at 60 °C for 6 h. The cooled reaction mixture was diluted with water (65 mL), acidified to pH 1 using 10% HCl, and then extracted with ether (3 × 150 mL). The combined ether extract was dried ($MgSO_4$) and concentrated. Distillation of the residue gave 1.85 g, (79%) of Mosher's acid, bp 90–93 °C (0.3 mmHg) [lit.[3] bp 105–110 °C (1.0 mmHg)]. Spectral data were in accord with that of an authentic sample.

Acknowledgment. We are grateful to the Natural Sciences and Engineering Research Council of Canada for support of this research.

Registry No. 1, 434-45-7; 3, 81655-41-6; 4, 141090-95-1; TTA, 25436-07-1; PEG-400, 25322-68-3; TDA-1, 70384-51-9; Cl_3CCO_2H·Na, 650-51-1; $Bu_4N^+·HSO_4^-$, 32503-27-8; $(n\text{-}C_8H_{17})_4N^+·Br^-$, 14866-33-2; 18-crown-6, 17455-13-9; dibenzo-18-crown-6, 14187-32-7; dicyclohexano-18-crown-6, 16069-36-6.

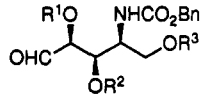
A Convenient Preparation of Terminally Differentiated, Selectively Protected Six-Carbon Synthons from D-Glucosamine

Robert S. Coleman,*[1a] Yong Dong, and Andrew J. Carpenter[1b]

Department of Chemistry and Biochemistry, University of South Carolina, Columbia, South Carolina 29208

Received March 2, 1992

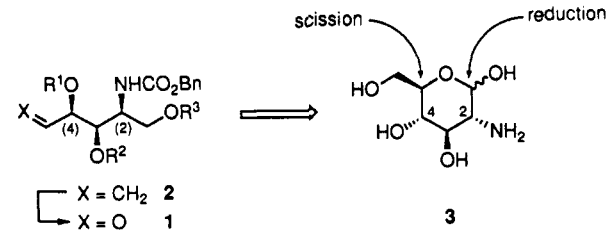
In the course of studies directed toward the total synthesis of the naturally occurring antitumor agents azinomycin A and B,[2] we developed a requirement for five-carbon fragments[3] bearing the absolute stereochemistry and selectively protected functional groups depicted by aldehyde **1**. This requirement was subject to several considerations, including the ability to smoothly unmask a potentially unstable aldehyde, to produce a selectively protected *syn*-1,2-diol ($R^1 \neq R^2$), and to readily access an unprotected primary hydroxyl group in **1** (R^3 = H). Economic considerations dictated that targets such as **1** must be available in homoenantiomeric form. Herein, we detail a high-yielding, effectual synthetic route to variably protected precursors of aldehyde **1**, subject to efficiently satisfying the conditions specified above.



1

The synthesis of systems related to **1** relied on the observation that the three stereogenic centers of aldehyde **1** possess the same absolute configuration as C2, C3, and C4 of D-glucosamine (**3**), a readily available and inexpensive starting material ($20/mol).[3] This strategic observation is outlined in Scheme I. Aldehyde **1** would be available

Scheme I



from olefin **2** by oxidative cleavage, conceptually providing a convertible precursor that in turn can be mapped onto the pyran skeleton of D-glucosamine (**3**). In turn, suitable protection of the C2–C4 amino diol functionality of **3**, pyran ring scission using a Vasella fragmentation,[4] and reduction of C1 to the alcohol oxidation state would provide ready entry into systems depicted by **2**.

Synthesis of the variously protected 6-deoxy-6-iodo-D-glucosamine derivatives **10a–d** is detailed in Scheme II. Reaction of carbamate **4**[5] with *p*-anisaldehyde or benzaldehyde dimethyl acetal (cat. CSA, DMF, 90 °C, 12–48 h)[6] afforded 4,6-*O*-benzylidene acetals **5a** (75%; PMP = *p*-methoxyphenyl) and **6a** (73%). Protection of the remaining C3-hydroxyl group as the corresponding benzyl ether (**5a**; KH, $PhCH_2Br$, cat. $n\text{-}Bu_4NI$, THF, 0 °C, 67%) or silyl ether (**6a**; *t*-$BuMe_2SiOTf$, 2,6-lutidine, CH_2Cl_2, 24 °C, 100%) afforded **5b** and **6b**, respectively. Cleavage of the labile *p*-methoxybenzylidene acetal of **5a** (2% HCl in CH_3OH, 24 °C, 92%) afforded diol **7**. Selective iodination of the primary C6-hydroxyl group of **8** (I_2, Ph_3P, pyridine, toluene, 70 °C, 87%)[7] afforded **8**; acetylation of the remaining C4-hydroxyl group of **9** (Ac_2O, Et_3N, CH_2Cl_2, 24 °C, 100%) afforded 6-deoxy-6-iodo-D-glucosamine derivative **10a**. Alternatively, the benzylidene acetal of **6b** was cleaved using the Hanessian–Hullar protocol[8] (*N*-bromosuccinimide, cat. AIBN, $BaCO_3$, CCl_4, reflux, 72%) to provide the fully protected 6-bromo-6-deoxy-D-glucosamine derivative **9**, which was converted to iodide **10b** (NaI, acetone, reflux, 100%).[9] Symmetrically protected 6-deoxy-6-iodo-D-glucosamine derivatives **10c** and **10d** were prepared from carbamate **4** by selective iodination of the primary C6-hydroxyl group (I_2, Ph_3P, pyridine, toluene, 80 °C, 69%)[7] and either silylation (*t*-$BuMe_2SiOTf$, 2,6-lutidine, CH_2Cl_2, 24 °C, 52%) or acylation (Ac_2O, pyridine, 24 °C, 100%) of the remaining secondary hydroxyl groups.

Scission of the pyran ring system (Scheme III) was achieved by Vasella fragmentation[4a] of iodides **10a–d** (activated Zn, 95% EtOH, 78 °C, 1 h), in a process that cleanly and in high yield afforded the corresponding 5-hexenal derivatives **11a–d** (X = O), with no detectable epimerization of the C2-stereogenic center (^1H NMR). In

(1) (a) Recipient of a Camille and Henry Dreyfus Foundation Distinguished New Faculty Award (1989–1994) and an American Cancer Society Junior Faculty Research Award (1991–1993). (b) Recipient of a U.S. Department of Education graduate fellowship (1991–1992).

(2) (a) Coleman, R. S.; Carpenter, A. J. *J. Org. Chem.* Submitted for publication. (b) Nagaoka, K.; Matsumoto, M.; Oono, J.; Yokoi, K.; Ishizeki, S.; Nakashima, T. *J. Antibiot.* **1986**, *39*, 1527. Yokoi, K.; Nagaoka, K.; Nakashima, T. *Chem. Pharm. Bull.* **1986**, *34*, 4554. Ishizeki, S.; Ohtsuka, M.; Irinoda, K.; Kukita, K.-I.; Nagaoka, K.; Nakashima, T. *J. Antibiot.* **1987**, *40*, 60.

(3) Hanessian, S. *Acc. Chem. Res.* **1979**, *12*, 159. Hanessian, S. *Total Synthesis of Natural Products: The 'Chiron' Approach*; Pergamon Press: Oxford, 1983. Schmidt, R. R.; Maier, M. *Synthesis* **1982**, 747.

(4) (a) Bernet, B.; Vasella, A. *Helv. Chim. Acta* **1984**, *67*, 1328. (b) For a closely related strategy in which tri-*O*-acetyl-D-galactal was converted via a series of functional group manipulations and a Vasella fragmentation into a six-carbon synthon for preparation of the C22–C27 fragment of FK-506, see: Linde, R. G., II; Egbertson, M.; Coleman, R. S.; Jones, A. B.; Danishefsky, S. J. *J. Org. Chem.* **1990**, *55*, 2771.

(5) Readily available from D-glucosamine hydrochloride by N-protection ($ClCO_2Bn$, $NaHCO_3$, dioxane/H_2O, 24 °C) and methyl glycoside formation (2% HCl in CH_3OH, reflux, 24 h). Chargaff, E.; Bovarnick, M. *J. Biol. Chem.* **1937**, *118*, 421. Neuberger, A.; Rivers, R. P. *J. Chem. Soc.* **1939**, 122.

(6) Evans, M. E. In *Methods in Carbohydrate Chemistry*; Whistler, R. L., BeMiller, J. N., Eds.; Academic Press: New York, 1980; Vol. 8, p 313.

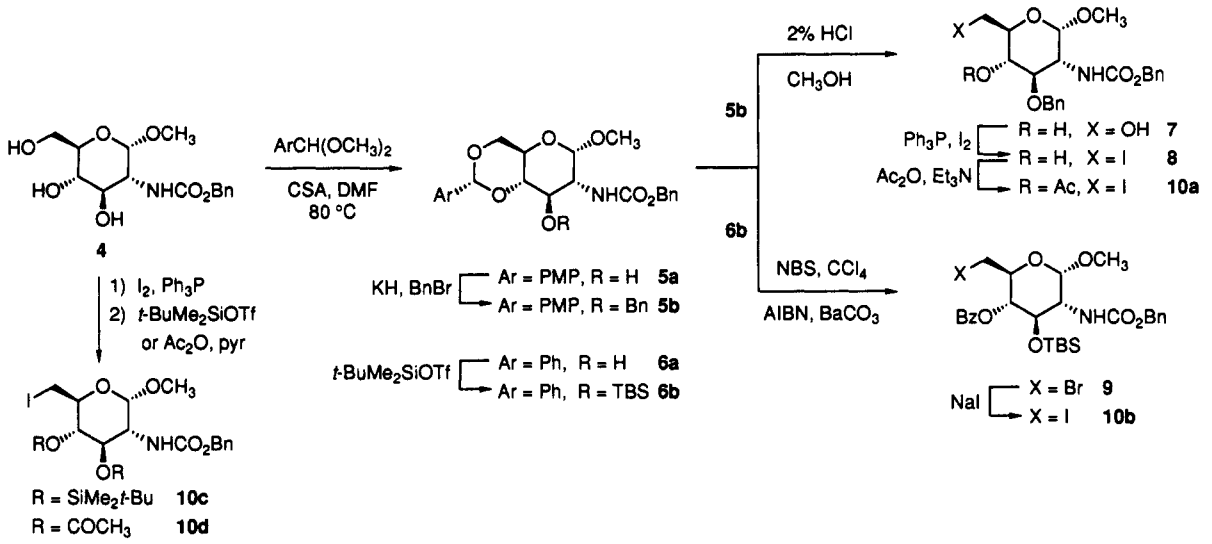
(7) Anisuzzaman, A. K. M.; Whistler, R. L. *Carbohydr. Res.* **1978**, *61*, 511.

(8) Hanessian, S.; Plessas, N. R. *J. Org. Chem.* **1969**, *34*, 1035, 1045, 1053. Hullar, T. L.; Siskin, S. B. *J. Org. Chem.* **1970**, *35*, 225.

(9) Bromide **9** failed to smoothly undergo Vasella fragmentation under standard conditions[4a] (activated Zn, 95% EtOH, 78 °C, 1–3 h).

0022-3263/92/1957-3732$03.00/0

Scheme II



practice, aldehydes **11a–d** proved moderately unstable and were reduced either in situ following filtration ($NaBH_4$, EtOH, 0 °C) or without purification ($NaBH_4$, 20:1 THF/H_2O, −43 °C) to the corresponding primary alcohols **12a–d** (X = H, OH) in excellent yields (69–84% from **10a–d**). Overall yields for the conversion of carbamate **4** to targets **12a–d** ranged from 30 to 42% for the multistep process.

Synthons **12a–d** represent potentially versatile intermediates for synthesis.[2,3] All functional groups of **12a–d** have been differentiated by selective protection or suitable masking, and the termini of **12a–d** are functionally equivalent, since either end can be selectively manipulated to provide reactive functionality for further elaboration.[10] In addition, we have shown that a variety of protecting groups (e.g., alkyl ethers, silyl ethers, esters) can be arrayed selectively in different configurations. The facile, short (4–7 steps), and high-yielding route from D-glucosamine to **12a–d** provides easy access to these chiral synthons.[3]

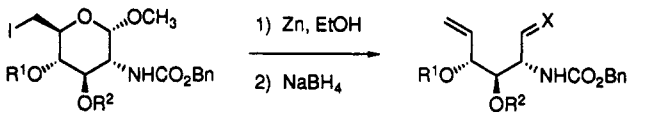
Experimental Section[11]

Methyl 2-[*N*-(Benzoxycarbonyl)amino]-2-deoxy-4,6-*O*-(4-methoxybenzylidene)-α-D-glucopyranoside (5a). A solution of triol **4**[5] (33.0 g, 101 mmol) in DMF (400 mL) was treated with *p*-anisaldehyde dimethyl acetal (52 mL, 303 mmol, 3.0 equiv) followed by a catalytic amount of camphorsulfonic acid (0.3 g). The reaction mixture was warmed under N_2 at 90 °C for 4 h and was then allowed to cool to ambient temperature. The mixture was diluted with water (200 mL) and EtOAc (400 mL). The aqueous layer was extracted with EtOAc (2 × 200 mL) and the combined organic extracts were washed with saturated aqueous $NaHCO_3$ (200 mL) and saturated aqueous NaCl (2 × 200 mL) and were dried ($MgSO_4$) and concentrated in vacuo to provide a light brown solid. Recrystallization (EtOAc) afforded **5a** (33.6 g, 44.9 g theoretical, 75%) as a white granular solid: mp 177–178 °C (EtOAc); ^1H NMR (300 MHz, $CDCl_3$) δ 7.41–7.32 (m, 7 H, ArH), 6.87 (m, 2 H, ArH), 5.49 (s, 1 H, $ArCH(OR)_2$), 5.12–5.06 (m, 3 H, overlapping NH and $PhCH_2$), 4.71 (d, J = 3.3 Hz, 1 H, C1-H), 4.24 (apparent dd, J = 9.2, 3.7 Hz, 1 H, C6-H), 3.89 (apparent td, J = 9.4, 3.3 Hz, 1 H, C2-H), 3.85–3.79 (m, 1 H, C3-H), 3.78 (s, 3 H, CH_3O-Ar), 3.77–3.72 (m, 2 H, overlapping C4-H and C6-H), 3.53 (apparent t, J = 9.4 Hz, 1 H, C5-H), 3.36 (s, 3 H, OCH_3), 2.69 (br s, 1 H, OH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.2, 156.8, 136.1, 129.6, 128.6, 128.3, 127.7, 113.7, 101.9, 99.2, 81.8, 70.4, 68.8, 67.3, 62.4, 55.7, 55.4, 55.3; IR (KBr) ν_{max} 1699, 827, 752 cm^{-1}; EIMS m/e (relative intensity) 445 (M^+, 10), 414 (3), 337 (5), 311 (13), 206 (26), 175 (15), 135 (57), 91 (base); HRMS, m/e calcd for $C_{23}H_{27}NO_8$ 445.1737, found 445.1725.

Anal. Calcd for $C_{23}H_{27}NO_8$: C, 62.01; H, 6.11, N, 3.14. Found: C, 61.94; H, 6.07; N, 3.09.

Methyl 2-[*N*-(Benzoxycarbonyl)amino]-3-*O*-benzyl-2-deoxy-4,6-*O*-(4-methoxybenzylidene)-α-D-glucopyranoside (5b). A slurry of potassium hydride (54 mg, 1.34 mmol, 1.2 equiv) in THF (12 mL) was treated with benzyl bromide (1.3 mL, 11.2 mmol, 10.0 equiv) and n-Bu_4NI (83 mg, 0.22 mmol, 0.2 equiv) at 0 °C under N_2. Alcohol **5a** (500 mg, 1.12 mmol) was added in one portion as a solid to the light yellow solution and the reaction mixture was stirred for 1.5 h at 0 °C. The reaction mixture was carefully quenched with saturated aqueous NH_4Cl (2 mL, caution!: liberation of H_2) and concentrated in vacuo to provide a yellow slurry. Et_2O (100 mL) was added and the resulting white precipitate was isolated by filtration (cold Et_2O wash). The solid was redissolved in CH_2Cl_2 (50 mL), and the solution was washed with saturated aqueous NaCl (2 × 25 mL), dried ($MgSO_4$), and concentrated in vacuo to provide **5b** (400 mg, 600 mg theoretical, 67%) as a white solid, which was used without further purification. A sample of crude **5b** was purified by flash chromatography (0.9 × 15 cm silica, $CHCl_3$) to afford pure **5b**, which was characterized: mp 196–198 °C (EtOAc); ^1H NMR (300 MHz, $CDCl_3$) δ 7.41–7.23

Scheme III



10a	R^1 = Ac	R^2 = Bn	**11a** (X = O)	**12a** (X = H, OH)
10b	R^1 = Bz	R^2 = TBS	**11b** (X = O)	**12b** (X = H, OH)
10c	R^1 = TBS	R^2 = TBS	**11c** (X = O)	**12c** (X = H, OH)
10d	R^1 = Ac	R^2 = Ac	**11d** (X = O)	**12d** (X = H, OH)

(10) In related studies, olefins related to **12a–d** were smoothly and quantitatively converted to the corresponding aldehydes (cf. **1**, Figure 1) by ozonolysis (O_3, CH_2Cl_2, −78 °C; Me_2S, 24 °C), thereby providing access to carbonyl groups at either termini of these systems (Coleman, R. S.; Dong, Y.; Carpenter, A. J. Unpublished observations).

(11) ^1H NMR and ^{13}C NMR spectra were recorded on Bruker AM-300 or AM-500 instruments. Mass spectra (EI, CI, and high resolution) were recorded on a VG 7070S high resolution instrument. Infrared spectra were recorded on a Varian 1600 FTIR. Elemental microanalyses were performed by Atlantic Microlabs, Norcross, GA. All extraction and chromatography solvents (EtOAc, hexanes, CH_2Cl_2) were distilled before use. Reaction solvents were distilled under N_2 immediately prior to use from the following drying agents: THF (Na, benzophenone), CH_2Cl_2 (CaH_2), toluene (CaH_2). Flash chromatography was performed using E. Merck silica gel (240–400 mesh) following the procedure of Still, Kahn, and Mitra (*J. Org. Chem.* **1978**, *43*, 2923). Thin layer chromatography was performed using precoated plates purchased from E. Merck (silica gel 60 PF254, 0.25 mm) that were visualized using either a phosphomolybdic acid or Ce(III) stain. 2,6-Lutidine and pyridine were distilled from CaH_2. Zinc metal was activated following the procedure of Tsuda, Ohki, and Nozoe (*J. Org. Chem.* **1963**, *28*, 783). All other reagents and solvents were used as received from commercial suppliers.

(m, 12 H, ArH), 6.89 (m, 2 H, ArH), 5.53 (s, 1 H, ArC*H*(OR)$_2$), 5.11 (AB q, J = 12.2 Hz, $\Delta\nu$ = 24.2 Hz, 2 H, NC(O)OCH_2Ph), 4.85 (br d, J = 9.6 Hz, 1 H, NH), 4.74 (AB q, J = 12.0 Hz, $\Delta\nu$ = 70.1 Hz, 2 H, OCH_2Ph), 4.71 (d, J = 3.7 Hz, 1 H, C1-H), 4.26 (apparent dd, J = 9.2, 3.7 Hz, 1 H, C6-H), 4.00 (apparent td, J = 9.6, 3.7 Hz, 1 H, C2-H), 3.80 (s, 3 H, CH_3O-Ar), 3.79–3.63 (m, 4 H, overlapping C3-H, C4-H, C5-H, and C6-H), 3.33 (s, 3 H, OCH$_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.1, 156.1, 138.5, 136.4, 129.9, 128.6, 128.3, 127.8, 127.5, 127.4, 113.6, 101.3, 99.6, 82.7, 76.6, 74.3, 69.0, 67.0, 62.7, 55.3, 55.2, 54.7; IR (KBr) ν_{max} 1698, 1548, 826, 736, 696 cm^{-1}; EIMS, m/e (relative intensity) 535 (M$^+$, 3), 444 (6), 397 (15), 278 (20), 179 (18), 135 (32), 91 (base); HRMS, m/e calcd for $C_{30}H_{33}NO_8$ 535.2206, found 535.2206.

Methyl 2-[*N*-(Benzoxycarbonyl)amino]-3-*O*-benzyl-2-deoxy-α-D-glucopyranoside (7). Acetal **5b** (4.37 g, 8.2 mmol) was added to a solution of 2% anhydrous HCl in CH_3OH (80 mL, prepared from 3 mL of CH_3COCl and 77 mL of CH_3OH) at 24 °C and the reaction mixture was stirred for 2 h. The reaction mixture was poured onto saturated aqueous $NaHCO_3$ (100 mL) and diluted with EtOAc (150 mL). The aqueous layer was extracted with EtOAc (2 × 150 mL), and the combined organic extracts were washed with saturated aqueous NaCl (2 × 150 mL), dried ($MgSO_4$), and concentrated in vacuo to provide diol **7** (3.14 g, 3.41 g theoretical, 92%) as a white solid that was used without further purification. A sample of crude diol **7** was purified by flash chromatography (0.9 × 12 cm silica, 75% EtOAc/hexanes) to afford pure **7** as a white solid: mp 147–148.5 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32–7.27 (m, 10 H, ArH), 5.09 (AB q, J = 12.1 Hz, $\Delta\nu$ = 22.9 Hz, 2 H, NC(O)OCH_2Ph), 4.96 (br d, J = 10.3 Hz, 1 H, NH), 4.67 (AB q, J = 11.5 Hz, $\Delta\nu$ = 29.9 Hz, 2 H, OCH_2Ph), 4.66 (d, J = 3.7 Hz, 1 H, C1-H), 4.94 (apparent td, J = 9.9, 3.7 Hz, 1 H, C2-H), 3.85–3.70 (m, 2 H, C6-H), 3.65 (dd, J = 9.2, 8.8 Hz, 1 H, C4-H), 3.59 (m, 1 H, C5-H), 3.52 (dd, J = 9.9, 8.8 Hz, 1 H, C3-H), 3.33 (s, 3 H, OCH$_3$), 2.61 (br s, 1 H, OH), 2.16 (br s, 1 OH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.3, 138.6, 136.7, 129.0, 128.9, 128.7, 128.3, 99.5, 96.5, 81.2, 74.8, 71.6, 71.1, 67.4, 62.8, 55.6, 54.8; IR (KBr) ν_{max} 3333, 1688, 1543, 848, 738, 697 cm^{-1}; EIMS m/e (relative intensity) 326 (M$^+$ – CH_2Ph, 6), 294 (10), 233 (15), 206 (12), 91 (base); HRMS m/e calcd for $C_{22}H_{27}NO_7$ + H 418.1866, found 418.1870.

Anal. Calcd for $C_{22}H_{27}NO_7$: C, 63.29; H, 6.52; N, 3.36. Found: C, 63.47; H, 6.55; N, 3.42.

Methyl 2-[*N*-(Benzoxycarbonyl)amino]-3-*O*-benzyl-2,6-dideoxy-6-iodo-α-D-glucopyranoside (8). Iodine (267 mg, 1.05 mmol, 1.6 equiv) was added to a solution of PPh_3 (328 mg, 1.25 mmol, 1.9 equiv) in toluene (6.5 mL), followed by pyridine (186 μL, 2.30 mmol, 3.5 equiv) and alcohol **7** (275 mg, 0.66 mmol). The reaction mixture was warmed at 70 °C for 4 h under N_2, during which time the brown precipitate disappeared and a granular white solid appeared. The reaction mixture was cooled and filtered, and the filtrate was concentrated in vacuo to provide a white slurry. The slurry was redissolved in EtOAc (50 mL) and was washed with 5% HCl (25 mL), saturated aqueous $NaHCO_3$ (25 mL), and saturated aqueous NaCl (2 × 25 mL), dried ($MgSO_4$), and concentrated in vacuo to give a colorless oil. Purification of the residue by flash chromatography (1.4 × 10 cm silica, 30% EtOAc/hexanes) afforded iodide **8** (260 mg, 347 mg theoretical, 75%) as a white solid: mp 135–136 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32–7.24 (m, 10 H, ArH), 5.10 (AB q, J = 12.1 Hz, $\Delta\nu$ = 25.2 Hz, 2 H, NC(O)OCH_2Ph), 4.99 (br d, J = 9.9 Hz, 1 H, NH), 4.67 (d, J = 3.7 Hz, 1 H, C1-H), 4.64 (AB q, J = 11.5 Hz, $\Delta\nu$ = 50.3 Hz, 2 H, OCH_2Ph), 4.00 (apparent td, J = 9.9, 3.7 Hz, 1 H, C2-H), 3.55–3.48 (m, 2 H, overlapping C3-H and C6-H), 3.45–3.37 (m, 2 H, overlapping C4-H and C6-H), 3.39 (s, 3 H, OCH$_3$), 3.29–3.26 (m, 1 H, C5-H), 2.35 (br s, 1 H, OH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.0, 138.2, 136.3, 128.6, 128.3, 128.0, 99.1, 80.3, 74.3, 74.0, 70.8, 67.1, 55.5, 54.5, 7.1; IR (KBr) ν_{max} 3314, 1685, 740, 698 cm^{-1}; CIMS (NH_3), m/e (relative intensity) 528 (M$^+$ + H, 47), 496 (23), 420 (33), 402 (65), 394 (33), 370 (62), 294 (base), 204 (40); HRMS, m/e calcd for $C_{21}H_{23}NO_5I$ (M$^+$ – OCH$_3$) 496.0621, found 496.0600.

Anal. Calcd for $C_{22}H_{26}NO_6I$: C, 50.10; H, 4.97; N, 2.66. Found: C, 50.17; H, 4.98; N, 2.67.

Methyl 2-[*N*-(Benzoxycarbonyl)amino]-4-*O*-benzoyl-6-bromo-3-*O*-(*tert*-butyldimethylsilyl)-2,6-dideoxy-α-D-glucopyranoside (9). A mixture of acetal **6b** (1.24 g, 2.33 mmol), *N*-bromosuccinimide (0.52 g, 2.92 mmol, 1.3 equiv), $BaCO_3$ (0.51 g, 2.57 mmol, 1.1 equiv), and a catalytic amount of azobis(isobutyronitrile) (AIBN) in anhydrous CCl_4 (20 mL) was warmed at reflux under N_2 for 3 h, during which time the color of the reaction mixture, originally colorless, became successively yellow, red, and finally pale yellow. A small amount of insoluble material was removed by filtration, and the filtrate was diluted with saturated aqueous $NaHCO_3$ (20 mL) and extracted with CH_2Cl_2 (3 × 20 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated in vacuo. The residue was purified by flash chromatography (3 × 20 cm Et_3N deactivated silica, 15–45% EtOAc/hexanes) to afford primary bromide **9** (1.02 g, 1.42 g theoretical, 72%) as a white foam: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.02 (d, J = 7.1 Hz, 2 H, PhCO), 7.59 (apparent t, J = 7.4 Hz, 1 H, PhCO), 7.43 (apparent t, J = 7.6 Hz, 2 H, PhCO), 7.36–7.30 (m, 5 H, $C_6H_5CH_2O$), 5.18–5.02 (m, 3 H, C4-H and PhCH_2O), 4.90 (d, J = 9.9 Hz, 1 H, NH), 4.74 (d, J = 3.4 Hz, 1 H, C1-H), 4.07–3.90 (m, 3 H, C2-H, C3-H, and C5-H), 3.43 (s, 3 H, OCH$_3$), 3.40–3.33 (m, 2 H, C6-H), 0.68 (s, 9 H, SiC(CH$_3$)$_3$), –0.05 (s, 3 H, SiCH$_3$), –0.24 (s, 3 H, SiCH$_3$); IR (neat) ν_{max} 1728, 1513, 1263, 711 cm^{-1}; ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.7, 156.1, 136.5, 133.9, 130.3, 129.9, 129.0, 128.9, 128.9, 128.7, 99.4, 74.8, 71.7, 70.4, 67.5, 56.2, 55.9, 32.2, 25.9, 18.1, –4.0, –4.0; EIMS, m/e (relative intensity) 610/608 (M$^+$, 3/3), 594/592 (10/10), 552/550 (25/25), 398/396 (8/8), 179 (40), 91 (base); CIMS (NH_3), m/e (relative intensity) 627/625 (M$^+$ + NH_4, base), 610/608 (M$^+$, 50/50), 578/576 (80/80), 498 (60).

Anal. Calcd for $C_{28}H_{38}NO_7SiBr$: C, 55.26; H, 6.29; N, 2.30. Found: C, 55.37; H, 6.36; N, 2.37.

Methyl 4-*O*-Acetyl-2-[*N*-(benzoxycarbonyl)amino]-3-*O*-benzyl-2,6-dideoxy-6-iodo-α-D-glucopyranoside (10a). A solution of alcohol **8** (4.8 g, 9.1 mmol) in CH_2Cl (100 mL) was treated with Et_3N (3.75 mL, 27.2 mmol, 3.0 equiv), Ac_2O (1.70 mL, 18.2 mmol, 2.0 equiv), and a catalytic amount of DMAP. The reaction mixture was stirred at 24 °C for 30 min under N_2. Aqueous 5% HCl (50 mL) and Et_2O (100 mL) were added and the aqueous layer was extracted with Et_2O (100 mL). The combined organic extracts were washed with saturated aqueous $NaHCO_3$ (100 mL) and saturated aqueous NaCl (2 × 100 mL), dried ($MgSO_4$), and concentrated in vacuo to afford acetate **10a** (5.1 g, 5.1 g theoretical, 100%) as a white solid that was used without further purification. A sample of crude acetate **10a** was purified by flash chromatography (0.9 × 15 cm silica, 20% EtOAc/hexanes) to afford pure **10a**, which was characterized: mp 160–162 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32–7.17 (m, 10 H, ArH), 5.07 (AB q, J = 12.1 Hz, $\Delta\nu$ = 34.7 Hz, 2 H, NC(O)OCH_2Ph), 4.88 (br d and m, J = 9.6 Hz, 2 H, overlapping NH and C4-H, respectively), 4.72 (d, J = 3.1 Hz, 1 H, C1-H), 4.55 (s, 2 H, OCH_2Ph), 4.05 (apparent td, J = 9.6, 3.1 Hz, 1 H, C2-H), 3.69 (apparent td, J = 9.8, 2.1 Hz, 1 H, C5-H), 3.65 (dd, J = 10.1, 9.8 Hz, 1 H, C6-H), 3.42 (s, 3 H, OCH$_3$), 3.23 (dd, J = 10.1, 2.1 Hz, 1 H, C6-H), 3.09 (apparent t, J = 10.1 Hz, 1 H, C3-H), 1.98 (s, 3 H, CH_3CO); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.7, 155.8, 137.9, 136.2, 128.6, 128.4, 128.3, 127.8, 127.7, 98.8, 77.8, 73.7, 70.1, 67.1, 55.7, 54.3, 21.0, 4.2; IR (KBr) ν_{max} 1736, 1691, 749, 697 cm^{-1}; CIMS (NH_3), m/e (relative intensity) 570 (M$^+$ + H, 35), 538 (30), 461 (49), 444 (65), 412 (base), 336 (45); HRMS, m/e calcd for $C_{24}H_{28}NO_7I$ + H 570.0989, found 570.0973.

Anal. Calcd for $C_{24}H_{28}NO_7I$: C, 50.62; H, 4.96; N, 2.46. Found: C, 50.65; H, 4.92; N, 2.47.

Methyl 2-[*N*-(Benzoxycarbonyl)amino]-4-*O*-benzoyl-3-*O*-(*tert*-butyldimethylsilyl)-6-iodo-2,6-dideoxy-α-D-glucopyranoside (10b). A mixture of bromide **9** (0.73 g, 1.2 mmol) and NaI (2.70 g, 18.0 mmol, 15 equiv) in acetone (20 mL) was warmed at reflux under N_2 for 5 h. The cooled reaction mixture was diluted with saturated aqueous $NaHCO_3$ (30 mL) and extracted with EtOAc (3 × 40 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated in vacuo, and the residue was passed through a pad of silica (Et_3N deactivated, 50% EtOAc/hexanes wash) to afford iodide **10b** (0.79 g, 0.79 g theoretical, 100%) as a white foam that was used without further purification. Iodide **10b** was characterized: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.01 (d, J = 7.1 Hz, 2 H, PhCO), 7.58 (apparent, J = 7.4 Hz, 1 H, PhCO), 7.44 (apparent t, J = 7.6 Hz, 2 H, PhCO), 7.39–7.26 (m, 5 H, *Ph*CH$_2$O), 5.12–5.03 (m, 3 H, C4-H, PhCH_2O), 4.90 (d, J = 9.9 Hz, 1 H, NH), 4.72 (d, J = 3.4 Hz, 1 H, C1-H), 4.02 (apparent td, J = 9.9, 9.9, 3.4 Hz, 1 H, C2-H), 3.89 (dd, J = 9.9, 8.5 Hz, 1

H, C3-H), 3.82 (ddd, J = 9.6, 9.2, 2.4 Hz, 1 H, C5-H), 3.45 (s, 3 H, OCH_3), 3.23 (dd, J = 10.3, 2.4 Hz, 1 H, C6-H_a), 3.13 (dd, J = 10.3, 9.2 Hz, 1 H, C6-H_b), 0.68 (s, 9 H, $SiC(CH_3)_3$), −0.05 (s, 3 H, $SiCH_3$), −0.24 (s, 3 H, $SiCH_3$); IR (neat) ν_{max} 1728, 1514, 1261 cm^{-1}; ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.7, 156.0, 136.5, 133.9, 130.3, 129.9, 128.9, 128.9, 128.9, 128.7, 99.5, 75.8, 71.4, 70.6, 67.6, 66.2, 56.3, 56.1, 26.2, 25.9, 18.1, 4.8, −4.0, −4.0; CIMS (NH_3), m/e (relative intensity) 656 (M^+ + H, 35), 624 (50), 547 (65), 530 (30), 498 (base).

Anal. Calcd for $C_{28}H_{38}NO_7SiI$: C, 51.30; H, 5.84; N, 2.14. Found: C, 51.36; H, 5.81; N, 2.11.

(2*S*,3*R*,4*R*)-4-Acetoxy-3-benzoxy-2-[*N*-(benzoxycarbonyl)amino]-5-hexenal (11a). A solution of iodo sugar **10a** (3.0 g, 5.3 mmol) in 95% EtOH (25 mL) was treated with activated zinc dust (6.9 g, 105.4 mmol, 20 equiv), and the reaction mixture was warmed at reflux for 1 h under N_2. The reaction mixture was cooled to ambient temperature, filtered through a plug of alumina and silica (EtOH wash, 3 × 25 mL), and concentrated in vacuo. The residue was redissolved in EtOAc (50 mL), washed with saturated aqueous $NaHCO_3$ (50 mL) and saturated aqueous NaCl (2 × 30 mL), dried (Na_2SO_4), and concentrated in vacuo to provide aldehyde **11a** (2.2 g, 2.2 g theoretical, 100%) as a pale yellow oil, which was used without further purification. A sample of crude aldehyde **11a** was purified by flash chromatography (0.9 × 15 cm silica, 30% EtOAc/hexanes) to afford pure **11a**, which was characterized: ^1H NMR (500 MHz, $CDCl_3$) δ 9.60 (s, 1 H, CHO), 7.35–7.27 (m, 10 H, ArH), 5.79 (ddd, J = 17.4, 10.7, 6.4 Hz, 1 H, C*H*=CHH), 5.64 (br d, J = 7.6 Hz, 1 H, NH), 5.43 (dd, J = 6.4, 5.2 Hz, 1 H, C4-H), 5.30 (d, J = 17.4 Hz, 1 H, *trans*-CH=C*H*H), 5.24 (d, J = 10.7 Hz, 1 H, *cis*-CH=CH*H*), 5.11 (AB q, J = 12.2 Hz, $\Delta\nu$ = 20.1 Hz, 2 H, NC(O)OCH_2Ph), 4.66 (AB q, J = 11.6 Hz, $\Delta\nu$ = 40.6, 2 H, OCH_2Ph), 4.43 (dd, J = 7.6, 3.4 Hz, 1 H, C2-H), 4.21 (dd, J = 5.2, 3.4 Hz, 1 H, C3-H), 2.00 (s, 3 H, CH_3CO); ^{13}C NMR (75 MHz, $CDCl_3$), δ 199.0, 169.7, 156.2, 137.0, 135.9, 132.1, 128.6, 128.5, 128.4, 128.3, 128.2, 128.1, 119.5, 78.5, 74.6, 73.4, 67.4, 60.3, 20.9; IR (neat) ν_{max} 3032, 2867, 1736, 1720 cm^{-1}; CIMS (NH_3), m/e (relative intensity) 412 (M^+ + H, 72), 352 (18), 304 (16), 246 (41), 197 (45), 169 (28), 108 (79), 91 (base).

(2*R*,3*R*,4*R*)-4-Acetoxy-3-benzoxy-2-[*N*-(benzoxycarbonyl)amino]-5-hexen-1-ol (12a). A solution of aldehyde **11a** (3.68 g, 9.0 mmol) in THF (50 mL) at −43 °C under N_2 was treated with solid sodium borohydride (3.38 g, 90 mmol, 10 equiv) followed by water (2.5 mL). The reaction mixture was allowed to stir overnight at −43 °C and was quenched by the slow addition of saturated aqueous NH_4Cl (15 mL, caution!: liberation of H_2). The aqueous layer was extracted with EtOAc (3 × 25 mL) and the combined organic extracts were washed with 5% aqueous HCl (15 mL), saturated aqueous $NaHCO_3$ (2 × 25 mL), and saturated aqueous NaCl (2 × 25 mL), dried ($MgSO_4$), and concentrated in vacuo to provide a colorless oil. Purification of the residue by flash chromatography (3.6 × 15 cm silica, 30–40% EtOAc/hexanes) afforded alcohol **12a** (2.53 g, 3.70 g theoretical, 68%) as a colorless oil: ^1H NMR (500 MHz, $CDCl_3$) δ 7.49–7.28 (m, 10 H, ArH), 5.82 (ddd, J = 17.4, 10.7, 6.7 Hz, 1 H, C*H*=CHH), 5.48 (dd, J = 7.3, 6.7 Hz, 1 H, C4-H), 5.30 (d, J = 17.4 Hz, 1 H, *trans*-CH=C*H*H), 5.27 (br d, J = 9.5 Hz, 1 H, NH), 5.22 (d, J = 10.7 Hz, 1 H, *cis*-CH=CH*H*), 5.05 (s, 2 H, NC(O)OCH_2Ph), 4.69 (AB q, J = 11.3 Hz, $\Delta\nu$ = 78.9 Hz, 2 H, OCH_2Ph), 3.89 (apparent dd, J = 9.5, 5.5 Hz, 1 H, C2-H), 3.84 (dd, J = 7.3, 1.5 Hz, 1 H, C3-H), 3.59 (dd, J = 10.7, 5.5 Hz, 1 H, C1-H), 3.45 (dd, J = 10.7, 7.6 Hz, 1 H, C1-H), 2.53 (s, 1 H, OH), 2.02 (s, 3 H, CH_3CO); ^{13}C NMR (125 MHz, $CDCl_3$), δ 170.4, 156.8, 138.1, 136.6, 132.8, 129.0, 128.9, 128.6, 128.5, 128.4, 128.3, 119.5, 78.2, 75.5, 75.4, 67.4, 63.0, 53.0, 21.5; IR (neat) ν_{max} 3438, 3032, 1722 cm^{-1}; EIMS, m/e (relative intensity) 413 (M^+, 1), 382 (3), 314 (12), 270 (7), 219 (4), 160 (15), 119 (10), 91 (base); HRMS, m/e calcd for $C_{23}H_{27}NO_6$ 413.1828, found 413.1846.

Anal. Calcd for $C_{23}H_{27}NO_6$: C, 66.81; H, 6.58; N, 3.39. Found: C, 66.72; H, 6.59; N, 3.36.

(2*R*,3*R*,4*R*)-2-[*N*-(Benzoxycarbonyl)amino]-4-(benzoyloxy)-3-[(*tert*-butyldimethylsilyl)oxy]-5-hexen-1-ol (12b). A solution of iodide **10b** (0.77 g, 1.18 mmol) in 95% EtOH (20 mL) was treated with activated zinc dust (1.52 g, 23.4 mmol, 20 equiv). The reaction mixture was warmed at reflux under N_2 for 1 h and the warm reaction mixture was filtered through a mixed pad of Celite and neutral Al_2O_3 (3 × 10 mL EtOH wash). The filtrate containing crude aldehyde **11b** was cooled to 0 °C and was treated with $NaBH_4$ (22.2 mg, 0.59 mmol, 2.0 equiv). After 15 min at 0 °C, aqueous 5% HCl was slowly added to the reaction mixture until gas evolution ceased. The mixture was diluted with saturated aqueous $NaHCO_3$ (40 mL) and extracted with EtOAc (4 × 40 mL). The combined organic extracts were washed with saturated aqueous NaCl (60 mL) and were dried ($MgSO_4$). The solvent was removed in vacuo and the residue was purified by flash chromatography (2 × 12 cm silica, 20–40% EtOAc/hexanes) to afford alcohol **12b** (0.50 g, 0.60 g theoretical, 84% based on iodide **10b**): ^1H NMR (300 MHz, $CDCl_3$) δ 8.06 (d, J = 7.2 Hz, 2 H, PhCO), 7.54 (apparent t, J = 7.4 Hz, 1 H, PhCO), 7.43 (apparent t, J = 7.5 Hz, 2 H, PhCO), 7.35–7.30 (m, 5 H, $C_6H_5CH_2O$), 5.93 (ddd, J = 17.3, 10.7, 5.9 Hz, 1 H, C*H*=CH_2), 5.56 (dd, J = 6.2, 5.9 Hz, 1 H, C4-H), 5.32 (d, J = 17.3 Hz, 1 H, *trans*-CH=C*H*H), 5.24 (d, J = 8.8 Hz, 1 H, NH), 5.14 (d, J = 10.7 Hz, 1 H, *cis*-CH=CH*H*), 5.06 (s, 2 H, PhCH_2O), 4.20 (apparent d, J = 6.2 Hz, 1 H, C3-H), 3.98 (apparent dd, J = 15.0, 6.9 Hz, 1 H, C2-H), 3.70–3.60 (m, 1 H, C1-H), 3.55–3.45 (m, 1 H, C1-H), 2.72 (t, J = 5.7 Hz, 1 H, OH), 0.86 (s, 9 H, $SiC(CH_3)_3$), 0.13 (s, 3 H, $SiCH_3$), 0.09 (s, 3 H, $SiCH_3$); IR (neat) ν_{max} 3442, 1722, 1504, 1267 cm^{-1}; ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.5, 156.4, 136.4, 133.3, 132.0, 130.0, 130.0, 130.0, 128.5, 128.3, 117.9, 75.8, 70.8, 67.0, 63.1, 53.2, 25.9, 18.1, −4.2, −4.8; EIMS, m/e (relative intensity) 499 (M^+, 2), 468 (15), 442 (10), 338 (25), 230 (30), 179 (80), 91 (base); HRMS, m/e calcd for $C_{23}H_{28}NO_6Si$ (M^+ − $C(CH_3)_3$) 442.1686, found 442.1691.

Anal. Calcd for $C_{27}H_{37}NO_6Si$: C, 64.90; H, 7.46; N, 2.80. Found: C, 64.78; H, 7.51; N, 2.74.

Acknowledgment. We thank the American Cancer Society (JFRA-319) and the Camille and Henry Dreyfus Foundation (NF-89-18) for their generous support of this work. We thank Molecular Design Ltd. for the use of their synthetic database. NMR spectra were obtained on instruments purchased with funds from the National Science Foundation (CHE-8411172 and CHE-8904942) and the National Institutes of Health (S10-RR02425).

Registry No. **4**, 4704-15-8; **5a**, 141438-52-0; **5b**, 141438-53-1; **6a**, 93000-10-3; **6b**, 141438-54-2; **7**, 87907-35-5; **8**, 141438-55-3; **9**, 141438-56-4; **10a**, 141438-57-5; **10b**, 141438-58-6; **10c**, 141438-59-7; **10d**, 56733-36-9; **11a**, 141438-60-0; **12a**, 141438-61-1; **12b**, 141438-62-2; **12c**, 141438-63-3; **12d**, 141438-64-4; *p*-anisaldehyde dimethyl acetal, 2186-92-7.

Supplementary Material Available: Experimental procedures and spectral characterization for **6a**, **6b**, **10c,d**, **11c,d**, and **12c,d** (6 pages). Ordering information is given on any current masthead page.

A Novel Photochemical Isomerization of *N*-(2′,2′-Dimethyl-3′-butenoyl) Cyclic Dithiocarbamates, Cyclic Thionocarbamates, and Thiolactams to Thiolactones

Masami Sakamoto,* Kazuya Obara, Tsutomu Fujita, and Shoji Watanabe

Department of Applied Chemistry, Faculty of Engineering, Chiba University, Yayoi-cho, Chiba, Japan 260

Takehiko Nishio and Ikuo Iida

Department of Chemistry, The University of Tsukuba, Tsukuba-shi, Ibaraki, Japan 305

Received November 8, 1991

Introduction

The photochemistry of thiocarbonyl compounds has received much attention from both synthetic and mechanistic viewpoints. It is well-known that thioamides[1] and

