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Carbohydrate Research 258 (1994) 299–306

CARBOHYDRATE RESEARCH

The 1,4-linked disaccharide of hyaluronan: synthesis of methyl 2-acetamido-2-deoxy-β-D-glucopyranosyl-(1 → 4)-β-D-glucopyranosiduronic acid

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(Received October 18th, 1993; accepted in revised form December 22nd, 1993)

Hyaluronan (HA, **1**), a major component of the extracellular matrix of mammalian tissues [1], is a repeating polymer of 2-acetamido-2-deoxy-D-glucopyranose (GlcNAc) linked β,1-4 to D-glucuronic acid (GlcA). The GlcA is bound β,1-3 to the GlcNAc residue of the next subunit, hence the sequence GlcNAc(β1-4)GlcA(β1-3)GlcNAc. During the course of high-resolution NMR studies on the solution conformations of HA, it became necessary to fully characterize the methyl β-glycosides **2** and **3** of the two possible disaccharides derivable from this sequence. While the β,1-3-linked dimer is available by chemical degradation [2] of polymeric HA, the β,1-4-linked dimer **3** cannot be obtained in this manner. Several studies on the synthesis of HA fragments have been published [3], but the preparation of unprotected **3** has not been recorded. We now describe the successful synthesis of **3**.

Our initial strategy involved glycosylation of the free 4-hydroxyl group of methyl 2,3-di-*O*-benzyl-6-*O*-(4-methoxybenzyl)-β-D-glucopyranoside (**7**) with *N*-(3,4,6-tri-*O*-benzyl-2-deoxy-2-iodo-α-D-mannopyranosyl)benzenesulfonamide [4] (**4**). Glucose derivative **7** is available from methyl β-D-glucopyranoside in three steps in 57%

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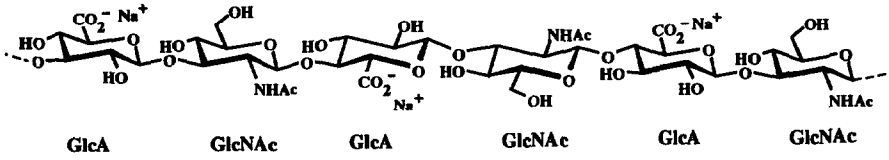
SSDI 0008-6215(93)00012-5



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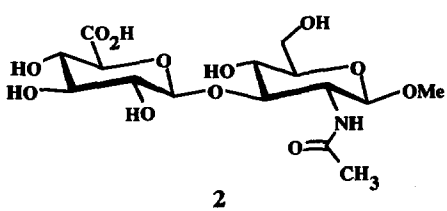

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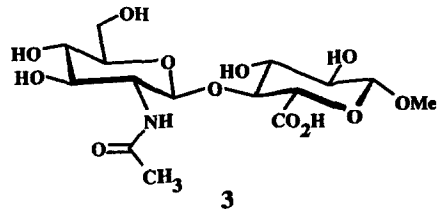


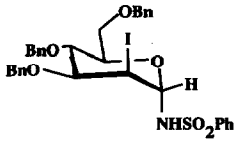
3

overall yield [1] (*1.* *p*-MeOPhCH(OMe)$_2$, TsOH · H_2O, DMF, −MeOH, 50–70°C; *2.* BnBr, NaH, RT; *3.* CF_3CO_2H, $NaBH_3CN$, 3A MS, DMF, RT) [5]. Treatment of a mixture of **4** and **7** with 2.2 equiv of lithium tetramethylpiperidide in THF containing AgOTf at −78°C, followed by warming to room temperature, afforded dimer **8** in 51% yield. Deprotection of the 6-OH (CAN, CH_3CN–H_2O, RT) [5], followed by Jones oxidation [6] and esterification (CH_2N_2, ether), produced **9** in 43% overall yield. Unfortunately, all attempts at removal of the *N*-sulfonyl and benzyl protecting groups to yield **3** resulted in incomplete deprotection and/or decomposition [2].

Since deprotection of **9** proved problematic, we sought a glycosyl donor with a more cooperative N-protecting group. After some exploration, we settled on the widely used glycosyl halide, 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-D-glucopyranosyl bromide [8] (**10**). An advantage of **10** was its ability to couple with a glycosyl acceptor (**13**) having C-6 already oxidized, thereby reducing the number of transformations required on the coupled product. Glucose derivative **13** is available from methyl β-D-glucopyranoside in five steps in 31% overall yield (*1.* *p*-MeOPhCH(OMe)$_2$, TsOH · H_2O, DMF, −MeOH, 50–70°C; *2.* BnBr, NaH, RT; *3.* Me_3SiCl, $NaBH_3CN$, 3A MS, CH_3CN, RT [5]; *4.* CrO_3 · 2 pyr, Ac_2O, ^{t}BuOH, CH_2Cl_2–DMF, RT [9]; *5.* CAN, CH_3CN–H_2O, RT [5]). The reaction of **13** and **10**

[1] Abbreviations used: CAN, ceric ammonium nitrate; MS, molecular sieves; pyr, pyridine; RT, room temperature; MPM, *p*-methoxyphenylmethyl; AgOTf, silver trifluoromethanesulfonate. In NMR assignments for **3** and its precursors G = glucopyranosyl unit or subunit; U = glucopyranosyluronic acid subunit; N = 2-acetamido-2-deoxy-β-D-glucopyranosyl subunit.

[2] Danishefsky and co-workers [7] have recently employed 2-(trimethylsilyl)ethanesulfonamide in their 'sulfonamidoglycosylation' procedure, in place of benzenesulfonamide. The eventual removal of the 2-(trimethylsilyl)ethylsulfonyl group is accomplished under conditions similar to those used for the removal of trimethylsilylethoxymethyl (SEM) protecting groups.



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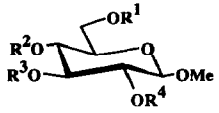
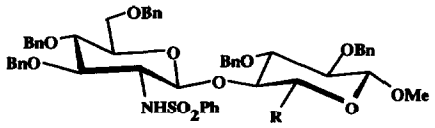


5: R^1, R^2 = CHPh-*p*-(OMe), $R^3 = R^4 = H$

6: R^1, R^2 = CHPh-*p*-(OMe), $R^3 = R^4$ = Bn

7: R^1 = MPM, R^2 = H, $R^3 = R^4$ = Bn

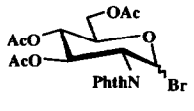


8: R = CH_2OMPM

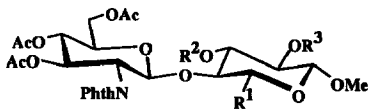
9: R = CO_2Me

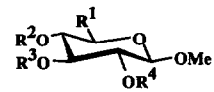
with AgOTf in the presence of *sym*-collidine [10] and 3A MS in CH_2Cl_2 at $-30 \rightarrow 25°C$ provided the protected disaccharide glycoside **14** in 94% yield. Removal of the benzyl protecting groups (30% Pd–C, H_2, EtOAc–H_2O) provided **15** in 75% yield. Unfortunately cleavage of the *tert*-butyl ester using formic acid [11] produced, in addition to **16**, an unidentified side product which we were unable to remove.

The reaction of **7** and **10** with AgOTf in the presence of *sym*-collidine and 3A MS in CH_2Cl_2 [10] at $-30 \rightarrow 25°C$ provided the protected disaccharide glycoside **17**, which could not be purified. However, removal of the 6-OH protecting group (CAN, CH_3CN–H_2O, RT) cleanly produced **18** in 70% yield from **7**. Jones



10





11: $R^1 = CH_2OH$, R^2 = MPM, $R^3 = R^4$ = Bn

12: $R^1 = CO_2{}^tBu$, R^2 = MPM, $R^3 = R^4$ = Bn

13: $R^1 = CO_2{}^tBu$, R^2 = H, $R^3 = R^4$ = Bn

14: $R^1 = CO_2{}^tBu$, $R^2 = R^3$ = Bn

15: $R^1 = CO_2{}^tBu$, $R^2 = R^3$ = H

16: $R^1 = CO_2H$, $R^2 = R^3$ = H

17: $R^1 = CH_2OMPM$, $R^2 = R^3$ = Bn

18: $R^1 = CH_2OH$, $R^2 = R^3$ = Bn

19: $R^1 = CO_2Me$, $R^2 = R^3$ = Bn

20: $R^1 = CO_2Me$, $R^2 = R^3$ = H

oxidation [6], followed by esterification (CH_2N_2, ether), provided **19** in 58% yield. Finally, a four-step sequence accomplished the removal of all protecting groups and the acylation of the free amine function (*1.* H_2, 30% Pd–C, EtOAc–H_2O; *2.* aq NaOH, MeOH, 0°C; *3.* $N_2H_4 \cdot H_2O$, EtOH, reflux; *4.* Ac_2O, MeOH) [8,11] to provide **3** in 52% overall yield from **19**.

1. Experimental

Spectroscopic measurements. —^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ on a Varian UNITY 500 MHz spectrometer at resonance frequencies of 499.84 and 125.67 MHz, respectively, at RT. Spectroscopic data for **3** were obtained at 37°C on a sample dissolved in D_2O, with HOD (δ 4.76 ppm) serving as the internal ^1H reference and the acetamido methyl carbon (δ 23.3 ppm) serving as the internal ^{13}C reference. Optical rotations were determined on a Perkin–Elmer model 141 polarimeter. The mass of compound **3** was determined by negative-ion high resolution FABMS at the University of Illinois School of Chemical Sciences Mass Spectrometry Laboratory.

Methyl 4,6-O-(4-methoxybenzylidene)-β-D-glucopyranoside (**5**).—A solution of methyl β-D-glucopyranoside (20.0 g, 103 mmol), 4-methoxybenzaldehyde dimethyl acetal [5] (28.6 g, 157 mmol), and *p*-toluenesulfonic acid monohydrate (0.18 g, 0.95 mmol) in anhyd DMF (103 mL) was heated at 50°C on a rotary evaporator under water aspirator pressure (~ 22 mmHg) for 1 h. The temperature was then increased to 70°C and the mixture was concentrated in volume to ca. 40 mL. This remaining solution was poured into a stirred slurry of ice (50 g), satd aq $NaHCO_3$ (100 mL), and diethyl ether (100 mL). The white precipitate that formed was filtered, washed with hexanes (3 × 100 mL), H_2O (2 × 100 mL), and dried in vacuo over P_2O_5 to yield 27.8 g (87%) of a white solid which was identified as **5**; mp 176–177°C (from EtOAc); MS: *m/z* calcd for $C_{15}H_{20}O_7$, 312.1209; found, 312.1222; ^1H NMR: 2.71 (s, 1 H, OH), 2.84 (s, 1 H, OH), 3.37 (ddd, 1 H, *J* 10, 9.5, 5.0 Hz, G5), 3.40–3.54 (m, 2 H, G2, G3), 3.50 (s, 3 H, OMe), 3.67–3.76 (m, 2 H, G6, G6'), 3.73 (s, 3 H, ArOMe), 4.25 (d, 1 H, *J* 7.5 Hz, G1), 4.27 (dd, 1 H, *J* 10.5, 5.0 Hz, G4), 5.42 (s, 1 H, ArCH), 6.82–6.84 (m, 2 H, Ar), 7.34–7.36 (m, 2 H, Ar);^{13}C NMR: δ 55.24, 57.40, 66.28, 68.55, 73.10, 74.40, 80.46, 101.75, 104.08, 113.65, 127.56, 129.40, 160.19.

Methyl 2,3-di-O-benzyl-4,6-O-(4-methoxybenzylidene)-β-D-glucopyranoside (**6**).—Sodium hydride (60%, 13.8 g, 346 mmol) was washed with anhyd hexanes (3 × 30 mL) and then dispersed in anhyd DMF (420 mL). A solution of **5** (26.9 g, 86 mmol) in anhyd DMF (78 + 38 + 12 mL) was added dropwise to the NaH slurry at RT. After 5 min BnBr (25.0 mL, 210 mmol) was added dropwise over a 15-min period. The reaction was quenched with MeOH (74 mL) after 3 h, diluted with EtOAc (1000 mL), and washed with H_2O (3 × 390 mL). The combined aq phases were extracted with ether (800 mL). The combined organic phases were dried ($MgSO_4$) and concentrated in vacuo to give 43.3 g of an off-white residue, which was

recrystallized from EtOH–acetone to yield 34.1 g (2 crops, 80%) of a white solid identified as **6**; mp 151°C (from EtOH–acetone); $[\alpha]_D$ −39.0° (*c* 1.19, $CHCl_3$); MS: *m/z* calcd for $C_{29}H_{32}O_7$, 492.2148; found, 492.2155; ^{1}H NMR: δ 3.41 (td, 1 H, *J* 10.0, 5.0 Hz, G5), 3.45 (dd, 1 H, *J* 8.3, 7.5 Hz, G2), 3.59 (s, 1 H, OMe), 3.67 (dd, 1 H, *J* 9.5, 9.0 Hz, G3), 3.77 (ABX, 2 H, J_{AB} 13.0, J_{AX} 10, J_{BX} 10 Hz, G6, G6′), 3.82 (s, 3 H, ArOMe), 4.35 (dd, 1 H, *J* 10.5, 5.0 Hz, G4), 4.42 (d, 1 H, *J* 7.5 Hz, G1), 4.82 (ABq, 2 H, *J* 11.0 Hz, CH_2Ph), 4.85 (ABq, 2 H, *J* 11.0 Hz, CH_2Ph), 5.54 (s, 1 H, ArCH), 6.90–6.92 (m, 2 H, Ar), 7.24–7.26 (m, 12 H, Ar); ^{13}C NMR: δ 57.18, 57.33, 65.89, 68.65, 74.96, 75.15, 80.74, 81.38, 82.11, 101.02, 105.12, 113.50, 127.24, 127.50, 127.57, 127.92, 127.95, 128.19, 128.24, 129.77, 138.37, 138.47, 159.93. Anal. Calcd for $C_{29}H_{32}O_7$ (492.571): C, 70.70; H, 6.55. Found: C, 70.57; H, 6.67.

Methyl 2,3-di-O-benzyl-4,6-O-(4-methoxybenzyl)-β-D-glucopyranoside (**7**).—A solution of CF_3CO_2H (15.6 mL, 203 mmol) in anhyd DMF (120 mL) over 3A MS at 0°C was added to a slurry of **6** (10.0 g, 20.3 mmol), $NaBH_3CN$ (6.72 g, 102 mmol), and crushed 3A MS (10.0 g) in anhyd DMF (160 mL) at RT. After 17 h the mixture was filtered through Celite into iced satd aq $NaHCO_3$ (280 mL). The aq phase was extracted with CH_2Cl_2 (5 × 160 mL). The combined organic phases were washed with satd aq $NaHCO_3$ (280 mL), water (280 mL), and satd aq NaCl (280 mL), dried ($MgSO_4$), and concentrated in vacuo to give a white solid. This was purified by flash column chromatography [12] (7 : 1 toluene–EtOAc) to yield 8.45 g (84%) of a colorless oil, which slowly solidified to a white solid and was identified as **7**: $[\alpha]_D$ −18.1° (*c* 1.10, $CHCl_3$); ^{1}H NMR: δ 3.33–3.38 (m, 1 H, G5), 3.34 (dd, 1 H, *J* 9.0, 7.5 Hz, G2), 3.39 (dd, 1 H, *J* 9.0, 9.0 Hz, G3), 3.50 (s, 3 H, OMe), 3.50–3.54 (m, 1 H, G4), 3.65 (ABX, 2 H, J_{AB} 10.4, J_{AX} 5.4, J_{BX} 4.6 Hz, G6,G6′), 3.74 (s, 3 H, ArOMe), 4.26 (d, 1 H, *J* 7.5 Hz, G1), 4.46 (ABq, 2 H, *J* 11.8 Hz, CH_2Ph), 4.75 (ABq, 2 H, *J* 11.3 Hz, CH_2Ph), 4.77 (ABq, 2 H, *J* 11.5 Hz, CH_2Ph), 6.79–6.83 (m, 2 H, Ar), 7.18–7.31 (m, 12 H, Ar); ^{13}C NMR: δ 55.14, 56.98, 69.90, 71.62, 73.21, 73.92, 74.55, 75.13, 81.67, 83.91, 104.64, 113.73, 127.54, 127.67, 127.83, 127.98, 128.25, 128.39, 129.26, 129.90, 138.42, 138.59, 159.19. Anal. Calcd for $C_{29}H_{34}O_7$ (494.584): C, 70.43; H, 6.93. Found: C, 70.57; H, 7.03.

Methyl O-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-(1 → 4)-β-D-glucopyranosiduronic acid (**3**).—A slurry of **7** (1.04 g, 2.1 mmol), AgOTf (1.88 g, 7.3 mmol), crushed 3A MS, and 2,4,6-collidine (0.83 mL, 6.3 mmol) in anhyd CH_2Cl_2 (20 mL) was stirred at RT for 1 h then cooled to −30°C. A slurry of **10** (3.75 g, 7.6 mmol) and crushed 3A MS in anhyd CH_2Cl_2 (10 mL) was stirred at RT for 1 h, then added dropwise to the above slurry at −30°C. After 0.5 h the mixture was allowed to warm to RT and stirred a further 4 h. The mixture was filtered through Celite, the solids were washed with CH_2Cl_2, and the combined filtrate was washed successively with satd aq $NaHCO_3$ (30 mL), M aq $Na_2S_2O_3$ (3 × 25 mL), water (25 mL), 10% aq citric acid (25 mL), satd aq $NaHCO_3$ (25 mL), H_2O (25 mL), and satd aq NaCl (25 mL), dried (Na_2SO_4), and concentrated in vacuo to give a bright-yellow foam. The foam was purified by flash column chromatography (5 : 1 toluene–EtOAc) to yield 1.85 g of a sticky off-white foam that was identified as impure methyl *O*-(3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1 → 4)-2,3-di-*O*-benzyl-6-*O*-(4-methoxybenzyl)-β-D-glucopyranoside (**17**).

CAN (2.30 g, 4.2 mmol) was added to a solution of crude **17** (1.85 g, ~0.56 mmol) in 9:1 CH_3CN–H_2O (32 mL). After 3.5 h the mixture was concentrated in vacuo and the residue was dissolved in EtOAc (125 mL). The solution was washed with satd aq $NaHCO_3$ (40 mL), H_2O (40 mL), and satd aq NaCl (40 mL), dried ($MgSO_4$), and concentrated in vacuo to give an off-white foam. This was purified by flash column chromatography (3:2 toluene–EtOAc) to yield 0.96 g (58% from **7**) of white foam identified as methyl *O*-(3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1 → 4)-2,3-di-*O*-benzyl-β-D-glucopyranoside: $[\alpha]_D$ +37.8° (*c* 0.50, $CHCl_3$); ^{1}H NMR: δ 1.82 (s, 3 H, Ac), 1.96 (s, 3 H, Ac), 1.98 (s, 3 H, Ac), 3.20 (dtd, 1 H, *J* 9.5, 2.0, 1.5 Hz, G5), 3.32 (dd, 1 H, *J* 8.8, 7.8 Hz, G2), 3.34–3.38 (m, 1 H, N5), 3.46 (s, 3 H, OMe), 3.47–3.50 (m, 1 H, G6), 3.56 (br d, 1 H, *J* 12.5 Hz, G6′), 3.65, (dd, 1 H, *J* 9.0, 9.0 Hz, G3), 3.75 (dd, 1 H, *J* 12.3, 2.3 Hz, N6), 3.83, (dd, 1 H, *J* 9.0, 8.5 Hz, G4), 4.02 (dd, 1 H, *J* 12.3, 3.8 Hz, N6′), 4.24 (dd, 2 H, *J* 10.3, 8.8 Hz, N2), 4.24 (d, 1 H, *J* 7.5 Hz, G1), 4.68 (ABq, 2 H, *J* 11.0 Hz, CH_2Ph), 4.97 (ABq, 2 H, *J* 12.0 Hz, CH_2Ph), 5.12 (dd, 1 H, *J* 10.0, 9.5 Hz, N4), 5.69 (dd, 1 H, *J* 10.8, 9.3 Hz, N3), 5.81 (d, 1 H, *J* 8.5 Hz, N1), 7.17–7.37 (m, 10 H, Ar), 7.75–7.89 (AA′BB′, 4 H, Phth); ^{13}C NMR: δ 20.30, 20.50, 20.61, 55.37, 57.05, 60.82, 61.33, 68.31, 70.76, 71.73, 74.04, 74.12, 74.58, 75.69, 82.10, 82.88, 98.09, 104.53, 123.40, 125.23, 126.10, 127.02, 127.54, 127.94, 128.16, 128.20, 128.27, 128.96, 131.54, 134.13, 138.14, 139.13, 169.34, 170.03, 170.57.

A solution of chromium trioxide (0.517 g, 5.17 mmol) in 3 M aq H_2SO_4 (0.27 mL concd H_2SO_4–1.40 mL H_2O) was added to a solution of **18** (0.43 g, 0.54 mmol) in 3:2 acetone–CH_2Cl_2 (7.0 mL) at 0°C. After 15 min the mixture was allowed to warm to RT. The reaction was quenched with EtOH after 4 h and the mixture was filtered. The filtrate was concentrated in vacuo to remove volatiles and the remaining aq phase was extracted with $CHCl_3$ (4 × 10 mL). The combined organic phases were washed with H_2O (10 mL) and satd aq NaCl (10 mL), dried (Na_2SO_4), and concentrated in vacuo to give a brown foam, which was treated with diazomethane generated from Diazald® [13]. The resulting brown solid was purified by flash column chromatography (5:1 toluene–EtOAc) to yield 0.26 g (58%) of a colorless oil identified as methyl *O*-(3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1 → 4)-(methyl 2,3-di-*O*-benzyl-β-D-glucopyranosid)uronate (**19**): $[\alpha]_D$ −1.9° (*c* 0.12, $CHCl_3$); ^{1}H NMR: δ 1.86 (s, 3 H, Ac), 2.00 (s, 6 H, Ac), 3.42 (dd, 1 H, *J* 9.0, 7.5 Hz, U2), 3.46 (s, 3 H, OMe), 3.63 (dd, 1 H, *J* 9.0, 9.0 Hz, U3), 3.64 (s, 3 H, CO_2Me), 3.61–3.65 (m, 1 H, N5), 3.71 (d, 1 H, *J* 10.0 Hz, U5), 3.91 (dd, 1 H, *J* 12.0, 2.0 Hz, N6), 4.11–4.16 (m, 2 H, N6′, U4), 4.24 (dd, 1 H, *J* 11.0, 8.5 Hz, N2), 4.27 (d, 1 H, *J* 7.5 Hz, U1), 4.70 (ABq, 2 H, *J* 11.3 Hz, CH_2Ph), 4.95 (ABq, 2 H, *J* 11.8 Hz, CH_2Ph), 5.14 (dd, 1 H, *J* 10.3, 9.3 Hz, N4), 5.58 (d, 1 H, *J* 8.0 Hz, N1), 5.78 (dd, 1 H, *J* 10.8, 9.3 Hz, N3), 7.17–7.40 (m, 10 H, Ar), 7.75–7.79 (m, 2 H, Phth), 7.89 (br s, 2 H, Phth); ^{13}C NMR: δ 20.36, 20.55, 20.62, 52.54, 55.06, 57.18, 61.54, 68.53, 70.53, 71.63, 74.06, 74.54, 74.60, 77.49, 81.30, 82.07, 97.54, 104.75, 123.38, 125.26, 126.69, 127.20, 127.56, 127.93, 128.19, 128.22, 129.00, 134.05, 134.08, 134.12, 134.16, 138.13, 138.93, 168.24, 169.43, 170.71, 170.61.

A slurry of **19** (0.209 g, 0.255 mmol) and 30% Pd–C in 10:1 EtOAc–H_2O (11 mL) was subjected to H_2 (51 psig) in a Parr apparatus. After 4 days the mixture

was filtered through Celite and concentrated in vacuo to give a yellow oil. The oil was purified by flash column chromatography (2:1 EtOAc–toluene) to yield 0.125 g (77%) of a white foam that was identified as **20**. Iced N aq NaOH (5.8 mL) was added to a solution of **20** (0.125 g, 0.195 mmol) in MeOH (23 mL) at 0°C. After 2.5 h the mixture was neutralized to pH 7 with glacial AcOH (0.6 mL) and concentrated in vacuo to give a white solid. The white solid was dissolved in anhyd EtOH (18 mL), the solution was degassed with N_2, hydrazinc monohydrate (3.1 mL, 64 mmol) was added, and the mixture was heated to 85°C. After 18.5 h the solution was concentrated in vacuo while removing the residual H_2O as a toluene–EtOH azeotrope to give a white solid. The solid was dissolved in anhyd MeOH (6.0 mL), the solution was cooled to 0°C, and Ac_2O (1.5 mL) was added. After 2 h the mixture was concentrated in vacuo and azeotroped with toluene to give a white solid, which was dissolved in H_2O, passed through a column of AG 50W-X4, and concentrated in vacuo to give a yellow solid. This solid was purified by flash column chromatography (1:1 $CHCl_3$–MeOH) to yield 0.0503 g (62%) of a white solid which was identified as **3**. The TLC and the ^1H and ^{13}C NMR spectra of **3** all showed it to be a single compound, > 99% pure based upon the signal-to-noise ratios of the NMR spectra. ^1H NMR (D_2O): 2.04 (s, 3 H, Ac), 3.32 (dd, 1 H, *J* 9.5, 8.0 Hz, U2), 3.45–3.49 (m, 2 H, N4, N5), 3.52 (dd, 1 H, *J* 10.5, 9.0 Hz, N3), 3.54 (s, 3 H, OMe), 3.58 (dd, 1 H, *J* 9.5, 8.5 Hz, U3), 3.69 (m, 1 H, N2) 3.70 (m, 1 H, U5), 3.73 (m, 1 H, U4), 3.76–3.77 (m, 1 H, N6′), 3.90–3.93 (m, 1 H, N6), 4.37 (d, 1 H, *J* 7.8 Hz, U1), 4.54 (d, 1 H, *J* 8.5 Hz, N1); ^{13}C NMR (D_2O): δ 23.3 ($CH_3C=O$), 55.96 (N2), 56.99 (OMe), 60.28 (N6), 69.46 (N4/N5), 72.43 (U2), 73.58 (U3,N3), 75.58 (N5/N4), 76.35 (U5), 79.70 (U4), 100.43 (N1), 103.86 (U1), 173.99 (C = O), 174.56 (C = O). MS: *m/z* calcd. for $C_{15}H_{24}NO_{12}$, 410.1299; found, 410.1294.

Acknowledgments

Financial support was provided by the Whitaker Foundation and the National Institutes of Health (R29 AR39801). We thank Signe Holmbeck for expert assistance in obtaining and analyzing the NMR spectra of **3**. The NMR spectrometer was purchased in part with funds from the NSF (CHE-8813550) and NIH (SIO RRO 4981) shared instrumentation programs. We are grateful to Dr. Steven L. Mullen, University of Illinois, for performing MS analysis of the final compound, **3**. The 70-SE-4F mass spectrometer used was purchased, in part, with funds from the National Institute of General Medical Sciences (GM 27029).

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