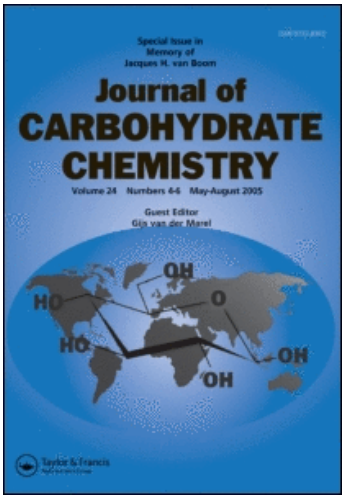

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N-Aryl-*O*-glycosyl Haloacetimidates as Glycosyl Donors

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N-Aryl-*O*-glycosyl Haloacetimidates as Glycosyl Donors

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Reaction of 1-*O*-unprotected tetra-*O*-acetyl- and tetra-*O*-benzyl-glucopyranose with *N*-aryl haloacetimidoyl chlorides in the presence of sodium hydride and 15-crown-5 afforded *N*-aryl-*O*-glucopyranosyl haloacetimidates. Mainly the β-anomers were obtained in this anomeric *O*-acylation-type reaction. The glycosyl donor properties of these haloacetimidates were investigated with 6-*O*- and 4-*O*-unprotected glucopyranosides as acceptors. The results were compared with those obtained with the corresponding *O*-glucopyranosyl trichloroacetimidates as glycosyl donors and the same acceptors. It was found that *N*-(2-chloro-6-methylphenyl)-*O*-glucopyranosyl trifluoroacetimidates (**16Ad**, **16Bd**) exhibit glycosyl donor properties closely related to those of the corresponding *N*-unsubstituted *O*-glucopyranosyl trichloroacetimidates (**12A**, **12B**).

Keywords Carbohydrates; Glycosidation; *N*-Aryl-*O*-glycosyl haloacetimidates; Synthesis; *O*-Imidoylation

INTRODUCTION

O-Glycosyl trichloroacetimidates have become highly useful glycosyl donors as they combine the most convenient preparation with excellent glycosyl donor properties under simple acid catalysis.[1–3] Replacement of the trichloromethyl group, for instance, by the trifluoromethyl group[4] or the dichloro-cyanomethyl group[5] was reported. So far, these modifications of the haloacetimidate leaving group did not exhibit advantages over the trichloroacetimidate group in glycosylation reactions.

Introduction of a substituent at the nitrogen of the imidate group can be reached by replacing the convenient base-catalyzed reversible addition of the anomeric hydroxy group to electron-poor nitriles permitting even anomeric

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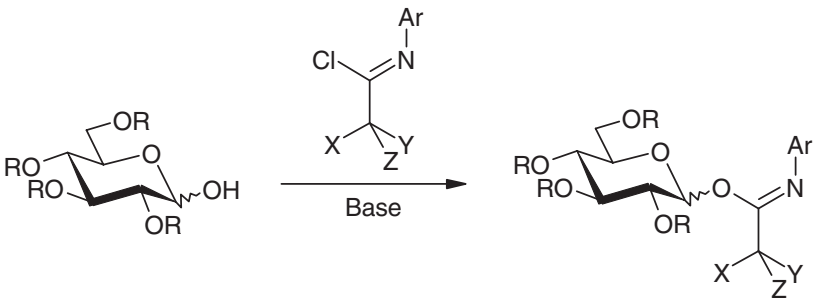
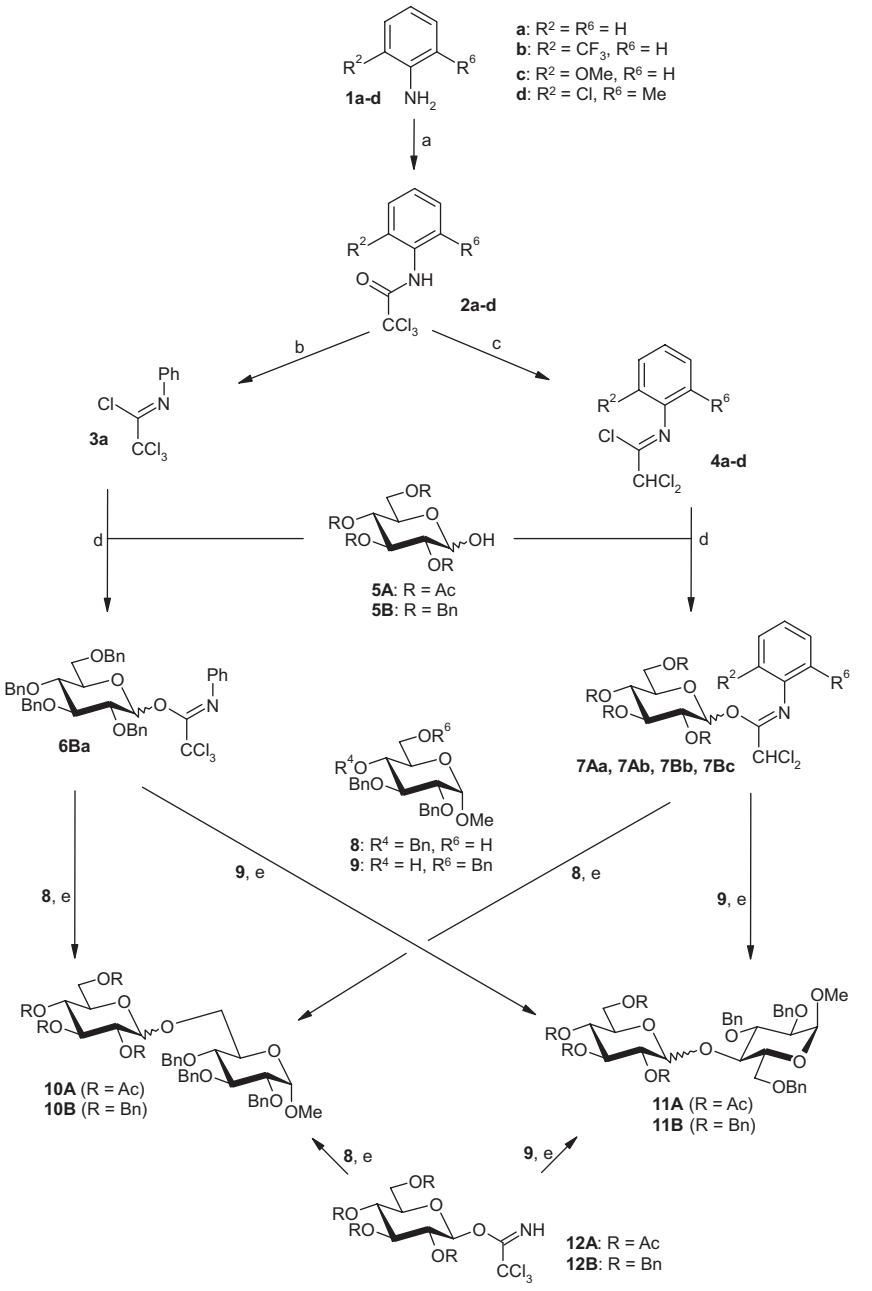


Figure 1: Imidoylation of 1-*O*-unprotected sugars by *N*-substituted imidoyl halides.

stereocontrol for a reaction with *N*-substituted imidoyl halides (Fig. 1).[6,7] Since this anomeric *O*-imidoylation reaction is generally irreversible, anomeric stereocontrol can hardly be achieved.[7,8] However, the available modification of the leaving group character may compensate for the less convenient preparation of such *N*-substituted *O*-glycosyl haloacetimidate donors. As *O*-glycosyl-*N*-phenyl-trifluoroacetimidates (Fig. 1, Ar=Ph, X=Y=Z=F) have previously been investigated as glycosyl donors in various glycosylation reactions,[8,9] earlier comparative studies by our group in this direction will be disclosed.[7]

RESULTS AND DISCUSSION

At first the synthesis and the reactions of *N*-aryl *O*-glucopyranosyl trichloroacetimidates were investigated (Sch. 1). To this end, aniline (**1a**) was transformed via the *N*-trichloroacetyl intermediate **2a** into known imidoyl chloride **3a**.[10,11] Anomeric *O*-imidoylation of *O*-benzyl-protected glucose **5B** with **3a** in the presence of sodium hydride as base and 15-crown-5 as complexing agent for sodium afforded the desired *O*-glucopyranosyl-*N*-phenyl trichloroacetimidate **6Ba** in excellent yield as anomeric mixture ($\alpha/\beta = 3{:}7$).[12] Following reaction of this donor with a primary and a secondary hydroxy group as acceptor, as, for instance, is present in the 6-*O*- and 4-*O*-unprotected glucopyranosides **8** and **9**, respectively, led under standard TMSOTf catalysis at rt to a mixture of the known anomers of **10B**[13,14] and **11B**[15] in good yield (Table 1, entry 1). Comparison of this glycosylation result with that for the corresponding *N*-unsubstituted β-configurated *O*-glucopyranosyl trichloroacetimidate **12B**[12,13] (that is most closely related to the anomeric mixture of **6Ba**) exhibited almost quantitative formation of **10B** and **11B** though in lower anomeric selectivity (Table 1, entry 7). Hence, the preference for the α-anomers in **10B** and **11B** with **6Ba** as donor reflects the lower reactivity of **6Ba** favoring an S_N2-type reaction, as also was observed for **12B** at low temperatures



Scheme 1: *N*-Aryl-*O*-glucopyranosyl-haloacetimidate formation and glycosylation of acceptors **8** and **9**. *Reagents and conditions*: (a) Cl_3C–COCl, Pyr; (b) $POCl_3$, PCl_5; (c) PPh_3, CCl_4, CH_2Cl_2; (d) NaH, 15-crown-15, CH_2Cl_2, rt; (e) TMSOTf (0.1 eq), CH_2Cl_2, rt (see Table 1).

Table 1: Glycosylation results with glycosyl donors **6**, **7**, **12,** and **16** and acceptors **8** and **9** leading to disaccharides **11A**, **B** and **11A**, **B**[a]

Entry	Glycosyl Donor (α/β)[b]	Product with Glycosyl Acceptor **8** ($R^6 = H$)	Product with Glycosyl Acceptor **9** ($R^4 = H$)
1	**6Ba** (3:7)	**10B** 82%, $\alpha:\beta = 4:1$	**11B** 71%, $\alpha:\beta = 5:1$
2	**7Aa** (β)	**10A** 80%, β	**11A** 71%, β
3	**7Ab** (2:3)	**10A** 70%, β	**11A** 62%, β
4	**7Bb** (1:7)	**10B** 77%, $\alpha:\beta = 5:1$	**11B** 69%, $\alpha:\beta = 5:1$
5	**7Bc** (1:9)	**10B** 87%, $\alpha:\beta = 3:1$	**11B** 78%, $\alpha:\beta = 2:1$
6	**12A** (β)	**10A** 82%, β	**11A** 74%, β
7	**12B** (β)	**10B** 98%, $\alpha:\beta = 3:2$	**11B** 85%, $\alpha:\beta = 1:1$
8	**16Aa** (1:3)	**10A** 74%, β	**11A** 67%, β
9	**16Ab** (1:2)	**10A** 59%, β	**11A** 53%, β
10	**16Ac** (1:4)	**10A** 80%, β	**11A** 71%, β
11	**16Ad** (2:1)	**10A** 85%, β	**11A** 74%, β
12	**16Ba** (β)	**10B** 85%, $\alpha:\beta = 1:1$	**11B** 74%, $\alpha:\beta = 1:1$
13	**16Bb** (1:5)	**10B** 71%, $\alpha:\beta = 1:1$	**11B** 63%, $\alpha:\beta = 1:1$
14	**16Bc** (β)	**10B** 91%, $\alpha:\beta = 1:1$	**11B** 82%, $\alpha:\beta = 1:1$
15	**16Bd** (β)	**10B** 98%, $\alpha:\beta = 1:1$	**11B** 89%, $\alpha:\beta = 1:1$

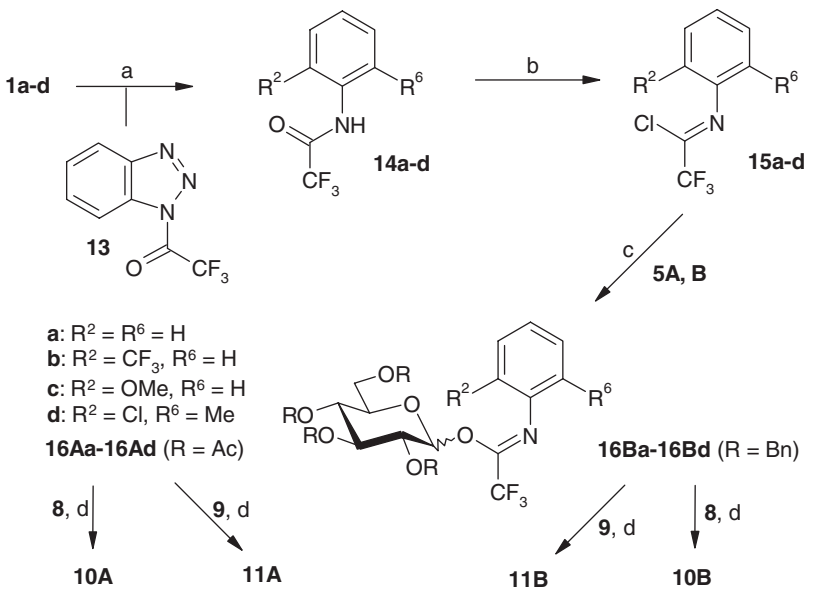
[a]All reactions were carried out in dichloromethane as solvent and TMSOTf (0.1 equivalents) as catalyst at rt.
[b]The anomeric ratio was taken from the ^{1}H NMR spectra.

or by using a less polar solvent; alternatively, through intimate ion pair formation of the activated glycosyl donor, a memory effect could influence the stereocontrol.[1,2]

Thereafter, the reaction of *O*-acetyl-protected **5A** with imidoyl chloride **3a** was investigated. However, presumably due to the lower reactivity of **5A** and the steric bulk of the trichloromethyl group, the reaction was met with difficulties. Therefore, we took advantage of a dehalogenation procedure found for the transformation of **2a** into dichloroacetimidoyl chloride **4a** with the help of triphenylphosphine and carbon tetrachloride[17]; this procedure was similarly applied to **2b–d**, furnishing the corresponding imidoyl chlorides **4b–d**. Reaction of **5A** with **4a** and **4b** readily provided *O*-acetyl-protected glucopyranosyl dihaloacetimidates **7Aa** and **7Ab**; similarly, reaction of **5B** with **4b** and **4c** afforded the *O*-benzyl-protected *O*-glucopyranosyl dichloroacetimidates **7Bb** and **7Bc**. The glycosylation results found for **7Aa** with **8**[18] and **9**[15] as acceptors (Table 1, entry 2) were closely related to those found for the related β-configurated *O*-glucopyranosyl trichloroacetimidate **12A**[1,2,16] with **8** and **9** as acceptors (Table 1, entry 6). Based on the neighboring group participation, as expected, in both cases only the β-linked disaccharides **10B** and **11B** were obtained. Introduction of an electron-withdrawing trifluoromethyl substituent into the *N*-phenyl group as in **7Ab** and **7Bb** did not improve the glycosylation yields with acceptors **8** and **9** (Table 1, entries 3 and 4). However, it is noteworthy that donor **7Bb** furnished mainly α-linked disaccharides (Table 1,

entry 4). The electron-donating 2-methoxy substituent in the *N*-phenyl group as in **7Bc** afforded almost glycosylation yields (Table 1, entry 5) as those found for **12B** (Table 1, entry 7).[1,2,16] This result is presumably due to bidentate complexation of the catalyst by the leaving group, thus exhibiting a remote activation effect, as previously found for the 3-methoxy-2-pyridyloxy (MOP) leaving group.[19]

In order to generate better and less bulky *N*-aryl-haloacetimidate leaving groups, the related trifluoroacetimidate analogs also were prepared (Sch. 2). To this end, anilines **1a–d** were transformed with *N*-trifluoroacetylbenzotriazole[20] (**13**) into the trifluoroacetanilides **14a–d**. Reaction with triphenylphosphine/carbon tetrachloride in dichloromethane readily gave the *N*-aryl imidoyl chlorides **15a–d** that led with **5A** and **5B** in the presence of sodium hydride and 15-crown-5 to the *O*-acetyl-protected glucopyranosyl trifluoroacetimidates **16Aa–16Ad** and to the *O*-benzyl-protected analogs **16Ba–16Bd**, respectively; generally, mainly or exclusively the β-anomers were formed. The glycosidation reaction with acceptors **8** and **9** under the aforementioned conditions clearly showed that donors **16** are superior to the trichloro- (**6Ba**) and dichloroacetimidate analogs **7** (Table 1, entries 8–15). However, only the compounds with 2,6-di-substitution in the *N*-phenyl ring (**16Ad** and **16Bd**) led to glycosylation results (Table 1, entries 11 and 15) as found for the corresponding trichloroacetimidates **12A** and **12B** (Table 1, entries 6 and 7). Hence,



Scheme 2: *N*-Aryl-*O*-glucopyranosyl-trifluoroacetimidate formation and glycosylation of acceptors **8** and **9**. *Reagents and conditions*: (a) CH_2Cl_2; (b) PPh_3, CCl_4, CH_2Cl_2; (c) NaH, 15-crown-15, CH_2Cl_2, rt; (d) TMSOTf (0.1 eq), CH_2Cl_2, rt (see Table 1).

these compounds possess similar glycosyl donor properties as **12A** and **12B**, which is presumably due to additional release of steric strain in the glycosylation step. Catalysis of these glycosylation reactions with $BF_3{\cdot}OEt_2$ was also possible.[7] With glycosyl donors **16Ba–16Bd,** the α,β-selectivities in the glycosidation reactions dropped (Table 1, entries 12–15) as was also found for trichloroacetimidate **12B** when reacted in dichloromethane at rt.[1,2] Hence, it seems that the ease of formation and the reactivity potential of the *O*-glycosyl trichloroacetimidates (as, for instance, **12A**, **B**) can be matched by structurally varied *N*-aryl-*O*-glycosyl haloacetimidates.

CONCLUSION

N-Aryl-*O*-glucopyransoyl haloacetimidates were prepared and their glycosyl donor properties were investigated. The best glycosyl donor properties were found for *N*-(2-chloro-6-methylphenyl)-*O*-glucopyranosyl trifluoroacetimidates (compounds **16Ad** and **16Bd**). Comparison of these glycosyl donors with the corresponding *O*-glucopyranosyl trichloroacetimidates (**12A** and **12B**) exhibited very similar behavior. Interestingly, the less reactive *N*-aryl-*O*-(tetra-*O*-benzyl-glucopyranosyl) dichloroacetimidates (**7Bd** and **7Bc**), having mainly β-configuration, furnished in the glycosylation reaction higher amounts of the inversion products than the more reactive glycosyl donors **12B** or **16Bd**. Yet, similar results were previously observed for **12B** when the reactivity was decreased by lowering the reaction temperature.

EXPERIMENTAL

Solvents were purified by standard procedures: ^{1}H NMR spectra: Bruker AC-250 (250 MHz): internal standard tetramethylsilane (TMS); flash chromatography: silica gel 60 (Baker: 0.04–0.063 mm); thin-layer chromatography (TLC): foil plates, silica gel 60 F_{254} (Merck: layer thickness 0.2 mm); optical rotations: Perkin-Elmer polarimeter 241 MC: 1-dm cell, 20°C; elemental analyses: Heraeus CHN-O-Rapid; MALDI-MS: Kratos (Kompac Maldi 1); ESI-MS: Bruker Esquire 3000 plus.

General Procedure A: Trichloroacetylation of Anilines (1a–d)

To a solution of aniline (2 eq) in dry dioxane (2 mL/1 mmol aniline) was added trichloroacetyl chloride (1 eq) under cooling with ice. After stirring for 30 min, water was added and the reaction mixture extracted three times with ethyl acetate (10 mL/1 mmol aniline). The organic phases were combined and dried with $MgSO_4$, the filtrate concentrated in vacuo, and the resulting product purified.

General Procedure B: Trifluoroacetylation of Anilines (1a–d)

The aniline (1 eq) was dissolved in dry dichloromethane (2 mL/1 mmol aniline). To this solution was added *N*-trifluoro-acetyl-benzotriazole (**13**, 1.1 eq) in portions and then the mixture was stirred for 3 h at rt. After concentration of this mixture, pure product was obtained by flash chromatography.

General Procedure C: Synthesis of the Imidoyl Chlorides 4a–d and 15a–d

The anilides (**2a–d**, **14a–d**) (1 eq) and triphenylphosphane (1.1 eq) were dissolved in a 1:1 mixture of carbon tetrachloride and dichloromethane (2 mL/1 mmol anilide) and the reaction mixture stirred for 4 h at 60°C. Then half of the solvent was removed in vacuo and the residue purified by flash chromatography on ALOX (Aluminia N32–63 active) with dry toluene as solvent.

General Procedure D: Synthesis of *N*-aryl-*O*-glucopyranosyl Haloacetimidates 6Ba, 7Aa, 7Ab, 7Bb, 7Bc, 16Aa–Ad and 16Ba–Bd

5A or **5B** (1 mmol) was dissolved in dry dichloromethane (5 mL) under argon and then 15-crown-5 (220 μL, 1.1 mmol) and sodium hydride (26 mg, 1.1 mmol) added under stirring at rt. After 5 min *N*-aryl-imidoyl chloride (1 to 1.1 mmol) was added and stirring continued for 30 min. The reaction mixture was neutralized with acetic acid and then concentrated in vacuo. The residue was purified by flash chromatography with dry solvents.

General Procedure E: Glycosylation Reactions Furnishing 10A, B and 11A, B

Under argon the glycosyl donor (0.26 mmol) and the acceptor **8** or **9** (0.2 mmol) were dissolved in dry dichloromethane (0.4 mL). A catalytic amount of TMSOTf (0.02 mmol) was then added at rt. After 1 h, the reaction mixture was neutralized with triethylamine and concentrated in vacuo. Flash chromatography with toluene/ethyl acetate (20:1) gave the disaccharides that were identical with independently synthesized material: **10A**, ref. 13; **10B**, ref. 14; **11A**, ref. 15; **11B**, ref. 15.

2,2,2-Trichloroacetyl-anilide (2a) and 2,2,2-Trichloro-*N*-phenyl-acetimidoyl Chloride (3a)

These compounds were obtained as previously described.[10,11]

N-(2-Trifluoromethylphenyl)-trichloroacetamide (2b)

Following general procedure A, from **1b** (2.51 mL, 20 mmol) **2b** (3.05 g, qu.) was obtained as yellow crystals. m.p. 46°C; R_f (toluene/ethyl acetate, 4:1) 0.68. ^{1}H NMR (250 MHz, $CDCl_3$): δ 8.75 (1 H, NH), 8.12 (m_c, 1 H, 6-H), 7.85 (m_c, 1 H, 3-H), 7.71–7.55 (m, 2 H, 4-H, 5-H). Anal. Calcd for $C_9H_5Cl_3F_3NO$ (306.50): C, 35.27; H, 1.64; N, 4.57. Found C, 35.20; H, 1.71; N, 4.67.

N-(2-Methoxyphenyl)-trichloroacetamide (2c)

Following general procedure A, from **1c** (12 g, 1 mol) **2c** (9.51 g, 36%) was obtained as clear viscous mass. R_f (toluene) 0.31. ^{1}H NMR (250 MHz, $CDCl_3$): δ 9.15 (1 H, NH), 8.30 (m_c, 1 H, 6-H), 7.17 (m_c, 1 H, 4-H), 7.01 (m_c, 1 H, 5-H), 6.93 (m_c, 1 H, 3-H), 3.91 (s, 3 H, OCH_3). Anal. Calcd for $C_9H_8Cl_3NO_2$ (268.52): C, 40.26; H, 3.00; N, 5.22. Found C, 40.45; H, 3.08; N, 5.23.

N-(2-Chloro-6-methylphenyl)-trichloroacetamide (2d)

Following general procedure A, from **1d** (6.15 mL, 0.05 mol) **2d** (6.10 g, 42%) was obtained as white crystals. m.p. 141°C; R_f (toluene) 0.15. ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.23–6.98 (m, 3 H, 3-H, 4-H, 5-H), 2.11 (s, 3 H, CH_3). Anal. Calcd for $C_9H_7Cl_4NO$ (286.97): C, 37.67; H, 2.46; N, 4.88. Found C, 37.38; H, 2.28; N, 4.86.

N-Phenyl-dichloroacetimidoyl Chloride (4a)

Following general procedure C, from **2a** (8.3 g, 35 mmol) **4a** (2.72 g, 35%) was obtained as colorless fluid. R_f (toluene) 0.89. ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.42–6.97 (m, 5 H, 2-H, 3-H, 4-H, 5-H, 6-H), 6.43 (s, 1 H, $CHCl_2$). Anal. Calcd for $C_8H_6Cl_3N$ (222.50): C, 43.18; H, 2.72; N, 6.30. Found C, 43.40; H, 2.73; N, 6.32.

N-(2-Trifluoromethylphenyl)-dichloroacetimidoyl Chloride (4b)

Following general procedure C, from **2b** (1.53 g, 5 mmol) **4b** (485 mg, 33%) was obtained as yellow fluid. R_f (toluene/ethyl acetate, 4:1) 0.98. ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.69 (m_c, 1 H, 6-H), 7.58 (m_c, 1 H, 4-H), 7.33 (m_c, 1 H, 5-H), 6.90 (m_c, 1 H, 3-H), 6.48 (s, 1 H, $CHCl_2$). Anal. Calcd for $C_9H_5Cl_3F_3N$ (290.50): C, 37.21; H, 1.73; N, 4.82. Found C, 37.56; H, 1.78; N, 5.01.

N-(2-Methoxyphenyl)-dichloroacetimidoyl Chloride (4c)

Following general procedure C, from **2c** (1.85 g, 7 mmol) **4c** (743 mg, 43%) was obtained as colorless oil. R_f (toluene) 0.81. ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.28–6.87 (m, 4 H, 3-H, 4-H, 5-H, 6-H), 6.53 (s, 1 H, $CHCl_2$), 3.84 (s, 3 H, CH_3).

Anal. Calcd for $C_9H_8Cl_3NO$ (252.52): C, 42.81; H, 3.19; N, 5.55. Found C, 43.31; H, 3.29; N, 5.50.

N-(2-Chloro-6-methylphenyl)-dichloroacetimidoyl Chloride (4d)

Following general procedure C, from **2d** (2.87 g, 10 mmol) **4d** (1.19 g, 44%) was obtained as viscous yellowish oil. R_f (toluene) 0.85. ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.29–6.99 (m, 3 H, 3-H, 4-H, 5-H), 6.53 (s, 1 H, $CHCl_2$), 2.08 (s, 3 H, CH_3). Anal. Calcd for $C_9H_7Cl_4N$ (270.97): C, 39.89; H, 2.60; N, 5.18. Found C, 40.36; H, 2.69; N, 5.18.

N-Phenyl-*O*-(2,3,4,6-tetra-*O*-benzyl-α,β-D-glucopyranosyl) Trichloroacetimidate (6Ba)

Following general procedure D, from **5B** (540 mg, 1 mmol) and **3a** (250 mg, 1 mmol) **6Ba** (647 mg, 85%) was obtained as yellowish oil. R_f (toluene/ethyl acetate, 4:1) 0.98, α/β 3:7. ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.01–6.73 (m, 25 H, 2′-H, 3′-H, 4′-H, 5′-H, 6′-H, 4 Ph), 6.67 (d, 0.3 H, $J_{1,2} = 3.6$ Hz, 1-H$_\alpha$), 5.91 (d, 0.7 H, $J_{1,2} = 8.4$ Hz, 1-H$_\beta$), 5.12–4.51 (m, 8 H, 4 CH_2Ph), 4.22 (dd, 0.3 H, $J_{3,2} = 9.7$, $J_{3,4} = 9.8$ Hz, 3-H$_\alpha$), 3.90–3.62 (m, 5.7 H, 2-H, 3-H$_\beta$, 4-H, 5-H, 6$_A$-H, 6$_B$-H). $C_{42}H_{40}Cl_3NO_6$ (759): ESI-MS (negative mode): m/z = 792 (M-2 H+Cl)$^-$, 758 (M−H)$^-$, 724 (M−Cl)$^-$.

N-Phenyl-*O*-(2,3,4,6-tetra-*O*-acetyl-α,β-D-glucopyranosyl) Dichloroacetimidate (7Aa)

Following general procedure D, from **5A** (340 mg, 1 mmol) and **4a** (230 mg, 1 mmol) **7Aa** (358 mg, 69%) was obtained as clear oil. R_f (toluene/ethyl acetate, 6:1) 0.18. ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.40–6.79 (m, 5 H, NPh), 6.12 (s, 1 H, $CHCl_2$), 5.93 (d, 1 H, $J_{1,2} = 8.2$ Hz, 1-H$_\beta$), 5.41–5.17 (m, 3 H, 2-H, 3-H, 4-H), 4.38–4.12 (dd, dd, 2-H, $J_{gem} = 12.3$, $J_{6A,5} = 4.5$, $J_{6B,5} = 2.3$ Hz, 6$_A$-H, 6$_B$-H), 3.90 (ddd, 1 H, $J_{5,4} = 9.5$, $J_{5,6A} = 4.5$, $J_{5,6B} = 2.3$ Hz, 5-H), 2.02–2.09 (4s, 12 H, 4 OAc). $C_{22}H_{25}Cl_2NO_{10}$ (534.43). FAB-MS (positive mode, matrix: NBOH with NaI): m/z = 533/535 (M)$^+$.

N-(2-Trifluoromethyl-phenyl)-*O*-(2,3,4,6-tetra-*O*-acetyl-α,β-D-glucopyranosyl) Dichloroacetimidate (7Ab)

Following general procedure D, from **5A** (340 mg, 1 mmol) and **4b** (280 mg, 1 mmol) **7Ab** (186 mg, 32%) was obtained as white foam. R_f (toluene/ethyl acetate, 6:1) 0.24. ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.68–7.14 (m, 3-H, 3′-H, 5′-H, 6′-H), 6.89–6.79 (m, 1 H, 4′-H), 6.60 (d, 0.4 H, $J_{1,2} = 3.7$ Hz, 1-H$_\alpha$), 5.99 (s, 0.4 H, $CHCl_2$), 5.97 (s, 0.6 H, $CHCl_2$), 5.92 (d, 0.6 H, $J_{1,2} = 7.9$ Hz, 1-H$_\beta$), 5.65 (dd, 0.4 H, $J_{3,2} = 10.3$, $J_{3,4} = 10.3$ Hz, 3-H$_\alpha$), 5.40–5.11 (m, 2.6 H, 2-H, 3-H$_\beta$, 4-H), 4.37–4.08 (m, 2.4 H, 5-H$_\alpha$, 6$_A$-H, 6$_B$-H), 3.90–3.82 (ddd, 0.6 H, $J_{5,4} = 9.8$, $J_{5,6A}$

= 4.5, $J_{5,6B}$ = 2.4 Hz, 5-H_β), 2.11–1.99 (m, 12 H, 4 OAc). $C_{23}H_{24}Cl_2F_3NO_{10}$ (601). FAB-MS (positive mode, matrix: NBOH with NaI): m/z = 601 $(M)^+$, 624 $(M+Na)^+$.

N-(2-Trifluoromethyl-phenyl)-*O*-(2,3,4,6-tetra-*O*-benzyl-α,β-D-glucopyranosyl) Dichloroacetimidate (7Bb)

Following general procedure D, from **5B** (540 mg, 1 mmol) and **4b** (280 mg, 1 mmol) **7Bb** (343 mg, 43%) was obtained as clear oil. R_f (toluene/ethyl acetate, 8:1) 0.64. ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.68–7.12 (m, 23 H, 3′-H, 5′-H, 6′-H, 4 Ph), 6.80 (m_c, 0.8 H, 4′-H_β), 6.71 (m_c, 0.2 H, 4′-H_α), 6.56 (d, 0.2 H, $J_{1,2}$ = 3.8 Hz, 1-H_α), 6.02 (s, 0.8 H, $CHCl_{2\beta}$), 5.98 (s, 0.2 H, $CHCl_{2\alpha}$), 5.82 (d, 0.8 H, $J_{1,2}$ = 7.9 Hz, 1-H_β), 5.08–3.52 (m, 8 H, 2-H, 3-H, 4-H, 5-H, 6_A-H, 6_B-H, 4 CH_2Ph).

$C_{43}H_{40}Cl_2F_3NO_6$ (793). FAB-MS (positive mode, matrix: NBOH with NaI): m/z = 816 $(M+Na)^+$.

N-(2-Methoxyphenyl)-*O*-(2,3,4,6-tetra-*O*-benzyl-α,β-D-glucopyranosyl) Dichloroacetimidate (7Bc)

Following general procedure D, from **5B** (540 mg, 1 mmol) and **4c** (269 mg, 1 mmol) **7Bc** (188 mg, 25%) was obtained as dark-yellow oil. R_f (toluene/ethyl acetate, 16:1) 0.68. ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.35–6.63 (m, 24 H, 1-H_α, 3′-H, 4′-H, 5′-H, 6′-H, 4 Ph), 6.01 (s, 0.9 H, $CHCl_{2\beta}$), 5.98 (s, 0.1 H, $CHCl_{2\alpha}$), 5.91 (d, 0.9 H, $J_{1,2}$ = 8.4 Hz, 1-H_β), 5.07–4.42 (m, 8 H, 4 CH_2Ph), 3.70–3.57 (m, 9 H, OCH_3, 2-H, 3-H, 4-H, 5-H, 6_A-H, 6_B-H).

N-Phenyl-trifluoroacetamide (14a)

Following general procedure B, from **1a** (0.93 g, 10 mmol) and **13** (2.32 g, 11 mmol) **14a** (1.61 g, 85%) was obtained as white solid. m.p. 87.7°C; R_f (toluene/ethyl acetate, 20:1) 0.63. ^{1}H NMR (250 MHz, $CDCl_3$): δ 8.22–8.01 (1 H, NH), 7.60 (m_c, 2 H, 2-H, 6-H), 7.26 (m_c, 1 H, 4 H). Anal. Calcd for $C_8H_6F_3NO$ (189.13): C, 50.80; H, 3.20; N, 7.41. Found C, 50.61; H, 3.09; N, 7.34.

N-(2-Trifluoromethylphenyl)-trifluoroacetamide (14b)

Following general procedure B, from **1b** (0.63 mL, 5 mmol) and **13** (1.16 g, 5.5 mmol) **14b** (1.23 g, 48%) was obtained as white crystals. m.p. 66°C; R_f (toluene/ethyl acetate, 6:1) 0.82. ^{1}H NMR (250 MHz, $CDCl_3$): δ 8.22 (1 H, NH), 8.08 (m_c, 1 H, 6-H), 7.72–7.57 (m, 2 H, 4-H, 5-H), 7.47 (m_c, 1 H, 3-H). Anal. Calcd for $C_9H_5F_6NO$ (257.16): C, 42.04; H, 1.96; N, 5.45. Found C, 42.52; H, 2.39; N, 5.45.

N-(2-Methoxyphenyl)-trifluoroacetamide (14c)

Following general procedure B, from **1c** (6.00 g, 48.7 mmol) and **13** (11.6 g, 53.9 mmol) **14c** (1.35 g, 62%) was obtained as white crystals. m.p. 39.9°C; R_f (toluene) 0.58. ^{1}H NMR (250 MHz, $CDCl_3$): δ 8.59 (m_c, 1 H, NH), 8.34 (m_c, 1 H, 6-H), 7.26–6.91 (m, 3 H, 3-H, 4-H, 5-H), 3.93 (s, 3 H, OCH_3). Anal. Calcd for $C_9H_8F_3NO_2$ (219.16): C, 49.32; H, 3.68; N, 6.39. Found C, 49.29; H, 3.68; N, 6.41.

N-(2-Chloro-6-methylphenyl)-trifluoroacetamide (14d)

Following general procedure B, from **1d** (0.62 mL, 5 mmol) and **13** (1.16 g, 5.5 mmol) **14d** (493 mg, 41%) was obtained as white crystals. m.p. 71°C; R_f (toluene/ethyl acetate, 2:1) 0.72. ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.68 (1 H, NH), 7.33–7.13 (m, 3 H, 3-H, 4-H, 5-H), 2.28 (s, 3 H, CH_3). Anal. Calcd for $C_9H_7ClF_3NO$ (237.69): C, 45.47; H, 2.96; N, 5.89. Found C, 45.65; H, 2.96; N, 5.91.

N-Phenyl-trifluoroacetimidoyl Chloride (15a)

Following general procedure C, from **14a** (380 mg, 2 mmol) **15a** (277 mg, 66%) was obtained as clear liquid. R_f (toluene) 0.90. ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.45 (m_c, 2 H, 3-H, 5-H), 7.28 (m_c, 1 H, 4-H), 7.09 (m_c, 2 H, 2-H, 6-H). Anal. Calcd for $C_8H_5ClF_3N$ (207.6): C, 46.28; H, 2.43; N, 6.75. Found C, 46.29; H, 2.43; N, 6.78.

N-(2-Trifluoromethylphenyl)-trifluoroacetimidoyl Chloride (15b)

Following general procedure C, from **14b** (514 mg, 2 mmol) **15b** (338 mg, 61%) was obtained as clear viscous liquid. R_f (toluene/ethyl acetate, 12:1) 0.91. ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.72 (m_c, 1 H, 6-H), 7.58 (m_c, 1 H, 4-H), 7.36 (m_c, 1 H, 5-H), 6.93 (m_c, 1 H, 3-H). Anal. Calcd for $C_9H_4ClF_6N$ (275.58): C, 39.22; H, 1.46; N, 5.08. Found C, 38.94; H, 1.50; N, 5.36.

N-(2-Methoxyphenyl)-trifluoroacetimidoyl Chloride (15c)

Following general procedure C, from **14c** (660 mg, 3 mmol) **15c** (473 mg, 66%) was obtained as clear liquid. R_f (toluene) 0.83. ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.28 (m_c, 1 H, 4-H), 7.08–6.96 (m, 3 H, 3-H, 5-H, 6-H), 3.89 (s, 3 H, OCH_3). Anal. Calcd for $C_9H_7ClF_3NO$ (237.61): C, 45.49; H, 2.96; N, 5.89. Found C, 45.68; H, 2.95; N, 6.28.

N-(2-Chloro-6-methylphenyl)-trifluoroacetimidoyl Chloride (15d)

Following general procedure C, from **14d** (474 mg, 2 mmol) **15d** (321 mg, 63%) was obtained as yellowish viscous oil. R_f (toluene/ethyl acetate, 6:1) 0.73. ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.30–7.04 (m, 3 H, 3-H, 4-H, 5-H), 2.08 (s, 3 H, CH_3). Anal. Calcd for $C_9H_6Cl_2N$ (256.05): C, 42.22; H, 2.36; N, 5.46. Found C, 42.39; H, 2.52; N, 5.59.

N-Phenyl-*O*-(2,3,4,6-tetra-*O*-acetyl-α,β-D-glucopyranosyl) Trifluoroacetimidate (16Aa)

Following general procedure D, from **5A** (340 mg, 1 mmol) and **15a** (230 mg, 1.1 mmol) **16Aa** (197 mg, 38%) was obtained as colorless oil. R_f (toluene/ethyl acetate, 4:1) 0.46, α/β 1:3. ^{1}H NMR (250 MHz, $CDCl_3$): δ Rotamere. 7.35–6.74 (5 H, 2′-H, 3′-H, 4′-H, 5′-H, 6′-H), 6.50 (0.25 H, 1-H$_\alpha$), 5.75 (0.75 H, 1-H$_\beta$), 6.54 (0.25 H, $J_{3,2} = 10.3$, $J_{3,4} = 10.4$ Hz, 3-H$_\alpha$), 5.78–5.06 (2.75 H, 2-H, 3-H$_\beta$, 4-H), 4.34–4.04 (2.25 H, 5-H$_\alpha$, 6$_A$-H, 6$_B$-H), 3.74 (0.75 H, 5-H$_\beta$), 2.11–1.99 (m, 12 H, 4 OAc). $C_{22}H_{24}F_3NO_{10}$ (518). FAB-MS (positive mode, matrix: NBOH with NaI): $m/z = 519$ $(M)^+$, 542 $(M+Na)^+$.

N-(2-Trifluoromethylphenyl)-*O*-(2,3,4,6-tetra-*O*-acetyl-α,β-D-glucopyranosyl) Trifluoroacetimidate (16Ab)

Following general procedure D, from **5A** (340 mg, 1 mmol) and **15b** (300 mg, 1.1 mmol) **16Ab** (211 mg, 36%) was obtained as white foam. R_f (toluene/ethyl acetate, 6:1) 0.31, α/β 1:2. ^{1}H NMR (250 MHz, $CDCl_3$): δ Rotamere. 7.33–6.77 (m, 4 H, 3′-H, 4′-H, 5′-H, 6′-H), 6.51 (m$_c$, 0.34 H, 1-H$_\alpha$), 5.76 (m$_c$, 0.66 H, 1-H$_\beta$), 5.31–5.07 (m, 3 H, 2-H, 3-H, 4-H), 4.33–4.03 (dddd, 2 H, $J_{gem} = 12.4$, $J_{6A,5} = 4.5$, $J_{6B,5} = 2.4$ Hz, 6$_A$-H, 6$_B$-H), 3.83–3.61 (m, 1 H, 5-H), 2.10–2.03 (m, 12 H, 4 OAc). $C_{23}H_{23}F_6NO_{10}$ (587.43). FAB-MS (positive mode, matrix: NBOH with NaI): $m/z = 587$ $(M)^+$, 610 $(M+Na)^+$.

N-(2-Methoxyphenyl)-*O*-(2,3,4,6-tetra-*O*-acetyl-α,β-D-glucopyranosyl) Trifluoroacetimidate (16Ac)

Following general procedure D, from **5A** (340 mg, 1 mmol) and **15c** (245 mg, 1 mmol) **16Ac** (197 mg, 36%) was obtained as yellowish oil. R_f (toluene/ethyl acetate, 4:1) 0.36, α/β 1:5. ^{1}H NMR (250 MHz, $CDCl_3$): δ Rotamere. 6.55 (0.2 H, 1-H$_\alpha$), 5.80 (0.8 H, 1-H$_\beta$), 5.57–5.08 (m, 3 H, 3 ring protons), 4.34–3.63 (m, 6 H, OCH_3, 4 ring protons), 2.11–1.98 (m, 12 H, 4 OAc). $C_{23}H_{26}F_3NO_{11}$ (549).

N-(2-Chloro-6-methylphenyl)-*O*-(2,3,4,6-tetra-*O*-acetyl-α,β-D-glucopyranosyl) Trifluoroacetimidate (16Ad)

Following general procedure D, from **5A** (340 mg, 1 mmol) and **15d** (265 mg, 1 mmol) **16Ad** (173 mg, 32%) was obtained as clear oil. R_f (toluene/

ethyl acetate, 6:1) 0.36, α/β 3:2. ^{1}H NMR (250 MHz, $CDCl_3$): δ Rotamere. 7.36–7.02 (m, 3 H, 3′-H, 4′-H, 5′-H), 6.38 (0.65 H, 1-H$_\alpha$), 6.14 (0.35 H, 1-H$_\beta$), 5.49–4.98 (m, 3 H, 2-H, 3-H, 4-H), 4.27–3.97 (m, 3 H, 5-H, 6$_A$-H, 6$_B$-H), 2.08 (s, 3 H, CH_3), 2.05–1.91 (m, 12 H, 4 OAc). $C_{23}H_{25}ClF_3NO_{10}$ (567.94). FAB-MS (positive mode, matrix: NBOH with NaI): $m/z = 590$ $(M+Na)^+$, 740 $(M+NaI+Na)^+$.

N-Phenyl-*O*-(2,3,4,6-tetra-*O*-benzyl-α,β-D-glucopyranosyl) Trifluoroacetimidate (16Ba)

Following general procedure D, from **5B** (540 mg, 1 mmol) and **15a** (230 mg, 1.1 mmol) **16Ba** (320 mg, 45%) was obtained as clear syrup. R_f (toluene/ethyl acetate, 9:1) 0.69. ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.43–6.68 (m, 25 H, 2′-H, 3′-H, 4′-H, 5′-H, 6′-H, 4 Ph), 3.80–3.58 (m, 15 H, 1-H, 2-H; 3-H, 4-H, 5-H, 6$_A$-H, 6$_B$-H, 4 CH_2Ph). $C_{42}H_{40}F_3NO_6$ (711). FAB-MS (positive mode, matrix: NBOH with NaI): $m/z = 711$ $(M)^+$, 734 $(M+Na)^+$.

N-(2-Trifluoromethylphenyl)-*O*-(2,3,4,6-tetra-*O*-benzyl-α,β-D-glucopyranosyl) Trifluoroacetimidate (16Bb)

Following general procedure D, from **5B** (540 mg, 1 mmol) and **15b** (300 mg, 1.1 mmol) **16Bb** (405 mg, 52%) was obtained as clear syrup. R_f (toluene/ethyl acetate, 9:1) 0.61, α/β 1:5. ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.53–6.65 (m, 24 H, 3′-H, 4′-H, 5′-H, 6′-H, 4 Ph), 6.44 (d, 0.17 H, $J_{1,2} = 3.8$ Hz, 1-H$_\alpha$), 5.67 (d, 0.83 H, $J_{1,2} = 8.0$ Hz, 1-H$_\beta$), 5.02–4.43 (m, 8 H, 4 CH_2Ph), 4.08–3.39 (m, 6-H, 2-H, 3-H, 4-H, 5-H, 6$_A$-H, 6$_B$-H). $C_{43}H_{39}F_6NO_6$ (779). FAB-MS (positive mode, matrix: NBOH with NaI): $m/z = 779$ $(M)^+$, 802 $(M+Na)^+$.

N-(2-Methoxphenyl)-*O*-(2,3,4,6-tetra-*O*-benzyl-α,β-D-glucopyranosyl) Trifluoroacetimidate (16Bc)

Following general procedure D, from **5B** (540 mg, 1 mmol) and **15c** (245 mg, 1.1 mmol) **16Bc** (310 mg, 42%) was obtained as yellowish oil. R_f (toluene/ethyl acetate, 9:1) 0.60. ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.40–6.67 (m, 24 H, 3′-H, 4′-H, 5′-H, 6′-H, 4 Ph), 5.01–3.58 (m, 18 H, OCH_3, 1-H, 2-H, 3-H, 4-H, 5-H, 6$_A$-H, 6$_B$-H, 4 CH_2Ph). $C_{43}H_{42}F_3NO_7$ (742).

N-(2-Chloro-4-methylphenyl)-*O*-(2,3,4,6-tetra-*O*-benzyl-α,β-D-glucopyranosyl) Trifluoroacetimidate (16Bd)

Following general procedure D, from **5B** (540 mg, 1 mmol) and **15d** (265 mg, 1.1 mmol) **16Bd** (743 mg, 98%) was obtained as colorless oil. R_f (toluene/ethyl acetate, 2:1) 0.93. ^{1}H NMR (250 MHz, $CDCl_3$): δ Rotamere. 7.37–6.85 (m, 23 H, 3′-H, 4′-H, 5′-H, 4 Ph), 5.54 (1 H, 1-H$_\beta$), 4.93–4.42 (m,

8 H, 4 CH_2Ph), 3.92–3.11 (m, 6 H, 2-H, 3-H, 4-H, 5-H, 6_A-H, 6_B-H), 2.02 (s, 3 H, CH_3). $C_{43}H_{41}ClF_3NO_6$ (760.24). EI-MS: $m/z = 759$ $(M-H)^+$.

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REFERENCES AND NOTES

1. Schmidt, R.R. New methods for the synthesis of glycosides and oligosaccharides—are there alternatives to the Koenigs-Knorr method? *Angew. Chem. Int. Ed. Engl.* **1986**, *25*, 212–235.

2. Schmidt, R.R.; Kinzy, W. Anomeric oxygen activation for glycoside synthesis. The trichloroacetimidate method. *Adv. Carbohydr. Chem. Biochem.* **1994**, *50*, 21–123.

3. Zhu, X.; Schmidt, R.R. New principles of glycoside bond formation. *Angew. Chem. Int. Ed.* **2009**, *48*, 1900–1935.

4. Schmidt, R.R.; Michel, J.; Roos, M. Direkte Synthese von *O*-α- und *O*-β-Glycosylimidaten. *Liebigs Ann. Chem.* **1984**, 1343–1357.

5. Schmelzer, U.; Zhang, Z.; Schmidt, R.R. Dichloro-cyano-acetimidates as glycosyl donors. *J. Carbohydr. Chem.* **2007**, *26*, 223–238.

6. Michel, J. α- und β-*O*-Glycosylimidate: Ihre Herstellung und Anwendung in der Glycosid- und Oligosaccharid-Synthese. Dissertation Universität Konstanz, **1983**. Verlag W. Hartung-Gorre, Konstanz, ISBN-3-923200-24-2.

7. Huchel, U. Neue Methoden zur diastereoselektiven Glycosylierung. Dissertation, Universität Konstanz, **1998**, Verlag Papierflieger, Clausthal-Zellerfeld, ISBN 3-89720-221-2.

8. Adinolfi, M.; Barone, G.; Iadonisi, A.; Schiatarella, M. Iodine/triethylsilane as a convenient promoter system for the activation of disarmed glycosyl trichloro- and *N*-(phenyl)trifluoroacetimidates. *Synlett* **2002**, 269–279; Adinolfi, M.; Iadonisi, A.; Ravidà, A.; Schiatarella, M. Versatile use of Ytterbium (III) Triflate and acid washed molecular sieves in the activation of Glycosyl Trifluoroacetimidate Donors. Assemblage of a biologically relevant Tetrasaccharide sequence of Globo H. *J. Org. Chem.* **2005**, *70*, 5316–5319.

9. Yu, B.; Tao, H. Glycosyl trifluoroacetimidates. Part 1: preparation and application as new glycosyl donors. *Tetrahedron Lett.* **2001**, *42*, 2405–2409; Yu. B.; Tao, H. Glycosyl trifluoroacetimidates. Part 2. Synthesis of dioscin and xiebai saponin I. *J. Org. Chem.* **2002**, *67*, 9099–9102.

10. Lee, J. B.; Nolan, T.J. Sugar Esters: III. New reagent for deoxyhalo sugar preparation. *Can. J. Chem.* **1966**, *44*, 1331.

11. Goerdeler, J.; Panshiri, F. M.; Vollrath, W. Über Imidoyl–isothiocyanate III. *Chem. Ber.* **1975**, *108*, 3071–3078.

12. For a discussion of anomeric *O*-acylation and *O*-alkylation reactions see reference 1 and Schmidt, R.R. Displacement by substitution processes: synthesis of glycosides. *Comprehensive Organic Synthesis,* Vol. 6, Trost, B.M.; Fleming, I.; Winterfeldt, E. Eds., Pergamon Press, Oxford, 1991, pp. 33–64.

13. Ito, Y.; Ogawa, T. Benzeneselenenyltriflate as a promoter of thioglycosides: a new method for O–glycosylation using thioglycosides. *Tetrahedron Lett.* **1988**, *29*, 1061–1064.

14. Pougny, J.R.; Jacquinet, J.C.; Nasr, M.; Duchet, D.; Milat, M.L.; Sinaÿ, P. A novel synthesis of 1,2-*cis*-disaccharides. *J. Am. Chem. Soc.* **1977**, *99*, 6762–6763.

15. Garegg, P.J.; Hultberg, H.; Wallin, S.A. A novel reductive ring-opening of carbohydrate benzylidene acetals. *Carbohydr. Res.* **1982**, *108*, 97–101.

16. Schmidt, R. R.; Stumpp, M. Glycosylimidate, 10. Glycosylphosphate aus Glycosyl (trichloracetimidaten). *Liebigs Ann. Chem.* **1984**, 680–691.

17. Petrova, T.D.; Savchenko, T.I.; Platonov, V.E.; Yacobson, G.G. Preparation and several reaction of *N*-(pentafluorophenyl)haloacetimidoyl chlorides. *Investiya Sibirskogo Otdeleniya Akademii Nank SSSR, Seriya Khimicheeskikh Nank* **1981**, *5*, 109–116.

18. Liptak, A.; Jodal, I.; Nanasi, P. Stereoselective ring-cleavage of 3-*O*-benzyl- and 2,3-di-*O*-benzyl-4,6-*O*-benzylidenehexopyranoside derivatives with the $LiAlH_4$–$AlCl_3$ reagent. *Carbohydr. Res.* **1975**, *44*, 1–11.

19. Hanessian, S.; Bacquet, C.; Leliang, N. Chemistry of the glycosidic linkage. Exceptionally fast and efficient formation of glycosides by remote activation. *Carbohydr. Res.* **1980**, *80*, C17; Hanessian, S. In *Preparative Carbohydrate Chemistry Chapter 16: Glycoside Synthesis Based on the Remote Activation Concept: An Overview.* Marcel Dekker, Inc., New York, **1997**, pp. 381–388, and references therein.

20. Katriztky, A.R.; Yang, B.; Semenzin, D. (Trifluoroacetyl)benzotriazole: a convenient trifluoroacetylating reagent. *J. Org. Chem.* **1997**, *62*, 726–728.