spectrometry of **4** dissolved in TFA (positive ion FAB) showed a signal at $m/z = 607.1631$, which corresponds to the calculated value of 607.1671 for $C_{42}H_{18}N_6$ $[M+H]^+$. The ^1H NMR spectrum ([D]TFA) of **4** contains only four signals in a 1:1:2:2 ratio: a singlet at $\delta = 12.98$, corresponding to the inner protons (H-20, H-22, and H-24), a singlet at $\delta = 9.90$ (H-6, H-12, and H-18), and two doublets at $\delta = 9.39$ and 8.98 for the twelve remaining protons. UV/Vis and fluorescence spectroscopy was carried out on **4** dissolved in $CHCl_3$/TFA (98/2). The solution shows absorptions at $\lambda_{max} = 429$, 404, 383, 332, and 249 nm and exhibits an intense blue fluorescence. The fluorescence emission was observed between 420 to 560 nm with maxima at 452, 481, and 514 nm (excitation at 331 nm). This new compound is insoluble in most organic solvents but exhibits low solubility in strong acids (methane sulfonic or trifluoroacetic acid), probably due to protonation of **4**.

We have prepared the first fully unsaturated heterocyclic analogue of **1**. The results of the mass spectrometry analysis indicate that the strategy used for synthesizing **4** should be also successful for preparing "expanded" heptaazahelicenes.[8]

Experimental procedure

6: Paraformaldehyde (0.026 g, 0.9 mmol) was added to a solution of **5** [7] (0.5 g, 1.8 mmol) in 12 N HCl (100 mL), and the mixture stirred at 50 °C for three weeks. The solution was then added dropwise to 10 N NaOH. The solid was filtered, washed with water and methanol, and dried (0.42 g, 0.75 mmol, 84% yield). An analytically pure sample was obtained by flash chromatography on silica gel (ethyl acetate); m.p. = 320 °C. ^1H NMR (200 MHz, [D$_6$]DMSO): $\delta = 11.30$ (s, 1H, H-17), 10.27 (s, 2H, 2 NH), 9.00 (s, 2H), 8.65 (s, 2H), 8.27 (d, 2H, $J = 9.4$ Hz), 8.18 (d, 2H, $J = 8.9$ Hz), 7.98 (d, 2H, $J = 9.4$ Hz), 7.85 (d, 2H, $J = 8.9$ Hz), 4.27 (m, 4H, CH_2), 1.35 (t, 6H, CH_3); ^{13}C NMR (100 MHz, [D$_6$]DMSO): $\delta = 153.56$, 151.07, 148.28, 147.035, 141.50, 135.73, 131.88, 129.34, 128.98, 127.08, 124.67, 123.22, 122.98, 120.46, 113.35, 60.62, 14.43; UV/Vis (EtOH): λ_{max} (ε) = 427 (7700), 362 (37400), 332 (41600), 280 (41300), 257 (71000); HR-MS (positive ion FAB, *m*-nitrobenyl alcohol matrix): calcd m/z: 556.1985, found: 556.1972 $[M+H]^+$.

7: A solution of **6** (1.6 g, 2.9 mmol) in EtOH (100 mL) and 10 N NaOH (10 mL) was stirred at 90 °C for 24 h. After the solution had cooled to room temperature, **7** was precipitated by addition of water. The solid was filtered, washed with water, methanol and diethyl ether, and dried (0.81 g, 1.9 mmol, 68% yield). An analytically pure sample was obtained by flash chromatography on silica gel (ethyl acetate); m.p. > 320 °C; elemental analysis calcd for $C_{27}H_{17}N_5 \cdot 1H_2O$: C 75.51, H 4.46, N 16.31; found: C 74.94, H 4.37, N 15.86; ^1H NMR (200 MHz, [D]TFA): $\delta = 12.24$ (s, 1H, H-17), 9.40 (s, 2H), 9.05 (d, 2H, $J = 8.8$ Hz), 8.62 (d, 2H, $J = 9.1$ Hz), 8.38 (d, 2H, $J = 8.8$ Hz), 7.72 (m, 4H,); ^{13}C NMR (100 MHz [D$_6$]DMSO): $\delta = 151.68$, 151.11, 150.22, 147.07, 135.56, 132.13, 129.47, 129.27, 125.23, 124.63, 120.98, 120.81, 120.59, 104.65; MS (positive ion FAB): $m/z = 412$ $[M+H]^+$.

4: A mixture of **7** (0.102 g, 0.25 mmol), proflavine (0.053 g, 0.26 mmol), and paraformaldehyde (0.015 g, 0.5 mmol) in 12 N HCl (30 mL) was stirred at 50 °C for 7d. After the solution had cooled, it was basified with diluted NH_4OH. The solid was filtered, washed with water, and dried (0.105 g). Washing the solid with CH_2Cl_2 (3 × 40 mL), DMF (3 × 40 mL), and MeOH (3 × 40 mL) provided pure **4** (0.017 g, 0.028 mmol, 10% yield), m.p. > 320 °C. ^1H NMR (200 MHz, [D]TFA): $\delta = 12.98$ (s, 3H, H-20,22,24), 9.9 (s, 3H, H-6, H-12, H-18), 9.39 (d, 6H, $J = 9.9$ Hz), 8.98 (d, 6H, $J = 9.9$ Hz); UV/Vis ($CHCl_3$/TFA 98/2): λ_{max} (ε) = 429 (13000), 404 (18900), 383 (18000), 332 (63700), 249 (62600); HR-MS (positive ion FAB): calcd $m/z = 607.1671$, found: 607.1631 $[M+H]^+$; elemental analysis calcd for $C_{42}H_{18}N_6 \cdot 10H_2O$: C 64.12, H 4.87, N 10.68; found: C 63.74, H 5.13, N 10.91.

Received: December 9, 1996 [Z 9863 IE]
German version: *Angew. Chem.* **1997**, *109*, 1238–1240

Keywords: arenes · azakekulenes · heterocycles · nitrogen · polycycles

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Stereoselective Synthesis of a C-Glycosidic Analog of *N*-Glucoasparagine**

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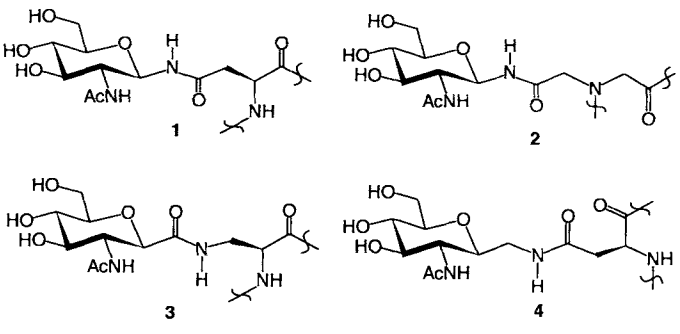
Dedicated to Professor Hans Paulsen on the occasion of his 75th birthday

In drug design glycopeptides are of interest for the modification of biologically active peptides. Recent investigations revealed that the attachment of carbohydrates to peptides improves bioavailability,[1] increases resistance to proteases,[2] improves water solubility,[3] or enables them to penetrate the blood–brain barrier.[4] Most synthetic glycopeptides contain the natural O- or N-glycosidic linkage between the sugar residue and the peptide backbone.[5] To improve the metabolic stability, C-glycosidic amino acids[6] are of interest because the carbon–carbon linkage at the anomeric center should increase the stability towards enzymes, acid, or base. Herein we present the synthesis of a C-glycosidic amino acid whose structure is analogous to that of N^4-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-L-asparagine (Asn(β-GlcNAc) **1**). Already existing analogs are the glycopeptoid **2**,[7] the retroamide **3**, which was recently described by our group,[8] and the C-glycosidic analog **4**.[9]



The key step in the synthesis described here is the coupling of the glycosyl dianion **10** with aldehyde **8**. Reactions of different glycosyl dianions with simple electrophiles have shown that a direct glycosylation is difficult and therefore the formation of a C–C bond with an aldehyde seemed most practical.[10] The

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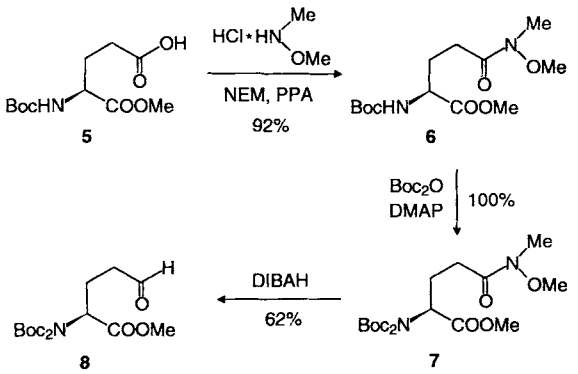
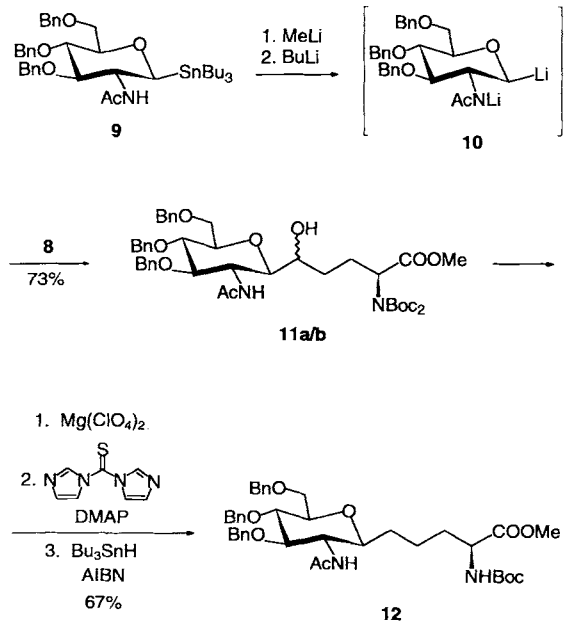
[**] This work was supported by the Fonds der Chemischen Industrie and the Deutsche Forschungsgemeinschaft.

  0570-0833/97/3611-1191 $ 17.50+.50/0

synthesis of the aldehyde **8** started from the *tert*-butoxycarbonyl(Boc)-protected methyl glutamate **5**, which was transformed into the Weinreb amide **6**[11] by using *N*,*O*-dimethylhydroxylamine hydrochloride, *N*-ethylmorpholine (NEM) and propylphosphonic acid anhydride (PPA) as coupling reagent. To prevent the protonation of the dianion **10**, the NH-proton was replaced by a second Boc-protecting group.[12] Subsequently, the protected Weinreb amide **7** was transformed into aldehyde **8** by reduction with diisobutylaluminum hydride (DIBAH).



To generate dianion **10**, the tin compound **9**[8] was first deprotonated with methyllithium and then transmetalated with butyllithium.[13] After addition of the aldehyde **8**,[14] the two diastereomeric C-glycosidic amino acids **11a,b** were obtained in equimolar amounts in a total yield of 73%. During this reaction no epimerization at the α-carbon atom was observed. After one Boc-protecting group had been removed with magnesium perchlorate,[15] the hydroxy group was transformed with 1,1′-thiocarbonyldiimidazole and 4-(dimethylamino)pyridine (DMAP) to give the corresponding thiocarbonyldiimidazole.[16] The subsequent radical reduction with tributyltin hydride and 2,2′-azobisisobutyronitrile (AIBN) gave the desired C-glycosylated amino acid **12** in 67% yield[17] with pure β-configuration at the C-1.[18]



The described procedure offers an easy access to a new C-glycosylated amino acid. The orthogonally protected building block can be prepared in few steps and good yields on a multigram scale.

Received: December 20, 1996 [Z99121E]
German version: *Angew. Chem.* **1997**, *109*, 1240–1241

Keywords: C-glycosides · glycoconjugates · glycopeptides · glycosylated amino acids · peptidomimetics

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[18] The coupling of the proton H-2, which can be easily assigned by DQF-COSY, with the proton H-1 was obtained from the total coupling of H-2 (width of the multiplet of the cross-peak) and the resulting value of about 8 Hz proves the β-configuration at C-1.

  0570-0833/97/3611-1192 $ 17.50+.50/0