Radical Trifluoromethylation of a D-Mannose Derived Ketene Dithioacetal. Synthesis of 2-*C*-Trifluoromethyl Derivatives of D-*glycero*-D-*galacto*- and D-*glycero*-D-*talo*-Heptopyranose

G. Foulard, T. Brigaud, and C. Portella*

Laboratoire "Réactions Sélectives et Applications", associé au CNRS (UMR no. 6519), Université de Reims, Faculté des Sciences, B.P. 1039, 51687 Reims Cedex 2, France

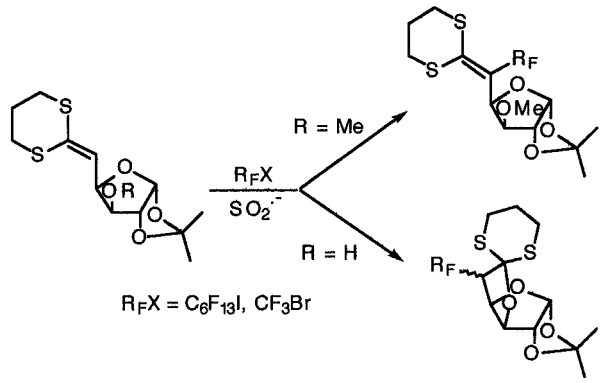
Received July 1, 1997[⊗]

Diacetone D-mannose was converted into ketene dithioacetals **3** by a Peterson reaction with 2-lithio-2-(trimethylsilyl)-1,3-dithiane or lithiobis(methylsulfanyl)(trimethylsilyl)methane. Radical addition of trifluoromethyl bromide (iodide) induced by electron transfer (from sulfoxylate radical anion) led selectively to a dithioketalized 2-deoxy-2-*C*-(trifluoromethyl)-D-*glycero*-D-*galacto*-heptopyranolactone (**5a**) or to the corresponding dithioketalized open sugar **9**, mainly according to the alkylsulfanyl group. Reaction conditions were found for complete or partial dethioketalization of these intermediates. A diisopropylidene-protected 2-deoxy-2-*C*-(trifluoromethyl)-D-*glycero*-D-*talo*-heptopyranolactone (**12**) was obtained from **5a**, with concomitant epimerization of C-2. Compound **9** was converted into either the corresponding sugar **14** or its methyl thioglycoside **13**. Most of these reactions gave preparative yields, and the overall sequence constitutes a three-step synthesis of 2-deoxy-2-*C*-(trifluoromethyl)-D-*glycero*-D-*galacto*-heptose or D-*talo*-heptose derivatives.

Radical addition of perfluoroalkyl iodide to a ω-hydroxy unsaturated alkene may be followed by nucleophilic cyclization into an oxygen heterocycle.[1] This cyclization step is either spontaneous[1a,1b] or needs a further basic treatment.[1b−e] In a preliminary account, we have reported the radical perfluoroalkylation of ketene dithioacetals. Applied to the dithioacetal derived from 1,2-*O*-isopropylidene-α-D-*xylo*-pentodialdo-1,4-furanose, a sugar derivative bearing a free hydroxyl group, this reaction led nonstereoselectively to a mixture of the corresponding cyclic dithioorthoesters, 5-deoxy-5-*C*-(perfluoroalkyl)-D-glucurono- and L-idurono lactone derivatives (Scheme 1).[2] The extension to trifluoromethylation led, with a similar poor stereoselectivity, to the trifluoromethyl analogues.[3] This paper is devoted to the radical trifluoromethylation of a dithioacetal derived from D-mannose, a highly stereoselective reaction which, after further transformations, leads selectively and in a few steps to various derivatives of 2-deoxy-2-*C*-(trifluoromethyl)heptopyranoses.

Fluorine substitution generally modifies strongly the chemical and biological properties of organic compounds, and the literature affords various illustrations in carbohydrates area.[4] Compounds such as 2-deoxy-2-fluoro- and 2-deoxy-2,2-difluoroglycosides are mechanism-based inhibitors of glycosidases, the fluorine atoms at C-2 inhibiting the development of a positive charge at the anomeric center.[5] The same effect could be expected after introduction of a trifluoromethyl group on C-2. Some 3-*C*-(trifluoromethyl)-[6] and 2-*C*-(trifluoromethyl)-D-ribose[7] derivatives have been reported, generally for applications in nucleoside analogues synthesis for antiviral investigations. In the hexose series the synthesis of a 2-*C*-(trifluoromethyl)-D-glucose was recently reported.[8] The method reported here allows both the homologation and the 2-*C*-trifluoromethylation of the diacetone D-mannose.

Scheme 1



Results and Discussion

Preparation of Starting Materials. The starting ketene dithioacetals were prepared from diacetone D-

[⊗] Abstract published in *Advance ACS Abstracts,* November 15, 1997.

(1) (a) Greiner, J; Milius, A; Riess, J. G. *J. Fluorine Chem.* **1992**, *56*, 285−293. (b) Kotora, M.; Hàjek, M.; Ameduri, B.; Boutevin, B. *J. Fluorine Chem.* **1994**, *68*, 49−56. (c) Foulard, G.; Brigaud, T.; Portella, C. *Tetrahedron* **1996**, *52*, 6187−6200. (d) Laurent, P.; Blancou, H.; Commeyras, A. *J. Fluorine Chem.* **1993**, *64*, 125−127. (e) Park, J. D.; Rogers, F. E.; Lacher, J. R. *J. Org. Chem.* **1961**, *26*, 2089−2095.

(2) Bergeron, S.; Brigaud, T.; Foulard, G.; Plantier-Royon, R.; Portella, C. *Tetrahedron Lett.* **1994**, *35*, 1985−1988.

(3) Further transformations of these trifluoromethylated derivatives are under investigation.

(4) (a) Ojima, I.; McCarthy, J. R.; Welch, J. T. *Biomedical Frontiers of Fluorine Chemistry*, ACS Symposium Series 639; American Chemical Society: Washington, DC, 1996. (b) Welch, J. T.; Eswarakrishnan, S. *Fluorine in Bioorganic Chemistry*; John Wiley and Sons, Inc.: New York, 1991. (c) Taylor, N.F. *Fluorinated Carbohydrates. Chemical and Biological Aspects*, ACS Symposium Series 374; American Chemical Society: Washington, DC, 1988. (d) Card, P. J. *J. Carbohydr. Chem.* **1985**, *4*, 451−487.

(5) (a) Stütz, A. E. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1926−1928. (b) Braun, C.; Brayers, G. D.; Withers, S. G. *J. Biol. Chem.* **1995**, *270*, 26778−26781. (c) Namchuk, M.; Braun, C.; McCarter, J. D.; Withers, S. G., see ref 4a, pp 279−293.

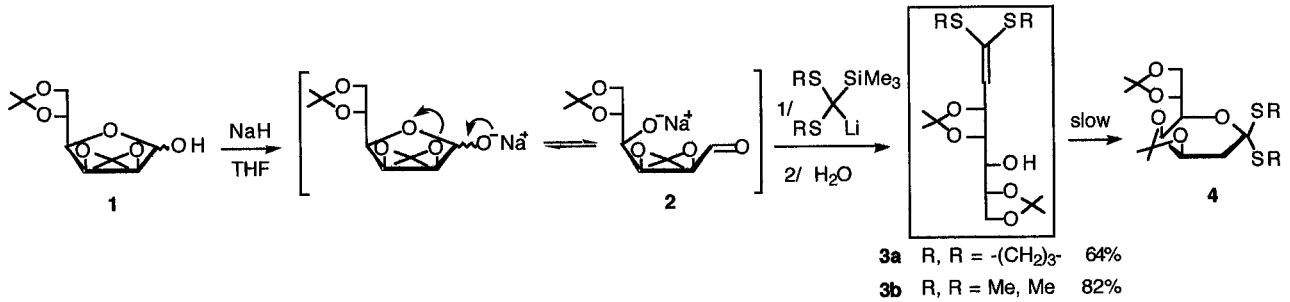
(6) (a) Ueda, S.; Yasumoto, S.; Yamashita, J.; Matsumoto, M.; Tada, T.; Kobayashi, K.; Naguchi, K. Jpn. Kokai Tokkyo Koho, Jp 0272,190 (9072,190) *Chem. Abstr.* **1990**, *113*, 152982m. (b) Morisawa, Y.; Yasuda, A.; Uchida, K. Jpn. Kokai Tokkyo Koho, Jp 02,270,893 (90,270,893); *Chem. Abstr.* **1991**, *114*, 143939w. (c) Johnson, C. R.; Bhumralkar, D. R.; De Clercq, E. *Nucleosides Nucleotides* **1995**, *14*, 185. (d) Lavaire, S.; Plantier-Royon, R.; Portella, C. *J. Carbohydr. Chem.* **1996**, *15*, 361−370.

(7) Schmit, C. *Synlett* **1994**, 241−242. Wucherpfennig, U.; Logothetis, T. A.; Eilitz, U. Burger, K. *Tetrahedron* **1996**, *52*, 143−148.

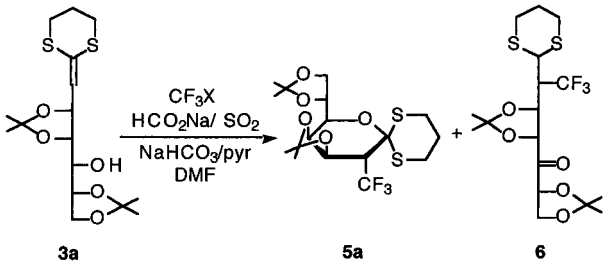
(8) Hiraoka, S.; Yamazaki, T.; Kitazume, T. *Synlett* **1997**, 669−670.

S0022-3263(97)01187-0 CCC: $14.00

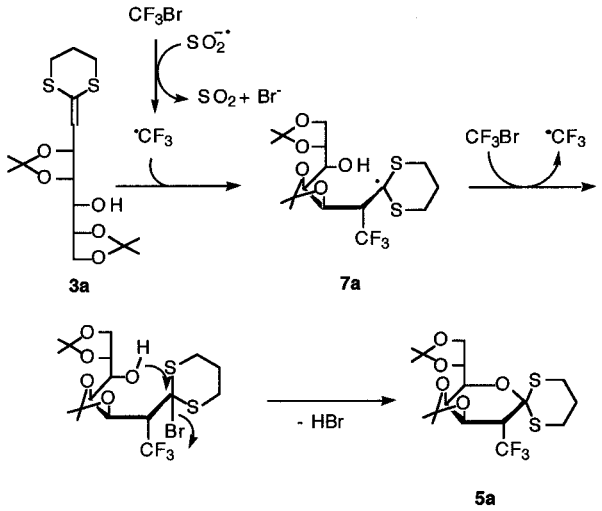
Scheme 2



Scheme 3



Scheme 4



mannose (**1**) according to the reaction pathway depicted in Scheme 2. Treatment of **1** with a base (NaH) allowed the equilibrium with the basic aldehyde **2** which was trapped by the lithio derivative of 2-(trimethylsilyl)-1,3-dithiane or bis(methylsulfanyl)(trimethylsilyl)methane, in a Peterson type reaction. We were gratified by good yields of the corresponding dithioacetals **3a**,**b** (64% and 82%, respectively) as the result of a selective reaction with electrophilic **2**. Moreover, no silicon transfer to the oxygen at C-4 was observed.

The dithioacetals **3** cyclized slowly into the 2-deoxyheptose derivative **4** by a spontaneous intramolecular addition. This cyclization may be slowed by storing **3** with a trace of triethylamine which is easily removed under vacuum before use. Nevertheless compounds **3** were reacted as quickly as possible within a short time after their synthesis.

Radical Trifluoromethylation. The trifluoromethylation of compounds **3** was carried out in an autoclave with an excess (7−10 bar) of trifluoromethyl bromide or trifluoromethyl iodide. The reaction was initiated by single-electron transfer from the sulfoxylate radical anion, itself obtained by reduction of sulfur dioxide with sodium formate.[9] The reaction was performed in the presence of sodium hydrogenocarbonate and pyridine in order to neutralize the halohydric acid released. Better results were observed with added pyridine, probably due to the more homogeneous medium. The results depended essentially on the alkylsulfanyl group and on the amount of reducing agent.

The dithiane derivative **3a** was reacted with trifluoromethyl bromide under the above-described conditions for 15 h to give the results depicted in Scheme 3. An addition−cyclization reaction was the major process leading to the expected protected lactone **5a** (56%) and a minor compound **6** (15%). The reaction is stereoselective: only one diastereomer was isolated for both **5a** and **6**, although the epimer of **5a** at C-2 (<10%) was observed in the ^{19}F NMR spectrum of the crude with a second nonidentified minor compound.

A coupling constant of 8.8 Hz between H-2 and H-3 of compound **5a** (measured after decoupling of H-4) indicated a trans diaxial relationship, with the trifluoromethyl group in the equatorial position. A bromine atom transfer followed by intramolecular nucleophilic substitution leads to **5a** (Scheme 4). The structure of compound **6** was deduced from spectral data: **6** exhibits the characteristic absorptions signals in ^{13}C NMR (208 ppm) and IR (1730 cm^{-1}) of a carbonyl group; the two signals in ^{1}H NMR at 3.66 (multiplet) and 4.47 ppm (doublet) are consistent with the two vicinal protons associated with the CF_3 and dithiane groups, respectively; on the other hand, the mass spectrum exhibits characteristic peaks corresponding to the fragmentation described in Scheme 5.

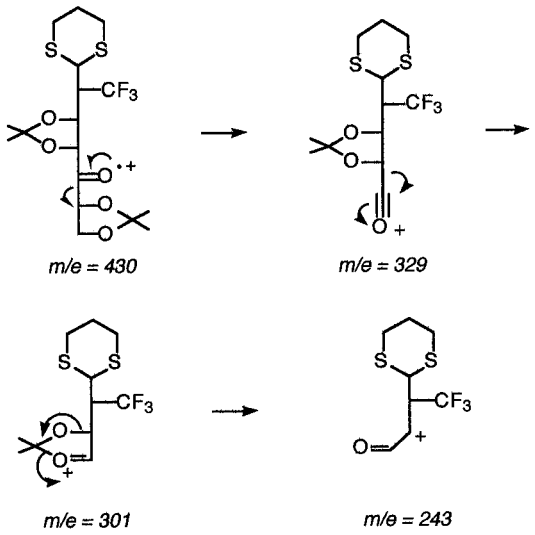
A tentative interpretation of the formation of compound **6** is illustrated in Scheme 6. The first radical adduct **7a** rearranges by an intramolecular 1,5-hydrogen shift leading to the highly oxidizable radical **8** which is transformed, after a back electron transfer (for example to SO_2[10]) and proton transfer, into the compound **6**.

According to this mechanism, the stereochemistry at C-2 is controlled during the radical addition step (as will be shown for the addition to **3b**) and then is assumed to be the same as for **5a**. From such a pathway we reasoned that the selectivity of the reaction toward **5a** could be

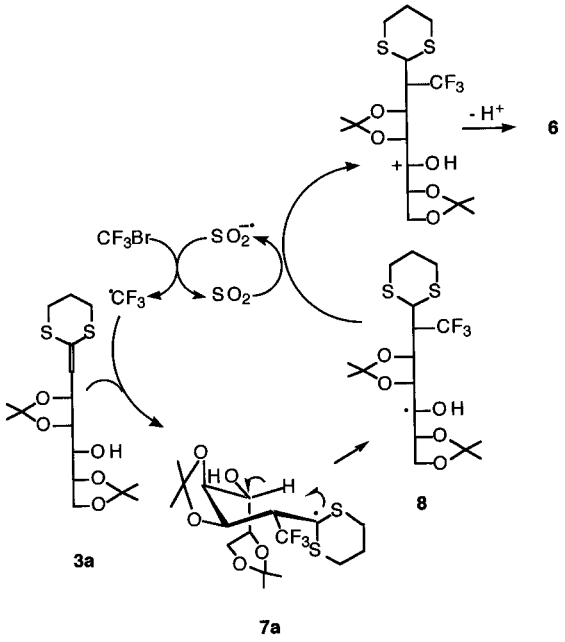
(9) Clavel, J.-L.; Langlois, B.; Nantermet, R.; Tordeux, M.; Wakselman, C. *J. Chem. Soc., Perkin Trans. 1* **1992**, 3371−3375.

(10) Tordeux, M.; Langlois, B.; Wakselman, C. *J. Chem. Soc., Perkin Trans. 1* **1990**, 2293−2299.

Scheme 5



Scheme 6

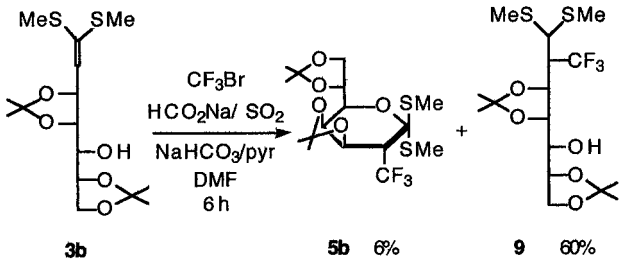


improved with a more competitive halogen transfer to **7a**. Hence, we then carried out the trifluoromethylation reaction with trifluoromethyl iodide, and indeed, the yield of **5a** increased to 75% (accompanied by its diastereomer: 8%)[11] whereas the product **6** resulting from hydrogen transfer decreased to 3% (Scheme 3).

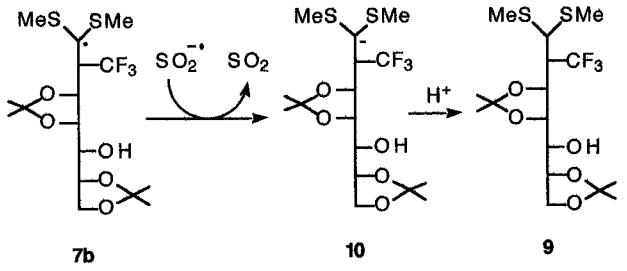
In contrast to the dithiane derivative **3a**, the reaction of the bis(methylsulfanyl) derivative **3b** with trifluoromethyl bromide led selectively, besides the cyclized adduct **5b** (6%), to compound **9** (60%) resulting from a hydrotrifluoromethylation process (Scheme 7).

A high stereoselectivity was also observed in this reaction (we were not able to isolate any other diastereomer). The configuration of C-2 in compound **9** was deduced from that of compound **13** (*vide infra*) assuming that the further transformations did not induce equilibration. Compound **9** probably results from a nonchain process consisting of a second electron transfer to the radical adduct **7b** leading to the sulfur-stabilized anion **10** and then to protonation (Scheme 8). We used an excess of the reducing species as standard reaction conditions for these reactions. When only 1 equiv was used, both the conversion of **3a** and the yield of **9** decreased dramatically. This observation is consistent with the hypothesis of a second electron transfer rather than a hydrogen transfer from the solvent. A remaining question is the different selectivity according to the substitution at sulfur. All other conditions being the same, the hydrotrifluoromethylation pathway should be favored by an increase in the reduction potential of the intermediate radical **7**. If we assume that the methyl subtituents in **7b** have a weaker donating effect than the alkyl type substitution in **7a**, the reduction potential of **7b** is expected to be slightly less negative, allowing a competitive second electron transfer, whereas an atom transfer is the major process for **7a**.

Scheme 7



Scheme 8



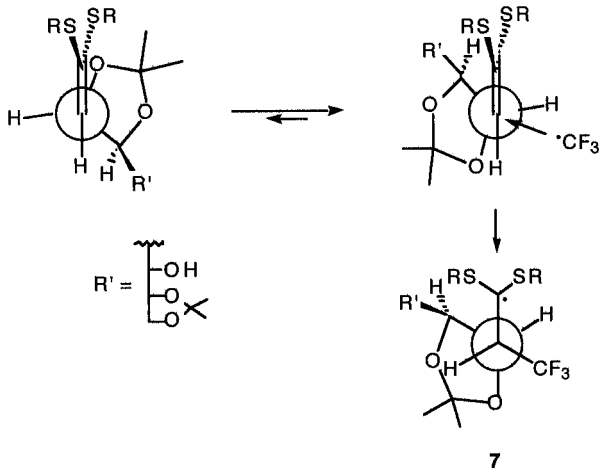
An outstanding feature of these trifluoromethylation reactions is the high stereoselectivity of the radical addition. The examination of the spatial structure of **3** with molecular models revealed that restricted mobility is highly probable owing to the dioxolane moiety and the cis relationship at C-3 and C-4. Furthermore, the C-2−C-3 bond is probably in a *s-trans* conformation to minimize the electronic interactions between the ketene dithioacetal moiety and the oxygens. A transition state like the one depicted in Scheme 9 is consistent with the observed stereoselectivity. The approach of the trifluoromethyl radical via the exo face of the less crowded conformation leads to the obtained *S* configuration at C-2.

Selective Transformation of the Trifluoromethyl Intermediates. The preceding reaction allowed us to have a selective access to derivatives of D-*glycero*-D-*galacto*-heptose, a component of a polysaccharide specific of *Chromobacterium violaceum*,[12] and of the corresponding lactone. We have investigated the reaction conditions liable to selectively remove the dithioacetal moiety and

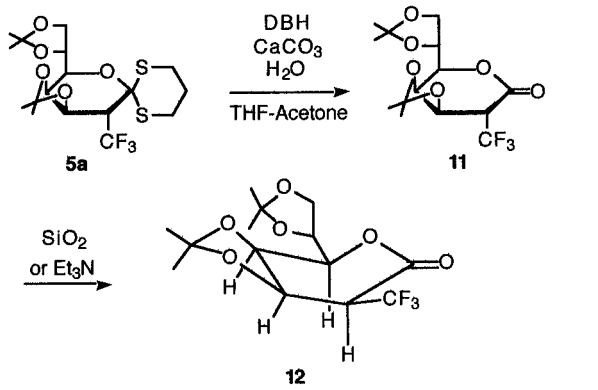
(11) In this experiment we were able to isolate a fraction containing this diastereomer as a major component having the following selected data: ^{19}F NMR δ ppm −62.26 (d, $^3J_{HF}$ = 10.3 Hz); ^{1}H NMR δ ppm 2.52 (dq, $^3J_{HF}$ = 10.3 Hz, $J_{2,3}$ = 1.9 Hz, H-2), 4.75 (dd, $J_{2,3}$ = 1.9 Hz, $J_{3,4}$ = 8.0 Hz, H-3); ^{13}C NMR δ ppm 51.02 (q, $^2J_{CF}$ = 26.9 Hz, C-2), 87.51 (C−1), 124.57 (q, $^1J_{CF}$ = 281 Hz, CF_3).

(12) *Carbohydrates*; Collins, P. M., Ed.; Chapman and Hall: London, 1987; p 269.

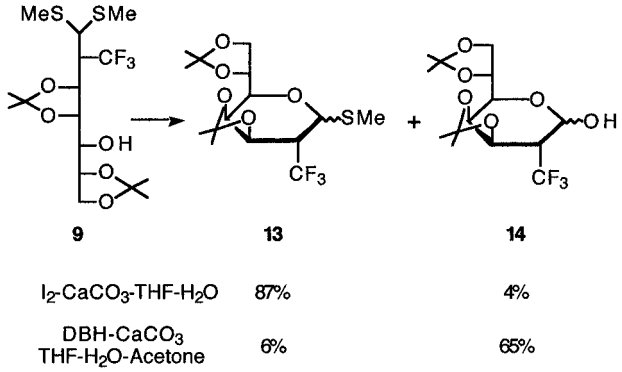
Scheme 9



Scheme 10



Scheme 11



	13	14
I_2-$CaCO_3$-THF-H_2O	87%	4%
DBH-$CaCO_3$ THF-H_2O-Acetone	6%	65%

to preserve the isopropylidene protective groups for an easier isolation and characterization of the products. Hence all reactions were attempted in a buffered medium. The removal of a dithioacetal group is generally not a trivial reaction as shown by the numerous available methods[13] and the continuous interest in the problem. After several attempts with mercuric perchlorate,[14,15] and claycop reagents,[16] which generally gave mixtures of products, we turned our attention to other mild and convenient reagents such as dibromodimethylhydantoin (DBH)[17] and iodine.[18]

The dithiane derivative **5a** reacted with DBH to quantitatively give the corresponding lactone **11** (Scheme 10). This lactone easily equilibrated into the epimeric D-*glycero*-D-*talo*-heptonolactone **12** upon contact with silica gel or treatment with a trace of triethylamine. The usual acidic character of the α-hydrogen in lactones is enhanced here by the trifluoromethyl group, thus explaining this easy epimerization which also implies a stabilization. Since an epimerization leading to an axial trifluoromethyl group is improbable, we have to consider a nonchair conformation. NOESY experiments associated with structural modelization[19] confirmed that **12** exists actually in a boatlike conformation where the trifluoromethyl group is in a pseudoequatorial position and where all axial positions are occupied by the hydrogen (Scheme 10). The coupling constants observed for **11** and **12** are in excellent accordance with the literature data for 2-deoxy-2-substituted-D-*glycero*-D-*galacto* and -D-*talo* analogues.[20]

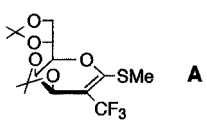
Compound **9** was either completely or partially deprotected according to the experimental conditions. Treatment with iodine as described in Scheme 11 gave the methyl thioglycoside **13** in 87% yield, which can be considered as an activated form of the corresponding sugar.[21] The anomeric mixture was separated to give **13**α and **13**β in a nonreproducible ratio. The thermodynamic ratio was determined by NMR in $CDCl_3$: the pure crystalline major compound **13**α was converted after several days at room temperature into a mixture of **13**α/**13**β = 85/15. The configuration of C-1 and C-2 was determined from the ^{1}H NMR. For the anomer **13**α, the coupling constants between H-2 and H-3 (9.9 Hz) and between H-1 and H-2 (4.8 Hz) are characteristic of a trans diaxial and cis relationship, respectively. The other compound (**13**β) exhibits a coupling constant of 9.2 Hz between H-1 and H-2, in accordance with a β-configuration, but the constant between H-2 and H-3 (6.1 Hz), smaller than that expected for a chair conformation, means a modification of the conformation, due to the bicyclic character of this compound. Indeed some examples found in the literature show the same range of coupling constants for β-thioglycosides containing a 3,4-di-*O*-alkylidene protection in the D-*glycero*-D-galactopyranose series.[22] As mentioned above, the stereochemical assignment of compound **9** was correlated to **13**.

The protected 2-deoxy-2-*C*-(trifluoromethyl)-D-*glycero*-D-*galacto*-heptopyranose **14** was the major product when

(13) Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*, 2nd ed.; Wiley-Interscience: New York, 1991; pp 198−207. Kocienski, P. J. *Protecting Groups*; Thieme Verlag: Stuttgart, 1994; pp 171−184.

(14) Bernardi, R.; Ghiringhelli, D. *J. Org. Chem.* **1987**, *52*, 5021−5022.

(15) From the reaction between **5b** and $Hg(ClO_4)_2 \cdot 3H_2O$ was isolated the unsaturated derivative **A** (14%) beside the lactone **12** (53%). Selected data for **A**: ^{19}F NMR δ ppm −57.3; ^{1}H NMR δ ppm 2.33 (s, SCH_3); ^{13}C NMR δ ppm 12.8 (SCH_3), 103.2 (q, ^2J = 31.5 Hz, C−2), 124.9 (q, ^1J = 272 Hz, CF_3), 159.4 (C−1); MS *m*/*z* (%) 370 (M^+, 13), 195 (100).



A

(16) (a) Balogh, M.; Cornélis, A.; Laszlo, P. *Tetrahedron Lett.* **1984**, *25*, 3313−3316. (b) Cornélis, A.; Lazslo, P. *Synthesis* **1985**, 909−918.

(17) Muzard, M.; Portella, C. *Synthesis* **1992**, 965−968.

(18) Russell, G. A.; Ochrymowycz, L. A. *J. Org. Chem.* **1969**, *34*, 3618−3624. Szarek, W. A.; Zamojski, A.; Tiwari, K. N.; Ison, E. R. *Tetrahedron Lett.* **1986**, *27*, 3827−3830.

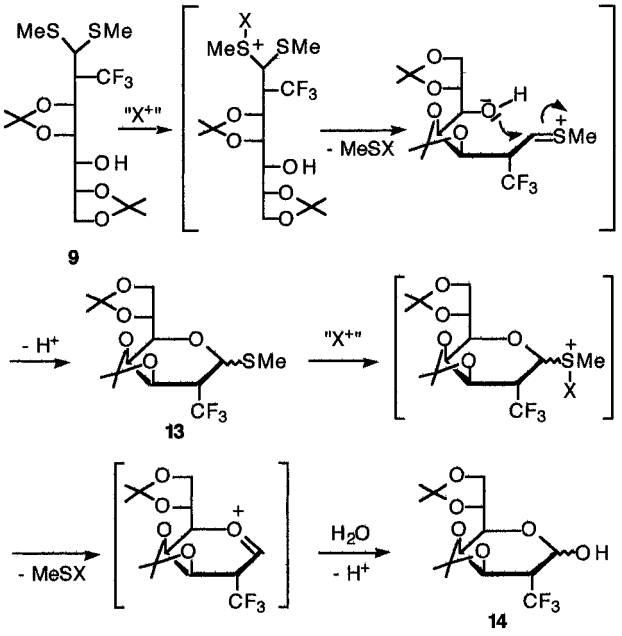
(19) Ourevitch, M.; Foulard, G.; Brigaud, T.; Portella, C. Unpublished results.

(20) Bruce, I.; Fleet, G. W. J.; Girdhar, A.; Haraldsson, M.; Peach, J. M.; Watkin, D. J. *Tetrahedron* **1990**, *46*, 19−32.

(21) Nicolaou, K. C.; Seitz, S. P.; Papahatjis, D. P. *J. Am. Chem. Soc.* **1983**, *105*, 2430−2434 and references therein.

(22) (a) Ziegler, T.; Herold, G. *Liebigs Ann. Chem.* **1994**, 859−866. (b) David, S.; Thieffry, A.; Veyrières, A. *J. Chem. Soc., Perkin Trans 1* **1981**, 1796−1801. (c) Vogel, C; Steffan, W.; Ott, A. Y.; Betaneli, V. I. *Carbohydr. Res.* **1992**, *237*, 115−129.

Scheme 12



9 was reacted with DBH under the conditions indicated in Scheme 11. Less than 10% of **13** was present in the crude product. Separation of the crude on silica gel allowed the isolation of a pure sample of the α-anomer which exhibits coupling constants between H-1 and H-2 (3.1 Hz) and H-3 and H-4 (9.5 Hz) in the same range as those observed for **13**α. The anomeric equilibrium was also established for **14**α/**14**β = 85/15 in $CDCl_3$ at room temperature.

This stepwise dethioketalization of **9** may be explained by the reaction sequence depicted in Scheme 12. The possibility of stopping the reaction at the thioglycoside level **13** is probably a consequence of the cation destabilizing effect of the trifluoromethyl group.

Summary

This study presents a three-step sequence for the stereo- and chemoselective synthesis of protected 2-deoxy-2-*C*-(trifluoromethyl)heptopyranoses from a very simple starting material, the diacetone D-mannose. The first step is the preparation of a ketene dithioacetal (**3**) via a Peterson reaction. The second one is a highly stereoselective radical trifluoromethylation which mainly leads to the dithioketalized heptonolactone **5a** or to the corresponding dithioketalized sugar **9**, according to the sulfur substitution and to the trifluoromethyl halide. In the third step, these intermediates are transformed into the corresponding epimerized lactone **12** and to the corresponding sugar **14** or its thioglycoside **13**, respectively. The new 2-*C*-trifluoromethyl derivatives were fully characterized, and comparison with corresponding 2-substituted sugars showed little or no conformational difference. Chemically, the main property modification induced by the trifluoromethyl group is the enhanced lability of H-2 leading to a very easy epimerization of the lactone derivative **11**.

Experimental Section

General Methods. See ref 1c.

Ketene Dithioacetals 3: General Procedure. A solution of *n*-butyllithium (1.2 equiv) in hexane was added dropwise to a solution of the silyl reagent (1−1.1 equiv) in anhydrous THF (1.9−2.6 mL/mmol) at low temperature (−60 °C for the bis(methylthio)methane, −30 °C for the 1,3-dithiane derivative). The resulting mixture was stirred for 2 h between −30 and −60 °C and then cooled to −78 °C before being slowly added to a prepared solution of **2** (addition of a solution of diacetone D-mannose (**1**) (1 equiv) in THF (1.2 mL/mmol) to a suspension of sodium hydride (1.2 equiv) in THF (20 mL) at 0 °C and stirring for 2 h). The reaction mixture was stirred overnight while the temperature was allowed to rise to room temperature. It was then poured into a saturated aqueous solution of ammonium chloride and extracted with ether or dichloromethane. Combined organic layers were washed with brine and dried over Na_2SO_4. After removal of the solvent, the crude product was submitted to flash chromatography over silica gel to give pure ketene dithioacetal **3**. A few drops of triethylamine could be added to the pure product to avoid its cyclization during storage.

1-Deoxy-1-(1,3-dithian-2-ylidene)-2,3:5,6-di-*O*-isopropylidene-D-mannitol (3a). Yield 64%. Chromatography: petroleum ether−ethyl acetate 4/1. White solid. Recrystallization from petroleum ether: mp 73 °C; ^{1}H NMR δ 1.35 (s, CH_3), 1.41 (s, $C(CH_3)_2$), 1.51 (s, CH_3), 2.12 (d, $^3J_{HH}$ = 8.0 Hz, OH), 2.17 (quint, $^3J_{HH}$ = 6.0 Hz, CH_2), 2.76−3.06 (m, 4H, SCH_2), 3.38 (ddd, $^3J_{HH}$ = 8.0 Hz, $J_{4,5}$ = 7.4 Hz, $J_{3,4}$ = 1.3 Hz, H-4), 3.95−4.08 (m, H-5, H-6, H-6′), 4.38 (dd, $J_{3,4}$ = 1.3 Hz, $J_{2,3}$ = 8.0 Hz, H-3), 5.28 (t, $J_{1,2}$ = $J_{2,3}$ = 8.0 Hz, H-2), 6.12 (d, $J_{1,2}$ = 8.0 Hz, H-1); ^{13}C NMR δ 24.3 (2C, CH_3 and CH_2), 25.3, 26.6, 26.8 (3 × CH_3), 29.0 and 29.4 ($SCH_2CH_2CH_2S$), 66.7 (C-6), 70.3, 74.3, 76.1, 76.3 (C-2, C-3, C-4, C-5), 108.4 and 109.2 ($C(CH_3)_2$), 129.4 (CH=), 134.2 (=$C(SR)_2$); IR (KBr) 3501 (vs), 1115 (s), 1053 (s), 839 (s) cm^{-1}; MS *m/e* (%) 362 (M^+, 27), 347 (32), 246 (39), 203 (41), 128 (100). Anal. Calcd for $C_{16}H_{26}O_5S_2$: C, 53.04; H, 6.91. Found: C, 53.33; H, 7.11.

1,2-Dideoxy-1,1-bis(methylsulfanyl)-3,4:6,7-di-*O*-isopropylidene-D-*manno*-hept-1-enitol (3b). Yield 82%. Chromatography: petroleum ether−ethyl acetate 85/15. **3b**: ^{1}H NMR δ 1.35, 1.39, 1.43, 1.52 (4 s, 2 × $C(CH_3)_2$), 2.13 (d, $^3J_{HH}$ = 8.4 Hz, OH), 2.33 and 2.36 (2 s, $C(SCH_3)_2$), 3.34 (m, H-5), 3.95−4.08 (m, H-6, H-7, H-7′), 4.42 (dd, $J_{3,4}$ = 8.0 Hz, $J_{4,5}$ = 1.3 Hz, H-4), 5.44 (t, $J_{2,3}$ = $J_{3,4}$ = 8.0 Hz, H-3), 5.93 (d, $J_{2,3}$ = 8.0 Hz, H-2); ^{13}C NMR δ 16.64 and 17.08 ($C(SCH_3)_2$), 24.41, 25.28, 26.63, 26.85 (4 s, 2 × $C(CH_3)_2$), 66.76 (C-7), 70.49 (C-6), 75.62, 76.25, 76.50 (C-3, C-4, C-5), 108.40 and 109.24 ($C(CH_3)_2$), 126.02 (CH=), 138.73 (=$C(SR)_2$).

Radical Trifluoromethylations: General Procedure. To a solution of the ketene dithioacetal **3** (2.5−3.5 mmol) in DMF (2.5 mL/mmol) were added sodium hydrogenocarbonate (3 equiv), pyridine (2 equiv), a solution of sulfur dioxide (3−4 M) in DMF (2 equiv), and sodium formate (3 equiv). The autoclave was closed and filled with CF_3Br (8 bar) or precondensed CF_3I (7 equiv) was added at low temperature. Vigorous stirring was maintained for 6 h. The reaction mixture was then poured into a round-bottom flask. Solvent and excess pyridine were removed under vacuum. The residue was diluted in dichloromethane and washed with water. The aqueous layer was extracted three times with CH_2Cl_2. Combined organic extracts were washed with brine and dried over $MgSO_4$. After removal of the solvent, products were separated by flash chromatography using petroleum ether−ethyl acetate as eluant (83/17 for products from **3a**; 90/10 to 85/15 for products from **3b**). Yields are reported in the schemes.

1,2-Dideoxy-3,4:6,7-di-*O*-isopropylidene-1,1-[propylenebis(sulfanediyl)]-2-*C*-(trifluoromethyl)-D-*glycero*-D-*galacto*-heptopyranose (5a). White solid (recrystallization from hexane) mp = 121 °C; ^{1}H NMR (C_6D_6) δ 1.10, 1.23, 1.30, 1.42 (4 s, 2 × $C(CH_3)_2$), 1.30−1.75 (m, CH_2), 1.90−2.10 (m, CH_2), 2.77 (m, 1H, SCH_2), 3.31 (m, 1H, SCH_2), 2.87 (dq, $J_{2,3}$ = 8.8 Hz, $^3J_{HF}$ = 8.4 Hz, H-2), 3.87 (dd, $J_{3,4}$ = 5.3 Hz, $J_{4,5}$ = 2.3 Hz, H-4), 4.02 (dd, J_{AB} = 8.6 Hz, $J_{6,7}$ = 6.3 Hz, H-7), 4.19 (dd, J_{AB} = 8.6 Hz, $J_{6,7'}$ = 5.7 Hz, H-7′), 4.21 (dd, $J_{5,6}$ = 5.7 Hz, $J_{4,5}$ = 2.3 Hz, H-5), 4.41 (q, $J_{5,6} \approx J_{6,7} \approx J_{6,7'}$ = 6 Hz, H-6), 4.45 (dd, $J_{2,3}$ = 8.8 Hz, $J_{3,4}$ = 5.3 Hz, H-3); ^{13}C NMR δ 24.3 (CH_2), 25.3 (CH_3), 25.7 (SCH_2), 26.2, 26.9 (2 × CH_3), 27.4 (SCH_2), 28.1 (CH_3), 53.9 (q, $^2J_{CF}$ = 24.7 Hz, $CH{-}CF_3$), 66.1 (C-7), 70.5 (2C), 71.1, 74.7 (C-3, C-4, C-5, C-6), 86.7 (C-1), 109.0 and 109.7 ($C(CH_3)_2$), 124.9 (q, $^1J_{CF}$ = 282 Hz, CF_3); ^{19}F NMR δ −61.46

(d, $^3J_{HF}$ = 8.4 Hz, CF_3); IR (KBr) 2998, 2936, 2897, 1379, 1254 (vs), 1179 (vs), 1128 (vs), 1053 (vs), 878 cm^{-1}; MS *m/e* (%) 430 (M^+, 35), 415 (19), 357 (22), 341 (67), 163 (60), 106 (100), 74 (81). Anal. Calcd for $C_{17}H_{25}O_5F_3S_2$: C, 47.43; H, 5.85. Found: C, 47.35; H, 5.44.

6,7-Dideoxy-7,7-[propylenebis(sulfanediyl)]-6-*C*-trifluoromethyl-L-*galacto*-hept-3-ulose (6): ^{1}H NMR δ 1.40 (s, $C(CH_3)_2$), 1.44 and 1.48 (2 s, $C(CH_3)_2$), 1.81 (m, 1H, CH_2), 2.08 (m, 1H, CH_2), 2.78−3.02 (m, 4H, SCH_2), 3.66 (ddq, $J_{6,7}$ = 3.4 Hz, $J_{5,6}$ = 6.5 Hz, $^3J_{HF}$ = 8.2 Hz, H-6), 4.16−4.20 (m, 2H, H-1, H-1′), 4.47 (d, $J_{6,7}$ = 3.4 Hz, H-7), 4.75 (t, $J_{5,6} \approx J_{4,5}$ = 6.5 Hz, H-5), 4.83 (t, $^3J_{HH}$ = 6.5 Hz, H-2), 4.99 (d, $J_{4,5}$ = 6.5 Hz, H-4); ^{13}C NMR δ 24.74 (CH_3), 25.22 (CH_2), 25.30 (CH_3), 26.00 (CH_3), 26.22 (CH_3), 30.55 (SCH_2), 31.24 (SCH_2), 44.90 (C-7), 45.81 (q, $^2J_{CF}$ = 25.6 Hz, C-6), 65.79 (C-1), 73.49, 76.88, 78.19 (C-2, C-4, C-5), 110.39 and 110.95 (2 × $C(CH_3)_2$), 125.26 (q, $^1J_{CF}$ = 283 Hz, CF_3), 205.78 (C=O); ^{19}F NMR δ −63.02 (d, $^3J_{HF}$ = 8.8 Hz, CF_3); IR (film) 2997, 2936, 2897, 1730 (vs), 1379, 1258, 1155, 1128 and 1065 (vs), 914, 852 cm^{-1}; MS *m/e* (%) 430 (M^+, 7), 415 (35), 329 (15), 301 (31), 243 (40), 213 (100), 202 (20), 119 (40).

1,2-Dideoxy-3,4:6,7-di-*O*-isopropylidene-1,1-bis(methylsulfanyl)-2-*C*-(trifluoromethyl)-D-*glycero*-D-*galacto*-heptopyranose (5b). White solid: mp 67.5 °C; ^{1}H NMR δ 1.38 and 1.39 (2 s, $C(CH_3)_2$), 1.45 (s, CH_3), 1.51 (s, CH_3), 2.16 (s, SCH_3), 2.17 (s, SCH_3), 2.97 (dq, $^3J_{HF}$ = 8.6 Hz, $J_{2,3}$ = 8.8 Hz, H-2), 4.10 (m, H-7, H-7′), 4.23 (m, H-4), 4.26 (dd, $J_{4,5}$ = 2.5 Hz, $J_{5,6}$ = 5.3 Hz, H-5), 4.42 (dt, $J_{5,6}$ = 5.3 Hz, $J_{6,7} \approx J_{6,7'}$ = 6.1 Hz, H-6), 4.58 (dd, $J_{2,3}$ = 8.8 Hz, $J_{3,4}$ = 5.0 Hz, H-3); ^{13}C NMR δ 11.20 (SCH_3), 12.57 (SCH_3), 25.53, 26.16, 26.60, 28.42 (2 × $C(CH_3)_2$), 50.45 (q, $^2J_{CF}$ = 23.6 Hz, $CH-CF_3$), 65.85 (C-7), 70.19, 70.93, 71.42, 75.06 (C-3, C-4, C-5, C-6), 91.35 ($C(SCH_3)_2$), 109.17 and 109.56 ($C(CH_3)_2$), 124.87 (q, $^1J_{CF}$ = 282 Hz, CF_3); ^{19}F NMR δ −61.35 (d, $^3J_{HF}$ = 8.6 Hz, CF_3); IR (KBr) 2988, 2932, 2903, 2869, 1728 (w), 1379 (vs), 1248 (vs), 1225 (vs), 1175 (vs), 1127 (vs), 1074 (vs), 993, 839, 791 cm^{-1}; MS *m/e* (%) 418 (M^+, 10), 403 (16), 371 (100), 313 (17), 255 (46), 163 (80). Anal. Calcd for $C_{16}H_{25}O_5F_3S_2$: C, 45.92; H, 6.02. Found: C, 46.27; H, 5.99.

1,2-Dideoxy-3,4:6,7-di-*O*-isopropylidene-1,1-bis(methylsulfanyl)-2-*C*-(trifluoromethyl)-D-*glycero*-D-*galacto*-heptitol (9). Oil: $[\alpha]^{24}_D$ = −13 (*c* 0.73, $CHCl_3$); ^{1}H NMR δ 1.36 (s, CH_3), 1.42 (s, $C(CH_3)_2$), 1.53 (s, CH_3), 2.21 (d, $^3J_{HH}$ = 8.4 Hz, OH), 2.24 (s, SCH_3), 2.27 (s, SCH_3), 3.44 (qdd, $^3J_{HF}$ = 9.2 Hz, $J_{2,3}$ = 7.6 Hz, $J_{1,2}$ = 2.7 Hz, H-2), 3.70 (m, H-5), 3.83 (d, $J_{1,2}$ = 2.7 Hz, H-1), 4.04−4.12 (m, H-6, H-7, H-7′), 4.56 (dd, $J_{3,4}$ = 6.9 Hz, $J_{4,5}$ = 1.2 Hz, H-4), 4.66 (dd, $J_{2,3}$ = 7.6 Hz, $J_{3,4}$ = 6.9 Hz, H-3); ^{13}C NMR δ 15.52 (SCH_3), 16.61 (SCH_3), 24.19, 25.28, 26.15, 26.91 (2 × $C(CH_3)_2$), 48.45 (q, $^2J_{CF}$ = 25.6 Hz, $CH-CF_3$), 53.58 (C-1), 66.92 (C-7), 70.58 (C-5), 73.55 (C-3), 76.10 (C-6), 76.15 (C-4), 108.64 and 109.38 ($C(CH_3)_2$), 125.50 (q, $^1J_{CF}$ = 285 Hz, CF_3); ^{19}F NMR δ −62.08 (d, $^3J_{HF}$ = 9.2 Hz, CF_3); IR (film) 3522 (br, OH), 2988 (vs), 2936 (vs), 2923 (vs), 1738, 1435, 1426, 1373 (vs), 1258 (vs), 1215 (vs), 1154 (vs), 1065 (vs), 972, 887, 847 cm^{-1}; MS *m/e* (%) 421 (M + 1, 7), 419 (M − 1, 14), 404 (19), 372 (14), 325 (8), 315 (31), 267 (31), 239 (29), 215 (37), 209 (35), 183 (41), 173 (49), 115 (81). Anal. Calcd for $C_{16}H_{27}O_5F_3S_2$: C, 45.70; H 6.47. Found: C, 45.79; H 6.79.

Transformation of 5a into the Corresponding Lactone. DBH (0.262 g, 0.92 mmol) and $CaCO_3$ (0.230 g, 2.30 mmol) were added to a solution of **5a** (0.198 g, 0.46 mmol) in THF/H_2O/acetone 1/2/1 (6 mL), and the mixture was stirred at 5−10 °C until complete consumption of **5a** (40 min). The solution was then poured into a water/dichloromethane mixture. The aqueous layer was extracted three times with CH_2Cl_2. Combined extracts were washed with aqueous ammonium chloride and dried over Na_2SO_4. After removal of the solvent, crude **11** (0.272 g) was adsorbed on silica gel contained in a chromatography column and left 2 h before elution (petroleum ether−ethyl acetate 85/15) to give the 1,5-heptonolactones **11** and **12** (0.148 g, 94%, **11**/**12** = 8/92). Analytically pure **12** was obtained after recrystallization in hexane.

2-Deoxy-3,4:6,7-di-*O*-isopropylidene-2-*C*-(trifluoromethyl)-D-*glycero*-D-*galacto*-heptono-1,5-lactone (11): ^{1}H NMR δ 1.38 (s, CH_3), 1.40 (s, CH_3), 1.44 (s, $C(CH_3)_2$), 3.60 (qd, $^3J_{HF}$ = 11.1 Hz, $J_{2,3}$ = 1.0 Hz, H-2), 4.09 (dd, J_{AB} = 9.2 Hz, $J_{6,7}$ = 4.2 Hz, H-7), 4.15 (dd, J_{AB} = 9.2 Hz, $J_{6,7'}$ = 5.5 Hz, H-7′), 4.30 (dd, $J_{5,6}$ = 8.4 Hz, $J_{4,5}$ = 1.5 Hz, H-5), 4.39 (m, H-6), 4.66 (dd, $J_{3,4}$ = 7.2 Hz, $J_{4,5}$ = 1.5 Hz, H-4), 4.83 (br d, $J_{3,4}$ = 7.2 Hz, H-3); ^{13}C NMR δ 24.25, 25.01, 26.20, 27.42 (2 × $C(CH_3)_2$), 51.82 (q, $^2J_{CF}$ = 27.6 Hz, $CH-CF_3$), 66.52 (C-7), 70.21, 71.06, 73.03, 76.72 (C-3, C-4, C-5, C-6), 109.97 and 110.44 (2 × $C(CH_3)_2$), 122.93 (q, $^1J_{CF}$ = 281 Hz, CF_3), 161.84 (C=O); ^{19}F NMR δ −63.78 (d, $^3J_{HF}$ = 11.1 Hz, CF_3); IR (film) 2290 (vs), 2940, 1765 (vs), 1375 (vs), 1254 (vs), 1219 (vs), 1181 (vs), 1163 (vs), 1132 (vs), 1074 (vs), 1057 (vs), 843 cm^{-1}; MS *m/e* (%) 341 (M + 1, 17), 325 (100), 283 (11), 267 (42), 163 (72), 155 (29), 123 (32), 115 (70).

2-Deoxy-3,4:6,7-di-*O*-isopropylidene-2-*C*-(trifluoromethyl)-D-*glycero*-D-*talo*-heptono-1,5-lactone (12): white solid (recrystallization from hexane); mp 117 °C; $[\alpha]^{24}_D$ = +53.0 (*c* 0.296, $CHCl_3$); ^{1}H NMR δ 1.38, 1.40, 1.45, 1.47 (4 s, 2 × $C(CH_3)_2$), 3.26 (dq, $^3J_{HF}$ = 7.6 Hz, $J_{2,3}$ = 2.7 Hz, H-2), 3.97 (dd, $J_{4,5}$ = 1.7 Hz, $J_{5,6}$ = 8.2 Hz, H-5), 4.07 (dd, J_{AB} = 9.5 Hz, $J_{6,7}$ = 3.8 Hz, H-7), 4.15 (dd, J_{AB} = 9.5 Hz, $J_{6,7'}$ = 5.7 Hz, H-7′), 4.42 (ddd, $J_{5,6}$ = 8.2 Hz, $J_{6,7}$ = 3.8 Hz, $J_{6,7'}$ = 5.7 Hz, H-6), 4.74 (dd, $J_{3,4}$ = 7.8 Hz, $J_{4,5}$ = 1.7 Hz, H-4), 4.98 (dd, $J_{2,3}$ = 2.7 Hz, $J_{3,4}$ = 7.8 Hz, H-3); ^{13}C NMR δ 24.36, 24.96, 25.78, 27.03 (2 × $C(CH_3)_2$), 47.77 (q, $^2J_{CF}$ = 28.2 Hz, $CH-CF_3$), 66.52 (C-7), 70.92 (C-3), 72.18, 72.43 (C-4, C-6), 77.72 (C-5), 110.08 and 111.56 (2 × $C(CH_3)_2$), 123.08 (q, $^1J_{CF}$ = 279 Hz, CF_3), 162.19 (C=O); ^{19}F NMR δ −66.31 (d, $^3J_{HF}$ = 7.6 Hz, CF_3); IR (KBr) 2298 (w), 2944 (w), 2901 (w), 1757 (vs), 1381, 1279, 1246, 1213 (vs), 1177, 1154, 1121, 1076, 1034, 947 cm^{-1}; MS *m/e* (%) 340 (M^+, 10), 325 (M − 15, 100), 267 (M − 58, 21), 163 (15). Anal. Calcd for $C_{14}H_{19}O_6F_3$: C, 49.41; H, 5.63. Found: C, 49.52; H, 5.50.

Conversion of 9 into the Thioglycosides 13 and the Sugar 14. 1,2-Dideoxy-3,4:6,7-di-*O*-isopropylidene-1-(methylsulfanyl)-2-*C*-(trifluoromethyl)-D-*glycero*-D-*galacto*-heptopyranoside (13). $CaCO_3$ (0.150 g, 1.50 mmol) and diiodine (0.381 g, 1.50 mmol) were added to a solution of **9** (0.210 g, 0.50 mmol) in a mixture of THF/H_2O 4/1 (6.5 mL) at rt and stirred for 1 h 30 min. The reaction mixture was washed with aqueous $Na_2S_2O_3$. The aqueous layer was extracted three times with CH_2Cl_2. Combined extracts were washed with aqueous NH_4Cl and dried over $MgSO_4$. After removal of the solvent, the ^{19}F NMR spectrum of the crude product showed both **13** and **14** (**13**/**14** ≈ 95/5). Flash chromatography (petroleum ether-ethyl acetate 87/13) led to **13** (0.162 g, 87%, **13**α /**13**β = 85/15) which was partially separated to give pure samples of **13**α and **13**β. **13**α: white solid; mp 76 °C; $[\alpha]^{24}_D$ = +178 (*c* 1.03, $CHCl_3$); ^{1}H NMR δ 1.38 (s, $C(CH_3)_2$), 1.44 (s, CH_3), 1.51 (s, CH_3), 2.08 (s, SCH_3), 2.92 (ddq, $^3J_{HF}$ = 8.5 Hz, $J_{2,3}$ = 9.9 Hz, $J_{1,2}$ = 4.8 Hz, H-2), 4.00 (dd, J_{AB} = 8.8 Hz, $J_{6,7}$ = 4.6 Hz, H-7), 4.08 (dd, J_{AB} = 8.8 Hz, $J_{6,7'}$ = 6.1 Hz, H-7′), 4.24 (dd, $J_{3,4}$ = 4.8 Hz, $J_{4,5}$ = 2.3 Hz, H-4), 4.36 (dd, $J_{4,5}$ = 2.3 Hz, $J_{5,6}$ = 6.9 Hz, H-5), 4.41 (m, H-6), 4.46 (dd, $J_{2,3}$ = 9.9 Hz, $J_{3,4}$ = 4.8 Hz, H-3), 5.28 (d, $J_{1,2}$ = 4.8 Hz, H-1); ^{13}C NMR δ 13.08 (SCH_3), 25.29, 26.29, 26.70, 28.23 (2 × $C(CH_3)_2$), 47.30 (q, $^2J_{CF}$ = 25.6 Hz, $CH-CF_3$), 66.49 (C-7), 68.26, 69.41, 71.53, 74.44 (C-3, C-4, C-5, C-6), 79.55 (C-1), 109.21 and 109.59 (2 × $C(CH_3)_2$), 125.20 (q, $^1J_{CF}$ = 282 Hz, CF_3); ^{19}F NMR δ −65.85 (d, $^3J_{HF}$ = 8.5 Hz, CF_3); IR (KBr) 2992 (vs), 2950, 2926, 2896, 1680, 1387 (vs), 1372 (vs), 1346 (vs), 1283, 1221 (vs), 1125 (vs), 1082 (vs), 1047 (vs), 1038, 1020, 882, 847 cm^{-1}; MS *m/e* (%) 372 (M^+, 7), 357 (35), 325 (22), 267 (100), 209 (91), 163 (67), 115 (66). Anal. Calcd for $C_{15}H_{23}O_5F_3S$: C, 48.38; H, 6.22. Found: C, 48.17; H, 6.05. **13**β: white solid; mp 63.5 °C; $[\alpha]^{21}_D$ = −3.3 (*c* 0.8, $CHCl_3$); ^{1}H NMR δ 1.37 (s, CH_3), 1.39 (s, CH_3), 1.43 (s, CH_3), 1.52 (s, CH_3), 2.23 (s, SCH_3), 2.62 (ddq, $^3J_{HF}$ = 9.3 Hz, $J_{1,2}$ = 9.2 Hz, $J_{2,3}$ = 6.1 Hz, H-2), 3.51 (dd, $J_{5,6}$ = 7.6 Hz, $J_{4,5}$ = 2.1 Hz, H-5), 4.03 (dd, J_{AB} = 8.8 Hz, $J_{6,7}$ = 4.6 Hz, H-7), 4.10 (dd, J_{AB} = 8.8 Hz, $J_{6,7'}$ = 6.1 Hz, H-7′), 4.29 (dd, $J_{3,4}$ = 6.1 Hz, $J_{4,5}$ = 2.1 Hz, H-4), 4.35 (ddd, $J_{5,6}$ = 7.6 Hz, $J_{6,7'}$ = 6.1 Hz, $J_{6,7}$ = 4.6 Hz, H-6), 4.45 (t, $J_{2,3} = J_{3,4}$ = 6.1 Hz, H-3), 4.50 (d, $J_{1,2}$ = 9.2 Hz, H-1); ^{13}C NMR δ 13.20 (SCH_3), 25.32, 25.73, 27.01, 27.51 (2 × $C(CH_3)_2$), 48.34 (q, $^2J_{CF}$ = 25.2 Hz, $CH-CF_3$), 66.73 (C-7), 70.65 (C-4), 71.54 (C-3), 74.10 (C-6), 76.50 (C-5), 79.52 (C-1), 109.46 and 110.06 (2 × $C(CH_3)_2$), 125.60 (q, $^1J_{CF}$ = 280 Hz, CF_3); ^{19}F NMR δ −67.35 (d, $^3J_{HF}$ = 9.3 Hz, CF_3); MS *m/e* (%) 372 (M^+, 21), 357 (56), 325 (56), 299

(17), 266 (92), 209 (100), 163 (52); IR (KBr) 2992, 2932, 2907, 2863, 1385 (vs), 1370 (vs), 1254 (vs), 1219, 1175 (vs), 1156, 1127 (vs), 1082, 1051, 1024 (vs), 878, 851, 694, 519 cm^{-1}. Anal. Calcd for $C_{15}H_{23}O_5F_3S$: C, 48.38; H 6.22. Found: C, 48.60; H 6.31.

2-Deoxy-3,4:6,7-di-*O*-isopropylidene-2-*C*-(trifluoromethyl)-D-*glycero*-D-*galacto*-heptopyranose (14). $CaCO_3$ (0.402 g, 4.02 mmol) and DBH (0.421 g, 1.47 mmol) were successively added to a solution of dithioacetal **9** (0.282 g, 0.67 mmol) in THF/H_2O/acetone 1/2/1 (8.5 mL) at 5 °C. The mixture was stirred for 3 h and slowly warmed to rt. An additional amount of DBH (0.057 g, 0.2 mmol) was added to complete the transformation of the thioglycoside **13** detected in the medium by TLC. After completion of the reaction, the mixture was poured into a mixture water/dichloromethane. The aqueous layer was extracted three times with CH_2Cl_2. Combined extracts were washed with aqueous ammonium chloride and dried over Na_2SO_4. After removal of the solvent, the ^{19}F NMR spectrum of the crude product showed the presence of both **13** and **14** (**13**/**14** < 10/90). Flash chromatography (petroleum ether−ethyl acetate 4/1) gave a first fraction containing mainly thioglycoside **13** (18 mg), the next one contained pure **14**α (69 mg, 30%) and the third one was a mixture of **14**α and **14**β (80 mg, 35%, **14**α/**14**β = 70/30). Total yield of **14** = 65%. **14**α: white solid; mp 141 °C; ^1H NMR δ 1.38 (s, CH_3), 1.39 (s, CH_3), 1.44 (s, CH_3), 1.51 (s, CH_3), 2.54 (qddd, $^3J_{HF}$ = 8.6 Hz, $J_{2,3}$ = 9.5 Hz, $J_{1,2}$ = 3.05 Hz, $^4J_{HH}$ = 1.5 Hz, H-2), 3.54 (br s, OH), 4.02 (dd, J_{AB} = 8.8 Hz, $J_{6,7}$ = 5.3 Hz, H-7), 4.08 (dd, J_{AB} = 8.8 Hz, $J_{6,7'}$ = 6.1 Hz, H-7′), 4.22−4.43 (m, H-4, H-5), 4.39 (m, H-6), 4.62 (dd, $J_{2,3}$ = 9.5 Hz, $J_{3,4}$ = 5.0 Hz, H-3), 5.47 (dd, $J_{1,2}$ = 3.05 Hz, $^3J_{HH}$ = 3.8 Hz, H-1); ^{13}C NMR δ 25.26, 26.39, 26.70, 28.23 (2 × C(CH_3)$_2$), 47.06 (q, $^2J_{CF}$ = 24.4 Hz, $CH-CF_3$), 66.36 (C-7), 67.30, 69.06, 71.20, 74.62 (C-2, C-3, C-4, C-5), 89.80 (C-1), 109.33 and 109.66 (2 × $C(CH_3)_2$), 125.67 (q, $^1J_{CF}$ = 280 Hz, CF_3); ^{19}F NMR δ −66.76 (d, $^3J_{HF}$ = 8.6 Hz, CF_3); MS *m/e* (%) 343 (M+1, 10), 327 (100), 269 (36), 209 (20), 163 (23), 115 (63); IR (KBr) 3333 (br, OH), 2996, 2909, 1460, 1387, 1377, 1350, 1275 (vs), 1246, 1223 (vs), 1167 (vs), 1134 (vs), 1042, 860, 804 cm^{-1}. Anal. Calcd for $C_{14}H_{21}O_6F_3$: C, 49.12; H, 6.18. Found: C, 49.16; H, 5.96. **14**β: ^1H NMR δ 2.42 (dq, $^3J_{HF}$ = 8.8 Hz, $J_{2,3}$ = 8.0 Hz, H-2), 4.81 (dd, $J_{2,3}$ = 8.0 Hz, $J_{3,4}$ = 6.1 Hz, H-3); ^{13}C NMR δ 50.83 (q, $^2J_{CF}$ = 23.6 Hz, $CH-CF_3$), 93.01(C-1); ^{19}F NMR δ −66.84 (d, $^3J_{HF}$ = 8.8 Hz, CF_3).

Acknowledgment. We thank the Ministère de l′Education Nationale de l′Enseignement Supérieur et de la Recherche for a fellowship (G.F.) and the Conseil Général de la Marne for financial support.

JO971187O