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Studies on Organic Fluorine Compounds. XLVII.[1] Synthesis of Trifluoromethylated Sugars through the Aldol Reaction of 2-Trimethylsilyloxy-4-trifluoromethylfuran

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Lewis acid-catalyzed aldol condensation of 2-trimethylsilyloxy-4-trifluoromethylfuran (**2a**) with aldehydes was found to proceed in a regio- and diastereoselective manner to give the 5-substituted 4-trifluoromethyl-2(5*H*)-furanone (**4**) in good yield. The aldol product (**4a**) derived from benzyloxyacetaldehyde was successfully converted to the branched sugar (**12**), the first reported example of a trifluoromethylated branched sugar, and its crystal structure was determined by X-ray analysis.

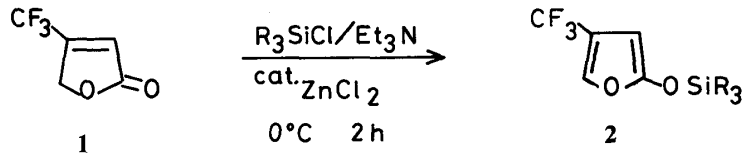
Keywords——2-trimethylsilyloxy-4-trifluoromethylfuran; 5-substituted 4-trifluoromethyl-2(5*H*)-furanone; aldol condensation; 3-trifluoromethylgulose; 3-trifluoromethyltalose

The synthetic utility of 2-silyloxyfuran derivatives, which have potential reactivities in the aldol condensation with carbonyl compounds or in the Diels–Alder reaction with dienophiles, has been reported.[2–6] In the course of our studies on the development of synthetic methods for trifluoromethylated compounds, directed toward fluorine-modified bioactive compounds such as lactones or sugars, we have investigated synthetic reactions based on 3-trifluoromethyl-Δ^2-butenolide (**1**)[1] as a building unit for trifluoromethylated molecules.

In this paper, we report the Lewis acid-catalyzed aldol reaction of silyloxyfuran (**2a**) (derived from **1**) with aldehydes, providing condensation products with high regio- and diastereoselectivity. Furthermore, the aldol product (**4a**) derived from benzyloxyacetaldehyde was successfully converted to branched sugars (**12** and **13**), the first reported examples of trifluoromethylated branched sugars. The crystal structure of **12** was determined by X-ray analysis, the result of which confirmed the *threo* selectivity in the aldol reaction of **2a** with benzyloxyacetaldehyde (**7c**).

Synthesis of 2-Trialkylsilyloxy-4-trifluoromethylfuran

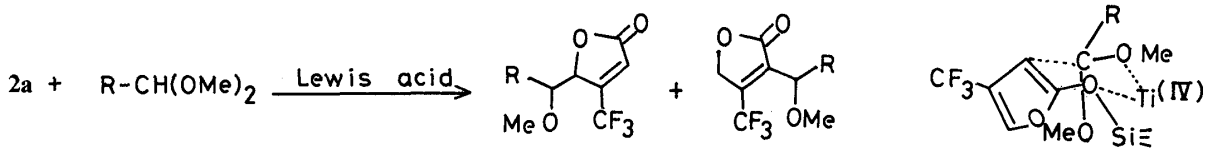
Under basic conditions the butenolide (**1**) was found to be unstable and gave a complex mixture. Therefore, **1** should be converted to a reactive compound which can be used under



1 → **2**

2a: R=Me 71%
2b: R=Et 63%

Chart 1



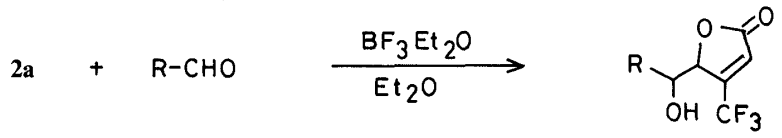
3a: R=Ph
3b: R=$PhCH_2CH_2$

4 **5** **6**

Chart 2

TABLE I. Reaction of **2a** with Acetals

Lewis acid	Acetal	Solvent	Temp (°C), (time, h)	4:5	Yield (%)
$TiCl_4$	**3a**	CH_2Cl_2	−78 (0.4)	Only **5**	26
$TiCl_4$	**3a**	CH_2Cl_2	−78 (3)	1:4	62
$TiCl_4$	**3a**	Et_2O	r.t (1)	1:1	56
BF_3Et_2O	**3a**	CH_2Cl_2	−78 (1.5)	1:1	36
BF_3Et_2O	**3a**	Et_2O	r.t (2)	2:1	78
$TiCl_4$	**3b**	CH_2Cl_2	−78 (3)	No reaction	
BF_3Et_2O	**3b**	Et_2O	r.t (3)	No reaction	



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4c: R=$BnOCH_2$ 74%
4d: R=n-C_6H_{13} 83%
4e: R=$PhCH_2CH_2$ 73%

Chart 3

acidic reaction conditions for the aldol reaction.

The silyloxyfuran derivatives (**2**) were obtained in moderate yields by treating **1** with trialkylchlorosilane and triethylamine in the presence of a catalytic amount of zinc chloride in dry ether (Chart 1). Since **2a** is immediately desilylated on contact with water, it was purified by distillation from the reaction mixture. In contrast, the triethyl derivative (**2b**) is rather stable to moisture and can be purified through extractive work-up. The reactivity of **2a** in aldol reactions is much higher than that of **2b**, as expected.

Aldol Reaction of 2a with Acetals and Aldehydes

The silyloxyfuran (**2a**) was found to react with acetals and aldehydes in the presence of a Lewis acid. To examine the effects of solvent and Lewis acid on the regioselectivity, we investigated the reaction of **2a** with acetals under a variety of reaction conditions. The results are summarized in Table I. The α-adduct (**5**) was predominant in the case of titanium tetrachloride ($TiCl_4$) in dichloromethane. The formation of the α-adduct can presumably be explained in terms of the cyclic transition state (**6**), which was proposed for the $TiCl_4$-catalyzed aldol reaction of silylenol ether with acetals or aldehydes in dichloromethane.[7,8] On the other hand, in the case of $BF_3 \cdot OEt_2$ in ether, the γ-adduct (**4**) was predominant.

On the basis of the above results, an attempt was made to react **2a** with aldehyde (**7**) in the presence of $BF_3 \cdot OEt_2$ in ether to prepare the corresponding γ-adduct (**4**). Thus, the reaction of **2a** with benzyloxyacetaldehyde (**7c**) and $BF_3 \cdot OEt_2$ (0.4 mol eq) in ether at 0 °C for 16 h gave only the γ-adduct (**4c**) in 74% yield as a single diastereoisomer. In a similar manner, the reaction of **2a** with heptanal (**7d**) and 3-phenylpropanal (**7e**) afforded the corresponding γ-

adduct (**4d** and **4e**, respectively). The adducts **4d** and **4e** were each identified as a single diastereoisomer from their proton nuclear magnetic resonance (^{1}H-NMR) and fluorine nuclear magnetic resonance (^{19}F-NMR) spectra, although their relative stereochemistry was unknown.

Compared with the reported example,[2-4] in which 2-silyloxyfuran without or with an electron-donating substituent such as an alkyl or methoxyl group at the 4-position reacted with acetals or aldehydes to give γ-adducts exclusively, the electron-with-drawing character of the trifluoromethyl group of **2a** affected the regioselectivity and the reactivity, since in the case of aliphatic aldehyde acetal (**3b**), no adduct was formed. Moreover, these examples were reported to proceed without stereoselectivity to give a diastereoisomeric mixture.

The *threo* configuration at C-5 and C-6 of **4c** was confirmed by X-ray analysis of the sugar derivative (**12**) derived from **4c** as described below, in addition to an NMR study of the lactone compound derived from **4c**[9]

Synthesis of 3-Trifluoromethylgulofuranose (12) and 3-Trifluoromethyltalofuranose (13)

The aldol product **4c** seems to be suitably functionalized for the synthesis of hexose derivatives. Thus, we attempted to introduce a protective group at the hydroxyl function and to generated a vicinal diol function at the trifluoromethylated double bond.

Under basic reaction conditions, benzylation (NaH-$C_6H_5CH_2Br$), methoxymethylation (NaH-CH_3OCH_2Cl) and silylation (2,6-lutidine-*tert*-$BuMe_2SiCl$) of **4c** were unsuccessful, resulting in the formation of complex mixtures. Treatment of **4c** with acetic anhydride and pyridine did not give the acetylated compound, but the olefinic product (**14**) in 69% yield. Thus, several attempts were made under acidic conditions.

Treatment of **4c** with an excess amount of dimethoxymethane in the presence of P_2O_5 in dichloromethane gave the methoxymethylated compound (**8**) in quantitative yield.[10]

Diisobutylaluminum hydride (DIBAL-H) reduction of **8** followed by the reaction of the resultant hemiacetal (**9**) with isopropanol in the presence of pyridinium *p*-toluenesulfonate gave the two isopropyl 3-trifluoromethyl-2,3-dideoxyhex-2-enofuranosides (**10** and **11**) in a ratio of 1.6:1, and these could be separated by silica gel column chromatography. At this stage the relative stereochemistry at C-1 and C-4 of **10** or **11** was unknown.

Introduction of the vicinal diol function into **10** or **11** was achieved by reaction with potassium permanganate in aqueous ethanol. Thus, the reaction of **10** with 1 mol eq of $KMnO_4$ in aqueous ethanol at 0 °C for 2 h gave the 3-trifluoromethylhexofuranoside (**12**) as crystals in 56% yield. Similarly, **11** gave the isomeric compound (**13**) in 47% yeild. The

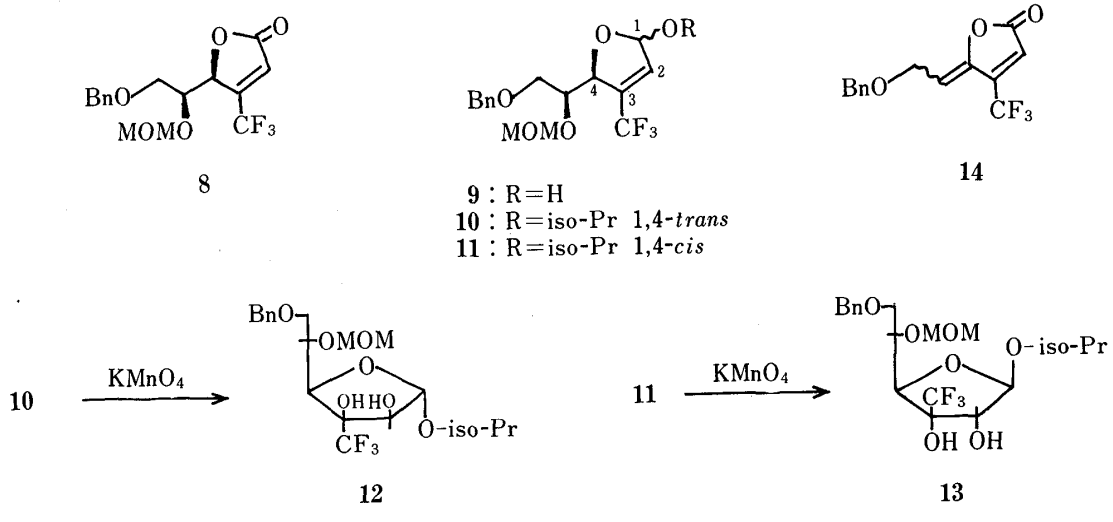

Chart 4

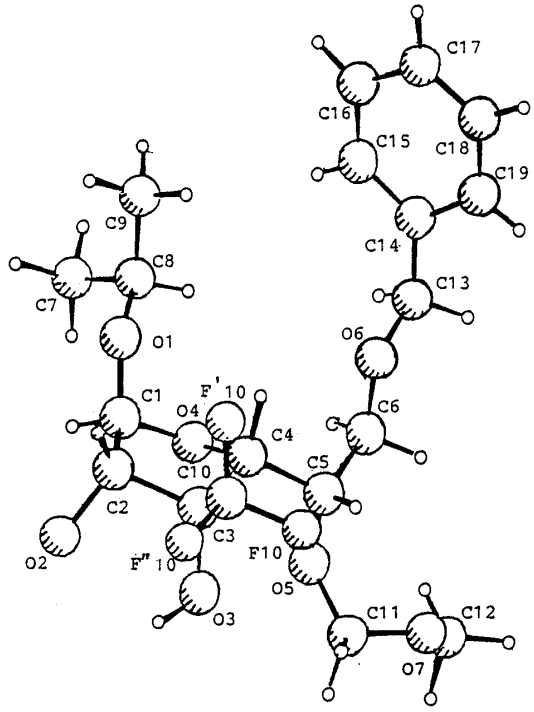

Fig. 1. Molecular Structure of **12**

structure of **12** was confirmed as (±)-isopropyl 6-*O*-benzyl-3-trifluoromethyl-5-*O*-methoxymethyl-α-gulofuranoside by X-ray analysis (Chart 4). This result shows that the relative stereochemistry at C-1 (Oiso-Pr) and C-4 (side chain) in the 2,3-dideoxyhex-2-enofuranoside (**10**) is *trans*, and demonstrates the *threo* configuration for the C-4 oxygen and C-5 oxygen functions. The former result suggests that permanganate attacks the double bond from the less-hindered side with respect to the isopropoxyl group at C-1, but not the side chain at C-4. The latter result supports the *threo*-selectivity in the aldol reaction of **2a** with benzyloxyacetaldehyde (**7c**). On the basis of these results, we tentatively deduced that the hexafuranoside (**13**) is (±)-isopropyl 6-*O*-benzyl-3-trifluoromethyl-5-*O*-methoxymethyl-β-talofuranoside. These two new branched sugars are the first reported examples of trifluoromethyl analogs, to our knowledge.

In conclusion, although the generality and the mechanistic aspects of the aldol reaction of the silyloxyfuran (**2a**) require further study, the potential synthetic utility of **2a** as a building unit for trifluoromethylated compounds seems clear. The synthesis of optically active trifluoromethylated sugars is now being investigated by using chiral aldehydes in the aldol reaction.

Experimental

Melting points were taken on a hot-stage microscope (Yanagimoto) and are uncorrected. Infrared (IR) spectra were recorded using a Jasco IRA-1 spectrophotometer. ^{1}H-NMR spectra were recorded on Varian EM 390L and JEOL FX-200 spectrometers. Chemical shifts are reported in parts per million (PPM) on the δ scale relative to tetramethylsilane as an internal standard. ^{19}F-NMR spectra were recorded on Varian EM 360L spectrometer. Chemical shifts are reported in parts per million relative to benzotrifluoride as an external standard, and a plus sign indicates high field. Mass spectra (MS) were recorded on Hitachi RMU-7L instrument.

4-Trifluoromethyl-2-trimethylsilyloxyfuran (2a)——Under an argon atmosphere, a mixture of chlorotrimethylsilane (2.6 g, 24 mmol) and triethylamine (2.4 g, 24 mmol) in ether (10 ml) was added to a solution of 4-trifluoromethyl-2(5*H*)-furanone (3.0 g, 20 mmol) and anhydrous zinc chloride (10 mg) in ether (15 ml), and the reaction mixture was stirred for 2 h at 0 °C. After removal of the solvent under a vacuum (*ca.* 80 mmHg, room temperature), the residue was flash-distilled (3 mmHg, 30 °C) into a trap cooled in a dry ice-acetone bath. The distillate was diluted with *n*-pentane and the precipitates were filtered off. The filtrate was subjected to Kugelrohr distillation to give **2a** (3.1 g, 71%). **2a**: bp 100—115 °C/100 mmHg. ^{1}H-NMR ($CDCl_3$) δ: 0.24 (9H, s, $SiMe_3$), 5.22

(1H, s, 3-H), 7.08 (1H, q, J=2.8 Hz, 5-H). ^{19}F-NMR ($CDCl_3$) δ: −3.5 (d, J=2.8 Hz).

The triethyl derivative (**2b**) was prepared in a similar manner. **2b**: bp 112 °C/42 mmHg. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3135, 2960, 2880, 1640, 1590, 1200—1100, 950, 840. ^{1}H-NMR ($CDCl_3$) δ: 0.50—1.17 [15H, m, $Si(CH_2CH_3)_3$], 5.29 (1H, s, 3-H), 7.13 (1H, q, J_{H-F}=1.8 Hz, 5-H). ^{19}F-NMR ($CDCl_3$) δ: −3.6 (d, J_{H-F}=1.8 Hz). MS m/z: 266 (M^+), 237.

Reaction of 2a with Benzaldehyde Dimethylacetal (3a)——Under an argon atmosphere, a catalytic amount of $TiCl_4$ (3 drops) was added to a mixture of **2a** (220 mg, 1.03 mmol) and benzaldehyde dimethylacetal (**3a**) (160 mg, 1.05 mol) in dichloromethane at −78 °C (dry ice–acetone bath), and the reaction mixture was stirred at the same temperature for 3 h, then diluted with water and extracted with ether. After being dried over $MgSO_4$, the extract was concentrated *in vacuo* and the residue was chromatographed on a silica gel column (*n*-hexane–AcOEt 10 : 1) to give 166 mg (62%) of a mixture of the α-adduct (**5a**) and the γ-adduct (**4a**). Further separation of this mixture was achieved by using medium-pressure liquid chromatography (MPLC) to give pure **5a** and **4a**.

4a: Pale yellow oil. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1800, 1180—1070. ^{1}H-NMR ($CDCl_3$) δ: 3.25 (3H, s, OCH_3), 4.60 (1H, br s, 5-H), 5.27 (1H, br s, CH-Ph), 6.61 (1H, m, 3-H), 7.47 (5H, s, aromatic-H). ^{19}F-NMR ($CDCl_3$) δ: −0.2 (s). MS m/z: 272 (M^+), 240.212. High-resolution MS: Calcd for $C_{12}H_7F_3O_2$ ($M^+ - CH_3OH$) 240.0397. Found: 240.0393.

5a: Pale yellow oil. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1780, 1080. ^{1}H-NMR ($CDCl_3$) δ: 3.40 (3H, s, OCH_3), 4.88 (2H, m, 5-H), 5.40 (1H, br s, CH-Ph), 7.30—7.78 (5H, m, aromatic-H). ^{19}F-NMR ($CDCl_3$) δ: −4.0 (s). MS m/z: 272 (M^+), 240, 212. High-resolution MS: Calcd for $C_{13}H_{11}F_3O_3$ 272.0659. Found: 272.0649.

4-Trifluoromethyl-5-(2-benzyloxy-1-hydroxy)ethyl-2(5*H*)-furanone (4c)——Under an argon atmosphere, $BF_3 \cdot OEt_2$ (100 μl, 0.8 mmol) was added to a solution of **2a** (550 mg, 2.45 mmol) and benzyloxyacetaldehyde (400 mg, 2.67 mmol) in ether (10 ml) at 0 °C, and the reaction mixture was stirred for 16 h, poured into ice-water, and extracted with ether. The extract was successively washed with $NaHCO_3$ solution and brine, then dried over $MgSO_4$ and concentrated *in vacuo*. The residue was chromatographed on a silica gel column (*n*-hexane–AcOEt 4 : 1) to give **4c** (547 mg, 74%) as a colorless oil. **4c**: IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3630—3200, 1800, 1780, 1190, 1160. ^{1}H-NMR ($CDCl_3$) δ: 3.70 (2H, d, J=6.6 Hz, $BnOCH_2$), 4.18 (1H, t, J=6.6 Hz, CH–OH), 4.20 (1H, br s, –OH), 4.62 (2H, s, $PhCH_2O$), 5.35 (1H, s, 5-H), 6.62 (1H, m, 3-H), 7.42 (5H, s, aromatic-H). ^{19}F-NMR ($CDCl_3$) δ: −0.1 (s). MS m/z: 302 (M^+), 272, 264, 254. High-resolution MS: Calcd for $C_{14}H_{13}F_3O_4$: 302.0765. Found: 302.0796.

4-Trifluoromethyl-5-(1-hydroxy)heptyl-2(5*H*)-furanone (4d)——In a manner similar to that used for the preparation of **4c**, the reaction of **2a** (300 mg, 1.34 mmol), *n*-heptanal (230 mg, 2.02 mmol) and $BF_3 \cdot OEt_2$ (100 μl) in ether (5 ml) gave **4d** (277 mg, 83%) as a colorless oil. **4d**: IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600—3240, 1780. ^{1}H-NMR ($CDCl_3$) δ: 1.06—1.88 [13H, m, $CH_3(CH_2)_5$], 2.15 (1H, br s, OH), 4.00 (1H, t, J=6 Hz, CH–OH), 5.17 (1H, br s, 5-H), 6.62 (1H, m, 3-H). ^{19}F-NMR ($CDCl_3$) δ: 0 (s). MS m/z: 267 (M^+), 180, 179. High-resolution MS: Calcd for $C_{12}H_{17}F_3O_2$: 266.1128. Found: 266.1106.

4-Trifluoromethyl-5-(1-hydroxy-3-phenyl)propyl-2(5*H*)-furanone (4e)——The reaction of **2a** (300 mg, 1.34 mmol), 3-phenylpropanal (220 mg, 1.64 mmol) and $BF_3 \cdot OEt_2$ (100 μl) in ether (5 ml) gave **4e** (280 mg, 73%) as colorless crystals. **4e**: mp 114—117 °C (from benzene). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600—3280, 1770. ^{1}H-NMR ($CDCl_3$) δ: 1.66 (1H, d, J= 8 Hz, OH), 2.06 [2H, m, –CH$_2$–CH(OH)–], 2.82 (2H, m, $PhCH_2$), 4.01 (1H, dd, J=8 and 13 Hz, CH–OH), 5.12 (1H, s, 5-H), 6.57 (1H, m, 3-H), 7.28 (5H, br s, aromatic-H). ^{19}F-NMR ($CDCl_3$) δ: −0.13 (s). MS m/z: 286 (M^+), 268.152. High-resolution MS: Calcd for $C_{14}H_{13}F_3O_3$: 286.0816. Found: 286.0824.

4-Trifluoromethyl-5-(2-benzyloxy-1-methoxymethoxy)ethyl-2(5*H*)-furanone (8)——Powdered P_2O_5 (total 300 mg) was added portionwise to a solution of **4c** (300 mg, 1 mmol) and dimethoxymethane (2 ml) in dichloromethane (5 ml) at room temperature, and the reaction mixture was stirred for 30 min at room temperature, then poured into ice-water and extracted with dichloromethane. The organic extract was successively washed with $NaHCO_3$ solution and brine, then dried over $MgSO_4$ and concentrated *in vacuo* to give **8** (340 mg, 98%) as a pale yellow oil. **8**: IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1800, 1780, 1200—1000. ^{1}H-NMR ($CDCl_3$) δ: 3.30 (3H, s, OCH_3), 3.78 (2H, m, $BnOCH_2$), 4.10 (1H, s, CHOMOM), 4.60 (4H, s, $PhCH_2$ and OCH_2OMe), 5.54 (1H, s, 5-H), 6.61 (1H, m, 3-H), 7.41 (5H, s, aromatic-H). ^{19}F-NMR ($CDCl_3$) δ: −0.7 (s). MS m/z: 346 (M^+), 301.

DIBAL-H Reduction of 8——Under an argon atmosphere, **8** (300 mg, 0.87 mmol) was treated with DIBAL-H (1.2 eq, *n*-hexane solution) in ether (5 ml) for 2 h at −78 °C. Then water (1 ml) was added and the reaction mixture was stirred for 1 h at room temperature. The precipitates were filtered off through Celite and washed with ether. The filtrate was dried over $MgSO_4$ and then chromatographed on a silica gel column (*n*-hexane–AcOEt 3 : 1) to give **9** (250 mg, 83%), which exists as an anomeric mixture in $CDCl_3$ (ratio 4 : 3) as judged from the integrals of the olefinic proton signals in its ^{1}H-NMR spectrum. **9**: Colorless oil. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3560—3200. ^{1}H-NMR ($CDCl_3$) δ: 3.32 (s, OCH_3), 5.18 (s, 5-H), 6.46 (m, 3-H) for one isomer; 3.36 (s, OCH_3), 5.36 (br s, 5-H), 6.55 (m, 3-H) for the other isomer. MS m/z: 330 ($M^+ - H_2O$), 303, 285. High-resolution MS: Calcd for $C_{16}H_{17}F_3O_4$ ($M^+ - H_2O$): 330. 1077. Found: 330.1058.

***trans*- and *cis*-4-Trifluoromethyl-5-(2-benzyloxy-1-methoxymethoxy)ethyl-2-isopropyloxy-2,5-dihydrofuran (10 and 11)**——A mixture of the hemiacetal **9** (400 mg, 1.15 mmol) and pyridinium *p*-toluenesulfonate (*ca.* 10 mg) in isopropanol (10 ml) was heated at 70—80 °C for 4 h. The reaction mixture was poured into water and extracted with ether. The extract was dried over $MgSO_4$, and concentrated *in vacuo*, and the residue was chromatographed on a silica gel column (*n*-hexane–AcOEt 6 : 1) to give **10** (186 mg, 42%) as a colorless oil. **10**: IR $\nu_{max}^{CCl_4}$ cm^{-1}: 2980, 2900,

1380, 1330, 1200—1000. ^{1}H-NMR ($CDCl_3$) δ: 1.20 (3H, d, J=6.6 Hz, $CHCH_3$), 1.30 (3H, d, J=6.6 Hz, $CHCH_3$), 3.34 (3H, s, OCH_3), 3.73 (2H, d, J=6 Hz, $BnOCH_2$), 3.98 (1H, sept, J=6.6 Hz, $-CHMe_2$), 3.96 (1H, t, J=6 Hz, CHOMOM), 4.60 (2H, s, $PhCH_2$), 4.70 (2H, s, $-OCH_2O-$), 5.33 (1H, br s, 5-H), 6.05 (1H, m, 2-H), 6.40 (1H, s, 3-H), 7.42 (5H, s, aromatic-H). ^{19}F-NMR ($CDCl_3$) δ: −1.8 (s). MS *m/e*: 358 ($M^+ - CH_3OH$), 330.

Further elution with the same solvent gave **11** (117 mg, 26%) as a colorless oil.

11: IR $\nu_{max}^{CCl_4}$ cm^{-1}: 2980, 2900, 1370, 1300, 1200—1000. ^{1}H-NMR ($CDCl_3$) δ: 1.17 (3H, d, J=6 Hz, $>CH-C\underline{H}_3$), 1.20 (3H, d, J=6 Hz, $>CH-C\underline{H}_3$), 3.73 (3H, s, OCH_3), 3.72 (2H, d, J=7.5 Hz, $BuOCH_2$), 3.93 (1H, t, J=7.5 Hz, >CHOMOM), 4.00 (1H, m, $-CHMe_2$), 4.58 (2H, s, $PhCH_2O$), 4.74 (2H, d, J=2.4 Hz, $-OCH_2O-$), 5.30 (1H, br s, 5-H), 5.93 (1H, m, 2-H), 6.38 (1H, m, 3-H), 7.40 (5H, s, aromatic-H). ^{19}F-NMR ($CDCl_3$) δ: −1.95 (s). MS *m/z*: 330 (M^+ − iso-PrOH).

(±)-Isopropyl 6-*O*-Benzyl-3-trifluoromethyl-5-*O*-methoxymethyl-α-gulofuranoside (12)——An aqueous solution (2 ml) of $KMnO_4$ (80 mg, 0.5 mmol) was added dropwise to a solution of **10** (190 mg, 0.49 mmol) in ethanol (10 ml) at 0 °C, and the reaction mixture was stirred for 2 h at 0 °C. The methanol (10 ml) was added, and the whole was warmed at 60 °C for 20 min to precipitate MnO_2. The precipitates were filtered off through Celite, and the filtrate was concentrated *in vacuo*. The residue was chromatographed on a silica gel column (MPLC, *n*-hexane–AcOHt 2 : 1) to give **10** (58 mg, 30% recovery) and **12** (116 mg, 56%) as colorless crystals.

12: mp 61—63 (from *n*-hexane). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600—3160, 1380, 1220—960. ^{1}H-NMR ($CDCl_3$) δ: 1.17 [6H, d, J=6.4 Hz, $-CH(C\underline{H}_3)_2$], 3.29 (1H, d, J=8.6 Hz, OH), 3.43 (3H, s, OCH_3), 3.66 (1H, dd, J=9.8 and 6.4 Hz, 6-H), 3.77 (1H, dd, J=9.8 and 5.9 Hz, 6-H), 3.86 (1H, sept, J=6.4 Hz, $CHMe_2$), 4.19 (1H, dd, J=8.5 and 2 Hz, 2-H), 4.31 (1H, t d, J=5.8 and 2.2 Hz, 5-H), 4.37 (1H, d, J=2.2 Hz, 4-H), 4.54 (2H, s, $PhCH_2$), 4.80 (1H, d, J=6.3 Hz, $-OCH_2O-$), 4.89 (1H, d, J=6.3 Hz, $-OCH_2O-$), 5.08 (1H, d, J=2 Hz, 1-H), 6.00 (1H, s, OH), 7.32 (5H, s, aromatic-H). ^{19}F-NMR ($CDCl_3$) δ: +14.5 (s). *Anal.* Calcd for: $C_{19}F_{27}F_3O_7$: C, 53.77; H, 6.41; F, 13.43. Found: C, 53.56; H, 6.38; F, 13.64.

(±)-Isopropyl 6-*O*-Benzyl-3-trifluoromethyl-5-*O*-methoxymethyl-β-talofuranoside (13)——In a manner similar to that described for the preparation of **12**, reaction of **11** (126 mg, 0.32 mmol) and $KMnO_4$ (51 mg, 0.32 mmol) gave **13** (64 mg, 47%), with some recovery of **12** (30 mg, 30%). **13**: colorless oil. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600—3200, 1380, 1200—1000, 980. ^{1}H-NMR ($CDCl_3$) δ: 1.18 (3H, d, J=5.8 Hz, $>CHC\underline{H}_3$), 1.21 (3H, d, J=5.8 Hz, $>CHC\underline{H}_3$), 3.35 (3H, s, OCH_3), 3.38 (1H, br s, OH), 3.70 (1H, dd, J=9.6 and 6.3 Hz, 6-H), 3.82 (1H, dd, J=9.6 and 4.9 Hz, 6-H), 3.93 (1H, ddd, J=6.3, 5.4 and 4.9 Hz, 5-H), 3.94 (1H, sept, J=6.1 Hz), 4.18 (1H d, J=5.4 Hz, 4-H), 4.28 (1H, d, J=4.4 Hz, 2-H), 4.28 (1H, br s, OH), 4.56 (2H, s, $PhCH_2$), 4.67 (1H, d, J=6.8 Hz, $-OCH_2O-$), 4.75 (1H, d, J=6.8 Hz, $-OCH_2O-$), 4.97 (1H, d, J=4.4 Hz, 1-H), 7.33 (5H, s, aromatic-H). ^{19}F-NMR ($CDCl_3$) δ: +11.2 (s). MS *m/z*: 392 ($M^+ - CH_3OH$), 379, 319. *Anal.* Calcd for $C_{19}H_{27}F_3O_7$: C, 53.77; H, 6.41. Found: C, 53.38; H, 6.28.

X-Ray Study of 12——A transparent colorless platy crystal of **12** grown in *n*-hexane solution was used for the X-ray study. The crystal data are: isopropyl 6-*O*-benzyl-3-trifluoromethyl-5-*O*-methoxymethyl-α-gulofuranoside, $C_{19}H_{27}O_7F_3$, M_r=424.4, orthorhombic, space group $Pna2_1$, z=4, D_{calc}=1.341 g cm^{-3}, a=11.002 (6), b=20.184 (10), c=9.462 (6) Å, U=2101 Å^3. We obtained 1943 out of 2550 possible reflections in the 2θ range of 6° through 156° using graphite-monochromated CuK_α radiation. The crystal structure was determined by the direct method and refined to an R value of 0.085, including 26 H atoms (HO3 bonded to 03 was not found on the different map).[12] The molecular structure is illustrated in Fig. 1, which was drawn by using the PLUTO program.[13] No abnormal bond lengths or angles were found in the structure. The C–F bond lengths were in the range of 1.31—1.37 Å. As is clear from Fig. 1, O1 and C5 are linked to the furanose ring with α-configuration and the oxygen atoms at C4 and C5 are in *threo* configuration. The isopropyl and benzyloxy side chains extend from C1 and C5 in such a way that the C2–C1–O1–C8–C9 chain and the O5–C5–C6–O6–C13–C14 chain adopt nearly *trans* planar conformations. The methoxymethyl group at C5, on the other hand, is strongly folded. The torsional angles are: ——C5 $\overset{116°}{}$ O5 $\overset{-72°}{}$ C11 $\overset{-71°}{}$ O7——C12.

References and Notes

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13) PLUTO, Cambridge Crystallographic Data Centre, University Chemical Laboratory, Leusfield Road, Cambridge CB2 1EW, U. K.