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An unprecedented access to trifluoromethylthiosugar derivatives from thiocyanate precursors upon treatment with trifluoromethyltrimethylsilane

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Abstract

Upon treatment with trifluoromethyltrimethylsilane (2 equiv) in oxolane at 0 °C in the presence of a catalytic amount of tetra-*n*-butylammonium fluoride (0.2 equiv), various protected sugar derivatives having a thiocyanato group attached to different positions (anomeric, secondary, primary) were converted into the corresponding trifluoromethylthio derivatives. Under these conditions, highly selective, albeit partial transformations of primary and secondary thiocyanate groups were achieved while a decreased selectivity was observed when the reaction involved a more reactive anomeric thiocyanate group. However, in this case, lowering the reaction temperature led to enhanced selectivity and higher isolated yields. The isopropylidene and benzoyl protecting groups in the resulting trifluoromethylthiosugar derivatives were removed by standard methods to afford the corresponding free trifluoromethylthio derivatives, generally in high yield and as crystalline solids. Hence, this method opens a practical access to new trifluoromethylthiosugars obtained under smooth conditions as protected or unprotected derivatives.

Keywords: Sugar thiocyanates; Trifluoromethylthiosugars; Trifluoromethyltrimethylsilane; Catalytic reaction

1. Introduction

Fluorosugars [1–3] represent a wide class of sugar derivatives having applications in synthesis, particularly for stereocontrolled glycosidation reactions [4], in enzymatic studies [5–10], in molecular recognition studies [11] and as bioactive compounds [12,13] because the introduction of fluorine or fluoroalkyl groups may significantly modify the chemical, physical and biological properties of such derivatives. Consequently, there is a continuing interest towards this class of compounds, and recent literature provides a variety of synthetic approaches dealing with the preparation of elaborated fluorosugars, containing either one [14–19], two [18,20–22] or three [18,23–28] fluorine atoms linked to the same carbon atom or polyfluoroalkyl moieties [29] so as to produce fluorine-containing compounds with specific properties arising from the high electronegativity and the hydrophobic/lipophilic character of this element.

In the frame of our continuing interest in organofluorine chemistry, we recently pro-

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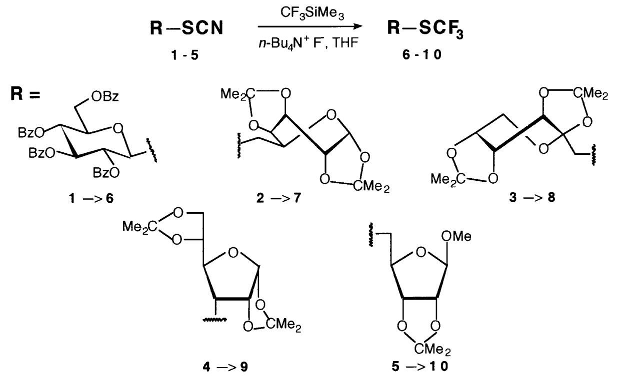
posed a new method for the preparation of trifluoromethylthio derivatives [30,31] from the corresponding thiocyanate precursors on treatment with trifluoromethyltrimethylsilane in the presence of a catalytic quantity of tetra-*n*-butylammonium fluoride [32]. Since it is well known that incorporation of fluorine atoms may dramatically modify the properties of the resulting glycomimetics, we decided to extend our studies to appropriately protected sugar thiocyanates [33] so as to develop an easy access to unknown structures. We were encouraged in this project by having in hand recent papers describing the introduction of trifluoromethyl group in sugar derivatives [18,23–28].

2. Results and discussion

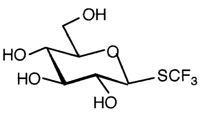
The trifluoromethylation reaction was applied to sugar thiocyanates **1** [34], **2**, **3**, **4** [35] and **5** [34]. The β-thiocyanate **1** [34] was prepared from the corresponding 2,3,4,6-tetra-*O*-benzoyl-α-D-glucopyranosyl bromide on treatment with potassium thiocyanate in acetone in the presence of 18-crown-6 as described. Applied to the preparation of the 2,3,4,6-tetra-*O*-acetyl-β-thiocyanate related to **1**, this protocol was found less satisfactory, due to competitive formation of the corresponding more stable isothiocyanate [34]. 6-Deoxy-1,2:3,4-di-*O*-isopropylidene-6-thiocyanato-α-D-galactopyranose (**2**), 1-deoxy-2,3:4,5-di-*O*-isopropylidene-1-thiocyanato-β-D-fructopyranose (**3**), 3-deoxy-1,2:5,6-di-*O*-isopropylidene-3-thiocyanato-α-D-allofuranose (**4**) [35] and methyl 2,3-*O*-isopropylidene-5-deoxy-5-thiocyanato-β-D-ribofuranoside (**5**) [34] were prepared under similar conditions from respectively 1,2:3,4-di-*O*-isopropylidene-6-*O*-trifluoromethanesulfonyl-α-D-galactopyranose [36], 2,3:4,5-di-*O*-isopropylidene-1-*O*-methanesulfonyl-β-D-fructopyranose [37], 2,3:4,5-di-*O*-isopropylidene-1-*O*-trifluoromethanesulfonyl-β-D-fructopyranose [38,39], 1,2:5,6-di-*O*-isopropylidene-3-*O*-trifluoromethanesulfonyl-α-D-glucofuranose [40,41] and from methyl 2,3-*O*-isopropylidene-5-*O*-*p*-toluenesulfonyl-β-D-ribofuranoside [42,43]. Nucleophilic displacement of the trifluoromethanesulfonate group in 1,2:5,6-di-*O*-isopropylidene-3-*O*-trifluoromethanesulfonyl-α-D-glucofuranose by the thiocyanate ion involved a S_N2 process leading to the corresponding 3-thiocyanato-α-D-allofuranose derivative [44].

Introduction of the trifluoromethyl group was achieved by treatment of a sugar thiocyanate in THF (1 mL for 1 mmol of the substrate) with trifluoromethyltrimethylsilane and tetra-*n*-butylammonium fluoride (1:2:0.2 ratio) generally from 0 °C to room temperature, resulting in good isolated yields for the trifluoromethylthio derivatives **6**–**10**. Under the applied conditions, transformation of the sugar thiocyanates was not complete (conversion $\geq 60\%$) and, except for the more labile anomeric thiocyanate **1** [34], the starting material was recovered by column chromatography. In the case of the isopropylidene-protected substrates, the transformation was highly selective, giving for example **9** as a single product from **4**. In this series, in spite of uncomplete conversions, the isolated yields were in the range 39–68% with selectivities as high as 98%. With the tetra-*O*-benzoyl thiocyanate **1**, another more polar product was detected by TLC when the reaction was conducted at 0 °C to afford **6** in a 30% isolated yield. Formation of this byproduct could be minimized by carrying out the trifluoromethylation reaction at a lower temperature followed by immediate product purification, as shown by improved isolated yields: 61% (−25 °C, 1 h); 76% (−78 °C, 40 min). Hence, a trifluoromethylthioether was conveniently prepared from a precursor having a thiocyanato group attached to the anomeric centre but the transformations involving unactivated thiocyanate groups at primary or secondary positions were found even more selective under ordinary conditions. The conversion of thiocyanatosugars into the corresponding trifluoromethylthio derivatives with trifluoromethyltrimethylsilane as reported here or into alkyl- and aryl-thioethers by means of Grignard reagents [34] are similar with respect to their mechanisms which both involve attack of a thiocyanate group by nucleophilic species with the cyano moieties acting as a leaving group [32].



Under acid-catalyzed transesterification in methanol containing formic acid, cleavage of the benzoyl groups in **6** led quantitatively to the corresponding trifluoromethyl β-D-thioglucopyranoside **11** within ~2 h. Transesterification also proceeded under base-catalyzed (MeONa, MeOH) conditions. However, with an excess of MeONa, we observed the complete transformation of **11** into methyl D-glucopyranoside (α anomer predominant as judged from the TLC plates). Fully unprotected reducing trifluoromethylthio sugars **12**, **13**, **14** and **16** were obtained from **7**, **8**, **9** and **10**, respectively, by acid-catalyzed hydrolysis. The methyl β-D-ribofuranoside **15** could also be separated by column chromatography from the main product **16**, in the deprotection reaction of **10**. In the case of the 2,3;4,5-di-*O*-isopropylidene-1-trifluoromethylthio-β-D-fructopyranose derivative **8**, complex mixtures were obtained under any of the acid-catalyzed conditions tried, the desired compound **13** being isolated in a ~10% yield.

The vicinal homonuclear coupling constants recorded for the D-galactopyranose derivatives **2** and **7** ($J_{1,2} \approx 5.0$, $J_{2,3} \approx 2.5$, $J_{3,4} \approx 7.8$, $J_{4,5} \approx 1.5$, $J_{5,6} \approx 6.5$ and $J_{5,6'} \approx 7$ Hz) showed that the pyranose ring assumes in both structures a skew-boat conformation [45,46] as a result of constraints in the tricyclic framework. Similarly, as judged from the vicinal couplings found for derivatives **3** and **8** ($J_{3,4} \approx 2.6$, $J_{4,5} \approx 7.9$, $J_{5,6} \approx 1.8$ and $J_{5,6'} \approx 1$ Hz), the D-fructopyranose adopted twist-boat conformations (${}^6S_4$) [46,47].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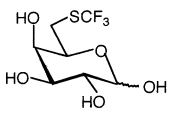
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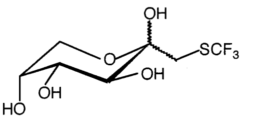
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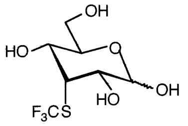
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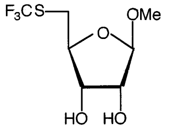
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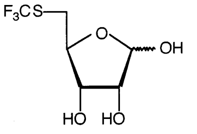
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Since it has been shown that the presence of a trifluoromethyl group attached to either the anomeric centre or the C-4 position in methyl furanosides decreases the rate of the acid-catalyzed glycosidic bond hydrolysis up to 2000 times [23], enzymatic studies were carried out with the deprotected compound **11**, so as to investigate its properties towards almond emulsin. However, **11** was found to be a weak competitive inhibitor of the almond β-glucosidase (K_i 9 mM) compared with D-glucono-1,5-lactone or phenylthio β-D-glucopyranoside [48]. It was not substrate of the enzyme. Compound **12** was found inactive.

In summary, treatment of protected sugar isothiocyanates with excess trifluoromethyl trimethylsilane in oxolane in the presence of a catalytic amount of tetra-*n*-butylammonium fluoride offers a direct route to unprecedented sugar-derived trifluoromethylthio derivatives, with potential applications to the synthesis of trifluoromethylthio analogues of biologically active methylthiosugars and nucleosides for example in the lincosamine [49] and 5′-deoxy-5′-(methylthio)-adenosine [50] series.

3. Experimental

General methods.—Melting points were determined with a Büchi capillary apparatus and were not corrected. Optical rotations were determined with a Perkin–Elmer 241 polarimeter. ^{1}H and ^{13}C NMR spectra were recorded with Bruker AC 200/AM 300 instruments for solutions in $CDCl_3$, unless indicated otherwise, with Me_4Si as the internal reference. ^{19}F NMR spectra were recorded with $CFCl_3$ as the internal reference at 188.31 MHz. Reactions were monitored by TLC on Silica Gel 60 F_{254} (E. Merck) plates sprayed with H_2SO_4 followed by charring. Spraying successively a fluorescein solution in absolute EtOH (0.1% w/v), then 1:1 H_2O_2 (30% in water)–AcOH followed by charring was used to detect a bromine-containing starting material which appeared as pink-coloured spots. Column chromatography was performed using Silica Gel Geduran Si 60 (E. Merck).

S-*Trifluoromethyl 2,3,4,6-tetra*-O-*benzoyl-1-thio-β-*D-*glucopyranoside* (**6**).—A solution of the tetra-*O*-benzoyl thiocyanate **1** [34] (637 mg, 1 mmol) in THF (1 mL) under an inert atmosphere (nitrogen or argon) was cooled down to −10 °C. After addition of trifluoromethyltrimethylsilane (300 μL, 2 mmol) and tetra-*n*-butylammonium fluoride (1.1 M in THF, 200 μL, 0.22 mmol, 0.22 equiv), the reaction mixture was stirred for 1 h at −25 °C and for 2 h at room temperature. After concentration and purification by column chromatography (7:3 petroleum ether–acetone), the *S*-trifluoromethyl 1-thio-β-D-glucopyranoside (415 mg, 61%) was obtained as a colourless solid, mp 141–142 °C; R_f 0.7 (7:3 petroleum ether–acetone); $[\alpha]_D^{25}$ + 34.5° (*c* 1, $CHCl_3$). The reaction of trifluoromethyltrimethylsilane with thiocyanate **1** was also carried out at −78 °C, 40 min or 0 °C, ~5 min to afford **6** in 76 and 30% yield, respectively. ^1H NMR (200.13 MHz): δ 7.81–8.10 (m, 8H, H *ortho*), 7.22–7.59 (m, 12H, H *meta* and *para*), 6.05 (t, 1H, $J_{2,3} = J_{3,4}$ 9.5 Hz, H-3), 5.72 (t, 1H, $J_{4,5}$ 9.7 Hz, H-4), 5.61 (t, 1H, H-2), 5.40 (d, 1H, $J_{1,2}$ 9.9 Hz, H-1), 4.67 (dd, 1H, $J_{6,6'}$ 12.2 Hz, $J_{5,6'}$ 2.8 Hz, H-6′), 4.51 (dd, 1H, $J_{5,6}$ 5.9 Hz, H-6), 4.31 (ddd, 1H, $J_{4,5}$ 9.8 Hz, H-5); ^{13}C NMR (50.32 MHz): δ 165.2–166.1 (C=O), 133.3–133.8 (C *para*), 129.8–130.0 (C *ortho*), 129.6 (C *ipso*), 129.5 (q, $^1J_{C,F}$ 309 Hz, CF_3), 128.5–128.6 (C *meta*), 82.0 (q, $^3J_{C,F}$ 2.8 Hz, C-1), 76.9, 73.7, 70.1, 69.2 (C-2 to C-5), 63.1 (C-6); ^{19}F NMR ($CDCl_3$): δ −40.3 (s, SCF_3). Anal. Calcd for $C_{35}H_{27}F_3O_9S$: C, 61.76; H, 4.00; S, 4.71. Found: C, 61.48; H, 4.15; S, 4.54.

S-*Trifluoromethyl 1-thio-β-*D-*glucopyranoside* (**11**).—*Procedure A: debenzoylation with sodium methoxide in MeOH.* *S*-Trifluoromethyl 2,3,4,6-tetra-*O*-benzoyl-1-thio-β-D-glucopyranoside **6** (500 mg, 0.735 mmol) was dissolved in MeOH (25 mL) containing a catalytic amount of NaOMe (30 drops) prepared by adding sodium (43 mg) to MeOH (2 mL). After 2.5 h, TLC monitoring showed the conversion of the starting material (R_f 0.9 in 6:1 CH_2Cl_2–MeOH) into **11** (R_f 0.2). Concentration and purification by column chromatography on silica gel (5.5:1 CH_2Cl_2–MeOH) afforded 152 mg (78% yield) of *S*-trifluoromethyl 1-thio-β-D-glucopyranose **11** which crystallized at −10 °C from MeOH upon addition of EtOAc and C_6H_6 as colourless crystals, mp 124 °C; R_f 0.2 (6:1 CH_2Cl_2–MeOH); $[\alpha]_D^{25}$ −36° (*c* 0.9, MeOH). Use of an excess of NaOMe resulted in further transformation of **11** to afford presumably, as suggested by TLC, a mixture of the corresponding methyl D-glucopyranosides. ^1H NMR (200.13 MHz, CD_3OD): δ 4.86 (d, 1H, $J_{1,2}$ 10 Hz, H-1), 3.84 (dd, 1H, $J_{5,6}$ 1.8 Hz, $J_{6,6'}$ 12.1 Hz, H-6), 3.70 (dd, 1H, $J_{5,6'}$ 4.2 Hz, H-6′), 3.42–3.20 (m, 4H, H-2, H-3, H-4, H-5); ^{13}C NMR (50.32 MHz, CD_3OD): δ 131.8 (q, $^1J_{C,F}$ 306.4 Hz, CF_3), 85.6 (q, $^3J_{C,F}$ 2.1 Hz, C-1), 82.3, 79.4, 73.6, 70.8 (C-2 to C-5), 62.4 (C-6); ^{19}F NMR (CD_3OD): δ −39.1 (s, SCF_3); CIMS (NH_3): *m*/*z* 282 $[M + NH_4]^+$. Anal. Calcd for $C_7H_{11}F_3O_5S$: C, 31.82; H, 4.20; S, 12.13; F, 21.57. Found: C, 31.91; H, 4.35; S, 11.74; F, 20.26.

Procedure B: debenzoylation in HCOOH-containing MeOH (10 ppm). Dissolution of compound **6** in 99% grade MeOH containing trace amounts of HCOOH (10 ppm), used as purchased from Prolabo, resulted upon stirring at room temperature for ~2 h in debenzoylation to afford **11** in a ~100% yield.

6-Deoxy-1,2:3,4-di-O-*isopropylidene-6-thiocyanato-α-*D-*galactopyranose* (**2**).—1,2:3,4-Di-*O*-isopropylidene-6-*O*-trifluoromethanesulfonyl-α-D-galactopyranose [36] (2.8 g, 7.2 mmol), dissolved in MeCN (180 mL), was stirred for 5 h at 75 °C in the presence of sodium thiocyanate (4.9 g, 50.4 mmol, 7 equiv), as described for the preparation of the 3-thiocyanato-D-*gluco*- and D-*allo*-furanose derivatives [35]. TLC monitoring showed that the starting material (R_f 0.7 in 3:7 EtOAc–petroleum ether) was converted to a new compound (R_f 0.6). After concentration under reduced pressure, water (70 mL) was added to the residue and the organic material was extracted with CH_2Cl_2 (3 × 70 mL). The combined organic phase was washed with brine

(70 mL) then with water (2 × 70 mL). After drying (Na_2SO_4) and concentration, the obtained brown oil was purified by column chromatography (1:5 EtOAc–petroleum ether) to give the thiocyanate **2** (1.9 g, 86%) as a syrup. IR (KBr): 2160 cm^{-1} (ν SCN); $[\alpha]_D^{25}$ $-4.5°$ (*c* 1, $CHCl_3$); ^1H NMR (200.13 MHz): δ 5.54 (d, 1H, $J_{1,2}$ 5 Hz, H-1), 4.68 (dd, 1H, $J_{2,3}$ 2.5 Hz, $J_{3,4}$ 7.8 Hz, H-3), 4.36 (dd, 1H, H-2), 4.28 (dd, 1H, $J_{4,5}$ 1.9 Hz, H-4), 4.06 (dt, 1H, $J_{5,6} = J_{5,6'}$ 6.7 Hz, H-5), 3.15 (d, 2H, H-6, H-6'), 1.59, 1.44, 1.35, 1.35 (4 s, 12H, isopropylidene); ^{13}C NMR (50.32 MHz): δ 112.2 (SCN), 109.9, 109.3 (2*C*Me_2), 96.5, 71.5, 71.0, 70.4, 66.7 (C-1 to C-5), 34.2 (C-6), 26.0, 25.9, 24.9, 24.4 (methyl). Anal. Calcd for $C_{13}H_{19}NO_5S$: C, 51.81; H, 6.35; O, 26.55. Found: C, 50.75; H, 6.33; O, 26.43.

*1,2:3,4-Di-*O*-isopropylidene-6-thio-6-*S*-trifluoromethyl-α-*D*-galactopyranose* (**7**).—A solution of thiocyanate **2** (808 mg, 2.7 mmol) in THF (2.7 mL) under argon was cooled down to -25 °C. After addition of trifluoromethyltrimethylsilane (800 μL, 5.4 mmol, 2 equiv) and tetra-*n*-butylammonium fluoride (1.1 M in THF, 533 μL, 0.59 mmol, 0.22 equiv) the reaction mixture was stirred for 1 h at -25 °C. TLC monitoring showed the partial conversion of the starting material (R_f 0.4 in 1:4 acetone–petroleum ether) into a new compound (R_f 0.7). After stirring was continued for 2 h at room temperature, TLC monitoring showed the presence of starting material ($\sim 40\%$) and formation of byproducts (R_f 0.6). Diethyl ether (5 mL) was added and the organic phase was washed with distilled water (2 × 5 mL), then dried over $MgSO_4$. Concentration under reduced pressure led to a brown oil which was purified by column chromatography (9:1 Et_2O–petroleum ether) to give 1,2:3,4-di-*O*-isopropylidene-6-thio-6-*S*-trifluoromethyl-α-D-galactopyranose (339 mg, 39% yield; based on the recovered starting material the yield was 62%) as an oil which solidified below room temperature. Another experiment conducted at a somewhat higher temperature (0 °C, 5 min then room temperature, 2 h) led with a similar selectivity to **2** (42% isolated yield); $[\alpha]_D^{21}$ $-48.4°$ (*c* 0.9, $CHCl_3$); ^1H NMR (300.13 MHz): δ 5.54 (d, 1H, $J_{1,2}$ 5.0 Hz, H-1), 4.66 (dd, 1H, $J_{3,4}$ 7.9 Hz, H-3), 4.35 (dd, 1H, $J_{2,3}$ 2.5 Hz, H-2), 4.32 (dd, 1H, $J_{4,5}$ 1.5 Hz, H-4), 4.00 (dt, 1H, $J_{5,6}$ 7.7 Hz, $J_{5,6'}$ 6.4 Hz, H-5), 3.15 (dd, 1H, $J_{6,6'}$ 14.2 Hz, H-6), 3.05 (dd, 1H, H-6'), 1.53, 1.46, 1.36, 1.35 (4 s, 12H, isopropylidene); ^{13}C NMR (75.47 MHz): δ 130.5 (q, $^1J_{C,F}$ 306.3 Hz, SCF_3), 109.1, 108.4 (2*C*Me_2), 95.9 (C-1), 70.7, 70.3, 69.8, 66.2 (C-2 to C-5), 29.1 (q, $^3J_{C,F}$ 2.1 Hz, C-6), 25.3, 25.2, 24.3, 23.8 (methyl); ^{19}F NMR ($CDCl_3$): δ -41.9 (SCF_3). EIMS: *m*/*z* 329, 22% $[M-15]^+$. Anal. Calcd for $C_{13}H_{19}F_3O_5S$: C, 45.34; H, 5.56. Found: C, 45.39; H, 5.71.

*6-Thio-6-*S*-trifluoromethyl-*D*-galactose* (**12**).—To a solution of 1,2:3,4-di-*O*-isopropylidene-6-thio-6-*S*-trifluoromethyl-α-D-galactopyranose **7** (316 mg, 0.9 mmol) in 1,4-dioxane (1.3 mL), a 1 M aq solution of hydrogen chloride (320 μL, 0.3 mmol, 0.35 equiv) was added. The mixture was heated to 100 °C for 3 h. TLC monitoring showed the transformation of the starting material (R_f 0.9 in 6:1 CH_2Cl_2–MeOH) into a polar new compound (R_f 0.3). After addition of sodium hydrogen carbonate (28 mg, 0.33 mmol), the solution was concentrated under reduced pressure to give an oil which was purified by column chromatography (6:1 CH_2Cl_2–MeOH). 6-Thio-6-*S*-trifluoromethyl-D-galactose **12** (232 mg, 80% yield) was obtained as an anomeric mixture ($\sim$4:1 α/β ratio) which crystallized from MeOH and EtOAc as colourless crystals, mp 117 °C; $[\alpha]_D^{25}$ $+82°$ (*c* 1, MeOH); ^1H NMR (300.13 MHz, CD_3OD), β anomer: $\sim 20\%$: δ 4.45 (d, $J_{1,2}$ 6.8 Hz, H-1); α anomer: $\sim 75\%$: δ 5.13 (d, 1H, $J_{1,2}$ 3.5 Hz, H-1), 4.20 (t, 1H, $J_{5,6}$ 8.2 Hz, $J_{5,6'}$ 5.8 Hz, H-5), 3.91 (broad d, 1H, $J_{3,4}$ 2.8 Hz, $J_{4,5} < 1$ Hz, H-4), 3.80 (dd, 1H, $J_{2,3}$ 10.1 Hz, H-3), 3.73 (dd, 1H, H-2), 3.22 (dd, 1H, $J_{6,6'}$ 13.5 Hz, H-6), 3.11 (dd, 1H, H-6'); ^{13}C NMR (75.47 MHz, CD_3OD), α anomer: δ 130.8 (q, $^1J_{C,F}$ 304.5 Hz, SCF_3), 92.3 (C-1), 69.5, 69.1, 68.1, 68.0 (C-2 to C-5), 29.4 (q, $^3J_{C,F}$ 2.2 Hz, C-6); β anomer: δ 96.8 (C-1), 72.8, 72.8, 71.3, 68.9 (C-2 to C-5), 32.3 (C-6); ^{19}F NMR (CD_3OD): δ -41.6 (SCF_3, β anomer); -41.7 (SCF_3, α anomer); CIMS (NH_3): *m*/*z* 282 $[M+18]^+$. Anal. Calcd for $C_7H_{11}F_3O_5S$: C, 31.82; H, 4.20; S, 12.13; F, 21.57. Found: C, 31.64; H, 4.24; S, 12.30; F, 21.11.

*1-Deoxy-2,3:4,5-di-*O*-isopropylidene-1-thiocyanato-β-*D*-fructopyranose* (**3**).—A mixture of 2,3:4,5-di-*O*-isopropylidene-1-*O*-trifluoromethanesulfonyl-β-D-fructopyranose [38,39] (325 mg, 0.83 mmol) and potassium thiocyanate (566 mg, 56.7 mmol, 7 equiv) in acetonitrile (21 mL) was refluxed for 19 h, whereupon TLC monitoring showed an almost complete conversion of the starting material (R_f 0.6 in 3:7 EtOAc–*n*-hexane) into the thiocyanate **3** (R_f 0.42). After removal of acetonitrile under reduced pressure, water (30 mL) was added to the residue. The organic materials were extracted with CH_2Cl_2 (3 × 30 mL), washed with water, dried ($MgSO_4$) and concentrated. Column chromatography (1.5:1 Et_2O–petroleum ether) gave the 1-thiocyanate **3** (181 mg, 0.6 mmol, 72% yield) which crystallized from Et_2O–petroleum ether as colourless crystals, mp 84 °C; $[\alpha]^{25}_{D}$ −10° (*c* 0.7, $CHCl_3$); IR (KBr) 2150 cm^{-1} (ν SCN); ^{1}H NMR (200.13 MHz): δ 4.62 (dd, 1H, $J_{3,4}$ 2.6 Hz, $J_{4,5}$ 7.8 Hz, H-4), 4.25 (d, 1H, H-3), 4.24 (dt, 1H, $J_{5,6}$ 1.8 Hz, $J_{5,6'} < 1$ Hz, H-5), 3.90 (dd, 1H, $J_{6,6'}$ 13 Hz, H-6), 3.78 (dd, 1H, H-6′), 3.47 (d, 1H, $J_{1,1'}$ 13.3 Hz, H-1), 3.22 (d, 1H, H-1′), 1.56, 1.48, 1.45, 1.35 (4 s, 12H, methyl); in acetone-d$_6$: δ 4.66 (dd, 1H, $J_{3,4}$ 2.6 Hz, $J_{4,5}$ 7.8 Hz, H-4), 4.36 (d, 1H, H-3), 4.27 (dt, 1H, $J_{5,6}$ 1.8 Hz, $J_{5,6'} < 1$ Hz, H-5), 3.87 (dd, 1H, $J_{6,6'}$ 13 Hz, H-6), 3.65 (dd, 1H, H-6′), 3.49 (s, 2H, H-1, H-1′), 1.51, 1.44, 1.42, 1.32 (4 s, 12H, methyl); ^{13}C NMR (50 MHz): δ 112.8 (SCN), 109.35, 109.3 (2*C*Me$_2$), 101.2 (C-2), 72.4, 70.4, 70.0 (C-3 to C-5), 61.9 (C-6), 42.2 (C-1), 26.3, 25.9, 25.0, 24.1 (CH_3). Anal. Calcd for $C_{13}H_{19}NO_5S$: C, 51.81; H, 6.35; O, 26.55; S, 10.64. Found: C, 51.70; H, 6.57; O, 27.10; S, 10.54.

Attempts to obtain **3** by nucleophilic displacement of a methanesulfonate group at position C-1 [37] by the thiocyanate anion in *N*,*N*-dimethylacetamide resulted in lower (31%) isolated yields.

*2,3:4,5-Di-*O*-isopropylidene-1-thio-1-*S*-trifluoromethyl-β-*D*-fructopyranose* (**8**).—Treatment of 1-deoxy-2,3:4,5-di-*O*-isopropylidene-1-thiocyanato-β-D-fructopyranose **3** (0.3 g, 1 mmol) with trifluoromethyltrimethylsilane (300 μL, 2 mmol) and tetra-*n*-butylammonium fluoride (1.1 M in THF, 200 μL, 0.22 mmol) at 0 °C as described for **7** led, after column chromatography (1:4 acetone–petroleum ether), to 2,3:4,5-di-*O*-isopropylidene-1-thio-1-*S*-trifluoromethyl-β-D-fructopyranose **8** (0.234 g, 68% isolated yield, 97% selectivity) in addition to unreacted starting material (~ 30%). Compound **8**, isolated as a white solid had mp 44 °C; R_f 0.7 (4:1 petroleum ether–acetone); $[\alpha]^{21}_{D}$ −9.2° (*c* 1, $CHCl_3$). ^{1}H NMR (200.13 MHz, acetone-d_6): δ 4.66 (dd, 1H, $J_{3,4}$ 2.6 Hz, $J_{4,5}$ 7.9 Hz, H-4), 4.35 (d, 1H, H-3), 4.27 (ddd, 1H, $J_{5,6}$ 1.8 Hz, $J_{5,6'}$ 1 Hz, H-5), 3.87 (dd, 1H, $J_{6,6'}$ 13 Hz, H-6), 3.64 (dd, 1H, H-6′), 3.44 (d, 1H, $J_{1,1'}$ 12.9 Hz, H-1), 3.31 (d, 1H, H-1′) 1.49 (s, 3H), 1.42 (broad s, 6H), 1.33 (s, 3H, isopropylidene); ^{13}C NMR (50.32 MHz): δ 130.9 (q, $^1J_{C,F}$ 306 Hz, SCF_3), 109.3, 109.1 (2*C*Me$_2$), 101.5 (C-2), 72.5, 70.7, 70.3 (C-3 to C-5), 61.8 (C-6), 37.9 (q, $^3J_{C,F}$ 2.2 Hz, C-1), 26.5, 25.8, 25.2, 24.1 (methyl); ^{19}F NMR ($CDCl_3$): δ −42.1 (s, SCF_3). EIMS: *m/z* 329, 73% $[M-15]^+$. Anal. Calcd for $C_{13}H_{19}F_3O_5S$: C, 45.34; F, 16.55; H, 5.56. Found: C, 45.88; F, 16.57; H, 5.51.

*1-Thio-1-*S*-trifluoromethyl-*D*-fructose* (**13**).—2,3:4,5-Di-*O*-isopropylidene-1-thio-1-*S*-trifluoromethyl-β-D-fructopyranose **8** (130 mg, 0.37 mmol) dissolved in a mixture of acetic acid (1.5 mL) and water (0.5 mL) was heated for 16 h at 100 °C. TLC examination of the reaction medium showed the presence of several compounds while the ^{1}H NMR spectrum of the crude reaction mixture showed resonances corresponding to acetyl groups. Therefore, the sample was kept for 72 h at room temperature in a 8:1:1 MeOH–NEt_3–H_2O mixture (2.5 mL) before purification by column chromatography (6:1 CH_2Cl_2–MeOH). Concentration of homogeneous fractions afforded the desired product (R_f 0.8 in 6:1 CH_2Cl_2–MeOH) as an anomeric mixture (10 mg, 0.038 mmol, 10% yield) showing complex NMR spectra. ^{1}H NMR (200.13 MHz, CD_3OD): δ 4.1–3.2 (m, 7 H); ^{13}C NMR (75.49 MHz, CD_3OD) major isomer (β pyranose): δ 132.7 (q, $^1J_{C,F}$ 304 Hz, SCF_3), 98.4 (C-2), 71.5, 70.9, 70.8 (C-3 to C-5), 64.9 (C-6), 37.8 (C-1); minor isomer (β furanose): δ 132.5 (q, $^1J_{C,F}$ 303 Hz, SCF_3), 98.4 (C-2), 83.7, 79.2, 76.5 (C-3 to C-5), 63.8 (C-6), 37.0 (C-1); other signals: δ 102.0, 85.1, 83.2, 72.9, 63.1; ^{19}F NMR (CD_3OD) δ (relative intensities) -41.6 (21%); -41.8 (11%); -42.0 (8%). CIMS (NH_3): *m*/*z* 282 $[M+18]^+$; 264 $[M]^+$.

*1,2:5,6-Di-*O*-isopropylidene-3-thio-3-*S*-trifluoromethyl-α-*D*-allofuranose* (**9**).—This compound was prepared from 3-deoxy-1,2:5,6-di-*O*-isopropylidene-3-thiocyanato-α-D-allofuranose **4** [35] (0.305 g, 1 mmol), trifluoromethyltrimethylsilane (300 μL, 2 mmol) and tetra-*n*-butylammonium fluoride (1.1 M in THF, 200 μL, 0.22 mmol) at 0 °C as described for **7**. Purification by column chromatography (1:4 acetone–petroleum ether) afforded some unreacted starting material (120 mg, 39%, R_f 0.4) and the desired trifluoromethylthio ether **9** (0.206 g, 60% isolated yield, 98% selectivity) as a syrup, R_f 0.7 (4:1 petroleum ether–acetone). $[\alpha]_D^{21}$ $+69.2°$ (*c* 1, $CHCl_3$). ^{1}H NMR (300.13 MHz): δ 5.86 (d, 1H, $J_{1,2}$ 3.7 Hz, H-1), 4.76 (dd, 1H, $J_{2,3}$ 4.4 Hz, H-2), 4.35 (dt, 1H, $J_{4,5}$ 4.2 Hz, $J_{5,6}=J_{5,6'}$ 6.5 Hz, H-5), 4.08–3.97 (m, 3H, H-4, H-6, H-6′), 3.33 (dd, 1H, $J_{3,4}$ 10.3 Hz, H-3), 1.54, 1.46, 1.37, 1.37 (4 s, 12H, isopropylidene); ^{13}C NMR (50.32 MHz): δ 130.5 (q, $^1J_{C,F}$ 307 Hz, SCF_3), 112.8, 110.1 (2CMe$_2$), 104.3 (C-1), 81.1, 79.4, 75.5 (C-2, C-4, C-5), 65.3 (C-6), 46.7 (q, $^3J_{C,F}$ 1.8 Hz, C-3), 26.6, 26.5, 26.3, 25.2 (isopropylidene); ^{19}F NMR ($CDCl_3$) δ -40.8 (s, SCF_3). EIMS: *m*/*z* 329, 18% $[M-15]^+$. Anal. Calcd for $C_{13}H_{19}F_3O_5S$: C, 45.34; H, 5.56. Found: C, 45.52; H, 5.55.

*3-Thio-3-*S*-trifluoromethyl-*D*-allose* (**14**).—1,2:5,6-Di-*O*-isopropylidene-3-thio-3-*S*-trifluoromethyl-α-D-allofuranose **9** (120 mg, 0.35 mmol) was dissolved in trifluoroacetic acid (5 mL) containing water (0.5 mL). The mixture was kept for 30 min at room temperature whereupon TLC showed the disappearance of the starting material (R_f 0.8 in 1:1 EtOAc–petroleum ether) and formation of a new compound (R_f 0.17). The volatiles were removed under reduced pressure and the residue was purified by column chromatography (1:1 petroleum ether–EtOAc then neat EtOAc) to afford the desired product **14** (96 mg, 0.36 mmol, 100% yield) as a crystalline anomeric mixture, mp 42 °C, giving complex NMR spectra. $[\alpha]_D^{20}$ $+2°$ (*c* 0.1, H_2O). ^{19}F NMR (CD_3OD): δ (relative intensities) -39.8 (25%); -40.5 (51%); -41.0 (8%); -41.3 (17%). CIMS (NH_3): *m*/*z* 282 $[M+18]^+$ 100%; 264 $[M]^+$ ~8%; 246 $[M-H_2O]^+$ ~10%.

*Methyl 2,3-*O*-isopropylidene-5-thio-5-*S*-trifluoromethyl-β-*D*-ribofuranoside* (**10**).—This compound was prepared from methyl 2,3-*O*-isopropylidene-5-deoxy-5-thiocyanato-β-D-ribofuranoside **5** (0.245 g, 1 mmol), trifluoromethyltrimethylsilane (300 μL, 2 mmol) and tetra-*n*-butylammonium fluoride (1 M in THF, 200 μL, 0.22 mmol) as described for **7**. Purification by column chromatography (1:9 acetone–petroleum ether) afforded first the desired trifluoromethylthioether **10** (R_f 0.8) as a colourless syrup (113 mg, 56% isolated yield, 89% selectivity) and unreacted starting material (R_f 0.4, 91 mg, 37%). $[\alpha]_D^{21}$ $-54°$ (*c* 1, $CHCl_3$). ^{1}H NMR (300.13 MHz): δ 4.99 (s, 1H, H-1), 4.66 (d, 1H, $J_{2,3}$ 6.0 Hz, H-2 or H-3), 4.63 (d, 1H, H-2 or H-3), 4.35 (dd, 1H, $J_{4,5}$ 8.1 Hz, $J_{4,5'}$ 7.7 Hz, H-4), 3.37 (s, 3H, OMe), 3.14 (dd, 1H, $J_{5,5'}$ 13.6 Hz, H-5′), 2.99 (dd, 1H, H-5), 1.48, 1.32 (2 s, each 3H, 2 Me); ^{13}C NMR (75 MHz): δ 130.9 (q, $^1J_{C,F}$ 306 Hz, SCF_3), 112.9 (CMe$_2$), 110.0 (C-1), 85.3, 85.2, 83.1 (C-2, C-3, C-4), 55.3 (OMe), 33.5 (q, $^3J_{C,F}$ 1.9 Hz, C-5), 26.4, 24.9 (isopropylidene); ^{19}F NMR ($CDCl_3$) δ -41.6 (s, SCF_3). EIMS: *m*/*z* 273, 42% $[M-15]^+$. Anal. Calcd for $C_{10}H_{15}F_3O_4S$: C, 41.66; H, 5.24; S, 11.12. Found: C, 41.45; H, 5.54; S, 11.21.

*5-Thio-5-*S*-trifluoromethyl-*D*-ribose* (**16**).—Methyl 2,3-*O*-isopropylidene-5-thio-5-*S*-trifluoromethyl-β-D-ribofuranoside **10** (200 mg, 0.7 mmol) was kept for 45 min in a mixture of trifluoroacetic acid (1 mL) and water (0.5 mL). TLC monitoring showed the disappearance of the starting material and formation of two compounds, among which the more polar was more abundant (R_f ~0.9, ~0.45 and ~0.25 respectively, in 1:1 EtOAc–petroleum ether). After concentration, the residue was applied to a column eluted with the same mixture of solvent, then neat EtOAc. Methyl 5-thio-5-*S*-trifluoromethyl-β-D-ribofuranoside **15** was eluted first to give a solid (mp 58 °C) after solvent removal (10 mg, 0.04 mmol, 6%). $[\alpha]_D^{21}$ $-11°$ (*c* 0.9, H_2O); ^{1}H NMR (CD_3OD, 200.13 MHz): δ 4.73 (s, 1H, H-1), 4.09 (m, 2H), 3.89 (d, 1H, J 3.8 Hz), 3.33 (s, 3H, OMe), 3.30 (m, 1H, H-5), 3.08 (dd, 1H, $J_{5,5'}$ 13 Hz, $J_{4,5'}$ 7.0 Hz, H-5′); ^{13}C NMR (75.48 MHz, D_2O): δ 131.2 (q, $^1J_{C,F}$ 305.4 Hz, SCF_3), 108.5 (C-1), 80.8, 74.7, 73.8 (C-2, C-3, C-4), 55.6 (OMe), 33.5 (q, $^3J_{C,F}$ 1 Hz, C-5), ^{19}F NMR (CD_3OD): δ 41.52 (s, SCF_3). Then, the 5-thio-5-*S*-trifluoromethyl-D-ribose **16** was obtained (70 mg, 0.3 mmol, 43% yield) as a solid (mp 44–45 °C). $[\alpha]_D^{21}$ $+34°$ (*c* 0.4, H_2O); ^{1}H NMR (CD_3OD, 200.13 MHz): δ 5.26, 5.11 (d and broad s, ~1/2 ratio, $J_{1,2}$ 4 Hz, ~0 Hz respectively, H-1), 4.2–3.8 (m, 3H), 3.4–3.0 (m, 2H); ^{13}C NMR (75.48 MHz, D_2O): major isomer: δ 131.2 (q, $^1J_{C,F}$ 305.3 Hz, SCF_3), 101.6 (C-1), 80.5, 75.6, 73.5 (C-2, C-3, C-4), 33.5 (q, $^3J_{C,F}$ 1 Hz, C-5); other isomer: δ 96.9 (C-1), 80.6, 72.8, 71.0 (C-2, C-3, C-4), 32.3 (q, $^3J_{C,F}$ 1 Hz, C-5); minor isomer: δ 103.8, 82.3, 80.1, 75.0, 72.2; ^{19}F NMR (CD_3OD): δ (relative intensities) -41.5 (10%); -41.5 (35%); -41.54 (55%). EIMS m/z 217, $[M-17]^+$, 3%; CIMS (NH_3) m/z 252, 100% $[M+18]^+$; 234, 46% $[M]^+$.

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References

[1] T. Tsuchiya, *Adv. Carbohydr. Chem. Biochem.*, 48 (1990) 91–277.

[2] J.T. Welch, S. Eswarakrishnan, in: *Fluorine in Bioorganic Chemistry*, *Ch. 8*, Wiley, New York, 1991, pp. 131–162.

[3] J.T. Welch, S. Eswarakrishnan, in: *Fluorine in Bioorganic Chemistry*, *Ch. 11*, Wiley, New York, 1991, pp. 220–233.

[4] K. Toshima, K. Tatsuta, *Chem. Rev.*, 93 (1993) 1503–1531.

[5] A. Konstantinidis, M.L. Sinnott, *Biochem. J.*, 279 (1991) 587–593.

[6] K. Srinivasan, A. Konstantinidis, M.L. Sinnott, B.G. Hall, *Biochem. J.*, 291 (1993) 15–17.

[7] J.D. McCarter, W. Yeung, J. Chow, D. Dolphin, S.G. Withers, *J. Am. Chem. Soc.*, 119 (1997) 5792–5797.

[8] S.M. Andersen, M. Ebner, C.W. Ekhart, G. Gradnig, G. Legler, I. Lundt, A.E. Stütz, S.G. Withers, T. Wrodnigg, *Carbohydr. Res.*, 301 (1997) 155–166.

[9] M. Namchuk, C. Braun, J.D. McCarter, S.G. Withers, in I. Ojima, J.R. McCarthy, J.T. Welch (Eds.), *Biomedical Frontiers of Fluorine Chemistry*, *ACS Symp. Ser. 639*, American Chemical Society, Washington, DC, 1996, pp. 279–293.

[10] J.R. McCarthy, P.S. Sunkara, D.P. Matthews, A.J. Bitonti, E.T. Jarvi, J.S. Sabol, R.J. Resvick, E.W. Huber, W.A. van der Donk, G. Yu, J. Stubbe, in I. Ojima, J.R. McCarthy, J.T. Welch (Eds.), *Biomedical Frontiers of Fluorine Chemistry*, *ACS Symp. Ser. 639*, American Chemical Society, Washington, DC, 1996, pp. 246–264.

[11] R.U. Lemieux, R. Cromer, U. Spohr, *Can. J. Chem.*, 66 (1988) 3083–3098.

[12] L.W. Hertel, R.J. Ternansky, in R. Filler, Y. Kobayashi, L.M. Yagupolskii (Eds.), *Organofluorine Compounds in Medicinal Chemistry and Biomedical Applications*, Elsevier, Amsterdam, 1993, pp. 23–71.

[13] L.W. Hertel, J.S. Kroin, C.S. Grossman, G.B. Grindey, A.F. Dorr, A.M.V. Storniolo, W. Plunkett, V. Gandhi, P. Huang, in I. Ojima, J.R. McCarthy, J.T. Welch (Eds.), *Biomedical Frontiers of Fluorine Chemistry*, *ACS Symp. Ser. 639*, American Chemical Society, Washington, DC, 1996, pp. 265–278.

[14] R. Miethchen, C. Hager, M. Hein, *Synthesis*, (1997) 159–161.

[15] R. Miethchen, H. Kowalek, A. Niemann, S. Diele, C. Schick, *Liebigs Ann. Recueil*, (1997) 279–284.

[16] M.D. Burkart, Z. Zhang, S.-C. Hung, C.-H. Wong, *J. Am. Chem. Soc.*, 119 (1997) 11743–11746.

[17] F. Yan, B.V. Nguyen, C. York, T. Hudlicky, *Tetrahedron*, 53 (1997) 11541–11548.

[18] S. Hiraoka, T. Yamazaki, T. Kitazume, *Synlett*, (1997) 669–670.

[19] I. Thomsen, B.V. Ernholt, M. Bols, *Tetrahedron*, 53 (1997) 9357–9364.

[20] T. Brigaud, O. Lefebvre, R. Plantier-Royon, C. Portella, *Tetrahedron Lett.*, 37 (1996) 6115–6116.

[21] J.-B. Behr, C.M. Evina, N. Phung, G. Guillerm, *J. Chem. Soc.*, *Perkin Trans. 1*, (1997) 1597–1599.

[22] T.F. Herpin, W.B. Motherwell, J.-M. Weibel, *J. Chem. Soc.*, *Chem. Commun.*, (1997) 923–924.

[23] P. Munier, A. Krusinski, D. Picq, D. Anker, *Tetrahedron*, 51 (1995) 1229–1244.

[24] C.R. Johnson, D.R. Bhumralkar, E. De Clercq, *Nucleosides Nucleotides*, 14 (1995) 185–194.

[25] G. Foulard, T. Brigaud, C. Portella, *J. Org. Chem.*, 62 (1997) 9107–9113.

[26] R. Miethchen, M. Hein, H. Reinke, *Eur. J. Org. Chem.*, (1998) 919–923.

[27] T. Yamazaki, K. Mizutani, T. Kitazume, in I. Ojima,

J.R. McCarthy, J.T. Welch (Eds.), *Biomedical Frontiers of Fluorine Chemistry*, *ACS Symp. Ser. 639*, American Chemical Society, Washington, DC, 1996, pp. 105–116.
[28] S. Hiraoka, T. Yamazaki, T. Kitazume, *Heterocycles*, 47 (1998) 129–132.
[29] J.G. Riess, J. Greiner, in G. Descotes (Ed.), *Carbohydrates as Organic Raw Materials II*, VCH, Weinheim, 1993.
[30] T. Billard, B.R. Langlois, *Tetrahedron Lett.*, 37 (1996) 6865–6868.
[31] B. Quiclet-Sire, R.N. Saicic, S.Z. Zard, *Tetrahedron Lett.*, 37 (1996) 9057–9058.
[32] T. Billard, S. Large, B.R. Langlois, *Tetrahedron Lett.*, 38 (1997) 65–68.
[33] Z.J. Witczak, *Adv. Carbohydr. Chem. Biochem.*, 44 (1986) 91–145.
[34] Z. Pakulski, D. Pierozynski, A. Zamojski, *Tetrahedron*, 50 (1994) 2975–2992.
[35] P.A. Risbood, T.S. Phillips, L. Goodman, *Carbohydr. Res.*, 94 (1981) 101–107.
[36] E.-P. Barrette, L. Goodman, *J. Org. Chem.*, 49 (1984) 176–178.
[37] J.E.G. Barnett, G.R.S. Atkins, *Carbohydr. Res.*, 25 (1972) 511–515.
[38] P.J. Card, W.D. Hitz, *J. Am. Chem. Soc.*, 106 (1984) 5348–5350.
[39] S.N. Noomen, G.J. Breel, C. Winkel, *Recl. Trav. Chim. Pays-Bas*, 114 (1995) 321–324.
[40] L.D. Hall, D.C. Miller, *Carbohydr. Res.*, 47 (1976) 299–305.
[41] R.N. Russell, T.M. Weigel, O. Han, H.-w. Liu, *Carbohydr. Res.*, 201 (1990) 95–114.
[42] P.A. Levene, E.T. Stiller, *J. Biol. Chem.*, 106 (1934) 421–429.
[43] C.H. Shunk, J.B. Lavigne, K. Folkers, *J. Am. Chem. Soc.*, 77 (1955) 2210–2212.
[44] J.M. García Fernandez, C. Ortiz Mellet, *Sulfur Rep.*, 19 (1996) 61–169.
[45] M.M. Midland, G. Asirwatham, J.C. Cheng, J.A. Miller, L.A. Morell, *J. Org. Chem.*, 59 (1994) 4438–4442.
[46] M.J. Costanzo, H.R. Almond Jr., A.D. Gauthier, B.E. Maryanoff, *Tetrahedron*: *Asymmetry*, 5 (1994) 2459–2473.
[47] B.E. Maryanoff, S.O. Nortey, J.F. Gardocki, R.P. Shank, S.P. Dodgson, *J. Med. Chem.*, 30 (1987) 880–887.
[48] J.-P. Praly, R. Faure, B. Joseph, L. Kiss, P. Rollin, *Tetrahedron*, 50 (1994) 6559–6568.
[49] P.M. Collins (Ed.), *Carbohydrates*, Chapman and Hall, London, 1987, pp. 318–319.
[50] J.R. Sufrin, A.J. Spiess, D.L. Kramer, P.R. Libby, C.W. Porter, *J. Med. Chem.*, 32 (1989) 997–1001.