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Novel Stereoselective Glycosidation by the Combined Use of Trityl Halide and Lewis Acid

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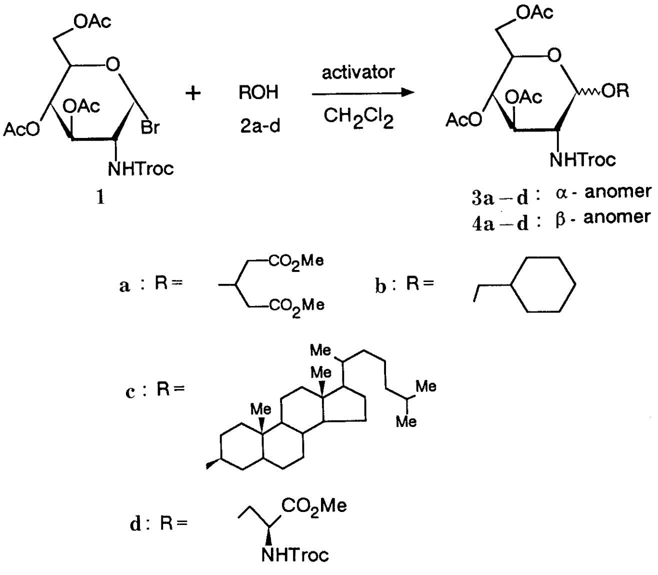
A Novel stereoselective glycosidation was achieved by the combined use of trityl halide and Lewis acid under mild reaction conditions. The stereoselectivity was found to be drastically changed by the presence of trityl halide.

Keywords glycosidation; trityl halide; zinc halide; glucosamine; Lewis acid

Stereoselective glycosidation has been one of the most actively investigated topics in the field of carbohydrate chemistry, with the result that a number of methods of producing glycosides in a highly stereoselective manner have been reported.[1] During the course of studies on the synthesis of biologically active D-glucosamine derivatives, it was necessary to develop a new method for the preparation of key intermediates (**3a**, **4a**) in fairly large quantities. Although several glycosidation reactions using D-glucosamine derivatives have been reported,[2] the catalysts used are usually explosive, toxic, or expensive. We report herein a stereoselective glycosidation reaction activated with Lewis acid alone or with the combination of Lewis acid and trityl halide as a non-toxic and non-explosive catalyst.

For the classical Koenigs–Knorr reaction or the modifications of it, silver salts and mercury compounds have been commonly used as activators.[1] The reaction of glycosyl bromide (**1**), prepared according to the method of Shiba *et al.*,[2h] and **2a** in the presence of silver perchlorate[3] in dichloromethane at 0 °C for 30 min afforded the β-anomer (**4a**) in 70% yield (Table I, run 1). In contrast to the above result, when the reaction was carried out at room temperature for 1.5 h, the α-anomer (**3a**) was obtained in 88% yield (Table I, run 2), suggesting that anomerization took place in the reaction system. No reaction occurred when Lewis acids such as $SnCl_4$,[2i] $TiCl_4$, and trimethylsilyl triflate[2a] were used as activators. Although we prepared the α- and β-anomers (**3a**, **4a**) stereoselectively using silver perchlorate as a catalyst, this reagent is an explosive substance, so that this procedure is thought not to be suitable for large-scale reactions. We therefore searched for a suitable agent for this reaction.

Recently, Mukaiyama *et al.*[4] have reported that trityl cation serves as a catalyst for the glycosidation reaction. They have also demonstrated that the combination of trityl chloride (TrCl) and $SnCl_2$ is effective for activating the aldol condensation reaction under mild reaction conditions.[5] From their studies, it seemed possible that trityl halide and Lewis acid might be combined and used as a catalyst for the glycosidation of **1** and **2a**. When the bromide (**1**) was treated with the alcohol (**2a**) in the presence of $SnCl_2$, no reaction occurred and the starting material was recovered.



Troc = 2,2,2-trichloroethoxycarbonyl

Chart 1

TABLE I. Reaction of **1** and **2a**—**d** by Activation with Lewis Acid or the Combined Use of Lewis Acid and Trityl Halide

Run	Alcohol[a]	Activator[a]	Temperature[b] (°C)	Time (h)	Yield[c] (%)	α : β[d]
1	**2a**	$AgClO_4$	0	0.5	70	1 : >99
2	**2a**	$AgClO_4$	25	1.5	88	>99 : 1
3	**2a**	TrCl–$SnCl_2$	25	120	55[e]	1 : >99
4	**2a**	TrCl–$ZnCl_2$	Reflux	10	93	3 : 97
5	**2a**	TrBr–$ZnBr_2$	Reflux	4	98	69 : 31
6	**2a**	$ZnCl_2$	25	12	75	>99 : 1
7	**2a**	$ZnBr_2$	25	12	80	>99 : 1
8	**2b**	TrCl–$ZnCl_2$	25	13	87	1 : >99
9	**2b**	$ZnCl_2$	25	13	88	>99 : 1
10	**2c**	TrCl–$ZnCl_2$	25	72	85	1 : >99
11	**2c**	$ZnCl_2$	25	72	73	>99 : 1
12	**2d**	TrCl–$ZnCl_2$	Reflux	10	75	1 : >99
13	**2d**	$ZnCl_2$	25	14	75	96 : 4

a) Equimolecular amounts of alcohol and activator were used in each case. *b*) All reactions were carried out in CH_2Cl_2. *c*) Combined yield of the two anomers. *d*) The α : β ratios were determined by isolation of the pure anomers. *e*) The starting material (**1**) was recovered in 31% yield.

Addition of 1 eq of TrCl to this reaction system, however, resulted in the stereoselective production of the β-glycoside (**4a**) in 55% yield along with the recovery of the starting material (**1**) in 31% yield, although the reaction rate was very slow (Table I, run 3). Since the combined use of TrCl and a relatively weak Lewis acid such as $SnCl_2$ was found to be effective for this reaction, we investigated other Lewis acids. The results are shown in Table I.

Treatment of **1** with the alcohol (**2a**) in the presence of TrCl (1 eq) and $ZnCl_2$ (1 eq) in dichloromethane for 10 h at reflux temperature afforded the α- and β-anomers (**3a**, **4a**) in 3% and 90% yields, respectively (Table I, run 4). When the combinaion of trityl bromide (TrBr, 1.0 eq) and $ZnBr_2$ (1.0 eq) was used, the ratio of α- and β-isomers became 69 : 31 in 98% combined yield (Table I, run 5). Attempted glycosidation using trityl tetrafluoroborate resulted in the recovery of the starting material (**1**).

Then, we studied the glycosidation using Lewis acid alone in order to ascertain how the ratio of **3a** and **4a** would change. When $ZnCl_2$ or $ZnBr_2$ was used alone as an activator, only the α-isomer (**3a**) was obtained in 75% and 80% yields, respectively (Table I, runs 6 and 7). It should be emphasized that the stereoselectivity of the glycosidation reaction was found to be changed drastically by the presence of trityl halide. In the course of the reaction, thin layer chromatography (TLC) analysis of the reaction mixture showed the formation of β-anomer (**4a**), which disappeared at the end point of the reaction. The results of these experiments would indicate that the β-anomer (**4a**), formed as a result of kinetic control, undergoes anomerization to the thermodynamically more stable α-anomer (**3a**) in the reaction system. Further studies on the effects of trityl halide on the stereochemistry and the anomerization mechanism are under way.

We have succeeded in developing a novel stereoselective glycosidation using zinc halide alone or in combination with trityl halide. To ascertain the limits of this methodology, we then investigated the reactions of **1** with one of the other alcohols (**2b**—**d**) as a glycosyl acceptor. The results are summarized in Table I. All the reactions of **1** and **2b**—**d** with the combined use of TrCl and $ZnCl_2$ resulted in the stereoselective formation of β-anomers (**4b**—**d**) in good yields (Table I, runs 8, 10, and 12). In contrast when zinc halide was used as the activator, α-anomers (**3b**—**d**) were obtained stereoselectively in good yields (Table I, runs 9, 11, and 13).

Experimental

Melting points were determined on a Yanagimoto melting point apparatus, and are uncorrected. Infrared (IR) spectra were taken on a Hitachi 270-30 infrared spectrophotometer. Proton nuclear magnetic resonance (^{1}H-NMR) spectra were obtained in deuteriochloroform on a JEOL-GSX 500 spectrometer (500 MHz). Chemical shifts are reported in parts per million relative to tetramethylsilane (δ units) as an internal standard. Optical rotations were measured with a Horiba SEDA 200 polarimeter. Column chromatography was performed with Merck Silica gel 60 (70—230 mesh). Preparative thin-layer chromatography (preparative TLC) was performed by using precoated silica gel (150A 1.0 mm thickness; PLK5F Whatman).

3,4,6-Tri-*O*-acetyl-2-deoxy-2-(2,2,2-trichloroethoxycarbonylamino)-α-D-glucopyranosyl Bromide (1)[2h] 1,3,4,6-Tetra-*O*-acetyl-2-deoxy-2-(2,2,2-trichloroethoxycarbonylamino)-α-D-glucopyranose (2.20 g, 4.21 mmol) was dissolved in 25% HBr–AcOH (5 ml) at room temperature. After being stirred for 2 h, the reaction mixture was poured into 5% $NaHCO_3$ and extracted with AcOEt. The organic layer was washed with H_2O and dried over $MgSO_4$. Evaporation of the solvent gave **1** as an oil (2.1 g, 92%). This oil was used without further purification.^{1}H-NMR δ: 2.05, 2.08 and 2.11 (each 3H, s, $OCOCH_3 \times 3$), 4.13 (2H, m, H-2, H-5), 4.27 (1H, m, H-6), 4.33 (1H, dd, J=13.0, 4.0 Hz, H-6), 4.66 (1H, d, J=11.9 Hz, CH_2CCl_3), 4.81 (1H, d, J=11.9 Hz, CH_2CCl_3), 5.24 (1H, t, J=9.0 Hz, H-4), 5.37 (1H, t, J=9.0 Hz, H-3), 6.53 (1H, d, J=4.0 Hz, H-1), 6.80 (1H, br, NH).

1,3-Di(methyloxycarbonyl)isopropyl 3,4,6-Tri-*O*-acetyl-2-deoxy-2-(2,2,2-trichloroethoxycarbonylamino)-α-D-glucopyranoside (3a) $AgClO_4$ (42. mg, 0.20 mmol) was added to a solution of **1** (110 mg, 0.20 mmol) and dimethyl 3-hydroxyglutarate (**2a**) (35 mg, 0.20 mmol) in dichloromethane (5 ml) under ice-cooling. After being stirred for 1.5 h at room temperature, the reaction mixture was diluted with AcOEt and poured into saturated aqueous $NaHCO_3$ solution. The insoluble mateials were filtered off through Celite 545 and washed with AcOEt. The separated organic layer was washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. The residue was chromatographed on silica gel (10 g) with $CHCl_3$–acetone (20 : 1) to give **3a** (110 mg, 88%) as an oil. $[\alpha]_D^{25}$ +46.0° (c=0.63, $CHCl_3$). *Anal.* Calcd for $C_{22}H_{30}Cl_3NO_{14}$: C, 41.36; H, 4.73; N, 2.19. Found: C, 40.84; H, 4.77; N, 2.16. IR (neat): 3358, 2956, 1743, 1533, 1443, 1371, 1227, 1176 cm^{-1}. ^{1}H-NMR δ: 1.99, 2.03 and 2.10 (each 3H, s, $OCOCH_3 \times 3$), 2.56—2.68 (3H, m, CH_2CO_2Me), 2.81 (1H, dd, J=15.9, 5.6 Hz, CH_2CO_2Me), 3.71 (3H, s, CO_2CH_3), 3.74 (3H, s, CO_2CH_3), 4.06 (2H, m, H-2, H-5), 4.12 (1H, dd, J=12.7, 2.4 Hz, H-6), 4.22 (1H, dd, J=12.7, 4.8 Hz, H-6), 4.48 (1H, m, $OC\underline{H}(CH_2COOMe)_2$), 4.62 (1H, d, J=12.7 Hz, CH_2CCl_3), 4.85 (1H, d, J=12.7 Hz, CH_2CCl_3), 5.06 (1H, d, J=4.0 Hz, H-1), 5.07 (1H, t, J=10.3 Hz, H-4), 5.18 (1H, t, J=10.3 Hz, H-3), 5.71 (1H, d, J=9.5 Hz, NH).

1,3-Di(methyloxycarbonyl)isopropyl 3,4,6-Tri-*O*-acetyl-2-deoxy-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside (4a) $AgClO_4$ (156 mg, 0.75 mmol) was added to a solution of **1** (420 mg, 0.75 mmol) and **2a** (133 mg, 0.75 mmol) in dichloromethane (5 ml) under ice-cooling. After being stirred for 0.5 h at the same temperature, the reaction mixture was diluted with AcOEt and poured into saturated aqueous $NaHCO_3$ solution. The insoluble materials were filtered off through Celite 545 and washed with AcOEt. The separated organic layer was washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. The residue was chromatographed on silica gel (30 g) with $CHCl_3$–acetone (20 : 1) to give **4a** (337 mg, 70%) as a powder. mp 95—100 °C, $[\alpha]_D^{25}$ +5.3° (c=0.58, $CHCl_3$). *Anal.* Calcd for $C_{22}H_{30}Cl_3NO_{14}$: C, 41.36; H, 4.73; N, 2.19. Found: C, 41.45; H, 4.72; N, 2.37. IR (KBr): 3364, 2962, 1749, 1551, 1443, 1383, 1293 cm^{-1}. ^{1}H-NMR δ: 2.00, 2.02 and 2.07 (each 3H, s, $OCOCH_3 \times 3$), 2.52—2.61 (2H, m, CH_2CO_2Me), 2.64 (1H, dd, J=17.5, 3.2 Hz, CH_2CO_2Me), 2.89 (1H, dd, J=15.9, 4.8 Hz, CH_2CO_2Me), 3.67 (3H, s, CO_2CH_3), 3.70 (3H, s, CO_2CH_3), 3.72 (2H, m, H-2, H-5), 4.10 (1H, dd, J=12.0, 2.4 Hz, H-6), 4.27 (1H, dd, J=12.0, 4.8 Hz, H-6), 4.45 (1H, m, $OC\underline{H}(CH_2COOMe)_2$), 4.60 (1H, d, J=12.0 Hz, CH_2CCl_3), 4.80 (1H, d, J=12.7 Hz, CH_2CCl_3), 4.80 (1H, d, J=8.0 Hz, H-1), 5.07 (1H, t, J=9.5 Hz, H-4), 5.16 (1H, t, J=9.5 Hz, H-3), 5.22 (1H, d, J=9.0 Hz, NH).

Reaction of 1 and 2a with $ZnCl_2$ $ZnCl_2$ (50 mg, 0.38 mmol) was added to a solution of **1** (210 mg, 0.38 mmol) and **2a** (70 mg, 0.38 mmol) in dichloromethane (4 ml). The reaction mixture was stirred for 12 h at room temperature, then diluted with AcOEt, washed with 5% $NaHCO_3$ and water, dried over $MgSO_4$ and concentrated under reduced pressure. The residue was chromatographed on silica gel (30 g) with $CHCl_3$–acetone (20 : 1) to give **3a** (180 mg, 75%).

Reaction of 1 and 2a with the Combined Use of TrCl and $ZnCl_2$ $ZnCl_2$ (32 mg, 0.23 mmol) was added to a solution of **1** (130 mg, 0.23 mmol), **2a** (45 mg, 0.23 mmol) and TrCl (65 mg, 0.23 mmol) in dichloromethane (2 ml). The reaction mixture was heated under reflux for 10 h. After being cooled, the reaction mixture was diluted with AcOEt, washed with 5% $NaHCO_3$ and water, dried over $MgSO_4$ and concentrated under reduced pressure. The residue was chromatographed on silica gel (15 g) with $CHCl_3$–acetone (20 : 1) to give **3a** (5 mg, 3%) and **4a** (132 mg, 90%), in order of elution.

Cyclohexylmethyl 3,4,6-Tri-*O*-acetyl-2-deoxy-2-(2,2,2-trichloroethoxycarbonylamino)-α-D-glucopyranoside (3b) $ZnCl_2$ (7.5 mg, 0.055 mmol) was added to a solution of **1** (30 mg, 0.055 mmol) and cyclohexylmethanol (**2b**) (6.5 mg, 0.057 mmol) in dichloromethane (1 ml). The reaction mixture was stirred for 13 h at room temperature. The reaction mixture was diluted with AcOEt, washed with 5% $NaHCO_3$ and water, dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by preparative TLC with $CHCl_3$–acetone (50 : 1) to give **3b** (28 mg, 88%) as an oil. $[\alpha]_D^{25}$ +72.5° (c=0.93, $CHCl_3$). *Anal.* Calcd for $C_{22}H_{32}Cl_3NO_{10}$: C, 45.81; H, 5.59; N, 2.43. Found: C, 45.78; H, 5.63; N, 2.66. IR (neat): 3454, 3358, 2932, 2854, 1845, 1755, 1515, 1455, 1371, 1233 cm^{-1}. ^{1}H-NMR

δ: 0.95 (3H, m), 1.19 (1H, m), 1.26 (1H, m), 1.72 (6H, m), 2.01, 2.04 and 2.10 (each 3H, s, $OCOCH_3 \times 3$), 3.25 (1H, dd, $J=10.1$, 6.4 Hz, OCH_2), 3.49 (1H, dd, $J=10.1$, 7.3 Hz, OCH_2), 3.96 (1H, m, H-5), 4.05 (1H, m, H-2), 4.10 (1H, m, H-6), 4.25 (1H, dd, $J=12.8$, 4.6 Hz, H-6), 4.67 (1H, d, $J=11.9$ Hz, CH_2CCl_3), 4.77 (1H, d, $J=11.9$ Hz, CH_2CCl_3), 4.85 (1H, d, $J=3.7$ Hz, H-1), 5.10 (1H, t, $J=10.1$ Hz, H-4), 5.20 (1H, d, $J=10.1$ Hz, NH), 5.24 (1H, t, $J=10.2$ Hz, H-3).

Cyclohexylmethyl 3,4,6-Tri-*O*-acetyl-2-deoxy-2-(2,2,2-trichloroethoxy carbonylamino)-β-D-glucopyranoside (4b) $ZnCl_2$ (45 mg, 0.33 mmol) was added to a solution of **1** (180 mg, 0.33 mmol), **2b** (45 mg, 0.39 mmol) and TrCl (92 mg, 0.33 mmol) in dichloromethane (2 ml). The reaction mixture was stirred for 13 h at room temperature, then diluted with AcOEt, washed with 5% $NaHCO_3$ and water, dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography with $CHCl_3$–acetone (50 : 1) to give **4b** (165 mg, 87%) as a powder. mp 104—105 °C $[\alpha]_D^{25}$ −2.9° ($c=0.41$, $CHCl_3$). *Anal.* Calcd for $C_{22}H_{32}Cl_3NO_{10}$: C, 45.81; H. 5.59; N, 2.43. Found: C, 45.58; H, 5.58; N, 2.61. IR (KBr): 3304, 2932, 2856, 1752, 1552, 1454, 1370, 1238 cm^{-1}. ^{1}NMR δ: 0.90 (2H, m), 1.19 (3H, m), 1.67 (6H, m), 2.02, 2.03 and 2.09 (each 3H, s, $OCOCH_3 \times 3$), 3.24 (1H, dd, $J=9.2$, 7.3 Hz, OCH_2), 3.62 (1H, m, H-2), 3.69 (2H, m, H-5, OCH_2), 4.13 (1H, dd, $J=11.9$, 1.8 Hz, H-6), 4.27 (1H, dd, $J=11.9$, 4.6 Hz, H-6), 4.58 (1H, d, $J=8.3$ Hz, H-1), 4.71 (2H, ABq, $J=11.0$ Hz, CH_2CCl_3), 5.06 (1H, t, $J=10.1$ Hz, H-4), 5.10 (1H, m, NH), 5.29 (1H, t, $J=10.1$ Hz, H-3).

Cholestan-3β-yl 3,4,6-Tri-*O*-acetyl-2-deoxy-2-(2,2,2-trichloroethoxycarbonylamino)-α-D-glucopyranoside (3c) $ZnCl_2$ (28 mg, 0.20 mmol) was added to a solution of **1** (110 mg, 0.20 mmol) and 3-β-chloestanol **(2c)** (79 mg, 0.20 mmol) in dichloromethane (1 ml). The reaction mixture was stirred for 72 h at room temperature. The reaction mixture was diluted with AcOEt, washed with 5% $NaHCO_3$ and water, dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by preparative TLC with $CHCl_3$–acetone (50 : 1) to give **3c** (125 mg, 73%) as a powder. mp 180—182 °C. $[\alpha]_D^{25}$ +79.1° ($c=0.43$, $CHCl_3$). *Anal.* Calcd for $C_{42}H_{66}Cl_3NO_{10} \cdot 0.15CHCl_3$: C, 58.24; H, 7.67; N, 1.61. Found: C, 58.62; H, 7.78; N, 1.81. IR (KBr): 3340, 2928, 2856, 1752, 1650, 1546, 1470, 1382, 1208 cm^{-1}. ^{1}H-NMR δ: 0.65—1.80 (46H, m), 2.00, 2.03 and 2.09 (each 3H, s, $OCOCH_3 \times 3$), 3.53 (1H, m, OCH), 4.01 (1H, td, $J=10.1$, 3.7 Hz, H-2), 4.08 (2H, m, H-5, H-6), 4.23 (1H, dd, $J=11.9$, 4.5 Hz, H-6), 4.66 (1H, d, $J=11.9$ Hz, CH_2CCl_3), 4.78 (1H, d, $J=11.9$ Hz, CH_2CCl_3), 5.01 (1H, d, $J=3.7$ Hz, H-1), 5.08 (1H, t, $J=10.1$ Hz, H-4), 5.19 (1H, d, $J=10.1$ Hz, NH), 5.23 (1H, t, $J=10.1$ Hz, H-3).

Cholestan-3β-yl 3,4,6-Tri-*O*-acetyl-2-deoxy-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside (4c) $ZnCl_2$ (11 mg, 0.083 mmol) was added to a solution of **1** (45 mg, 0.083 mmol), **2c** (32 mg, 0.083 mmol) and TrCl (23 mg, 0.083 mmol) in dichloromethane (1 ml). The reaction mixture was stirred for 72 h at room temperature, then diluted with AcOEt, washed with 5% $NaHCO_3$ and water, dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by preparative TLC with $CHCl_3$–acetone (50 : 1) to give **4c** (60 mg, 85%) as a powder. mp 176—178°C. $[\alpha]_D^{25}$ +14.4° ($c=0.39$, $CHCl_3$). *Anal.* Calcd for $C_{42}H_{66}Cl_3NO_{10}$:C, 59.25; H, 7.81; N, 1.65. Found: C, 59.06; H, 7.82; N, 1.54. IR (KBr): 3396, 2940, 2872, 1750, 1532, 1470, 1382, 1232 cm^{-1}. ^{1}H-NMR δ: 0.60—2.00 (46H, m), 2.02, 2.03 and 2.08 (each 3H, s, $OCOCH_3 \times 3$), 3.48 (1H, m, H-2), 3.58 (1H, m, OCH), 3.68 (1H, m, H-5), 4.11 (1H, m, H-6), 4.27 (1H, dd, $J=11.9$, 4.6 Hz, H-6), 4.67 (1H, d, $J=11.9$ Hz, CH_2CCl_3), 4.76 (1H, d, $J=11.9$ Hz, CH_2CCl_3), 4.81 (1H, d, $J=8.3$ H, H-1), 5.04 (1H, t, $J=10.1$ Hz, H-4), 5.11 (1H, d, $J=7.3$ Hz, NH), 5.38 (1H, t, $J=10.1$ Hz, H-3).

Reaction of 1 and 2d with $ZnCl_2$ $ZnCl_2$ (23 mg, 0.17 mmol) was added to a solution of **1** (90 mg, 0.17 mmol) and *N*-(2,2,2-trichloroethoxycarbonyl)-L-serine methyl ester **(2d)**[6] (59 mg, 0.20 mmol) in dichloromethane (1 ml). The reaction mixture was stirred for 14 h under nitrogen at room temperature, then diluted with AcOEt, washed with 5% $NaHCO_3$ and water, dried over $MgSO_4$ and concentrated under reduced pressure. The residue was chromatographed on a silica gel (15 g) with $CHCl_3$–acetone (20 : 1) to give *N*-(2,2,2-trichloroethoxycarbonyl)-*O*-(3,4,6-tri-*O*-acetyl-2-deoxy-2-(2,2,2-trichloroethoxycarbonylamino)-α-D-glucopyranosyl)-L-serine methyl ester **(3d)** (72 mg, 72%) and *N*-(2,2,2-trichloroethoxycarbonyl)-*O*-(3,4,6-tri-*O*-acetyl-2-deoxy-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranosyl)-L-serine methyl ester **(4d)** (4 mg, 3.2%) in order of elution.

3d: mp 61—64 °C. $[\alpha]_D^{25}$ +75.6° ($c=0.36$, $CHCl_3$). *Anal.* Calcd for $C_{22}H_{28}Cl_6N_2O_{14} \cdot 0.15CHCl_3$: C, 34.32; H, 3.66; N, 3.61. Found: C, 34.17; H, 3.50; N, 3.90. IR (KBr): 3360, 2964, 1748, 1532, 1442, 1372, 1226, 1170 cm^{-1}. ^{1}H-NMR δ: 2.01, 2.04 and 2.11 (each 3H, s, $OCOCH_3 \times 3$), 3.84 (3H, s, CO_2CH_3), 3.93 (1H, m, OCH_2), 3.95 (1H, m, H-5), 4.03 (2H, m, OCH_2, H-2), 4.11 (1H, d, $J=11.9$ Hz, H-6), 4.22 (1H, dd, $J=11.9$, 4.6 Hz, H-6), 4.59 (1H, m, $NCHCO_2CH_3$), 4.66 (1H, d, $J=11.9$ Hz, CH_2CCl_3), 4.74 (1H, d, $J=11.9$ Hz, CH_2CCl_3), 4.78 (1H, d, $J=11.9$ Hz, CH_2CCl_3), 4.80 (1H, d, $J=11.9$ Hz, CH_2CCl_3), 4.88 (1H, d, $J=2.8$ Hz, H-1), 5.08 (1H, t, $J=10.1$ Hz, H-4), 5.19 (1H, t, $J=10.1$ Hz, H-3), 5.31 (1H, d, $J=9.2$ Hz, NH), 6.11 (1H, d, $J=7.3$ Hz, NH).

***N*-(2,2,2-Trichloroethoxycarbonyl)-*O*-(3,4,6-tri-*O*-acetyl-2-deoxy-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranosyl)-L-serine Methyl Ester (4d)** $ZnCl_2$ (40 mg, 0.29 mmol) was added to a solution of **1** (160 mg, 0.29 mmol), **2d** (87 mg, 0.29 mmol) and TrCl (82 mg, 0.29 mmol) in dichloromethane (2 ml). The reaction mixture was heated under reflux for 10 h. After being cooled, the reaction mixture was diluted with AcOEt, washed with 5% $NaHCO_3$ and water, dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by preparative TLC with $CHCl_3$–acetone (20 : 1) to give **4d** (166 mg, 75%) as a powder mp 59—64 °C. $[\alpha]_D^{25}$ +7.8° ($c=0.72$, $CHCl_3$). *Anal.* Calcd for $C_{22}H_{28}Cl_6N_2O_{14} \cdot 0.15CHCl_3$: C, 34.32; H, 3.66; N, 3.61. Found: C, 34.26; H, 3.61; N, 3.91. IR (KBr): 3372, 2964, 1754, 1540, 1442, 1372, 1236, 1170 cm^{-1}. ^{1}H-NMR δ: 2.03 (6H, s, $OCOCH_3 \times 2$), 2.10 (3H, s, $OCOCH_3$), 3.63 (1H, m, H-2), 3.68 (1H, m, H-5), 3.79 (3H, s, $COOCH_3$), 3.92 (1H, dd, $J=10.1$, 2.8 Hz, OCH_2), 4.13 (1H, dd, $J=11.9$, 1.8 Hz, H-6), 4.26 (2H, m, H-6, OCH_2), 4.51 (1H, m, $NCHCO_2CH_3$), 4.65 (1H, d, $J=7.3$ Hz, H-1), 4.68 (1H, d, $J=11.0$ Hz, CH_2CCl_3), 4.74 (1H, d, $J=11.9$ Hz, CH_2CCl_3), 4.79 (1H, d, $J=11.9$ Hz, CH_2CCl_3), 4.84 (1H, d, $J=11.0$ Hz, CH_2CCl_3), 5.06 (1H, t, $J=10.1$ Hz, H-4), 5.23 (1H, t, $J=10.1$ Hz, H-3), 5.25 (1H, br, NH), 5.97 (1H, br, NH).

References and Notes

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