Organofluorine Compounds and Fluorinating Agents. 27 [1]

New Trifluoromethyl Substituted 1,2,3-Triazoles Linked to *D*-Galactose and *D*-Gulose

Christian Hager, Ralf Miethchen*, and **Helmut Reinke**

Rostock, Fachbereich Chemie, Lehrstuhl Organische Chemie II, Universität

Received, January 26th, 2000, respectively March 14th, 2000

Dedicated to Professor Dr. Peter Gründler on the Occasion of his 60th Birthday

Keywords: Azides, Carbohydrates, Fluorine, Heterocycles, 1,2,3-Triazoles

Abstract. The title compounds were synthesized by 1,3-dipolar cycloaddition of 3,3,3-trifluoropropinyl benzene (**2**) to the azido sugars 2,3,4,6-tetra-*O*-acetyl-β-*D*-galactopyranosyl azide (**1**), 6-*O*-acetyl-4-*O*-cyclohexylcarbamoyl-2,3-*O*-(2,2,2-trichloroethylidene)-β-*D*-gulopyranosyl azide (**6**), 6-azido-6-deoxy-1,2:3,4-di-*O*-isopropylidene-α-*D*-galactopyranose (**12**), and methyl 6-azido-4-*O*-cyclohexylcarbamoyl-6-deoxy-2,3-*O*-(2,2,2-trichloroethylidene)-β-*D*-gulopyranoside (**16**), respectively. Because of the dissymmetry of the dipolarophile **2**, always two regioisomeric products were obtained, the nucleoside-analogous compounds **3**/**4** (from **1**) and **7**/**8** (from **6**), respectively, and the reversed nucleosides **13**/**14** (from **12**) and **17**/**18** (from **16**), respectively. Protecting group chemistry like transesterification, deacetalation, hydrodechlorination is demonstrated in some cases. Thus, the trichloroethylidene derivatives **7**, **8**, **17**, and **18** were converted into the corresponding ethylidene derivatives (**9**, **10**, **19**, **20**) by treatment with tributylstannane/AIBN. An X-ray analysis is given for the 1-(2,3,4,6-tetra-*O*-acetyl-β-*D*-galactopyranosyl)-4-trifluoromethyl-5-phenyl-1,2,3-triazole (**4**) and for the 1-[6-*O*-acetyl-4-*O*-cyclohexylcarbamoyl-2,3-*O*-(2,2,2-trichloroethylidene)-β-*D*-gulopyranosyl]-4-trifluoromethyl-5-phenyl-1,2,3-triazole (**7**).

Various 1,2,3-triazole derivatives are biologically active [2, 3], among them also nucleoside-analogous compounds like *N*-glycosylated 4-halomethyl 1*H*- or 2*H*-1,2,3-triazoles. The latter show bactericide and viricide action [4–6] or are usable as radiomimetic substances [7]. The properties of such mimetic products may be commonly influenced by modifications of the heterocyclic but also of the carbohydrate moiety.

An effective method of preparation for 1,2,3-triazole–based nucleoside analogues and reversed nucleoside analogues, respectively, is the 1,3-dipolar cycloaddition starting from azidosugars. Some examples were reported in the literature [8–11]; (see ref. [12] as well). Recently, we synthesised fluorinated 1,2,3-triazole–based reversed nucleoside analogues by 1,3-dipolar cycloaddition from azido-deoxy sugar derivatives (*D*-galactose, *D*-altrose) and *(E)*-1-(F-alkyl)-2-phenylsulfonyl-ethenes [1]. As everybody knows, fluorine atoms or trifluoromethyl groups strategically positioned in target molecules may greatly modify their properties, biological activity and selectivity; for typical examples see ref. [13–17].

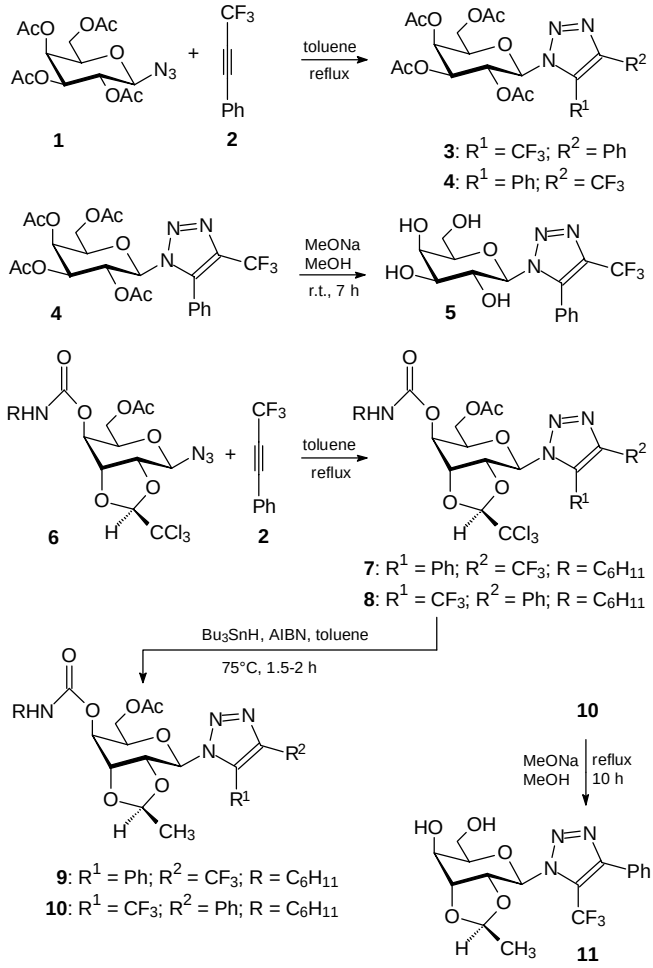
In this paper we report on 1,3-dipolar cycloadditions of sugar azides (*D*-galactose and *D*-gulose) with 3,3,3-trifluoropropinyl-benzene. This dipolarophile was already used by Meazza and Zanardi [18] to synthesise various aryl-trifluoromethyl-1,2,3-triazoles from aromatic azides.

Results and Discussion

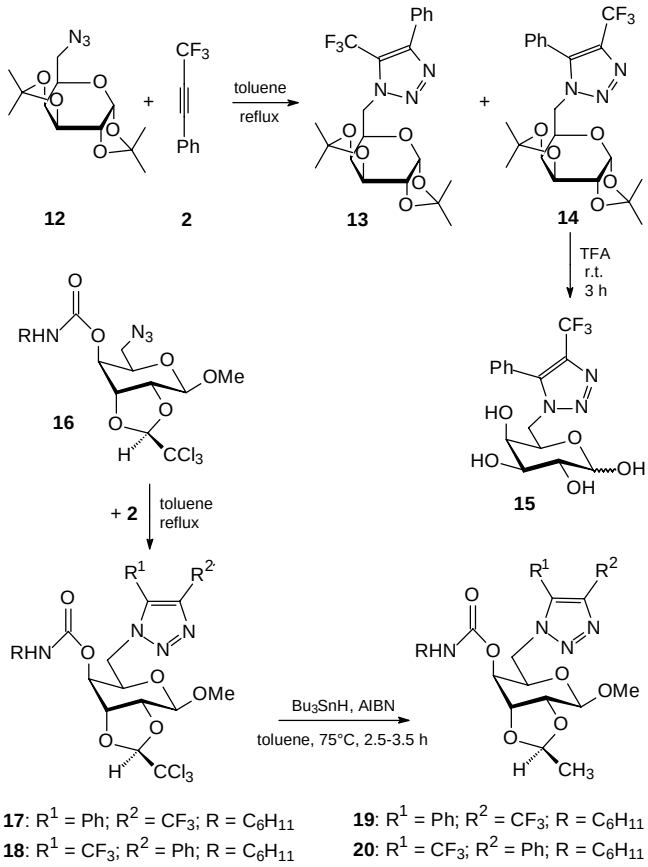
1,3-Dipolar cycloadditions of 2,3,4,6-tetra-*O*-acetyl-β-*D*-galactopyranosyl azide (**1**) [19], 6-*O*-acetyl-4-*O*-cyclohexylcarbamoyl-2,3-*O*-(2,2,2-trichloroethylidene)-β-*D*-gulopyranosyl azide (**6**) [20], 6-azido-6-deoxy-1,2:3,4-di-*O*-isopropylidene-α-*D*-galactopyranose (**12**) [21], and methyl 6-azido-4-*O*-cyclohexylcarbamoyl-6-deoxy-2,3-*O*-(2,2,2-trichloroethylidene)-β-*D*-gulopyranoside (**16**) [22] with 3,3,3-trifluoropropinyl-benzene (**2**) [23] were carried out by refluxing the reactants in toluene; Schemes 1 and 2.

In order to achieve a complete conversion of the azido sugars, an excess of 3,3,3-trifluoropropinyl-benzene (**2**) was required. However, non-specific side reactions occurred due to the relatively long reaction times (10–19 h) and a reaction temperature of 110 °C. They were indicated by carbonisation of the solutions and could be only partially suppressed by working under an argon atmosphere. Nevertheless, the two expected major products, 4-trifluoromethyl-5-phenyl and 5-trifluoromethyl-4-phenyl-1,2,3-triazole, were obtained in good yields (Tab. 1). Thus, 2,3,4,6-tetra-*O*-acetyl-β-*D*-galactopyranosyl azide (**1**) and 3,3,3-trifluoropropinyl-benzene (**2**) yielded the 5-trifluoromethyl-4-phenyl-1,2,3-triazole derivative **3** and its 4-trifluoromethyl-5-phenyl regioisomer **4** after 14 h refluxing. After separation by

  1436-9966/99/3410X-414 $ 17.50 + .50/0



Scheme 1 Trifluoromethyl substituted nucleoside-analogous 1,2,3-triazoles



Scheme 2 Trifluoromethyl substituted reversed nucleoside-analogous 1,2,3-triazoles

HPLC, the compounds were isolated in yields of 30% (**3**) and 49% (**4**), respectively.

The results of the cycloadditions of 6-*O*-acetyl-4-*O*-cyclohexylcarbamoyl-2,3-*O*-(2,2,2-trichloroethylidene) -*β*-*D*-gulopyranosyl azide (**6**), 6-azido-6-deoxy-1,2:3,4-di-*O*-isopropylidene-*α*-*D*-galactopyranose (**12**), and methyl 6-azido-4-*O*-cyclohexylcarbamoyl-6-2,3-deoxy-*O*-(2,2,2-trichloroethylidene)-*β*-*D*-gulopyranoside (**16**) with 3,3,3-trifluoropropinyl-benzene **2** are summarised in Tab.1, Scheme 1 and Scheme 2. Two regioisomeric trifluoromethyl-1,2,3-triazoles are formed as found for azi-de **1**. It is noteworthy that cycloadditions of sugar azides with *(E)*-1-(F-alkyl)-2-phenylsulfonyl-ethenes yield only a single isomer – the corresponding 4-(F-alkyl)-1,2,3-triazole derivative [1]; see also ref. [11, 24].

The assignment of the structures of the regioisomeric pairs **3**/**4**, **7**/**8**, **13**/**14**, and **17**/**18** based on ^{1}H NOE measurements, ^{19}F NMR data, and X-ray analyses. Thus, the 4-trifluoromethyl-5-phenyl-1,2,3-triazole derivative **4** shows, in contrast to its regioisomer **3**, couplings between 1-H of the sugar moiety and the phenyl protons. G. Meazza, G. Zanardi [18] reported that trifluoromethyl groups linked to a 1,2,3-triazole ring show a characteristic alteration of their chemical shifts in ^{19}F NMR spectra in dependence of their location. ^{19}F signals of trifluoromethyl groups in 4-position are shifted 2–4 ppm to higher field than those of trifluoromethyl groups lo-

Tab. 1 1,3-Dipolar cycloadditions of **1**, **6**, **12**, and **16** with 3,3,3-trifluoropropinyl-benzene (**2**)

Azide	Reaction time (h)	Yield (%) [a]	Ratio of the isomeric products	^{19}F NMR data of the products (δ/ppm) 5-CF_3	4-CF_3
1	14	79	**3** : **4** = 1 : 1.6	−55.5 (**3**)	−59.2 (**4**)
6	19	78	**8** : **7** = 1 : 1.5	−56.2 (**8**)	−59.1 (**7**)
12	13	82	**13** : **14** = 1 : 1.4	−55.5 (**13**)	−58.9 (**14**)
16	10	83	**18** : **17** = 1 : 1.5	−55.5 (**18**)	−59.0 (**17**)

[a]) After column chromatographic separation

cated in 5-position [18]. The same applies to all pairs of regioisomers described in this paper (Table 1). Moreover, the structures of the crystalline 4-trifluoromethyl isomers **4** (Fig. 1) and **7** (Fig. 2) could be confirmed by X-ray analyses. The Puckering parameters (Q = 0.525 Å, θ = 19.0°, φ = 342°) indicate a conformation between an ideal $^4C_1$-chair, an ^OE-half boat and an $^OH_5$-half chair conformation for the β-*D*-gulopyranosyl rest of **7**. X-ray analyses of two other gulose derivatives shown similar structures [20].

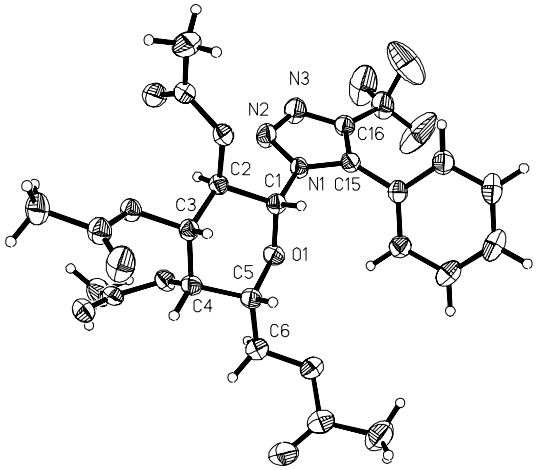


Fig. 1 X-ray structure of 1-(2,3,4,6-tetra-*O*-acetyl-β-*D*-galactopyranosyl)-4-trifluoromethyl-5-phenyl-1,2,3-triazole (**4**); 30% probability of the terminal ellipsoids

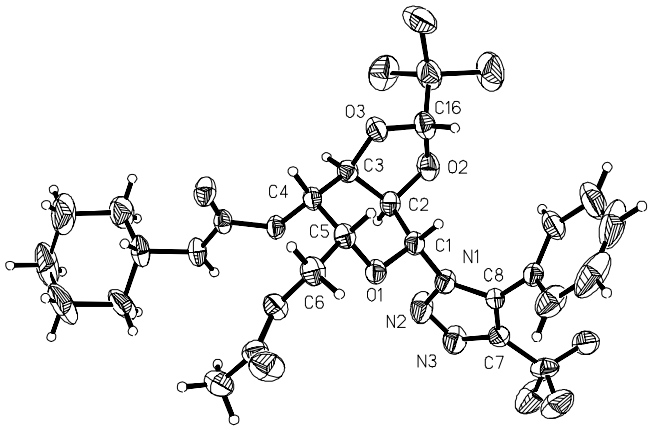


Fig. 2 X-ray structure of 1-[6-*O*-acetyl-4-*O*-cyclohexylcarbamoyl-2,3-*O*-(2,2,2-trichloroethylidene)-β-*D*-gulopyranosyl]-4-trifluormethyl-5-phenyl-1,2,3-triazole (**7**); 30% probability of the terminal ellipsoids.

Deprotection of the sugar moieties: Well-known methods of carbohydrate chemistry were used to generate 1,2,3-triazoles which are connected with a deprotected carbohydrate rest. Thus, 1-(2,3,4,6-tetra-*O*-acetyl-β-*D*-galactopyranosyl)-4-trifluoromethyl-5-phenyl-1,2,3-triazole (**4**) was deacetylated by Zemplén reagent. The syrupy 1-(β-*D*-galactopyranosyl)-4-trifluoromethyl-5-phenyl-1,2,3-triazole (**5**), isolated in quantitative yield after a reaction time of 7 h, crystallized from acetone (Scheme 1). Simultaneous transesterification of acetyl and carbamoyl groups is possible with boiling Zemplén reagent. Thus, the crystalline 1-(2,3-*O*-ethylidene-β-*D*-gulopyranosyl)-5-trifluoromethyl-4-phenyl-1,2,3-triazole (**11**) was generated from **10** after 10 h in 81% yield (Scheme 1). 1-(6-Deoxy-1,2:3,4-di-*O*-isopropylidene-α-*D*-galactopyranos-6-yl)-4-trifluoromethyl-5-phenyl-1,2,3-triazole (**14**) was deacetalated with 60% aqueous trifluoroacetic acid (TFA) at room temperature. After 3 h, 1-(6-deoxy-*D*-galactopyranos-6-yl)-4-trifluoromethyl-5-phenyl-1,2,3-triazole (**15**) was isolated in quantitative yield (Scheme 2).

Because a trichloroethylidene group is acid-stable, deacetalation of the *D*-gulose derivatives **7**, **8**, **17**, and **18** occurs only after conversion of this group into an ethylidene acetal. On heating of **7**, **8**, **17**, and **18**, respectively, with tributylstannane/AIBN in toluene for 1.5–3.5 h, the ethylidene derivatives **9**, **10**, **19**, and **20**, respectively, were isolated in yields of 90–97% [25] (Scheme 1 and 2); for previous applications of this procedure see *e.g.* ref. [26, 27]. An ethylidene group may be cleaved by treatment of the acetals with TFA; see *e.g.* ref. [27]. However, the test to remove selectively the ethylidene group of compound **11** by treatment with TFA at 50 °C was not successful. The glycosidic bond was also cleaved under these reaction conditions; concerning this see also ref. [8–10, 28].

Experimental

Column chromatography: Silica Gel 60 (63–200 μm, Merck); thin-layer chromatography (TLC): Silica Gel foils 60 F_{254} (Merck). NMR spectra: Bruker AC 250 equipment, ^{1}H NMR and ^{13}C(^{1}H) NMR referred to TMS. Melting points: Polarizing microscope Leitz (Laborlux 12 Pol) equipped with a hot stage (Mettler FP 90).

Details of the Crystal Structure Analysis: For the X-ray structure determination crystals of **4** and **7** were checked by rotational photographs and suitable reduced cells were found by the automatic cell determination routine. The data collections were performed in routine ω-scan, the structures were solved by direct methods (Siemens SHELXTL, Vers. 5.10 SGI/IRIX 5.3 for **4** and Vers. 5.03 MS-DOS for **7**) and refined by the full matrix least-squares method of SHELXL-97 (G. M. Sheldrick Universität Göttingen 1997). All non-hydrogen atoms were refined anisotropically. The H-atoms were put into theoretical positions and refined using the riding model. Diffractometer: Siemens P4; radiation: λ = 0.71073 Å (Mo-K_α) with graphite monochromator.

Further details for **4**: Crystal size: 0.76 × 0.66 × 0.44 mm^3; formula: $C_{23}H_{24}F_3N_3O_9$; formula weight: 543.45; temperature: 293(2) K; crystal system: monoclinic; space group: $P2_1$; unit cell dimensions: a = 9.6260(10) Å, b = 9.511(1) Å, c = 14.591(1) Å, β =106.19(1); volume: 1282.9(2) Å^3; Z = 2; density (calculated): 1.407 Mg/m^3; absorption coefficient: 0.122 mm^{-1}; F(000): 564; Θ range for data collection: 2.20 to 22.00°; index ranges: –10 < = h < = 10; – 10 < = k < = 10, – 15

< = l < = 15; reflections collected: 3582; independent reflections: 3142, R(int) = 0.0199; completeness to Θ = 22.00°, 99.9% ; data/restraints/parameters: 3142/1/343; goodness-of fit on F^2: 1.048; final R indices [$I > 2\sigma(I)$]: R1 = 0.0462; wR2 = 0.1271; R indices (all data): R1 = 0.0479; wR2 = 0.1293; largest diff. peak and hole: 0.408/-0.228 e/Å^3.
Further details for **7**: Crystal size: 0.62 × 0.60 × 0.57 mm^3; formula: $C_{26}H_{28}Cl_3F_3N_4O_7$; formula weight: 671.87; temperature: 293(2) K; crystal system: orthorhombic; space group: $P2_12_12_1$; unit cell dimensions: a = 10.203(2) Å, b = 13.665(3)Å, c = 22.587(5)Å; volume: 3149.2(11) Å^3; Z = 4; density (calculated): 1.417Mg/m^3; absorption coefficient: 0.357mm^{-1}; F(000): 1384; Θ range for data collection: 1.80 to 22.00°; index ranges: −10 < = h < = 10; −14 < = k < = 14; −23 < = l < = 23; reflections collected: 4391; independent reflections: 3828, R (int) = 0.0294; completeness to Θ = 22.00°, 99.9%; data/restraints/parameters: 3828/0/401; goodness-of fit on F^2: 1.019; final R indices [$I > 2\sigma(I)$]: R1 = 0.0543; wR2 = 0.1289; R indices (all data): R1 = 0.0781; wR2 = 0.1448; largest diff. peak and hole: 0.208/−0.235 e/Å^3.
Crystallographic data (excluding structure factors) for the structures have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-139500 (4) and CCDC-139501 (7). Copies of the data can be obtained, free of charge on application to The Director; CCDC; 12 Union Road, Cambridge CB2 1EZ, UK, (fax: Int.code + (1223) 336-033; e-mail: deposit@ccdc.cam.ac.uk).

1-(2,3,4,6-Tetra-O-acetyl-β-D-galactopyranosyl)-5-trifluoromethyl-4-phenyl-1,2,3-triazole (**3**) and *1-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-4-trifluoromethyl-5-phenyl-1,2,3-triazole* (**4**)

A solution of 2,3,4,6-tetra-*O*-acetyl-*β*-*D*-galactopyranosyl azide (**1**) (1.12 g, 3.0 mmol) and 3,3,3-trifluoropropinyl-benzene (**2**) [23] (0.68 g, 4.0 mmol) in 15 ml of toluene were refluxed for 14 h under argon atmosphere. After the mixture was concentrated under reduced pressure, the two regioisomers were isolated from the residue by column chromatographic separation (toluene/EtOAc 10 : 1 v/v). Yield of compound 3: 0.49 g (30%), R_f = 0.17; *m.p.* 141–143 °C; $[\alpha]_D^{21}$ −11.1 ($CHCl_3$, c = 1.01); compound **4**: 0.80 g (49%), R_f = 0.13; *m.p.* 114–115 °C; $[\alpha]_D^{20}$ −9.1 ($CHCl_3$, c = 1.01).
3: ^{1}H NMR (250 MHz, $CDCl_3$): *δ*/ppm = 7.57–7.65 (m, 2H, phenyl-H), 7.41–7.49 (m, 3H, phenyl-H), 6.14 (dd, 1H, $^3J_{1\text{-H}/2\text{-H}} \approx 9.1$, $^3J_{2\text{-H}/3\text{-H}} \approx 10.1$, 2-H), 5.87 (d, 1H, 1-H), 5.54 (dd, 1H, $^3J_{3\text{-H}/4\text{-H}} \approx 3.4$, 4-H), 5.27 (dd, 1H, 3-H), 4.09–4.27 (m, 3H, 5-H, 6-H, 6'-H), 2.20 (s, 3H, acetyl-CH_3), 2.04 (s, 3H, acetyl-CH_3), 2.02 (s, 3H, acetyl-CH_3), 1.92 (s, 3H, acetyl-CH_3). – ^{13}C{^{1}H} NMR (75.5 MHz, $CDCl_3$): *δ*/ppm = 170.3, 170.1, 169.9, 168.4 (4 acetyl-CO), 148.9 (triazole C-4), 129.6, 129.1, 128.4, 128.3, 128.1 (phenyl-C), 123.6 (q, $^2J_{\text{triazole C-5/F-A,B,C}} \approx 40.8$, triazole C-5), 120.0 (q, $^1J_{\text{CF3/F-A,B,C}} \approx 269.5$, CF_3), 86.3 (C-1), 74.0, 71.3, 66.9, 66.8 (C-2,3,4,5), 61.2 (C-6), 20.5, 20.4, 20.3 (acetyl-CH_3). – ^{19}F{^{1}H} NMR (235.4 MHz, $CDCl_3$): *δ*/ppm = −55.5 (CF_3).
$C_{23}H_{24}F_3N_3O_9$ (543.5) Calcd.: C 50.83 H 4.45 N 7.73 Found: C 50.77 H 4.44 N 7.88.
4: ^{1}H NMR (250 MHz, $CDCl_3$): *δ*/ppm = 7.44–7.62 (m, 5H, phenyl-H), 5.77 (dd, 1H, $^3J_{1\text{-H}/2\text{-H}} \approx 9.2$, $^3J_{2\text{-H}/3\text{-H}} \approx 10.1$, 2-H), 5.60 (d, 1H, 1-H), 5.38 (dd, 1H, $^3J_{3\text{-H}/4\text{-H}} \approx 3.3$, $^3J_{4\text{-H}/5\text{-H}} \approx 1.2$, 4-H), 5.07 (dd, 1H, 3-H), 4.11 (dd, 1H, $^3J_{5\text{-H}/6\text{-H}} \approx 8.4$, $^2J_{6\text{-H}/6'\text{-H}} \approx 11.9$, 6-H), 4.05 (dd, 1H, $^3J_{5\text{-H}/6'\text{-H}} \approx 4.6$, 6'-H), 4.02 (ddd, 1H, 5-H), 2.05 (s, 3H, acetyl-CH_3), 2.02 (s, 3H, acetyl-CH_3), 1.95 (s, 3H, acetyl-CH_3), 1.87 (s, 3H, acetyl-CH_3). – ^{13}C{^{1}H} NMR (75.5 MHz, $CDCl_3$): *δ*/ppm = 170.2, 169.9, 169.8, 168.4 (4 acetyl-CO), 138.6 (q, $^3J_{\text{triazole C-5/F-A,B,C}} \approx 1.9$, triazole C-5), 137.2 (q, $^2J_{\text{triazole C-4/F-A,B,C}} \approx 38.2$, triazole C-4), 130.8, 130.4, 128.6 (5 phenyl-CH), 123.8 (phenyl-C), 120.5 (q, $^1J_{\text{CF3/F-A,B,C}} \approx 269.0$, CF_3), 85.6 (C-1), 74.0, 71.1, 66.9, 66.7 (C-2,3,4,5), 61.3 (C-6), 20.6, 20.5, 20.4, 20.2 (4 acetyl-CH_3). – ^{19}F{^{1}H} NMR (235.4 MHz, $CDCl_3$): *δ*/ppm = −59.2 (CF_3).
$C_{23}H_{24}F_3N_3O_9$ (543.5) Calcd.: C 50.83 H 4.45 N 7.73 Found: C 50.75 H 4.55 N 7.65.

1-(β-D-Galactopyranosyl)-4-trifluoromethyl-5-phenyl-1,2,3-triazole (**5**)

A solution of **4** (1.0 g, 1.84 mmol) in 1% methanolic sodium methoxide (30 ml) was stirred for 7 h at r.t., and subsequently neutralized with an acidic ion exchanger resin (Amberlite IR-120). After evaporation of the solvent under reduced pressure, the residue was recrystallized from acetone yielding 0.69 g (100%) of **5**, $[\alpha]_D^{24}$ −2.9 (MeOH, c = 1.00). On heating decomposition was observed above 110 °C. – ^{1}H NMR (250 MHz, CD_3OD): *δ*/ppm = 7.51–7.65 (m, 5H, phenyl-H), 5.60 (d, 1H, $^3J_{1\text{-H}/2\text{-H}} \approx 9.2$, 1-H), 4.65 (dd, 1H, $^3J_{2\text{-H}/3\text{-H}} \approx 9.5$, 2-H), 3.89 (dd, 1H, $^3J_{3\text{-H}/4\text{-H}} \approx 3.3$, $^3J_{4\text{-H}/5\text{-H}} \approx 1.0$, 4-H), 3.81 (dd, 1H, $^3J_{5\text{-H}/6\text{-H}} \approx 7.5$, $^2J_{6\text{-H}/6'\text{-H}} \approx 11.9$, 6-H), 3.70 (dd, 1H, $^3J_{5\text{-H}/6'\text{-H}} \approx 4.2$, 6'-H), 3.61 (ddd, 1H, 5-H), 3.53 (dd, 1H, 3-H). – ^{13}C{^{1}H} NMR (75.5 MHz, CD_3OD): *δ*/ppm = 132.0, 131.3, 130.1 (phenyl-CH), 125.3 (phenyl-C), 87.9 (C-1), 80.3, 75.6, 70.4, 70.0 (C-2,3,4,5), 62.6 (C-6). – ^{19}F{^{1}H} NMR (235.4 MHz, CD_3OD): *δ*/ppm = −56.5 (CF_3).
$C_{15}H_{16}F_3N_3O_5$ (375.3) Calcd.: C 48.01 H 4.30 N 11.20 Found: C 48.20 H 4.50 N 10.82.

1-[6-O-Acetyl-4-O-cyclohexylcarbamoyl-2,3-O-(2,2,2-trichloroethylidene)-β-D-gulopyranosyl]-4-trifluoromethyl-5-phenyl-1,2,3-triazole (**7**) and *1-[6-O-acetyl-4-O-cyclohexylcarbamoyl-2,3-O-(2,2,2-trichloroethylidene)-β-D-gulopyranosyl]-5-trifluoromethyl-4-phenyl-1,2,3-triazole* (**8**)

A solution of the azide **6** (1.51 g, 3.0 mmol) and 3,3,3-trifluoropropinyl-benzene **2** [23] (0.68 g, 4.0 mmol) in toluene (15 ml) was refluxed for 19 h under argon atmosphere. After the mixture was concentrated under reduced pressure, the two regioisomers (**7**) and (**8**) were isolated from the residue by column chromatographic separation (toluene/EtOAc 40 : 1 v/v). Yield of compound **7** 0.95 g (47%), R_f = 0.14; *m.p.* 161–162 °C; $[\alpha]_D^{24}$ −59.7 ($CHCl_3$, c = 0.94); yield of **8** [1], 0.62 g (31%), R_f = 0.17.
7: ^{1}H NMR (250 MHz, $CDCl_3$): *δ*/ppm = 7.44–7.67 (m, 5H, phenyl-H), 5.68 (dd, 1H, $^3J_{1\text{-H}/2\text{-H}} \approx 8.2$, $^3J_{2\text{-H}/3\text{-H}} \approx 5.3$, 2-H), 5.27 (dd, 1H, $^3J_{3\text{-H}/4\text{-H}} \approx 2.5$, $^3J_{4\text{-H}/5\text{-H}} \approx 1.7$, 4-H), 5.23 (s, 1H, acetal-H), 5.10 (d, 1H, 1-H), 4.88 (dd, 1H, 3-H), 4.83 (d, 1H, $^3J_{\text{carbamoyl-NH/cyclohexyl-CH}} \approx 8.1$, carbamoyl-NH), 4.23 (dd, 1H,

[1]) Compound **8** was contaminated by small amounts of the starting material; complete purification by HPLC was not successful. Therefore, a full analytical characterization was carried out only after the reduction of **8** to the ethylidene acetal **10**.

$^3J_{5\text{-H/6-H}} \approx 4.9$, $^2J_{6\text{-H/6'-H}} \approx 11.5$, 6-H), 4.15 (dd, 1H, $^3J_{5\text{-H/6'-H}} \approx 7.0$, 6'-H), 4.07 (ddd, 1H, 5-H), 3.30–3.60 (m, 1H, cyclohexyl-CH), 2.09 (s, 3H, acetyl-CH_3), 1.87–2.02 (m, 2H, cyclohexyl-CH_2), 1.54–1.82 (m, 3H, cyclohexyl-CH_2), 1.06–1.47 (m, 5H, cyclohexyl-CH_2). – $^{13}C\{^1H\}$ NMR (62.9 MHz, $CDCl_3$): δ/ppm = 170.2 (acetyl-C=O), 153.4 (carbamoyl-CO), 131.2, 129.9, 129.2, (phenyl-CH), 123.6 (phenyl-C), 106.6 (acetal-C), 98.2 (-CCl_3), 82.9 (C-1), 76.7, 73.8, 73.5, 65.4 (C-2,3,4,5), 62.0 (C-6), 50.4 (cyclohexyl-CH), 33.1, 25.4, 24.7 (cyclohexyl-CH_2), 20.7 (acetyl-CH_3). – $^{19}F\{^1H\}$ NMR (235.4 MHz, $CDCl_3$): δ/ppm = –59.1 (CF_3).

$C_{26}H_{28}Cl_3F_3N_4O_7$ (671.9) Calcd.: C 46.48 H 4.20 N 8.34 Found: C 46.55 H 4.20 N 8.26.

8: ^1H NMR (250 MHz, $CDCl_3$): δ/ppm = 7.57–7.68 (m, 2H, phenyl-H), 7.41–7.51 (m, 3H, phenyl-H), 5.90 (dd, 1H, $^3J_{1\text{-H/2-H}} \approx 7.9$, $^3J_{2\text{-H/3-H}} \approx 5.4$, 2-H), 5.67 (d, 1H, 1-H), 5.59 (s, 1H, acetal-H), 5.35 (dd, 1H, $^3J_{3\text{-H/4-H}} \approx 2.5$, $^3J_{4\text{-H/5-H}} \approx 1.6$, 4-H), 4.98 (dd, 1H, 3-H), 4.77 (d, 1H, $^3J_{\text{carbamoyl-NH/cyclohexyl-CH}} \approx 8.1$, carbamoyl-NH), 4.08–4.26 (m, 3H, 5-H, 6-H, 6'-H), 3.32–3.58 (m, 1H, cyclohexyl-CH), 2.07 (s, 3H, acetyl-CH_3), 1.83–2.03 (m, 2H, cyclohexyl-CH_2), 1.51–1.80 (m, 3H, cyclohexyl-CH_2), 1.03–1.45 (m, 5H, cyclohexyl- CH_2). – $^{13}C\{^1H\}$ NMR (62.9 MHz, $CDCl_3$): δ/ppm = 170.4 (acetyl-CO), 153.4 (carbamoyl-CO), 129.7, 129.1, 128.6, (phenyl-CH), 128.2 (phenyl-C), 106.8 (acetal-C), 98.4 (-CCl_3), 84.8 (C-1), 76.1, 73.2, 71.8, 65.6 (C-2,3,4,5), 61.8 (C-6), 50.3 (cyclohexyl-CH), 33.1, 25.4, 24.7 (cyclohexyl-CH_2), 20.6 (acetyl-CH_3). – $^{19}F\{^1H\}$ NMR (235.4 MHz, $CDCl_3$): δ/ppm = –56.2 (CF_3).

1-(6-O-Acetyl-4-O-cyclohexylcarbamoyl-2,3-O-ethylidene-β-D-gulopyranosyl)-4-trifluoromethyl-5-phenyl-1,2,3-triazole (**9**)

A solution of **7** (0.67 g, 1.0 mmol), Bu_3SnH (0.92 ml, 3.5 mmol) and AIBN (10 mg, 0,06 mmol) in dry toluene (10 ml) was heated at 75 °C under stirring (Ar atmosphere). When the reaction was finished (1.5 h, TLC control) the solution was cooled down and was shaken with 30% aq KF (5 ml) for 45 min. Bu_3SnF precipitated and was removed by filtration. Subsequently, the organic phase was separated, washed with 3% aq. $NaHSO_4$ (5 ml) and twice with water (5 ml), dried ($MgSO_4$), and concentrated under reduced pressure. The residue was purified by column chromatography (R_f = 0.27, toluene/EtOAc = 9 : 1 v/v). Yield 0.54 g (95%), *m.p.* 145–147 °C (*i*-PrOH), $[\alpha]_D^{23}$ –93.1 ($CHCl_3$, c = 1.11). – ^1H NMR (250 MHz, $CDCl_3$): δ/ppm = 7.37–7.64 (m, 5H, phenyl-H), 5.35 (dd, 1H, $^3J_{1\text{-H/2-H}} \approx 8.4$, $^3J_{2\text{-H/3-H}} \approx 4.7$, 2-H), 5.25 (q, 1H, $^3J_{\text{acetal-H/ethylidene-CH3}} \approx 4.9$, acetal-H), 5.17 (dd, 1H, $^3J_{3\text{-H/4-H}} \approx 2.6$, $^3J_{4\text{-H/5-H}} \approx 1.5$, 4-H), 5.07 (d, 1H, 1-H), 4.82 (d, 1H, $^3J_{\text{carbamoyl-NH/cyclohexyl-CH}} \approx 7.9$, carbamoyl-NH), 4.31 (dd, 1H, 3-H), 4.22 (dd, 1H, $^3J_{5\text{-H/6-H}} \approx 5.1$, $^2J_{6\text{-H/6'-H}} \approx 11.7$, 6-H), 4.14 (dd, 1H, $^3J_{5\text{-H/6'-H}} \approx 1.4$, 6'-H), 4.04 (ddd, 1H, 5-H), 3.30–3.62 (m, 1H, cyclohexyl-CH), 2.08 (s, 3H, acetyl-CH_3), 1.87–2.02 (m, 2H, cyclohexyl-CH_2), 1.52–1.80 (m, 3H, cyclohexyl-CH_2), 1.26 (d, 3H, ethylidene-CH_3), 1.06–1.48 (m, 5H, cyclohexyl-CH_2). – $^{13}C\{^1H\}$ NMR (75.5 MHz, $CDCl_3$): δ/ppm = 170.3 (acetyl-CO), 153.8 (carbamoyl-CO), 139.1 (q, $^3J_{\text{triazole C-5/F-A,B,C}} \approx 2.1$, triazole C-5), 136.3 (q, $^2J_{\text{triazole C-4/F-A,B,C}} \approx 38.0$, triazole C-4), 130.9, 129.8, 129.0, (phenyl-CH), 123.8 (phenyl-C), 102.6 (acetal-C), 82.6 (C-1), 73.9, 73.5, 71.6, 66.3 (C-2,3,4,5), 62.4 (C-6), 50.3 (cyclohexyl-CH), 33.2, 25.4, 24.7 (cyclohexyl-CH_2), 21.4, 20.7 (ethylidene-CH_3, acetyl-CH_3). – $^{19}F\{^1H\}$ NMR (235.4 MHz, $CDCl_3$): δ/ppm = –59.1 (CF_3).

$C_{26}H_{31}F_3N_4O_7$ (568.5) Calcd.: C 54.93 H 5.50 N 9.85 Found: C 55.22 H 5.66 N 9.62.

1-(6-O-Acetyl-4-O-cyclohexylcarbamoyl-2,3-O-ethylidene-β-D-gulopyranosyl)-5-trifluoromethyl-4-phenyl-1,2,3-triazole (**10**)

The trichloroethylidene moiety of **8** (0.67 g, 1.0 mmol) was hydrodechlorinated with Bu_3SnH/AIBN as described for compound **9** (reaction time 2 h). After column chromatographic purification (R_f = 0.29, toluene/EtOAc = 9 : 1 v/v), 0.53 g (93%) of **10** was obtained as an amorphous solid, $[\alpha]_D^{23}$ –51.1 ($CHCl_3$, c = 1.01). – ^1H NMR (250 MHz, $CDCl_3$): δ/ppm = 7.55–7.66 (m, 2H, phenyl-H), 7.41–7.49 (m, 3H, phenyl-H), 5.60 (d, 1H, $^3J_{1\text{-H/2-H}} \approx 8.4$, 1-H), 5.60 (q, 1H, $^3J_{\text{acetal-H/ethylidene-CH3}} \approx 5.0$, acetal-H), 5.51 (dd, 1H, $^3J_{2\text{-H/3-H}} \approx 4.6$, 2-H), 5.27 (dd, 1H, $^3J_{3\text{-H/4-H}} \approx 2.6$, $^3J_{4\text{-H/5-H}} \approx 1.6$, 4-H), 4.83 (d, 1H, $^3J_{\text{carbamoyl-NH/cyclohexyl-CH}} \approx 8.1$, carbamoyl-NH), 4.42 (dd, 1H, 3-H), 4.32 (ddd, 1H, $^3J_{5\text{-H/6-H}} \approx 4.1$, $^3J_{5\text{-H/6'-H}} \approx 8.0$, 5-H), 4.26 (dd, 1H, $^2J_{6\text{-H/6'-H}} \approx 11.7$, 6-H), 4.19 (dd, 1H, 6'-H), 3.30–3.64 (m, 1H, cyclohexyl-CH), 2.05 (s, 3H, acetyl-CH_3), 1.85–2.01 (m, 2H, cyclohexyl-CH_2), 1.52–1.80 (m, 3H, cyclohexyl-CH_2), 1.37 (d, 3H, ethylidene-CH_3), 1.04–1.48 (m, 5H, cyclohexyl-CH_2). – $^{13}C\{^1H\}$ NMR (62.9 MHz, $CDCl_3$): δ/ppm = 170.6 (acetyl-CO), 153.8 (carbamoyl-CO), 129.6, 129.1, 128.5, (phenyl-CH), 123.6 (phenyl-C), 103.0 (acetal-C), 84.5 (C-1), 74.0, 73.9, 71.3, 66.4 (C-2,3,4,5), 62.1 (C-6), 50.2 (cyclohexyl-CH), 33.1, 25.3, 24.7 (cyclohexyl-CH_2), 21.5, 20.6 (ethylidene-CH_3, acetyl-CH_3). – $^{19}F\{^1H\}$ NMR (235.4 MHz, $CDCl_3$): δ/ppm = –56.3 (CF_3).

$C_{26}H_{31}F_3N_4O_7$ (568.5) Calcd.: C 54.93 H 5.50 N 9.85 Found: C 55.27 H 5.33 N 9.71.

1-(2,3-O-Ethylidene-β-D-gulopyranosyl)-5-trifluoromethyl-4-phenyl-1,2,3-triazole (**11**)

A solution of compound **10** (1.14 g, 2.0 mmol) in 1% methanolic sodium methoxide (10 ml) was heated for 10 h under reflux (TLC control). The mixture was cooled down, neutralized with an acidic ion exchanger (Amberlite IR 120), filtered, and the filtration residue was washed twice with methanol (10 ml). The combined methanolic solutions were concentrated under reduced pressure and the crude product **11** obtained was purified by column chromatography (R_f = 0.15, toluene/EtOAc = 2 : 1 v/v). Yield of **11**: 0.65 g (81%); *m.p.* 155 °C, $[\alpha]_D^{24}$ –71.0 ($CHCl_3$, c = 1.10). – ^1H NMR (250 MHz, $CDCl_3$): δ/ppm = 7.51–7.59 (m, 2H, phenyl-H), 7.41–7.50 (m, 3H, phenyl-H), 5.63 (d, 1H, $^3J_{1\text{-H/2-H}} \approx 8.3$, 1-H), 5.59 (q, 1H, $^3J_{\text{acetal-H/ethylidene-CH3}} \approx 5.0$, acetal-H), 5.50 (dd, 1H, $^3J_{2\text{-H/3-H}} \approx 4.7$, 2-H), 4.46 (dd, 1H, $^3J_{3\text{-H/4-H}} \approx 2.5$, 3-H), 4.26 (dd, 1H, $^3J_{4\text{-H/5-H}} \approx 1.5$, 4-H), 4.00 (ddd, 1H, $^3J_{5\text{-H/6-H}} \approx 3.7$, $^3J_{5\text{-H/6'-H}} \approx 5.2$, 5-H), 3.86–3.94 (m, 2H, 6-H, 6'-H), 1.37 (d, 3H, ethylidene-CH_3). – $^{13}C\{^1H\}$ NMR (62.9 MHz, $CDCl_3$): δ/ppm = 129.7, 129.2, 128.5, (phenyl-CH), 128.2 (phenyl-C), 102.9 (acetal-C), 85.3 (C-1), 76.3, 76.3, 71.5, 67.3 (C-2,3,4,5), 62.7 (C-6), 21.6, (ethylidene-CH_3). – $^{19}F\{^1H\}$ NMR (235.4 MHz, $CDCl_3$): δ/ppm = –56.1 (CF_3).

$C_{17}H_{18}F_3N_3O_5$ (401.3) Calcd.: C 50.88 H 4.52 N 10.47 Found: C 50.90 H 4.49 N 10.35.

1-(6-Deoxy-1,2:3,4-di-O-isopropylidene-α-D-galactopyranos-6-yl)-5-trifluoromethyl-4-phenyl-1,2,3-triazole (**13**) and *1-(6-deoxy-1,2:3,4-di-O-isopropylidene-α-D-galactopyranos-6-yl)-4-trifluoromethyl-5-phenyl-1,2,3-triazole* (**14**)

A solution of the azide **12** [1] (0.86 g, 3.0 mmol) and 3,3,3-trifluoropropinyl-benzene **2** [23] (0.68 g, 4.0 mmol) in toluene (15 ml) was refluxed for 13 h under argon atmosphere. After the mixture was concentrated under reduced pressure, the two regioisomers **13** and **14** were isolated from the residue by column chromatographic separation (toluene/EtOAc 40 : 1 v/v). Yield of syrupy compound **13**: 0.46 g (34%), R_f = 0.19, $[\alpha]_D^{23}$ −47.4 ($CHCl_3$, c = 0.98); compound **14**: 0.66 g (48%), R_f = 0.16; *m.p.* 88–90 °C, $[\alpha]_D^{23}$ −59.7 ($CHCl_3$, c = 1.33).

13: ^{1}H NMR (250 MHz, $CDCl_3$): δ/ppm = 7.98–8.08 (m, 2H, phenyl-H), 7.78–7.88 (m, 3H, phenyl-H), 5.48 (d, 1H, $^3J_{1\text{-H}/2\text{-H}} \approx 5.1$, 1-H), 4.75 (dd, 1H, $^3J_{5\text{-H}/6\text{-H}} \approx 8.0$, $^2J_{6\text{-H}/6'\text{-H}} \approx 14.1$, 6-H), 4.68 (dd, 1H, $^3J_{5\text{-H}/6'\text{-H}} \approx 5.5$, 6'-H), 4.67 (dd, 1H, $^3J_{2\text{-H}/3\text{-H}} \approx 3.0$, $^3J_{3\text{-H}/4\text{-H}} \approx 7.7$, 3-H), 4.45 (ddd, 1H, $^3J_{4\text{-H}/5\text{-H}} \approx 2.0$, 5-H), 4.33 (dd, 1H, 2-H), 4.30 (dd, 1H, 4-H), 1.51 (s, 3H, isopropylidene-CH_3), 1.46 (s, 3H, isopropylidene-CH_3), 1.36 (s, 3H, isopropylidene-CH_3), 1.28 (s, 3H, isopropylidene-CH_3). – ^{13}C{^{1}H} NMR (75.5 MHz, $CDCl_3$): δ/ppm = 129.2, 129.0, 128.4 (phenyl-CH), 110.1, 109.1 (2 ketal-C), 96.2 (C-1), 71.1, 71.0, 70.4 (C-2,3,4), 67.0 (C-5), 50.7 (C-6), 25.9, 25.8, 24.9, 24.6 (4 isopropylidene-CH_3). – ^{19}F{^{1}H} NMR (235.4 MHz, $CDCl_3$): δ/ppm = −55.5 (CF_3).

$C_{21}H_{24}F_3N_3O_5$ (455.4) Calcd.: C 55.38 H 5.32 N 9.22 Found: C 55.53 H 5.25 N 9.05.

14: ^{1}H NMR (250 MHz, $CDCl_3$): δ/ppm = 7.39–7.52 (m, 5H, phenyl-H), 5.42 (d, 1H, $^3J_{1\text{-H}/2\text{-H}} \approx 4.9$, 1-H), 4.62 (dd, 1H, $^3J_{2\text{-H}/3\text{-H}} \approx 2.7$, $^3J_{3\text{-H}/4\text{-H}} \approx 7.9$, 3-H), 4.51 (ddd, 1H, $^3J_{4\text{-H}/5\text{-H}} \approx 2.1$, $^3J_{5\text{-H}/6\text{-H}} \approx 5.8$, $^3J_{5\text{-H}/6'\text{-H}} \approx 7.3$, 5-H), 4.31–4.37 (m, 2H, 6-H, 6'-H), 4.30 (dd, 1H, 2-H), 4.17 (dd, 1H, 4-H), 1.49 (s, 3H, isopropylidene-CH_3), 1.28 (s, 3H, isopropylidene-CH_3), 1.27 (s, 3H, isopropylidene-CH_3), 1.27 (s, 3H, isopropylidene-CH_3). – ^{13}C{^{1}H} NMR (75.5 MHz, $CDCl_3$): δ/ppm = 130.2, 130.2, 128.6 (phenyl-CH), 124.7 (phenyl-C), 109.9, 109.3 (2 ketal-C), 96.1 (C-1), 71.1, 70.9, 70.4 (C-2,3,4), 67.1 (C-5), 48.1 (C-6), 25.9, 25.8, 24.9, 24.6 (4 isopropylidene-CH_3). – ^{19}F{^{1}H} NMR (235.4 MHz, $CDCl_3$): δ/ppm = −58.9 (CF_3).

$C_{21}H_{24}F_3N_3O_5$ (455.4) Calcd.: C 55.38 H 5.32 N 9.22 Found: C 55.60 H 5.10 N 8.99.

1-(6-Deoxy-D-galactopyranos-6-yl)-4-trifluoromethyl-5-phenyl-1,2,3-triazole (**15**)

A solution of **14** (0.45 g, 1.0 mmol) in 60% aq. TFA (10 ml) was stirred at r.t. When the deacetalation was complete after about 3 h (TLC control with $CHCl_3$/MeOH = 5:1 v/v, R_f = 0.34), 10 ml of water was added and the mixture was concentrated under reduced pressure. To remove remainders of TFA and H_2O, the residue was dissolved in toluene (5 ml) and the solution was concentrated under reduced pressure. After repetition of this procedure the residue was crystallized from acetone. Yield 0.38 g (100%); *m.p.* 219 °C (decomp.). – ^{1}H NMR (250 MHz, DMSO-d_6): δ/ppm = 7.47–7.64 (m, 5H, phenyl-H). – ^{13}C{^{1}H} NMR (75.5 MHz, DMSO-d_6): δ/ppm = 129.3, 128.8, 128.6 (phenyl-CH), 101.8, 92.6 (C-1), 82.4, 81.9, 75.9, 69.5, 69.3, 68.8, 68.5, 68.3 (C-2,3,4,5), 54.0, 51.9 (C-6). – ^{19}F{^{1}H} NMR (235.4 MHz, DMSO-d_6): δ/ppm = – 54.8 (CF_3).

$C_{15}H_{16}F_3N_3O_5$ (375.3) Calcd.: C 48.01 H 4.30 N 11.20 Found: C 48.25 H 4.49 N 10.92.

1-[Methyl 4-O-cyclohexylcarbamoyl-6-deoxy-2,3-O-(2,2,2-trichloroethylidene)-β-D-gulopyranos-6-yl]-4-trifluoromethyl-5-phenyl-1,2,3-triazole (**17**) and *1-[methyl 4-O-cyclohexylcarbamoyl-6-deoxy-2,3-O-(2,2,2-trichloroethylidene)-β-D-gulopyranos-6-yl]-5-trifluoromethyl-4-phenyl-1,2,3-triazole* (**18**)

A solution of methyl 6-azido-4-*O*-cyclohexylcarbamoyl-6-deoxy-2,3-*O*-(2,2,2-trichloroethylidene)-β-*D*-gulopyranoside **16** [22] (1.42 g, 3.0 mmol) and 3,3,3-trifluoropropinyl-benzene **2** [23] (0.68 g, 4.0 mmol) in toluene (15 ml) was refluxed for 10 h under argon atmosphere. After the mixture was concentrated under reduced pressure, the two regioisomers **17** and **18** were isolated from the residue by column chromatographic separation (toluene/EtOAc 40 : 1 v/v). Yield of **17**: 0.97 g (50%), R_f = 0.22; *m.p.* 140–142 °C, $[\alpha]_D^{23}$ −41.8 ($CHCl_3$, c = 0.97); isomer 18: 0.64 g (33%), R_f = 0.25; *m.p.* 146–148 °C, $[\alpha]_D^{23}$ −46.8 ($CHCl_3$, c = 1.00).

17: ^{1}H NMR (250 MHz, $CDCl_3$): δ/ppm = 7.48–7.56 (m, 3H, phenyl-H), 7.36–7.43 (m, 2H, phenyl-H), 5.45 (s, 1H, acetal-H, 5.20 (dd, 1H, $^3J_{3\text{-H}/4\text{-H}} \approx 2.5$, $^3J_{4\text{-H}/5\text{-H}} \approx 1.5$, 4-H), 4.65 (dd, 1H, $^3J_{2\text{-H}/3\text{-H}} \approx 5.3$, 3-H), 4.59 (d, 1H, $^3J_{\text{carbamoyl-NH/cyclohexyl-CH}} \approx 8.2$, carbamoyl-NH), 4.55 (ddd, 1H, $^3J_{5\text{-H}/6\text{-H}} \approx 3.3$, $^3J_{5\text{-H}/6'\text{-H}} \approx 10.1$, 5-H), 4.42 (dd, 1H, $^2J_{6\text{-H}/6'\text{-H}} \approx 14.2$, 6-H), 4.32 (dd, 1H, $^3J_{1\text{-H}/2\text{-H}} \approx 6.8$, 2-H), 4.25 (d, 1H, 1-H), 4.21 (dd, 1H, 6'-H), 3.32–3.43 (m, 1H, cyclohexyl-CH), 3.31 (s, 3H, OMe), 1.80–1.93 (m, 2H, cyclohexyl-CH_2), 1.48–1.78 (m, 3H, cyclohexyl-CH_2), 1.05–1.46 (m, 5H, cyclohexyl-CH_2). – ^{13}C{^{1}H} NMR (75.5 MHz, $CDCl_3$): δ/ppm = 153.6 (carbamoyl-CO), 138.4 (q, $^3J_{\text{triazole-C5/F-A,B,C}} \approx 2.0$, triazole-C5), 135.9 (q, $^2J_{\text{triazole-C4/F-A,B,C}} \approx 38.2$, triazole-C4), 130.6, 129.9, 129.0 (phenyl-CH), 124.3 (phenyl-C), 120.8 (q, $^1J_{\text{CF3/F-A,B,C}} \approx 268.7$, CF_3), 106.7 (acetal-C), 101.7 (C-1), 98.8 (CCl_3) , 76.8, 76.6, 71.0, 66.4 (C-2,3,4,5), 56.9 (MeO), 50.2 (cyclohexyl-CH), 48.1 (C-6), 33.0, 25.3, 24.5 (cyclohexyl-CH_2). – ^{19}F{^{1}H} NMR (235.4 MHz, $CDCl_3$): δ/ppm = −59.0 (CF_3).

$C_{25}H_{28}Cl_3F_3N_4O_6$ (643.9) Calcd.: C 46.64 H 4.38 N 8.70 Found: C 46.57 H 4.29 N 8.69.

18: ^{1}H NMR (250 MHz, $CDCl_3$): δ/ppm = 7.68–7.55 (m, 2H, phenyl-H), 7.39–7.53 (m, 3H, phenyl-H), 5.47 (s, 1H, acetal-H), 5.31 (dd, 1H, $^3J_{3\text{-H}/4\text{-H}} \approx 2.6$, $^3J_{4\text{-H}/5\text{-H}} \approx 1.6$, 4-H), 4.88 (d, 1H, $^3J_{\text{carbamoyl-NH/cyclohexyl-CH}} \approx 8.0$, carbamoyl-NH), 4.74 (dd, 1H $^3J_{5\text{-H}/6\text{-H}} \approx 4.2$, $^2J_{6\text{-H}/6'\text{-H}} \approx 14.2$, 6-H), 4.74 (dd, 1H, $^3J_{2\text{-H}/3\text{-H}} \approx 5.2$, 3-H), 4.67 (dd, 1H, $^3J_{5\text{-H}/6'\text{-H}} \approx 8.8$, 6'-H), 4.51 (ddd, 1H, 5-H), 4.40 (dd, 1H, $^3J_{1\text{-H}/2\text{-H}} \approx 7.1$, 2-H), 4.30 (d, 1H, 1-H), 3.43–3.58 (m, 1H, cyclohexyl-CH), 3.36 (s, 3H, OMe), 1.86–2.02 (m, 2H, cyclohexyl-CH_2), 1.52–1.82 (m, 3H, cyclohexyl-CH_2), 1.05–1.46 (m, 5H, cyclohexyl-CH_2). – ^{13}C{^{1}H} NMR (75.5 MHz, $CDCl_3$): δ/ppm = 153.7 (carbamoyl-CO), 129.5, 128.9, 128.5 (phenyl-CH), 128.7 (phenyl-C), 120.3 (q, $^1J_{\text{CF3/F-A,B,C}} \approx 269.9$, CF_3), 106.7 (acetal-C), 101.6 (C-1), 98.8 (CCl_3), 76.8, 76.6, 71.0, 66.5 (C-2,3,4,5), 56.8 (MeO), 50.5 (C-6), 50.3 (cyclohexyl-CH), 33.1, 25.3, 24.6 (cyclohexyl-CH_2). – ^{19}F{^{1}H} NMR (235.4 MHz, $CDCl_3$): δ/ppm = −55.5 (CF_3).

$C_{25}H_{28}Cl_3F_3N_4O_6$ (643.9) Calcd.: C 46.64 H 4.38 N 8.70 Found: C 46.87 H 4.38 N 8.58.

1-(Methyl 4-O-cyclohexylcarbamoyl-6-deoxy-2,3-O-ethylidene-β-D-gulopyranos-6-yl)-4-trifluoromethyl-5-phenyl-1,2,3-triazole (**19**)

1-[Methyl 4-*O*-cyclohexylcarbamoyl-6-deoxy-2,3-*O*-(2,2,2-trichloroethylidene)-*β*-*D*-gulopyranos-6-yl]-4-trifluoromethyl-5-phenyl-1,2,3-triazole (**17**) (0.64 g, 1.0 mmol) was hydrodechlorinated with Bu_3SnH/AIBN as described for compound **9** (reaction time 2.5 h). After column chromatographic purification (R_f = 0.25, toluene/EtOAc = 9 : 1 v/v), 0.52 g (97%) of the crystalline product **19** were obtained; *m.p*. 106–108 °C (*i*-PrOH), $[\alpha]_D^{23}$ −44.9 ($CHCl_3$, c = 0.98). – ^{1}H NMR (250 MHz, $CDCl_3$): δ/ppm = 7.34–7.56 (m, 5H, phenyl-H), 5.42 (q, 1H, $^3J_{\text{acetal-H/ethylidene-CH3}} \approx 5.0$, acetal-H), 5.08 (dd, 1H, $^3J_{\text{3-H/4-H}} \approx 2.5$, $^3J_{\text{4-H/5-H}} \approx 1.5$, 4-H), 4.60 (d, 1H, $^3J_{\text{carbamoyl-NH/cyclohexyl-CH}} \approx 8.2$, carbamoyl-NH), 4.50 (ddd, 1H, $^3J_{\text{5-H/6-H}} \approx 3.4$, $^3J_{\text{5-H/6'-H}} \approx 10.0$, 5-H), 4.71 (dd, 1H, $^2J_{\text{6-H/6'-H}} \approx 14.0$, 6-H), 4.24 (dd, 1H, 6'-H), 4.22 (d, 1H, $^3J_{\text{1-H/2-H}} \approx 7.2$, 1-H), 4.13 (dd, 1H, $^3J_{\text{2-H/3-H}} \approx 5.1$, 3-H), 3.99 (dd, 1H, 2-H), 3.29 (s, 3H, MeO), 3.25–3.46 (m, 1H, cyclohexyl-CH), 1.48–1.80 (m, 5H, cyclohexyl-CH_2), 1.30 (d, 3H, ethylidene-CH_3), 1.00–1.44 (m, 5H, cyclohexyl-CH_2). – ^{13}C{^{1}H} NMR (62.9 MHz, $CDCl_3$): δ/ppm = 153.9 (carbamoyl-CO), 138.3 (q, $^3J_{\text{triazole C-5/F-A,B,C}} \approx 1.9$, triazole C-5), 135.8 (q, $^2J_{\text{triazole C-4/F-A,B,C}} \approx 38.2$, triazole C-4), 130.5, 129.9, 129.0 (phenyl-CH), 124.4 (phenyl-C), 120.8 (q, $^1J_{\text{CF3/F-A,B,C}} \approx 268.6$, CF_3), 102.4, 101.4 (acetal-C, C-1), 74.8, 74.2, 71.0, 67.3 (C-2,3,4,5), 56.8 (MeO), 50.1 (cyclohexyl-CH), 48.3 (C-6), 33.0, 25.3, 24.6 (cyclohexyl-CH_2), 21.4 (ethylidene-CH_3). – ^{19}F{^{1}H} NMR (235.4 MHz, $CDCl_3$): δ/ppm = −59.1 (CF_3).

$C_{25}H_{31}F_3N_4O_6$ (540.5) Calcd.: C 55.55 H 5.78 N 10.36 Found: C 55.46 H 5.74 N 10.05.

1-(Methyl 4-O-cyclohexylcarbamoyl-6-deoxy-2,3-O-ethylidene-β-D-gulopyranos-6-yl)-5-trifluoromethyl-4-phenyl-1,2,3-triazole (**20**)

1-[Methyl 4-*O*-cyclohexylcarbamoyl-6-deoxy-2,3-*O*-(2,2,2-trichloroethylidene)-*β*-*D*-gulopyranos-6-yl]-5-trifluoromethyl-4-phenyl-1,2,3-triazole (**18**) (0.64 g, 1.0 mmol) was hydrodechlorinated with Bu_3SnH/AIBN as described for compound **9** (reaction time 3.5 h). After column chromatographic purification (R_f = 0.28, toluene/EtOAc = 9 : 1 v/v), 0.49 g (90%) of the crystalline product **20** were obtained; *m.p*. 180 °C (*i*-PrOH), $[\alpha]_D^{21}$ −44.0 ($CHCl_3$, c = 1.06). – ^{1}H NMR (250 MHz, $CDCl_3$): δ/ppm = 7.55–7.66 (m, 2H, phenyl-H), 7.40–7.49 (m, 3H, phenyl-H), 5.45 (q, 1H, $^3J_{\text{acetal-H/ethylidene-CH3}} \approx 5.0$, acetal-H), 5.20 (dd, 1H, $^3J_{\text{3-H/4-H}} \approx 2.6$, $^3J_{\text{4-H/5-H}} \approx 1.5$, 4-H), 4.88 (d, 1H, $^3J_{\text{carbamoyl-NH/cyclohexyl-CH}} \approx 8.2$, carbamoyl-NH), 4.71 (d, 2H, $^3J_{\text{5-H/6-H,6'-H}} \approx 6.4$, 6-H, 6'-H), 4.32 (dt, 1H, 5-H), 4.27 (d, 1H, $^3J_{\text{1-H/2-H}} \approx 7.2$, 1-H), 4.21 (dd, 1H, $^3J_{\text{2-H/3-H}} \approx 5.0$, 3-H), 4.07 (dd, 1H, 2-H), 3.34 (s, 3H, MeO), 3.40–3.60 (m, 1H, cyclohexyl-CH), 1.86–2.03 (m, 2H, cyclohexyl-CH_2), 1.53–1.80 (m, 3H, cyclohexyl-CH_2), 1.32 (d, 3H, ethylidene-CH_3), 1.06–1.47 (m, 5H, cyclohexyl-CH_2). – ^{13}C{^{1}H} NMR (62.9 MHz, $CDCl_3$): δ/ppm = 154.0 (carbamoyl-CO), 129.4, 129.0 (phenyl-CH), 128.8 (phenyl-C), 128.5 (phenyl-CH), 102.5, 101.3 (acetal-C, C-1), 74.8, 74.1, 71.1, 67.4 (C-2,3,4,5), 56.8 (MeO), 50.7 (cyclohexyl-CH), 50.2 (C-6), 33.1, 25.4, 24.7 (cyclohexyl-CH_2), 21.5 (ethylidene-CH_3). – ^{19}F{^{1}H} NMR (235.4 MHz, $CDCl_3$): δ/ppm = −55.4 (CF_3).

$C_{25}H_{31}F_3N_4O_6$ (540.5) Calcd.: C 55.55 H 5.78 N 10.36 Found: C 55.65 H 5.72 N 10.22.

References

[1] Part 26.: Chr. Hager, R. Miethchen, H. Reinke, J. Fluorine Chem. **2000**, *104*, in press
[2] R. Böhm, C. Karow, Pharmazie **1981**, *36*, 243
[3] H. Dehne, 1,2,3-Triazoles, in Houben-Weyl, Vol. E 8d, Thieme-Verlag, Stuttgart 1994, 308 and papers cited therein
[4] G. R. Revankar, V. C. Solan, R. K. Robins, Nucl. Acid Res. – Symp. Ser. **1981**, *9*, 65
[5] O. Makabe, H. Suzuki, S. Umezawa, Bull. Chem. Soc. Jpn. **1977**, *50*, 2689
[6] P. Wigerinck, A. v. Aerschot, P. Claes, J. Balzarini, E. De Clercq, P. Herdewijn, J. Heterocycl. Chem. **1989**, *26*, 1635
[7] A. Contreras, R. M. Sánchez-Pérez, G. Alonso, Cancer Chemother. Pharmacol. **1978**, *1*, 243
[8] W. Bröder, H. Kunz, Synlett **1990**, 252
[9] W. Bröder, H. Kunz, Carbohydr. Res. **1993**, *249*, 221
[10] W. Bröder, H. Kunz, Bioorg. Med. Chem. **1997**, *5*, 1
[11] P. Norris, D. Horton, B. R. Levine, Heterocycles **1996**, *43*, 2643 and papers cited therein.
[12] D. F. Ewing, G. Goethals, G. MacKenzie, P. Martin, G. Ronco, L. Vanbaelinghem, and P. Villa, J. Carbohydr. Chem. **1999**, *18*, 441
[13] R. Filler, J. Fluorine Chem. **1986**, *33*, 361
[14] J. T. Welch, Tetrahedron **1987**, *43*, 3123
[15] R. Filler, Y. Kobayashi, L. M. Yagupolskii (Eds.), Organofluorine Compounds in Medical Chemistry and Biomedical Applications, Elsevier, Amsterdam 1993 and papers cited therein
[16] J. T. Welch, S. Eswarakrishnan (Eds.), Fluorine in Bioorganic Chemistry, J. Wiley & Sons, New York 1991 and papers cited therein
[17] Reviews in the special issue "Fluorinated Sugars", Carbohydr. Res. **2000**, in press
[18] G. Meazza, G. Zanardi, J. Fluorine Chem. **1991**, *55*, 199
[19] H. Paulsen, Z. Györgydeák, M. Friedmann, M., Chem. Ber. **1974**, *107*, 1568
[20] Chr. Hager, R. Miethchen, H. Reinke, Synthesis, **2000**, 226
[21] A. B. Reitz, R. W. Tuman, C. S. Marchione, A. D. Jordan, C. R. Bowden, B. E. Maryanoff, J. Med. Chem. **1989**, *32*, 2210
[22] Chr. Hager, R. Miethchen, R. Kempe, J. Carbohydr. Chem. **2000**, accepted for publication
[23] Y. Kobayashi, T. Yamashita, M. Takahashi, H. Kuroda, I. Kumadaki, Tetrahedron Lett. **1982**, *23*, 343
[24] G. Beck, D. Günther, Chem. Ber. **1973**, *106*, 2758
[25] The hydrodechlorinations proceed *via* the corresponding dichloro- and the monochloro intermediates, easily to detect by TLC.
[26] S. Jacobsen, F. Sløk, Acta Chem. Scand. **1993**, *47*, 1012
[27] D. Rentsch, R. Miethchen, Carbohydr. Res. **1996**, *293*, 139
[28] C. Peto, G. Batta, Z. Györgydeak, F. Sztairicskai, J. Carbohydr. Chem. **1996**, *4*, 465

Address for correspondence:
Prof. Dr. Ralf Miethchen
Fachbereich Chemie, Universität Rostock
Buchbinderstr.
D-18051 Rostock
Fax: Internat. code (0) 381 498 1819
e-Mail: ralf.miethchen @chemie.uni-rostock.de