commercially and used without further purification. THF, Et_2O, CH_2Cl_2, and MeCN were dried using a MB-SPS-800 system (M. Braun). Reactions were monitored by TLC using silica gel 60 plates provided by Merck and Macherey-Nagel. Visualization was accomplished with UV light (254 nm), ceric ammonium molybdate, $KMnO_4$, or anisaldehyde.

^1H, ^{13}C, ^{19}F, and ^{29}Si NMR spectra were recorded with Bruker Avance III HD (400–600 MHz) and calibrated against residual solvent peaks. IR spectra were obtained with a PerkinElmer Spectrum Two UATR spectrophotometer. Mass spectra were recorded with a Thermo Fisher Scientific TSQ (LCMS-ESI) and a Thermo Electron LTQ Orbitrap spectrometer (HPLC-ESI).

(3*R*,4*S*,5*R*,6*R*)-6-(Acetoxymethyl)tetrahydro-2*H*-pyran-2,3,4,5-tetrayltetraacetate (**1**),[12] (2*R*,3*R*,4*S*,5*R*,6*R*)-2-(acetoxymethyl)-6-bromotetrahydro-2*H*-pyran-3,4,5-triyltriacetate,[13] (2*R*,3*R*,4*S*,5*R*,6*R*)-2-(acetoxymethyl)-6-azidotetrahydro-2*H*-pyran-3,4,5-triyltriacetate (**2**),[14] (2*R*,3*R*,4*S*,5*S*,6*R*)-2-azido-6-(hydroxymethyl)tetrahydro-2*H*-pyran-3,4,5-triol,[15] (2*R*,3*R*,4*S*,5*R*,6*R*)-2-(acetoxymethyl)-6-(prop-2-yn-1-yloxy)tetrahydro-2*H*-pyran-3,4,5-triyltriacetate (**6**),[16] (2*R*,3*S*,4*S*,5*R*,6*R*)-2-(hydroxymethyl)-6-(prop-2-yn-1-yloxy)tetrahydro-2*H*-pyran-3,4,5-triol,[17] (2*S*,3*R*,4*S*,5*R*,6*R*)-6-(acetoxymethyl)-5-{[(2*R*,3*R*,4*S*,5*R*,6*R*)-3,4,5-triacetoxy-6-(acetoxymethyl)-tetrahydro-2*H*-pyran-2-yl]oxy}tetrahydro-2*H*-pyran-2,3,4-triyltriacetate,[18] (2*R*,3*R*,4*S*,5*R*,6*R*)-2-(acetoxymethyl)-6-{[(2*R*,3*R*,4*S*,5*R*,6*R*)-4,5-diacetoxy-2-(acetoxymethyl)-6-bromotetrahydro-2*H*-pyran-3-yl]oxy}tetrahydro-2*H*-pyran-3,4,5-triyltriacetate,[19] (2*R*,3*R*,4*S*,5*R*,6*R*)-2-(acetoxymethyl)-6-{[(2*R*,3*R*,4*S*,5*R*,6*R*)-4,5-diacetoxy-2-(acetoxymethyl)-6-azidotetrahydro-2*H*-pyran-3-yl]oxy}tetrahydro-2*H*-pyran-3,4,5-triyltriacetate,[20] (2*R*,3*R*,4*S*,5*S*,6*R*)-2-{[(2*R*,3*S*,4*R*,5*R*,6*R*)-6-azido-4,5-dihydroxy-2-(hydroxymethyl)tetrahydro-2*H*-pyran-3-yl]oxy}-6-(hydroxymethyl)tetrahydro-2*H*-pyran-3,4,5-triol (**9a**),[21] (2*R*,3*R*,4*S*,5*R*,6*R*)-2-(acetoxymethyl)-6-{[(2*R*,3*R*,4*S*,5*R*,6*R*)-4,5-diacetoxy-2-(acetoxymethyl)-6-(prop-2-yn-1-yloxy)tetrahydro-2*H*-pyran-3-yl]oxy}tetrahydro-2*H*-pyran-3,4,5-triyltriacetate,[22] (2*R*,3*R*,4*S*,5*S*,6*R*)-2-{[(2*R*,3*S*,4*R*,5*R*,6*R*)-4,5-dihydroxy-2-(hydroxymethyl)-6-(prop-2-yn-1-yloxy)tetrahydro-2*H*-pyran-3-yl]oxy}-6-(hydroxymethyl)tetrahydro-2*H*-pyran-3,4,5-triol (**9b**),[23] (3*R*,4*S*,5*R*,6*R*)-6-(acetoxymethyl)-5-{[(2*S*,3*R*,4*S*,5*S*,6*R*)-3,4,5-triacetoxy-6-(acetoxymethyl)-tetrahydro-2*H*-pyran-2-yl]oxy}tetrahydro-2*H*-pyran-2,3,4-triyltriacetate,[24] (2*R*,3*S*,4*S*,5*R*,6*S*)-2-(acetoxymethyl)-6-{[(2*R*,3*R*,4*S*,5*R*,6*R*)-4,5-diacetoxy-2-(acetoxymethyl)-6-bromtetrahydro-2*H*-pyran-3-yl]oxy}-tetrahydro-2*H*-pyran-3,4,5-triyltriacetate,[19] (2*R*,3*S*,4*S*,5*R*,6*S*)-2-(acetoxymethyl)-6-{[(2*R*,3*R*,4*S*,5*R*,6*R*)-4,5-diacetoxy-2-(acetoxymethyl)-6-azidotetrahydro-2*H*-pyran-3-yl]oxy}tetrahydro-2*H*-pyran-3,4,5-triyltriacetate,[20] (2*S*,3*R*,4*S*,5*R*,6*R*)-2-{[(2*R*,3*S*,4*R*,5*R*,6*R*)-6-azido-4,5-dihydroxy-2-(hydroxymethyl)tetrahydro-2*H*-pyran-3-yl]oxy}-6-(hydroxymethyl)tetrahydro-2*H*-pyran-3,4,5-triol (**12a**),[25] (2*R*,3*S*,4*S*,5*R*,6*S*)-2-(acetoxymethyl)-6-{[(2*R*,3*R*,4*S*,5*R*,6*R*)-4,5-diacetoxy-2-(acetoxymethyl)-6-(prop-2-yn-1-yloxy)tetrahydro-2*H*-pyran-3-yl]oxy}tetrahydro-2*H*-pyran-3,4,5-triyltriacetate,[26] (2*S*,3*R*,4*S*,5*R*,6*R*)-2-{[(2*R*,3*S*,4*R*,5*R*,6*R*)-4,5-dihydroxy-2-(hydroxymethyl)-6-(prop-2-yn-1-yloxy)tetrahydro-2*H*-pyran-3-yl]oxy}-6-(hydroxymethyl)tetrahydro-2*H*-pyran-3,4,5-triol (**12b**),[26] and (4a*R*,6*S*,7*R*,8*R*)-

6-{[(2*R*,3*S*,4*R*,5*R*,6*R*)-6-azido-4,5-dihydroxy-2-(hydroxymethyl)tetrahydro-2*H*-pyran-3-yl]oxy}-2-phenylhexahydropyrano[3,2-*d*][1,3]dioxin-7,8-diol (**15**)[10] are known compounds and were prepared according to literature procedures.

[(2*R*,3*S*,4*S*,5*R*,6*R*)-6-Azido-3,4,5-trihydroxytetrahydro-2*H*-pyran-2-yl]methyl 4-Methylbenzolsulfonate (3)

A solution of (2*R*,3*R*,4*S*,5*S*,6*R*)-2-azido-6-(hydroxymethyl)tetrahydro-2*H*-pyran-3,4,5-triol (585 mg, 2.85 mmol, 1.0 equiv) in anhyd pyridine (6 mL) was cooled to 0 °C and treated with *p*TsCl (706 mg, 3.71 mmol, 1.3 equiv) in anhyd pyridine (3 mL). The mixture was stirred at rt for 24 h. The solvent was removed under reduced pressure, and the crude product was purified by column chromatography (silica gel, EtOAc); yield: 742 mg (72%); colorless solid.

IR (ATR): 3354, 3290, 2115, 1347, 1248, 1188, 1167, 1106, 1079, 1057, 1012, 967, 894, 813, 781, 705, 663, 552, 505 cm^{-1}.

^1H NMR (600 MHz, DMSO-d_6): δ = 7.78 (d, *J* = 8.3 Hz, 2 H, ArH), 7.48 (d, *J* = 8.2 Hz, 2 H, ArH), 5.57 (d, *J* = 5.6 Hz, 1 H, CHO*H*), 5.34 (d, *J* = 5.7 Hz, 1 H, CHO*H*), 5.23 (d, *J* = 5.3 Hz, 1 H, CHO*H*), 4.51 (d, *J* = 8.7 Hz, 1 H, β-H_1), 4.24 (dd, J_1 = 10.8 Hz, J_2 = 1.7 Hz, 1 H), 3.52 (ddd, J_1 = 9.8 Hz, J_2 = 6.5 Hz, J_3 = 1.7 Hz, 1 H), 3.16 (td, J_1 = 8.9 Hz, J_2 = 5.2 Hz, 1 H), 3.04 (td, J_1 = 9.4 Hz, J_2 = 5.6 Hz, 1 H), 2.95 (td, J_1 = 8.8 Hz, J_2 = 5.6 Hz, 1 H), 2.43 (s, 3 H, ArCH_3).

^{13}C NMR (150 MHz, DMSO-d_6): δ = 132.6 (s, *ipso*-Ar), 130.6, 128.1 (2 d, Ar), 90.1 (d, CHN_3), 76.5 (d, *C*HCH$_2$), 75.7, 73.5, 70.3 (3 d, CHOH), 69.5 (t, CH_2OH), 21.6 (q, ArCH_3).

4-(Di-*tert*-butylfluorsilyl)benzenethiol (4)

The procedure published previously[8] was improved as follows. A solution of *t*BuLi in pentane (8.05 mL, 1.9 M, 15.3 mmol, 2.0 equiv) was added dropwise under magnetic stirring to a –78 °C cold solution of (4-bromophenylsulfanyl)-*tert*-butyldimethylsilane (2.32 g, 7.65 mmol, 1.0 equiv) in Et_2O (50 mL). After stirring the reaction mixture for 25 min at –78 °C, di-*tert*-butyldifluorosilane (1.52 g, 8.41 mmol, 1.1 equiv) was added dropwise. The reaction mixture was allowed to warm up to rt over a period of 24 h and brine (50 mL) was added. The organic layer was separated, and the aqueous layer was extracted with Et_2O (4 × 50 mL). The combined organic layers were dried ($MgSO_4$). The filtrate was concentrated in vacuo to give 1-(*tert*-butyldimethylsilanylsulfanyl)-4-(di-*tert*-butylfluorosilanyl)benzene as a yellow oil that solidified (2.58 g, 6.70 mmol, 88%). The subsequent deprotection to afford **4** was carried out as described previously.[8]

(2*R*,3*R*,4*S*,5*S*,6*S*)-2-Azido-6-({[4-(di-*tert*-butylfluorosilyl)phenyl]thio}methyl)tetrahydro-2*H*-pyran-3,4,5-triol (5)

A solution of **4** (50 mg, 0.18 mmol, 1.2 equiv) in anhyd DMSO (1 mL) was treated with *t*BuOK (20 mg, 0.18 mmol, 1.2 equiv). The mixture was stirred at 50 °C for 30 min. After the addition of **3** (54 mg, 0.15 mmol, 1 equiv) in anhyd DMSO (1 mL), the mixture was stirred at 50 °C for 24 h. Cooling to rt was followed by addition of excess aq 1 M HCl. The mixture was dissolved to Et_2O and washed with aq 1 M HCl (3 × 20 mL) and H_2O (3 × 20 mL). After drying ($MgSO_4$), the solvent was removed under reduced pressure, and the crude product was purified by column chromatography (silica gel) using a gradient starting with pentane/Et_2O (15:1) and ending with Et_2O/MeOH (20:1); yield: 51.1 mg (74%); colorless powder.

IR (ATR): 3354 (br), 2933, 2859, 2117, 1582, 1471, 1386, 1365, 1245, 1064, 1011, 969, 936, 836, 824, 811, 740, 715, 646, 599 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ = 7.52 (d, *J* = 8.1 Hz, 2 H, ArH), 7.39 (d, *J* = 8.1 Hz, 2 H, ArH), 4.59 (d, *J* = 8.4 Hz, 1 H, β-H_1), 3.69–3.66 (m, 1 H), 3.59–3.48 (m, 4 H), 3.34 (t, *J* = 8.5 Hz, 1 H), 3.31 (dd, J_1 = 14.1 Hz, J_2 = 7 Hz, 1 H), 1. 05 [s, 18 H, 2 × C$(CH_3)_3$].

^{13}C NMR (150 MHz, $CDCl_3$): δ = 138.4 (s, Ar), 134.5 (d, *J* = 4.1 Hz, Ar), 130.8 (s, *J* = 13.8 Hz, Ar), 127.2 (d, Ar), 90.0 (d, CHN_3), 76.9, 76.4, 73.5, 72.5 (4 d, CH), 34.5 (t, CH_2S), 27.3 [q, C(*C*$H_3)_3$], 20.3 [s, *J* = 12.4 Hz, *C*$(CH_3)_3$].

^{19}F NMR (565 MHz, $CDCl_3$): δ = –188.9 (d, *J* = 297.8 Hz).

^{29}Si NMR (119 MHz, $CDCl_3$): δ = 15.3 (d, *J* = 297.8 Hz).

HRMS (ESI): *m*/*z* calcd for $C_{20}H_{33}FN_3O_4SSi$ $[M + H]^+$: 458.19396; found: 458.19396.

[(2*R*,3*S*,4*S*,5*R*,6*R*)-3,4,5-Trihydroxy-6-(prop-2-yn-1-yloxy)tetrahydro-2*H*-pyran-2-yl]methyl 4-Methylbenzolsulfonate (7)

A solution of (2*R*,3*S*,4*S*,5*R*,6*R*)-2-(hydroxymethyl)-6-(prop-2-yn-1-yloxy)tetrahydro-2*H*-pyran-3,4,5-triol (847 mg, 3.88 mmol, 1.0 equiv) in anhyd pyridine (7 mL) was cooled to 0 °C and treated with *p*TsCl (962 mg, 5.05 mmol, 1.3 equiv) in anhyd pyridine (3 mL). The mixture was stirred at rt for 24 h. The solvent was removed under reduced pressure, and the crude product was purified by column chromatography (silica gel, EtOAc); yield: 1.22 g (84%); colorless solid.

IR (ATR): 3325, 2899, 1596, 1446, 1356, 1188, 1176, 1080, 1046, 997, 925, 833, 814, 687, 656, 620, 550, 502 cm^{-1}.

^1H NMR (600 MHz, CD_3OD): δ = 7.81 (d, *J* = 8.3 Hz, 2 H, ArH), 7.45 (d, *J* = 8.1 Hz, 2 H, ArH), 4.37 (d, *J* = 7.8 Hz, 1 H, β-H_1), 4.34 (dd, J_1 = 10.9 Hz, J_2 = 1.8 Hz, 1 H), 4.29–4.26 (m, 1 H), 4.21 (s, 1 H), 4.19–4.15 (m, 1 H), 3.39 (ddd, J_1 = 9.8 Hz, J_2 = 5.9 Hz, J_3 = 1.9 Hz, 1 H), 3.30–3.28 (m, 1 H), 3.22–3.19 (m, 1 H), 3.11 (dd, J_1 = 9.2 Hz, J_2 = 7.9 Hz, 1 H), 2.46 (s, 3 H, ArCH_3). OH groups were not detected.

^{13}C NMR (150 MHz, CD_3OD): δ = 146.7, 134.6 (2 s, Ar), 131.2, 129.3 (2 d, Ar), 102.1 (d, *C*HOCH$_2$), 80.0 (s, C≡C), 77.9 (d, CH), 76.5 (s, C≡C), 75.2, 74.8, 71.2 (2 d, CH), 70.8 (t, *C*H_2OTs), 56.7 (t, *C*H_2C≡C), 21.8 (Ar*C*H_3).

HRMS (ESI): *m*/*z* calcd for $C_{16}H_{20}O_8SNa$ $[M + Na]^+$: 395.07711; found: 395.07671.

(2*S*,3*S*,4*S*,5*R*,6*R*)-2-({[4-(Di-*tert*-butylfluorosilyl)phenyl]thio}methyl)-6-(prop-2-yn-1-yloxy)tetrahydro-2*H*-pyran-3,4,5-triol (8)

A solution of **4** (50 mg, 0.18 mmol, 1.2 equiv) in anhyd DMSO (1 mL) was treated with *t*BuOK (20 mg, 0.18 mmol, 1.2 equiv). The mixture was stirred at 50 °C for 30 min. After the addition of **7** (56 mg, 0.15 mmol, 1 equiv) in anhyd DMSO (1 mL), the mixture was stirred at 50 °C for 24 h. Cooling to rt was followed by addition of excess aq 1 M HCl. The mixture was dissolved in Et_2O and washed with aq 1 M HCl (3 × 20 mL) and H_2O (3 × 20 mL). After drying ($MgSO_4$), the solvent was removed under reduced pressure, and the crude product was purified by column chromatography (silica gel) using a gradient starting with pentane/Et_2O (15:1) and ending with Et_2O/MeOH (20:1); yield: 36.8 mg (52%); colorless powder.

IR (ATR): 3347, 3293, 2934, 2859, 1582, 1470, 1387, 1365, 1262, 1180, 1066, 1007, 824, 811, 740, 716, 645 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.57–7.49 (m, 2 H, ArH), 7.39–7.36 (m, 2 H, ArH), 4.50 (d, *J* = 7.3 Hz, 1 H, β-H_1), 4.36 (dd, J_1 = 15.7 Hz, J_2 = 2.4 Hz, 1 H), 4.25 (dd, J_1 = 15.9 Hz, J_2 = 2.2 Hz, 1 H), 3.61–3.48 (m, 4 H), 3.46–3.41 (m, 1 H), 3.17 (dd, J_1 = 14.2 Hz, J_2 = 7.3 Hz, 1 H), 2.48 (t, *J* = 2.4 Hz, 1 H), 1.60 (br s, 3 H, CHO*H*), 1. 05 [s, 18 H, 2 × C$(CH_3)_3$].

^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.8 (s, Ar), 134.4 (d, Ar), 130.4 (s, Ar), 127.1 (d, Ar), 100.1 (d, $CHOCH_2$), 77.2 (s, C≡C), 76.3 (d, CH), 75.4 (s, C≡C), 75.3, 73.6, 72.9 (3 d, CH), 55.9 (t, CH_2C≡C), 34.5 (t, CH_2S), 27.3 [q, $C(CH_3)_3$], 20.3 [s, J = 12.5 Hz, $C(CH_3)_3$].

^{19}F NMR (565 MHz, $CDCl_3$): δ = –188.9 (d, J = 297.6 Hz).

^{29}Si NMR (119 MHz, $CDCl_3$): δ = 15.3 (d, J = 297.8 Hz).

HRMS (ESI): m/z calcd for $C_{23}H_{35}FO_5SSiNa$ [M + Na]$^+$: 493.18507; found: 493.18476.

((2*R*,3*S*,4*S*,5*R*,6*R*)-6-{[(2*R*,3*S*,4*R*,5*R*,6*R*)-6-Azido-4,5-dihydroxy-2-[(tosyloxy)methyl]tetrahydro-2*H*-pyran-3-yl]oxy}-3,4,5-trihydroxytetrahydro-2*H*-pyran-2-yl)methyl 4-Methylbenzenesulfonate (10a)

A solution of **9a** (100 mg, 0.27 mmol, 1.0 equiv) in anhyd pyridine (2.4 mL) was cooled to –20 °C and treated with $ZnBr_2$·2 H_2O (243 mg, 1.08 mmol, 4.0 equiv) and then with *p*TsCl (257 mg, 1.35 mmol, 5.0 equiv) in anhyd pyridine (1 mL). The mixture was stirred at –20 °C for 1 h. The reaction was carried out three times in separate flasks. The reaction mixtures were combined, the solvent was removed under reduced pressure, and the crude product was purified by column chromatography (silica gel, EtOAc); yield: 367 mg (50%); colorless solid.

IR (ATR): 3375, 2363, 2330, 2119, 1598, 1450, 1353, 1190, 1173, 1141, 1071, 973, 928, 812, 688, 660, 551, 502 cm^{-1}.

^{1}H NMR (500 MHz, CD_3OD): δ = 7.82–7.77 (m, 4 H, ArH), 7.44 (d, J = 7.1 Hz, 4 H, ArH), 4.97 (d, J = 3.7 Hz, 1 H, α-$H_{1'}$), 4.43 (d, J = 8.7 Hz, 1 H, β-H_1), 4.32–4.30 (m, 2 H), 4.19–4.16 (m, 2 H), 3.71–3.68 (m, 1 H), 3.63–3.60 (m, 1 H), 3.52 (m, 2 H), 3.36–3.33 (m, 1 H), 3.25 (t, J = 9.5 Hz, 1 H), 3.07 (t, J = 9 Hz, 1 H), 2.46 (d, J = 5.3 Hz, 6 H, ArCH_3). OH groups were not detected.

^{13}C NMR (125 MHz, CD_3OD): δ = 146.8, 146.6, 134.5, 134.4 (4 s, Ar), 131.3, 131.2, 129.4, 129.3 (4 d, Ar), 103.0 (d, CHO), 91.7 (d, CHN_3), 80.7, 77.6, 75.6, 74.9, 74.0, 73.8, 72.4, 70.7 (8 d), 70.5, 70.4 (2 t, CH_2OTs), 21.8 (q, ArCH_3).

HRMS (ESI): m/z calcd for $C_{26}H_{33}N_3O_{14}S_2Na$ [M + Na]$^+$: 698.12962; found: 698.12955.

(2*S*,3*R*,4*S*,5*S*,6*S*)-2-{[(2*S*,3*S*,4*R*,5*R*,6*R*)-6-Azido-2-({[4-(di-*tert*-butylfluorosilyl)phenyl]thio}methyl)-4,5-dihydroxytetrahydro-2*H*-pyran-3-yl]oxy}-6-({[4-(di-*tert*-butylfluorsilyl)phenyl]thio}methyl)tetrahydro-2*H*-pyran-3,4,5-triol (11a)

A solution of **4** (192.2 mg, 0.71 mmol, 2.4 equiv) in anhyd DMSO (3 mL) was treated with *t*BuOK (79.7 mg, 0.71 mmol, 2.4 equiv). The mixture was stirred at 50 °C for 30 min. After the addition of **10a** (200 mg, 0.30 mmol, 1 equiv) in anhyd DMSO (1 mL), the mixture was stirred at 50 °C for 48 h. Cooling to rt was followed by addition of excess aq 1 M HCl. The mixture was dissolved in Et_2O and washed with aq 1 M HCl (3 × 20 mL) and H_2O (3 × 20 mL). After drying ($MgSO_4$), the solvent was removed under reduced pressure, and the crude product was purified by column chromatography (silica gel) using a gradient starting with cyclohexane/EtOAc (3:1) and ending with EtOAc/MeOH (10:1); yield: 174 mg (67%); colorless solid.

IR (ATR): 3325, 2934, 2859, 2117, 1715, 1582, 1470, 1373, 1250, 1056, 1012, 939, 816, 740, 645, 600, 504 cm^{-1}.

^{1}H NMR (600 MHz, DMSO-d_6): δ = 7.42–7.36 (m, 6 H, ArH), 7.25 (d, J = 8 Hz, 2 H, ArH), 5.84–5.83 (m, 1 H), 5.75 (d, J = 6.3 Hz, 1 H), 5.66 (d, J = 5.5 Hz, 1 H), 5.32 (d, J = 5.8 Hz, 1 H), 5.13–5.08 (m, 2 H), 4.57 (d, J = 8.7 Hz, 1 H, β-H_1), 3.79 (t, J = 7.2 Hz, 1 H), 3.70–3.67 (m, 1 H), 3.56 (d, J = 12.3 Hz, 1 H), 3.49–3.41 (m, 3 H), 3.25–3.20 (m, 1 H), 3.16–3.11 (m, 1 H), 3.09–3.05 (m, 1 H), 3.03–3.00 (m, 1 H), 1.00–0.94 [m, 36 H, 4 × $C(CH_3)_3$].

^{13}C NMR (150 MHz, DMSO-d_6): δ = 140.0, 139.7 (2 s, Ar), 133.9 (d, J = 4.1 Hz, Ar), 133.8 (d, J = 3.9 Hz, Ar), 128.6 (s, J = 13.8 Hz, Ar), 128.4 (s, J = 13.8 Hz, Ar), 126.4, 125.9 (2 d, Ar), 101.4 (d, CHO), 89.6 (d, CHN_3), 82.6, 75.8, 75.5, 72.8, 72.7, 72.5, 72.3, 72.1 (8 d, CH), 59.7 (t, CH_2S), 39.0 (t, CH_2S), 28.0 [q, J = 6.1 Hz, $C(CH_3)_3$], 27.0 [q, J = 6.6 Hz, $C(CH_3)_3$], 19.8 [s, J = 12.4 Hz, $C(CH_3)_3$], 19.7 [s, J = 12.4 Hz, $C(CH_3)_3$].

^{19}F NMR (565 MHz, DMSO-d_6): δ = –187.5 (d, J = 297.8 Hz).

^{29}Si NMR (119 MHz, DMSO-d_6): δ = 15.4 (d, J = 297.8 Hz).

HRMS (ESI): m/z calcd for $C_{40}H_{63}F_2N_3O_8S_2Si_2Na$ [M + H + Na]$^+$: 894.34609; found: 894.34644.

((2*R*,3*S*,4*S*,5*R*,6*R*)-6-{[(2*R*,3*S*,4*R*,5*R*,6*R*)-4,5-Dihydroxy-6-(prop-2-yn-1-yloxy)-2-[(tosyloxy)methyl]tetrahydro-2*H*-pyran-3-yl]oxy}-3,4,5-trihydroxytetrahydro-2*H*-pyran-2-yl)methyl 4-Methylbenzenesulfonate (10b)

A solution of **9b** (100 mg, 0.26 mmol, 1.0 equiv) in anhyd pyridine (2.4 mL) was cooled to –20 °C and treated with $ZnBr_2$·2 H_2O (237 mg, 1.05 mmol, 4.0 equiv) and then with *p*TsCl (248 mg, 1.3 mmol, 5.0 equiv) in anhyd pyridine (1 mL). The mixture was stirred at –20 °C for 1 h. The reaction was carried out twice in separate flasks. The reaction mixtures were combined, the solvent was removed under reduced pressure, and the crude product was purified by column chromatography (silica gel, EtOAc); yield: 115 mg (31%); colorless solid.

IR (ATR): 3284, 2924, 1731, 1598, 1354, 1173, 993, 928, 812, 691, 660, 551 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.79–7.71 (m, 4 H, ArH), 7.46 (ddd, J_1 = 10.0 Hz, J_2 = 8.6 Hz, J_3 = 0.6 Hz, 4 H, ArH), 5.54 (d, J = 3.2 Hz, 1 H, OH), 5.49 (d, J = 6.4 Hz, 1 H, OH), 5.33 (d, J = 5.4 Hz, 1 H, OH), 5.23 (d, J = 5.8 Hz, 1 H, OH), 5.03 (d, J = 5.1 Hz, 1 H, OH), 4.93 (d, J = 3.7 Hz, 1 H, α-$H_{1'}$), 4.29–4.23 (m, 2 H), 4.22–4.19 (m, 1 H), 4.14–4.06 (m, 4 H), 3.51–3.56 (m, 1 H), 3.48 (t, J = 2.5 Hz, 2 H), 3.37 (d, J = 3.2 Hz, 1 H), 3.26–3.30 (m, 1 H), 3.21–3.26 (m, 1 H), 3.13–3.18 (m, 1 H), 3.08 (dd, J_1 = 9.7 Hz, J_2 = 5.7 Hz, 1 H), 2.96 (dd, J_1 = 5.3 Hz, J_2 = 1.1 Hz, 1 H), 2.41 (s, 6 H, ArCH_3).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 145.0, 144.9, 132.4, 132.3 (4 s, Ar), 130.1, 127.7, 127.5 (3 d, Ar), 100.7 (d), 100.4 (d), 79.5 (d), 78.9 (d), 77.6 (s), 75.8, 72.8, 72.4 (3 d), 71.9 (t, CH_2OTs), 71.5 (d), 70.4 (t, CH_2OTs), 69.3, 68.8 (2 d), 55.1 (t, CH_2C≡CH), 21.2 (q, ArCH_3).

HRMS (ESI): m/z calcd for $C_{29}H_{37}O_{15}S_2$ [M + H]$^+$: 689.15684; found: 689.15570.

(2*S*,3*S*,4*S*,5*R*,6*S*)-2-({[4-(Di-*tert*-butylfluorsilyl)phenyl]thio}methyl)-6-{[(2*S*,3*S*,4*R*,5*R*,6*R*)-2-({[4-(di-*tert*-butylfluorsilyl)phenyl]thio}methyl)-4,5-dihydroxy-6-(prop-2-yn-1-yloxy)tetrahydro-2*H*-pyran-3-yl]oxy)}tetrahydro-2*H*-pyran-3,4,5-triol (11b)

A solution of **4** (144.1 mg, 0.53 mmol, 2.4 equiv) in anhyd DMSO (3 mL) was treated with *t*BuOK (59.8 mg, 0.53 mmol, 2.4 equiv). The mixture was stirred at 50 °C for 30 min. After the addition of **10b** (152.9 mg, 0.22 mmol, 1 equiv) in anhyd DMSO (1 mL), the mixture was stirred at 50 °C for 2 d. Cooling to rt was followed by addition of excess aq 1 M HCl. The mixture was dissolved in Et_2O and washed with aq 1 M HCl (3 × 20 mL) and H_2O (3 × 20 mL). After drying ($MgSO_4$), the solvent was removed under reduced pressure, and the crude product was purified by column chromatography (silica gel) using a gradient starting with cyclohexane/EtOAc (3:1) and ending with EtOAc/MeOH (10:1); yield: 109 mg (55%); colorless solid.

IR (ATR): 3298, 2933, 2859, 1732, 1582, 1471, 1365, 1245, 1062, 1012, 824, 812, 741, 646, 601, 504, 430 cm^{-1}.

^1H NMR (600 MHz, DMSO-d_6): δ = 7.44–7.39 (m, 4 H, ArH), 7.36 (d, *J* = 8.1 Hz, 2 H, Ar*H*), 7.26 (d, *J* = 8.1 Hz, 2 H, ArH), 5.72 (d, *J* = 2.6 Hz, 1 H, OH), 5.64 (d, *J* = 6.6 Hz, 1 H, OH), 5.34–5.29 (m, 2 H, 2 × OH), 5.13 (d, *J* = 3.7 Hz, 1 H, α-$H_{1'}$), 5.06 (d, *J* = 5.1 Hz, 1 H, OH), 4.93 (td, J_1 = 6.5 Hz, J_2 = 3.9 Hz, 1 H), 4.29 (d, *J* = 7.7 Hz, 1 H, β-H-1), 4.11 (d, *J* = 2.6 Hz, 1 H), 3.99 (d, *J* = 13.6 Hz, 1 H, H-7b), 3.80–3.77 (m, 1 H, H-3), 3.53–3.44 (m, 2 H), 3.43–3.34 (m, 7 H), 3.23–3.18 (m, 1 H), 3.14–3.08 (m, 1 H), 3.08–2.98 (m, 2 H), 0.97 [d, *J* = 8.1 Hz, 36 H, 4 × C(CH_3)$_3$].

^{13}C NMR (150 MHz, DMSO-d_6): δ = 140.0, 139.8 (2 s, Ar), 133.9 (d, *J* = 4.1 Hz, Ar), 133.8 (d, *J* = 4.1 Hz, Ar), 128.5 (s, *J* = 13.9 Hz, Ar), 128.3 (s, *J* = 13.9 Hz, Ar), 126.4 (d, Ar), 125.8 (d, Ar), 101.2 (d), 100.5 (d), 82.9 (d), 79.3 (s), 77.5 (s), 76.0, 74.2 (2 d), 72.8 (d, *J* = 7.1 Hz), 72.6, 72.3 (2 d), 72.01 (d, *J* = 3.4 Hz), 68.8 (d), 58.3 (d), 54.7 (t), 31.4, 28.0 (2 t), 27.0 [q, C(*C*H_3)$_3$], 19.8, 19.7 [2 s, *J* = 4.7 Hz, *C*(CH_3)$_3$].

^{19}F NMR (565 MHz, $CDCl_3$): δ = –187.5, –187.5 (2 d, *J* = 297.8 Hz).

^{29}Si NMR (119 MHz, $CDCl_3$): δ = 15.5, 13.0 (2 d, *J* = 298.1 Hz).

HRMS (ESI): *m*/*z* calcd for $C_{44}H_{67}F_2O_{11}S_2Si_2$ [M + HCOO]$^-$: 929.36259; found: 929.36097.

((2*R*,3*R*,4*S*,5*R*,6*S*)-6-{[(2*R*,3*S*,4*R*,5*R*,6*R*)-6-Azido-4,5-dihydroxy-2-[(tosyloxy)methyl]tetrahydro-2*H*-pyran-3-yl]oxy}-3,4,5-trihydroxytetrahydro-2*H*-pyran-2-yl)methyl 4-Methylbenzolsulfonate (13a)

A solution of **12a** (100 mg, 0.27 mmol, 1.0 equiv) in anhyd pyridine (2.4 mL) was cooled to –20 °C and treated with $ZnBr_2$·2 H_2O (243 mg, 1.08 mmol, 4.0 equiv) and then with *p*TsCl (257 mg, 1.35 mmol, 5.0 equiv) in anhyd pyridine (1 mL). The mixture was stirred at –20 °C for 15 min. The reaction was carried out twice in separate flasks. The reaction mixtures were combined, the solvent was removed under reduced pressure, and the crude product was purified by column chromatography (silica gel) using a gradient starting with EtOAc/cyclohexane (30:1) and ending with EtOAc/MeOH (10:1); yield: 160 mg (44%); colorless solid.

IR (ATR): 3369, 2912, 2116, 1728, 1598, 1451, 1352, 1255, 1173, 1060, 971, 811, 769, 689, 662, 550 cm^{-1}.

^1H NMR (500 MHz, DMSO-d_6): δ = 7.83–7.76 (m, 4 H, ArH), 7.49–7.45 (m, 4 H, ArH), 5.82 (d, *J* = 5.6 Hz, 1 H), 5.16 (d, *J* = 3.8 Hz, 1 H), 4.96 (d, *J* = 4.7 Hz, 1 H), 4.82 (d, *J* = 4.7 Hz, 1 H), 4.59–4.55 (m, 2 H), 4.46 (d, *J* = 9.9 Hz, 1 H), 4.20–4.10 (m, 3 H), 3.91 (t, *J* = 9.2 Hz, 1 H), 3.76–3.72 (m, 2 H), 3.30–3.23 (m, 3 H), 3.04–3.01 (m, 1 H), 2.42 (d, *J* = 1.5 Hz, 6 H, 2 × Ar*CH*$_3$). OH groups were not detected.

^{13}C NMR (125 MHz, DMSO-d_6): δ = 145.2, 144.9, 132.3, 131.8 (4 s, Ar), 130.3, 130.1, 127.9, 127.7 (4 d, Ar), 102.8 (d, CHO), 89.2 (d, CHN_3), 78.5, 74.0, 73.3, 72.6, 72.4, 72.2 (6 d, CH), 69.9 (t, CH_2OTs) 69.8 (d, CH), 69.2 (t, *C*H_2OTs), 68.0 (d, CH), 21.2 (q, Ar*C*H_3).

HRMS (ESI): *m*/*z* calcd for $C_{26}H_{33}N_3O_{14}S_2Na$ [M + Na]$^+$: 698.12962; found: 698.12936.

(2*R*,3*R*,4*S*,5*R*,6*S*)-2-{[(2*S*,3*S*,4*R*,5*R*,6*R*)-6-Azido-2-({[4-(di-*tert*-butylfluorosilyl)phenyl]thio}methyl)-4,5-dihydroxytetrahydro-2*H*-pyran-3-yl]oxy}-6-({[4-(di-*tert*-butylfluorsilyl)phenyl]thio}methyl)tetrahydro-2*H*-pyran-3,4,5-triol (14a)

A solution of **4** (136 mg, 0.5 mmol, 2.4 equiv) in anhyd DMSO (3 mL) was treated with *t*BuOK (57 mg, 0.5 mmol, 2.4 equiv). The mixture was stirred at 50 °C for 30 min. After the addition of **13a** (142 mg, 0.21 mmol, 1 equiv) in anhyd DMSO (1 mL), the mixture was stirred at 50 °C for 48 h. Cooling to rt was followed by addition of excess aq 1 M HCl. The mixture was dissolved in Et_2O and washed with aq 1 M HCl (3 × 20 mL) and H_2O (3 × 20 mL). After drying ($MgSO_4$), the solvent was removed under reduced pressure, and the crude product was purified by column chromatography (silica gel) using a gradient starting with cyclohexane/EtOAc (3:1) and ending with EtOAc; yield: 61 mg (33%); colorless solid.

IR (ATR): 3371, 2935, 2860, 2117, 1582, 1470, 1366, 1249, 1054, 936, 816, 741, 646, 600, 505 cm^{-1}.

^1H NMR (600 MHz, DMSO-d_6): δ = 7.49–7.44 (m, 4 H, ArH), 7.39–7.33 (m, 4 H, ArH), 5.75 (d, *J* = 5.6 Hz, 1 H), 5.33 (d, *J* = 5 Hz, 1 H), 4.93 (d, *J* = 5.6 Hz, 1 H), 4.88 (d, *J* = 5 Hz, 1 H), 4.70 (d, *J* = 1.9 Hz, 1 H), 4.59 (d, *J* = 8.7 Hz, 1 H), 4.36 (d, *J* = 7.8 Hz, 1 H), 4.03 (q, *J* = 7.1 Hz, 1 H), 3.80–3.71 (m, 3 H), 3.65 (t, *J* = 6.7 Hz, 1 H), 3.45–3.41 (m, 3 H), 3.23–3.11 (m, 3 H), 1.01–1.00 [m, 36 H, 4 × C(CH_3)$_3$].

^{13}C NMR (150 MHz, DMSO-d_6): δ = 139.5, 139.0 (2 s, Ar), 134.1 (d, *J* = 4.1 Hz, Ar), 134.0 (d, *J* = 3.9 Hz, Ar), 128.8 (s, *J* = 13.8 Hz, Ar), 128.3 (s, *J* = 13.8 Hz, Ar), 126.2, 125.9 (2 d, Ar), 103.2 (d, CHO), 89.4 (d, CHN_3), 81.4, 75.4, 74.0, 73.3 (4 d, CH), 73.1 (d, *J* = 7.4 Hz, CH), 70.1, 69.2 (2 d, CH), 32.4 (t, CH_2S), 32.2 (t, CH_2S), 28.0 [q, *J* = 6.1 Hz, C(*C*H_3)$_3$], 27.0 [q, C(*C*H_3)$_3$], 19.8 [s, *C*(CH_3)$_3$], 19.7 [s, *C*(CH_3)$_3$].

^{19}F NMR (565 MHz, DMSO-d_6): δ = –187.4 (d, *J* = 297.5 Hz).

^{29}SiNMR (119 MHz, DMSO-d_6): δ = 15.6 (d, *J* = 297.5 Hz).

HRMS (ESI): *m*/*z* calcd for $C_{40}H_{64}F_2N_3O_8S_2Si_2$ [M + H]$^+$: 872.36359; found: 872.36441.

((2*R*,3*R*,4*S*,5*R*,6*S*)-6-{[(2*R*,3*S*,4*R*,5*R*,6*R*)-4,5-Dihydroxy-6-(prop-2-yn-1-yloxy)-2-[(tosyloxy)methyl]-tetrahydro-2*H*-pyran-3-yl]oxy}-3,4,5-trihydroxytetrahydro-2*H*-pyran-2-yl)methyl 4-Methylbenzolsulfonate (13b)

A solution of **12b** (100 mg, 0.26 mmol, 1.0 equiv) in anhyd pyridine (2.3 mL) was cooled to –20 °C and treated with $ZnBr_2$·2 H_2O (237 mg, 1.05 mmol, 4.0 equiv) and then with *p*TsCl (251 mg, 1.3 mmol, 5.0 equiv) in anhyd pyridine (1 mL). The mixture was stirred at –20 °C for 90 min. The reaction was carried out twice in separate flasks. The reaction mixtures were combined, the solvent was removed under reduced pressure, and the crude product was purified by column chromatography (silica gel, EtOAc); yield: 130 mg (36%); colorless solid.

IR (ATR): 3334, 2912, 1728, 1598, 1451, 1352, 1173, 1122, 1049, 1019, 971, 931, 836, 813, 769, 691, 661, 551 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 7.84–7.77 (m, 4 H, ArH), 7.50–7.46 (m, 4 H, ArH), 5.46 (d, *J* = 5.4 Hz, 1 H), 5.16 (d, *J* = 4.1 Hz, 1 H), 4.96 (d, *J* = 5 Hz, 1 H), 4.82 (d, *J* = 4.9 Hz, 1 H), 4.54 (d, *J* = 2.1 Hz, 1 H), 4.47 (d, *J* = 9.3 Hz, 1 H), 4.31 (d, *J* = 7.8 Hz, 1 H), 4.23–4.07 (m, 5 H), 4.02 (t, *J* = 6.8 Hz, 1 H), 3.91 (dd, J_1 = 9.9 Hz, J_2 = 8.5 Hz, 1 H), 3.78–3.76 (m, 1 H), 3.59–3.51 (m, 3 H), 3.27–3.24 (m, 3 H), 3.04–2.99 (m, 1 H), 2.43 (s, 6 H, 2 × Ar*CH*$_3$).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 145.1, 144.8, 132.5, 131.8 (4 s, Ar), 130.3, 130.1, 127.9, 127.7 (4 d, Ar), 102.7 (d, CHO), 100.3 (d, *C*HOCH$_2$), 79.6 (s, C≡CH), 77.6 (d, *C*≡CH), 74.0, 72.6, 72.5, 72.2, 71.4, 69.8, 69.4, 68.0 (8 d), 62.3 (t, CH_2OTs), 55.0 (t, CHO*C*H$_2$), 21.2 (q, Ar*C*H_3).

HRMS (ESI): *m*/*z* calcd for $C_{29}H_{37}O_{15}S_2$ [M + H]$^+$: 689.15684; found: 689.15712.

(2*S*,3*R*,4*S*,5*R*,6*R*)-2-({[4-(Di-*tert*-butylfluorsilyl)phenyl]thio}methyl)-6-{[(2*S*,3*S*,4*R*,5*R*,6*R*)-2-({[4-(di-*tert*-butylfluorsilyl)phenyl]thio}methyl)-4,5-dihydroxy-6-(prop-2-yn-1-yloxy)tetrahydro-2*H*-pyran-3-yl]oxy}tetrahydro-2*H*-pyran-3,4,5-triol (14b)

A solution of **4** (94 mg, 0.35 mmol, 2.4 equiv) in anhyd DMSO (1.5 mL) was treated with *t*BuOK (39 mg, 0.35 mmol, 2.4 equiv). The mixture was stirred at 50 °C for 30 min. After the addition of **13b** (100 mg, 0.15 mmol, 1 equiv) in anhyd DMSO (1 mL), the mixture was stirred at 50 °C for 2 d. Cooling to rt was followed by addition of excess aq 1 M HCl. The mixture was dissolved in Et_2O and washed with aq 1 M HCl (3 × 20 mL) and H_2O (3 × 20 mL). After drying ($MgSO_4$), the solvent was removed under reduced pressure, and the crude product was purified by column chromatography (silica gel) using a gradient starting with cyclohexane/EtOAc (3:1) and ending with EtOAc/MeOH (10:1); yield: 47 mg (36%); colorless solid.

IR (ATR): 3396, 2934, 2859, 1715, 1582, 1471, 1365, 1074, 825, 812, 741, 646, 601, 505, 430 cm^{-1}.

^1H NMR (600 MHz, DMSO-d_6): δ = 7.46 (dd, J_1 = 19.8 Hz, J_2 = 8.1 Hz, 4 H ArH), 7.38 (d, J = 8.2 Hz, 2 H, ArH), 7.34 (d, J = 8.2 Hz, 2 H, ArH), 5.38 (d, J = 5.3 Hz, 1 H, OH), 5.30 (d, J = 4.8 Hz, 1 H, OH), 4.91 (d, J = 5.4 Hz, 1 H, OH), 4.86 (d, J = 4.9 Hz, 1 H, OH), 4.64 (d, J = 1.8 Hz, 1 H, OH), 4.37–4.32 (m, 2 H), 4.19 (dd, J_1 = 15.6 Hz, J_2 = 2.4 Hz, 1 H), 4.11–4.04 (m, 2 H), 3.77–3.70 (m, 2 H), 3.67–3.64 (m, 1 H), 3.59–3.54 (m, 1 H), 3.43–3.37 (m, 4 H), 3.26–3.21 (m, 1 H), 3.16–3.08 (m, 3 H), 1.00 [d, J = 5.0 Hz, 36 H, 4 × $C(CH_3)_3$].

^{13}C NMR (150 MHz, DMSO-d_6): δ = 140.2, 139.6 (2 s, Ar), 134.6 (d, J = 4.4 Hz, Ar), 134.4 (d, J = 4.4 Hz, Ar), 129.2 (s, J = 14.3 Hz, Ar), 128.7 (s, J = 14.3 Hz, Ar), 126.7, 126.4 (2 d, Ar), 103.6 (d), 100.9 (d), 82.2 (d), 79.9 (s), 77.9, 74.6, 74.4, 73.7 (4 d), 73.5 (d, J = 2.2 Hz), 70.5 (d), 69.7 (d), 67.7 (d, J = 12.1 Hz), 55.3 (t), 33.0, 32.8 (2 t), 27.5 [q, $C(CH_3)_3$], 20.2 [s, J = 12.1 Hz, $C(CH_3)_3$].

^{19}F NMR (565 MHz, $CDCl_3$): δ = –187.4, –187.4 (2 d, J = 297.8 Hz).

^{29}Si NMR (119 MHz, $CDCl_3$): δ = 15.5, 13.6 (2 d, J = 297.6 Hz).

HRMS (ESI): m/z calcd for $C_{43}H_{66}F_2O_9S_2Si_2$ [M + Na]$^+$: 907.35471; found: 907.35541.

((2*R*,3*S*,4*R*,5*R*,6*R*)-6-Azido-3-{[(4a*R*,6*S*,7*R*,8*R*)-7,8-dihydroxy-2-phenylhexahydropyrano[3,2-*d*][1,3]dioxin-6-yl]oxy}-4,5-dihydroxytetrahydro-2*H*-pyran-2-yl)methyl 4-Methylbenzensulfonate (16) and (4a*R*,6*S*,7*R*,8*R*)-6-{[(2*R*,3*S*,4*R*,5*R*,6*R*)-6-Azido-4,5-dihydroxy-2-[(tosyloxy)methyl]tetrahydro-2*H*-pyran-3-yl]oxy}-7-hydroxy-2-phenylhexahydropyran[3,2-*d*][1,3]dioxin-8-yl 4-Methylbenzenesulfonate (17)

A solution of **15** (100 mg, 0.22 mmol, 1.0 equiv) in anhyd pyridine (2 mL) was cooled to –20 °C and treated with $ZnBr_2$·2 H_2O (198 mg, 0.88 mmol, 4.0 equiv) and then with *p*TsCl (209 mg, 1.1 mmol, 5.0 equiv) in anhyd pyridine (1 mL). The mixture was stirred at –20 °C for 30 min. The solvent was removed under reduced pressure, and the crude product was purified by column chromatography (silica gel) using a gradient starting with EtOAc/cyclohexane (1:1, + 1% Et_3N) and ending with EtOAc/MeOH (30:1, + 1% Et_3N).

16

Yield: 66 mg (49%); colorless solid.

IR (ATR): 3334, 2911, 2113, 1598, 1359, 1248, 1174, 1095, 1033, 994, 964, 903, 839, 810, 774, 741, 698, 670, 597, 554, 520, 481 cm^{-1}.

^1H NMR (600 MHz, DMSO-d_6): δ = 7.76 (d, J = 8.1 Hz, 2 H, ArH), 7.44 (dd, J_1 = 6.1 Hz, J_2 = 2.4 Hz, 2 H, ArH), 7.41–7.35 (m, 5 H, ArH), 5.74 (d, J = 5.6 Hz, 1 H, OH), 5.56 (s, 1 H), 5.19 (d, J = 4.1 Hz, 1 H, OH), 5.06–4.99 (m, 2 H, OH), 4.63–4.56 (m, 2 H), 4.33 (d, J = 7.4 Hz, 1 H), 4.13 (dd, J_1 = 11.0 Hz, J_2 = 7.2 Hz, 1 H), 4.09–4.05 (m, 2 H), 3.96 (d, J = 12.2 Hz, 1 H), 3.79 (t, J = 8.3 Hz, 1 H), 3.58 (s, 1 H), 3.48–3.39 (m, 3 H), 3.36 (d, J = 9.5 Hz, 1 H), 3.03 (td, J_1 = 8.6 Hz, J_2 = 5.8 Hz, 1 H), 2.38 (s, 3 H, ArCH_3).

^{13}C NMR (150 MHz, DMSO-d_6): δ = 145.3 (s, Ar), 139.0 (s, Ar), 132.7 (s, Ar), 130.5, 129.2 (2 d, Ar), 128.4 (d, Ar), 128.1, 126.7 (2 d, Ar), 102.8 (d), 100.2 (d), 89.7 (d), 77.5, 76.1, 74.6 73.9, 73.3, 72.0, 70.0 (7 d), 69.8, 68.9 (2 t), 66.8 (d), 21.6 ArCH_3).

HRMS (ESI): m/z calcd for $C_{26}H_{32}N_3O_{12}S$ [M + H]$^+$: 610.17012; found: 610.17125.

17

Yield: 52 mg (31%); colorless solid.

IR (ATR): 3486, 3037, 2875, 2116, 1729, 1598, 1357, 1246, 1173, 1093, 1043, 963, 905, 868, 812, 697, 669, 552 cm^{-1}.

^1H NMR (600 MHz, DMSO-d_6): δ = 7.82 (d, J = 8.2 Hz, 2 H, ArH), 7.74 (d, J = 8.2 Hz, 2 H, ArH), 7.42 (d, J = 8.2 Hz, 2 H, ArH), 7.39–7.35 (m, 5 H, ArH), 7.29–7.26 (m, 2 H, ArH), 5.76 (d, J = 5.5 Hz, 1 H, OH), 5.61 (d, J = 5.5 Hz, 1 H, OH), 5.35 (s, 1 H), 5.04 (d, J = 3.1 Hz, 1 H, OH), 4.62–4.51 (m, 4 H), 4.48 (d, J = 7.6 Hz, 1 H), 4.25 (d, J = 3.4 Hz, 1 H), 4.03–4.09 (m, 2 H), 3.99–3.95 (m, 1 H), 3.78–3.73 (m, 1 H), 3.70 (s, 1 H), 3.54 (ddd, J_1 = 9.5 Hz, J_2 = 7.9 Hz, J_3 = 5.5 Hz, 1 H), 3.43–3.36 (m, 2 H,), 3.01 (td, J_1 = 8.5 Hz, J_2 = 5.8 Hz, 1 H), 2.38 (d, J = 3.7 Hz, 6 H, 2 × ArCH_3).

^{13}C NMR (150 MHz, DMSO-d_6): δ = 145.1 (s, Ar), 144.9 (s, Ar), 138.1 (s, Ar), 134.0 (s, Ar), 132.3 (s, Ar), 130.2, 130.0, 129.1, 128.2 (4 d, Ar), 127.8 (d, J = 13.6 Hz, Ar), 126.2 (d, Ar), 102.8 (d), 100.2 (d), 89.7 (d), 77.5, 76.1, 74.6 73.9, 73.3, 72.0, 70.0 (7 d), 69.8, 68.9 (t), 66.8 (d), 21.6 (q, ArCH_3).

LRMS (ESI): m/z calcd for $C_{26}H_{31}N_3O_{12}SNa$ [M + Na]$^+$: 786.16; found: 786.32.

X-ray Crystal Data[11]

Intensity data for the colorless crystal of compound **17** were collected on a D8 Venture Bruker Diffractometer, SC-XRD using Cu-Kα radiation at 173(2) K. The molecular structure was solved with direct methods using SHELXS-2014/7 or SHELXT-2014/7 and refinements were carried out against *F*2 by using SHELXL-2014/7[27] or OLEX2.[28] The data obtained by the measurement were treated in the refinement procedure as a 2-component twin. Applying the TwinRotMat option in the program PLATON[29] revealed a twin law (BASF 0. 0.13258).

(4a*R*,6*S*,7*R*,8*R*)-6-{[(2*S*,3*S*,4*R*,5*R*,6*R*)-6-Azido-2-({[4-(di-*tert*-butylfluorsilyl)phenyl]thio}methyl)-4,5-dihydroxytetrahydro-2*H*-pyran-3-yl]oxy}-2-phenylhexahydropyrano[3,2-*d*][1,3]dioxin-7,8-diol (18)

A solution of **4** (110 mg, 0.41 mmol, 1.2 equiv) in anhyd DMSO (3 mL) was treated with *t*BuOK (45.8 mg, 0.41 mmol, 1.2 equiv). The mixture was stirred at 50 °C for 30 min. After the addition of **16** (207 mg, 0.34 mmol, 1 equiv) in anhyd DMSO (1 mL), the mixture was stirred at 50 °C for 2 d. Cooling to rt was followed by addition of excess aq 1 M HCl. The mixture was dissolved in Et_2O and washed with aq 1 M HCl (3 × 20 mL) and H_2O (3 × 20 mL). After drying ($MgSO_4$), the solvent was removed under reduced pressure, and the crude product was purified by column chromatography (silica gel) using a gradient starting with cyclohexane/EtOAc (2:1) and ending with EtOAc; yield: 146 mg (61%); colorless solid.

IR (ATR): 3385, 2934, 2933, 2859, 2115, 1733, 1582, 1471, 1365, 1245, 1163, 1027, 901, 812, 740, 699, 647, 601, 505, 431 cm^{-1}.

^1H NMR (600 MHz, DMSO-d_6): δ = 7.47 (d, *J* = 7.7 Hz, 4 H, ArH), 7.42–7.35 (m, 5 H, ArH), 5.70 (d, *J* = 5.5 Hz, 1 H, OH), 5.58 (s, 1 H), 5.47 (d, *J* = 4.4 Hz, 1 H, OH), 5.13–5.07 (m, 1 H, OH), 4.83–4.77 (m, 1 H, OH), 4.64 (d, *J* = 8.4 Hz, 1 H), 4.50–4.46 (m, 1 H), 4.11 (d, *J* = 2.6 Hz, 2 H), 4.00 (d, *J* = 12.1 Hz, 1 H), 3.85–3.81 (m, 1 H), 3.75 (br s, 1 H), 3.65 (s, 1 H), 3.54–3.47 (m, 2 H), 3.45–3.43 (m, 2 H), 3.18–3.08 (m, 2 H), 1.01 [s, 18 H, 2 × $C(CH_3)_3$].

^{13}C NMR (150 MHz, DMSO-d_6): δ = 139.8, 138.9, 135.3 (3 s, Ar), 134.4 (d, *J* = 4.4 Hz, Ar), 129.1, 128.3, 126.6, 126.2 (4 d, Ar), 103.7 (d, C-1′), 100.1 (d), 89.9 (d), 82.3, 76.1, 75.8, 74.5, 73.7, 72.2, 70.3 (7 d), 68.8 (t), 66.8 (d), 32.7 (t), 28.4, 27.4 [2 q, $C(CH_3)_3$)], 20.2 [d, *J* = 12.1 Hz, $C(CH_3)_3$].

^{19}F NMR (565 MHz, $CDCl_3$): δ = –187.4 (d, *J* = 296.5 Hz).

^{29}Si NMR (119 MHz, $CDCl_3$): δ = 15.6 (d, *J* = 297.1 Hz).

HRMS (ESI): *m*/*z* calcd for $C_{34}H_{47}FN_3O_{11}SSi$ [M + HCOO]$^-$: 752.26791; found: 752.26732.

(2*S*,3*R*,4*S*,5*R*,6*R*)-2-{[(2*S*,3*S*,4*R*,5*R*,6*R*)-6-Azido-2-({[4-(di-*tert*-butylfluorsilyl)phenyl]thio}methyl)-4,5-dihydroxytetrahydro-2*H*-pyran-3-yl]oxy}-6-(hydroxymethyl)tetrahydro-2*H*-pyran-3,4,5-triol (19)

A mixture of **18** (124 mg, 0.18 mmol, 1.0 equiv) and 80% aq AcOH (4 mL) was stirred at 70 °C for 4 h. After cooling to rt, the mixture was extracted with toluene (3 × 20 mL). After drying ($MgSO_4$), the solvent was removed under reduced pressure, and the crude product was purified by column chromatography (silica gel) using a gradient starting with EtOAc and ending with EtOAc/MeOH (10:1); yield: 71 mg (64%); colorless solid.

IR (ATR): 3359, 2933, 2859, 2121, 1583, 1366, 1245, 1172, 1068, 1034, 878, 814, 778, 741, 700, 645, 599, 503, 437 cm^{-1}.

^1H NMR (600 MHz, DMSO-d_6): δ = 7.53–7.30 (m, 4 H, Ar), 5.69 (d, *J* = 5.5 Hz, 1 H, OH), 5.33–5.25 (m, 1 H, OH), 4.88–4.82 (m, 2 H), 4.67 (t, *J* = 5.0 Hz, 1 H, OH), 4.62 (d, *J* = 8.4 Hz, 1 H), 4.55 (d, *J* = 4.8 Hz, 1 H), 4.44 (br. s., 1 H, OH), 4.28 (d, *J* = 7.7 Hz, 1 H), 3.82–3.77 (m, 1 H), 3.73–3.68 (m, 1 H), 3.63 (br s, 1 H), 3.57–3.45 (m, 3 H), 3.40–3.34 (m, 4H), 3.15–3.06 (m, 2 H), 1.02–0.95 [m, 18 H, 2 × $C(CH_3)_3$].

^{13}C NMR (150 MHz, DMSO-d_6): δ = 139.5 (s, Ar), 134.1 (d, *J* = 4.4 Hz, Ar), 128.3 (s, *J* = 13.2 Hz, Ar), 126.0 (d, Ar), 104.3 (d), 89.5 (d), 83.1, 75.8, 75.4, 74.6, 73.5, 73.1, 70.6, 68.3 (8 d), 60.5 (t), 32.4 (t), 28.1, 27.2 [2 q, $C(CH_3)_3$], 19.9 [s, *J* = 13.2 Hz, $C(CH_3)_3$].

^{19}F NMR (565 MHz, $CDCl_3$): δ = –187.4 (d, *J* = 297.2 Hz).

^{29}Si NMR (119 MHz, $CDCl_3$): δ = 15.6 (d, *J* = 297.3 Hz).

HRMS (ESI): *m*/*z* calcd for $C_{26}H_{42}FN_3O_9SSiNa$ [M + Na]$^+$: 642.22873; found: 642.22877.

Funding Information

Natural Sciences and Engineering Research Council of Canada (NSERC) research grant to R.S.

Acknowledgment

We thank Matthias Mawick for synthesizing compound **4**.

Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0037-1611656.

References

(1) Shukla, A. K.; Kumar, U. *J. Med. Phys.* **2006**, *31*, 13.
(2) (a) Ametamey, S. M.; Honer, M.; Schubiger, P. A. *Chem. Rev.* **2008**, *108*, 1501. (b) Schirrmacher, R.; Wängler, C.; Schirrmacher, E. *Mini-Rev. Org. Chem.* **2007**, *4*, 317. (c) Miller, P. W.; Long, N. J.; Vilar, R.; Gee, A. D. *Angew. Chem. Int. Ed.* **2008**, *47*, 8998.
(3) (a) Ying, L. *Sci. China Chem.* **2013**, *56*, 1682. (b) Gao, Z.; Gouverneur, V.; Davis, B. G. *J. Am. Chem. Soc.* **2013**, *135*, 13612. (c) Brust, P.; Van den Hoff, J.; Steinbach, J. *Neurosci. Bull.* **2014**, *30*, 777. (d) Liang, S. H.; Vasdev, N. *Angew. Chem. Int. Ed.* **2014**, *53*, 2. (e) Fehler, S. K.; Maschauer, S.; Höfling, S. B.; Bartuschat, A. L.; Tschammer, N.; Hübner, H.; Gmeiner, P.; Prante, O.; Heinrich, M. R. *Chem. Eur. J.* **2014**, *20*, 370. (f) Van der Born, D.; Pees, A.; Poot, A. J.; Orru, R. V. A.; Windhorst, A. D.; Vugts, D. J. *Chem. Soc. Rev.* **2017**, *46*, 4709. (g) Jakobsson, J. E.; Grønnevik, G.; Riss, P. J. *Chem. Commun.* **2017**, *53*, 12906.
(4) Gens, T. A.; Wethongton, J. A.; Brosi, A. R. *J. Phys. Chem.* **1958**, *62*, 1593.
(5) (a) Smith, G. E.; Sladen, H. L.; Biagini, S. C. G.; Blower, P. J. *Dalton Trans.* **2011**, *40*, 6196. (b) Chansaenpak, K.; Vabre, B.; Gabbai, F. P. *Chem. Soc. Rev.* **2016**, *45*, 954. (c) Gauthier, V. B.; Bailey, J. J.; Liu, Z.; Wängler, B.; Wängler, C.; Jurkschat, K.; Perrin, D. M.; Schirrmacher, R. *Bioconjugate Chem.* **2016**, *27*, 267. (d) Wilson, T. C.; Cailly, T.; Gouverneur, V. *Chem. Soc. Rev.* **2018**, *47*, 6990. (e) Schirrmacher, R.; Bernard-Gauthier, V.; Schirrmacher, E.; Bailey, J. J.; Jurkschat, K.; Wängler, C.; Wängler, B. In *Fluorine in Life Sciences: Pharmaceuticals, Medicinal Diagnostics, and Agrochemicals*; Haufe, G., Ed.; Elsevier: Amsterdam, **2019**, Chap. 15.
(6) Mu, L. J.; Hohne, A.; Schubiger, R. A.; Ametamey, S. M.; Graham, K.; Cyr, J. E.; Dinkelborg, L.; Stellfeld, T.; Srinivasan, A.; Voigtmann, U.; Klar, U. *Angew. Chem. Int. Ed.* **2008**, *47*, 4922.
(7) (a) Schirrmacher, R.; Bradtmöller, G.; Schirrmacher, E.; Thews, O.; Tillmanns, J.; Siessmeier, T.; Buchholz, H. G.; Bartenstein, P.; Wängler, B.; Niemeyer, C. M.; Jurkschat, K. *Angew. Chem. Int. Ed.* **2006**, *45*, 6047. (b) Tietze, L. F.; Schmuck, K. *Synlett* **2011**, 1697. (c) Joyard, Y.; Azzouz, R.; Bischoff, L.; Papamicaël, C.; Labar, D.; Bol, A.; Bol, V.; Vera, P.; Grégoire, V.; Levacher, V.; Bohn, P. *Bioorg. Med. Chem.* **2013**, *21*, 3680. (d) Jana, S.; Al-huniti, M. H.; Yang, B. Y.; Lu, S.; Pike, V. W.; Lepore, S. D. *J. Org. Chem.* **2017**, *82*, 2329. (e) Tisseraud, M.; Schulz, J.; Vimont, D.; Berlande, M.; Fernandez, P.; Hermange, P.; Fouquet, E. *Chem. Commun.* **2018**, *54*, 5098. (f) Boutureira, O.; Bernardes, G. J. L.; D'Hooge, F.; Davis, B. G. *Chem. Commun.* **2011**, *47*, 10010.
(8) Iovkova, L.; Wängler, B.; Schirrmacher, E.; Schirrmacher, R.; Quandt, G.; Boening, G.; Schürmann, M.; Jurkschat, K. *Chem. Eur. J.* **2009**, *15*, 2140.
(9) Yamamura, H.; Kawasaki, J.; Saito, H.; Araki, S.; Kawai, M. *Chem. Lett.* **2001**, *30*, 706.
(10) Ying, L.; Gervay-Hague, J. *Carbohydr. Res.* **2003**, *338*, 835.
(11) CCDC 1866515 contains the supplementary crystallographic data for this paper. The data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/getstructures.
(12) Lai, Y.-C.; Luo, C.-H.; Chou, H.-C.; Yang, C.-J.; Lu, L.; Chen, C.-S. *Tetrahedron Lett.* **2016**, *57*, 2474.

(13) Bernardes, G. J. L.; Marston, J. P.; Batsanov, A. S.; Howard, J. A. K.; Davis, B. G. *Chem. Commun.* **2007**, 3145.
(14) Jha, A. K.; Jain, N. *Tetrahedron Lett.* **2013**, *54*, 4738.
(15) Liu, F.; Tang, P.; Ding, R.; Liao, L.; Wang, L.; Wang, M.; Wang, J. *Dalton Trans.* **2017**, *46*, 7515.
(16) Tong, Z.; Pu, S.; Xiao, Q.; Liu, G.; Cui, S. *Tetrahedron Lett.* **2013**, *54*, 474.
(17) Mauceri, A.; Borocci, S.; Galantini, L.; Giansanti, L.; Mancini, G.; Martino, A.; Manni, L. S.; Sperduto, C. *Langmuir* **2014**, *30*, 11301.
(18) Chatterjee, D.; Paul, A.; Yadav, R.; Yadav, S. *RSC Adv.* **2015**, *5*, 29669.
(19) Yuan, X.; Cheng, S.; Shi, Y.; Xue, W. *Synthesis* **2014**, *46*, 331.
(20) Okafor, I. S.; Wang, G. *Carbohydr. Res.* **2017**, *451*, 81.
(21) Eisink, N. N. H. M.; Lohse, J.; Witte, M. D.; Minnaard, A. J. *Org. Biomol. Chem.* **2016**, *14*, 4859.
(22) Ma, D.-L.; Shum, T. Y.-T.; Zhang, F.; Che, C.-M.; Yang, M. *Chem. Commun.* **2005**, 4675.
(23) Maki, T.; Ishida, K. *J. Org. Chem.* **2007**, *72*, 6427.
(24) Sun, B.; Jiang, H. *Tetrahedron Lett.* **2012**, *53*, 5711.
(25) Calatrava-Pérez, E.; Bright, S. A.; Achermann, S.; Moylan, C.; Senge, M. O.; Veale, E. B.; Williams, D. C.; Gunnlaugsson, T.; Scanlan, E. M. *Chem. Commun.* **2016**, *52*, 13086.
(26) Abellán Flos, M.; García Moreno, M. I.; Ortiz Mellet, C.; García Fernández, J. M.; Nierengarten, J.-F.; Vincent, S. P. *Chem. Eur. J.* **2016**, *22*, 11450.
(27) Sheldrick, G. M. *Acta Crystallogr., Sect. C* **2015**, *71*, 3.
(28) Dolomanov, O. V.; Bourhis, L. J.; Gildea, R. J.; Howard, J. A. K.; Puschmann, H. *J. Appl. Cryst.* **2009**, *42*, 339.
(29) Spek, A. L. *Acta Crystallogr., Sect. D* **2009**, *65*, 148.