acidified and extracted with three 25-mL portions of CH_2Cl_2. Removal of the solvent left the carboxylic acid **3**.

***exo*-1-Methoxy-7-phenyl-*cis*-bicyclo[4.2.0]octan-8-one (7)**: ^1H NMR ($CDCl_3$) δ 7.26 (m, 5 H), 4.13 (d, 1 H, J = 11 Hz, O=CCH), 3.41 (s, 3 H, CH_3), 2.88 (dd, 1 H, J = 11, 5 Hz), 2.05 (br d, 1 H, J = 15 Hz), 2-1.4 (m, 7 H); ^{13}C NMR ($CDCl_3$) δ 206.9 (keto CO), 135.5, 128.5, 127.5, 127.1, 88.5 (s), 57.0 (d), 52.9 (q), 35.5 (d), 28.1, 21.8, 20.4, 20.3; IR (neat) 1765 cm^{-1}; MS (CI) m/e 231 (M + 1), 199 (M - MeOH). Anal. (7 semicarbazone). Calcd for $C_{16}H_{21}N_3O_2$: C, 66.87; H, 7.38. Found: C, 66.94; H, 7.39.

***exo*-1-Methoxy-9-phenyl-*cis*-bicyclo[6.2.0]decan-10-one (14)**: ^1H NMR ($CDCl_3$) δ 7.3 (m, 5 H), 3.70 (d, 1 H, J = 10 Hz, O=CCH), 3.46 (s, 3 H), 2.51 (ddd, 1 H, J = 12, 10, 3 Hz, OCCH), 2.1-1.2 (m, 12 H); ^{13}C NMR δ 211.2 (keto CO), 135.7, 128.7, 127.4, 127.1, 92.9 (s), 63.6 (d), 52.4 (q), 43.9 (d), 28.2, 27.9, 27.3, 25.1, 23.8, 23.7; IR (neat) 1770 cm^{-1}; MS (CI) m/e 258 (M + 1), 277 (M - MeOH).

Methyl *cis*-2-[2-(*p*-tolylsulfonyl)cyclohexyl]-2-phenylacetate (13): ^1H NMR δ 7.78 (2 H, Ar), 7.38 (2 H, Ar), 7.3 (5 H, Ph), 4.31 (d, 1 H, J = 9 Hz, PhCH), 3.55 (s, 3 H), 2.94 (q, 1 H, J = 5.5 Hz, $CHSO_2$), 2.84 (dq, 1 H, J = 9, 5 Hz, $CHCHSO_2$), 2.64 (s, 3 H), 2.05-1.7 (m, 5 H), 1.4-1.2 (m, 3 H), 0.98 (m, 1 H); ^{13}C NMR δ 173.9 (ester CO), 144.4, 136.0, 135.5, 129.7, 129.6, 128.7, 128.5, 127.5, 62.4 (d), 52.0 (d), 43.35 (d), 23.8, 23.2, 22.1, 21.1, 20.1; MS (CI) m/e 355 (M - MeOH), 327, 231.

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Synthesis of Acyclic Sugar Aldehydes by Ozonolysis of Oximes

David J. Weitz and Mark D. Bednarski*

Department of Chemistry and The Center for Advanced Materials, Lawrence Berkeley Laboratories, University of California, Berkeley, Berkeley, California 94720

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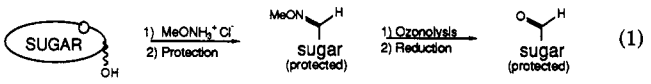
This note reports on an efficient method for the synthesis of acyclic sugar aldehydes based on the ozonolysis of methyloxime-protected aldoses. Readily accessible protected sugar oximes are converted into the corresponding aldehydo sugars in good yield and high purity on a multigram scale. This methodology eliminates problems associated with decomposition of these aldehydes by β-elimination and the formation of side products that contaminate the aldehyde after deprotection. The availability of these aldehydes should further facilitate their use in organic synthesis.[1-3]



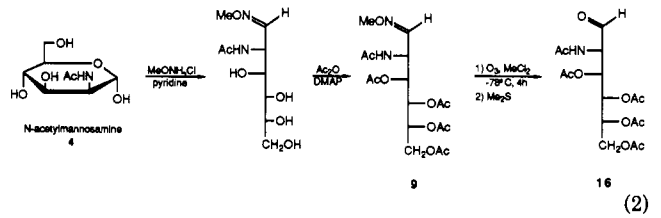
(1)

The mechanism of the cleavage of a carbon-nitrogen double bond by ozonolysis was thoroughly investigated in 1969 by Erikson and co-workers.[4] More recently, Enders has used this reaction to regenerate ketones (and aldehydes) from hydrazones after asymmetric alkylation reactions.[5] We reasoned that acyclic sugar oximes, which are readily accessible from carbohydrates by treatment with methoxyamine hydrochloride, can be protected and the oxime ozonized to generate acyclic aldehydo sugars. Deprotection of aldehydo sugars by ozonolysis produces volatile and water-soluble byproducts that can easily be removed from the reaction mixture. The mild reaction conditions also allow for the synthesis of acyclic α-acylamino sugar aldehydes without problems associated with decomposition by β-elimination[6] or participation of the acylamino group during deprotection.[7] The reaction can be performed on a multigram scale to give aldehydo sugars in greater than 95% purity and in good overall yields (approximately 90%). Oximes have been previously converted to aldehydes by using $TiCl_3$/AcOH,[8] aqueous NaH_2SO_3,[9] $(PhSeO)_2O$,[10] and $Pb(OAc)_4$.[11] These methods generally use acidic or basic reaction conditions that lead to decomposition of acyclic sugar aldehydes by β-elimination and limit the use of acid- or base-sensitive protecting groups. Other methods used to generate aldehydo sugars such as the cleavage of dithianes using mercury salts,[12] electrochemical oxidation,[13] *N*-bromosuccinimide,[6] or methyl iodide and cadmium carbonate[14] also result in β-elimination and loss of labile protecting groups. Corey has reported the synthesis of ketones from ketoxime acetates under mild conditions using chromous acetate.[15] Acetylation of aldose hydroxyoximes, however, yield the corresponding peracetylated sugar nitriles.[16]

Table I

sugar	protecting group	oxime	aldehyde
glucose (1)	acetates	85% 6	87% 13
arabinose (2)	acetates	82% 7	90% 14
mannose (3)	acetates	87% 8	92% 15
N-acetylmannosamine (4)	acetates	92% 9	93% 16
	benzoates	42% 10	99% 17
N-acetylglucosamine (5)	acetates	86% 11	85% 18
	isopropylidenes	62% 12	90% 19

Sugars **1-5** (see Table I) were treated with methoxyamine hydrochloride in pyridine (12 h) and then acetylated or benzoylated in situ by the addition of acetic anhydride or benzoylchloride (an outline of this sequence is shown in eq 2 for *N*-acetylmannosamine). To investigate the use



(2)

of the acid labile isopropylidene protecting group, the *N*-acetylglucosamine methyloxime derivative **12** was syn-

(1) Hanessian, S. *Total Synthesis of Natural Products: The Chiron Approach*; Pergamon Press: New York, 1983.
(2) Fraser-Reid, B.; Magdzinski, L.; Molino, B *Curr. Trends Org. Synth., Proc. Int. Conf., 4th Meeting Date* **1982**, 197-204.
(3) Mukaiyama, T. *Lect. Heterocycl. Chem.* **1984**, *7*, 53-7.
(4) Erickson, R. E.; Andrulis, P. J.; Collins, J. C.; Lungle, M. L.; Mercer, G. D. *J. Org. Chem.* **1969**, *34*, 2961-6.
(5) Enders, D. *Asymmetric Synth.* **1984**, *3*, Chapter 4.
(6) Miljkovic, M.; Dropkin, D.; Hagel, P.; Marino, M. *Carbohydr. Res.* **1984**, *128*, 14-20.
(7) Julina, R.; Muller, I.; Vasella, A.; Wyler, R. *Carbohydr. Res.* **1987**, *164*, 415-32.
(8) Timms, G.; Wildsmith, E. *Tetrahedron Lett.* **1971**, *2*, 195-8.
(9) Pines, S.; Chemerda, J.; Kozlowski, M. *J. Org. Chem.* **1966**, *31*, 3446-7.
(10) Barton, D.; Lester, D.; Ley, S. *J. Chem. Soc., Perkin Trans. 1* **1980**, 1212-7.
(11) Yakawa, Y.; Sakai, M.; Suzuki, S.*Bull. Chem. Soc. Jpn.* **1966**, *39*, 2266-9.
(12) Corey, E. J.; Erickson, B. W. *J. Org. Chem.* **1971**, *36*, 3553-3560.
(13) Lebouc, A.; Simonet, J.; Gelas, J.; Dehbi, A. *Synthesis* **1987**, *4*, 3201-2.
(14) Lichtenthaler, F.; Lorenz, K.; Ma, W. *Tetrahedron Lett.* **1987**, *28*, 47-50.
(15) Corey, E. J.; Richman, J. E. *J. Am. Chem. Soc.* **1970**, *92*, 5276-7.
(16) Mowry, D. *Chem. Rev.* **1948**, *42*, 189-283.

0022-3263/89/1954-4957$01.50/0

thesized by using 2,2-dimethoxypropane and *p*-toluenesulfonic acid.[17] The resulting protected methyloximes **6–12** were purified by either chromatography on silica gel or recrystallization. Oximes **6–12** were treated with a saturated solution of ozone in methylene chloride at −78 °C for 8–10 h followed by reduction with dimethyl sulfide to generate aldehydes **13–19**. The crude aldehydes were isolated in greater than 95% purity and 85% yield after a bicarbonate–brine wash followed by evaporation of the volatiles in vacuo. The major impurity (DMSO) was removed by evaporation under high vacuum for 48 h.

This procedure provides a short and efficient synthetic route to protected acyclic sugar aldoses. Unlike previous methods,[6-14] the ozonolysis can be performed in the presence of acid and base labile protecting groups, eliminates problems associated with β-elimination, and operates on a multigram scale. Sensitive α-acylamino sugar aldehydes such as **16** and **18** are now available in large quantities and in high purity. The availability of aldehydes **13–19** by this straightforward procedure should further facilitate the use of sugars in natural product synthesis.

Experimental Section

Unless otherwise noted, materials were obtained from commercial suppliers and were used without further purification. Dichloromethane was distilled from calcium hydride. Melting points (Pyrex capillary) are uncorrected. The silica gel used in column chromatography was Kieselgel 60 (Merck, 230–400 mesh). IR spectra were determined with a Perkin-Elmer Model 1420 infrared ratio-recording spectrometer. ^{1}H NMR spectra were determined at 400 or 500 MHz on Bruker superconducting Fourier transform spectrometers. Chemical shifts are reported in δ values, positive values indicating shifts downfield of tetramethylsilane. The internal reference for ^{1}H NMR spectra determined in $CDCl_3$ was $(CH_3)_4Si$. $^{13}C\{^1H\}$NMR spectra were measured at 100.6 or 125.7 MHz on Bruker spectrometers. ^{13}C NMR spectra chemical shifts are reported relative to the central peak of $CDCl_3$ as δ 77.0. ^{1}H NMR data are tabulated in the following order: multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; br, broad; m, multiplet), number of protons, coupling constant(s) in hertz. Elemental analyses were performed by the Microanalytical Laboratory, operated by the College of Chemistry, University of California, Berkeley, CA.

Procedure for the Synthesis of Acetylated Methyloximes. 2-Acetamido-2-deoxy-3,4,5,6-tetra-*O*-acetyl-D-mannose Methyloxime (9). To a 250-mL round-bottom flask were added *N*-acetyl-D-mannosamine (5.00 g, 22.6 mmol), methoxyamine hydrochloride (2.27 g, 27.1 mmol, 1.2 equiv), and 80 mL of dry pyridine. The reaction was stirred at room temperature, and the disappearance of starting material was followed by thin-layer chromatography (*n*-BuOH:AcOH:H_2O 5:3:2). Acetic anhydride (13.83 g, 135.6 mmol, 1.1 equiv) and (dimethylamino)pyridine (DMAP, 100 mg, 0.82 mmol) were added to the reaction mixture when the spot on TLC corresponding to the starting material disappeared (approximately 4 h). After 12 h, the reaction mixture was transferred to a 500-mL separatory funnel, and 225 mL of ethyl acetate was added. The organic layer was washed repeatedly with a saturated solution of $CuSO_4$ (150 mL per wash) until the aqueous layer remained light blue. The organic layer was then washed twice with a brine solution (100 mL), dried over Na_2SO_4, and concentrated by rotary evaporation. The crude material was dried under high vacuum to remove excess acetic anhydride. Purification by recrystallization (ethyl acetate:hexanes 1:2) yielded **9** as a white crystalline solid (7.14 g, 76%): mp 99–100 °C; IR (NaCl) 3300 (br), 2980, 1750, 1660, 1550, 1370, 1210, 1040 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.96 (s, 3 H), 2.02 (s, 3 H), 2.03 (s, 3 H), 2.05 (s, 3 H), 2.10 (s, 3 H), 3.80 (s, 3 H), 4.05 (dd, 1 H, *J* = 5.7, 12.4 Hz), 4.22 (dd, 1 H, *J* = 2.9, 12.4 Hz), 4.80 (ddd, 1 H, 6.7, 8.7, 12.6 Hz), 5.10 (ddd, 1 H, *J* = 2.9, 5.7, 8.2 Hz), 5.36 (dd, 1 H, *J* = 3.0, 6.8 Hz), 5.41 (dd, 1 H, *J* = 3.0, 8.0 Hz), 6.25 (d, 1 H, *J* = 8.7 Hz), 7.28 (d, 1 H, *J* = 5.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.58, 20.61, 20.68, 20.73, 23.06, 48.97, 60.34, 61.84, 68.29, 68.52, 70.21, 145.38, 169.69, 169.75, 169.92, 170.05, 170.53. Anal. Calcd for $C_{17}H_{26}N_2O_{10}$ (418.40): C, 48.80; H, 6.26; N, 6.70. Found: C, 48.47; H, 6.26; N, 6.39.

Compounds **6**, **7**, **8**, and **11** were synthesized according to the above procedure by substituting the appropriate sugar for *N*-acetylmannosamine. The data for these compounds are given below.

2,3,4,5,6-Penta-*O*-acetyl-D-glucose methyloxime (6): yield 85%; mp 75–76 °C; IR (NaCl) 3430 (br), 1740, 1440, 1365, 1210, 1030 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.06 (s, 6 H), 2.08 (s, 3 H) 2.09 (s, 3 H), 2.14 (s, 3 H), 3.86 (s, 3 H), 4.06 (dd, 1 H, *J* = 5.6, 12.4 Hz), 4.24 (dd, 1 H, *J* = 3.3, 12.4 Hz), 5.10 (ddd, 1 H, *J* = 3.3, 5.7, 8.1 Hz), 5.38 (dd, 1 H, *J* = 2.8, 7.9 Hz), 5.51 (m, 2 H), 7.27 (d, 1 H, *J* = 3.2 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.50, 20.63, 20.70, 20.73, 61.75, 62.15, 68.29, 68.40, 69.31, 69.53, 143.42, 169.39, 169.75, 170.46. Anal. Calcd for $C_{17}H_{25}NO_{11}$ (419.38): C, 48.69; H, 6.01; N, 3.33. Found: C, 48.37; H, 6.00; N, 3.49.

2,3,4,5-Tetra-*O*-acetyl-D-arabinose methyloxime (7): yield 82%; mp 46–47 °C; IR (NaCl) 3640, 3480, 2960, 2940, 2900, 1740 (m), 1440, 1360, 1220 (br), 1140 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.06 (s, 3 H), 2.07 (s, 3 H), 2.11 (s, 3 H), 2.12 (s, 3 H), 3.86 (s, 3 H), 4.16, (dd, 1 H, *J* = 4.9, 12.5 Hz), 4.27 (dd, 1 H, *J* = 2.8, 12.5 Hz), 5.23 (m, 1 H), 5.45 (dd, 1 H, *J* = 3.7, 8.4 Hz), 5.65 (dd, 1 H, *J* = 3.6, 6.0 Hz), 7.20 (d, 1 H, *J* = 5.9 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.44, 20.54, 20.57, 20.60, 20.66, 61.56, 62.10, 68.18, 68.26, 68.57, 144.06, 169.40, 169.50, 169.60, 171.10. Anal. Calcd for $C_{14}H_{21}NO_9$ (347.32): C, 48.41; H, 6.09; N, 4.03. Found: C, 48.27; H, 6.21; N, 4.21.

2,3,4,5,6-Penta-*O*-acetyl-D-mannose methyloxime (8): yield 87%; mp 75–77 °C; IR (NaCl) 2980, 2940, 1740, 1430, 1360, 1210, 1040 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.06 (s, 9 H), 2.08 (s, 3 H), 2.09 (s, 3 H), 3.84 (s, 3 H), 4.08 (dd, 1 H, *J* = 5.0, 12.5 Hz), 4.20 (dd, 1 H, *J* = 2.7, 12.5 Hz), 5.11 (m, 1 H), 5.36 (t, 1 H, *J* = 7.4 Hz), 5.46 (dd, 1 H, *J* = 2.1, 7.5 Hz), 5.49 (dd, 1 H, *J* = 2.1, 9.6 Hz), 7.23 (d, 1 H, *J* = 7.4 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.55, 20.62, 20.74, 61.77, 62.08, 67.18, 67.86, 68.41, 68.51, 144.61, 169.17, 169.5, 169.82, 170.00. Anal. Calcd for $C_{17}H_{25}NO_{11}$ (419.38): C, 48.69; H, 6.01; N, 3.33. Found: C, 48.64; H, 6.19; N, 3.55.

2-Acetamido-2-deoxy-3,4,5,6-tetra-*O*-acetyl-D-glucose methyloxime (11): yield 86%; mp 74–76 °C; IR (NaCl) 3300 (br), 2980, 1750, 1660, 1550, 1370, 1210, 1040 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.97 (s, 3 H), 1.98 (s, 3 H), 1.99 (s, 3 H), 2.02 (s, 3 H), 2.03 (s, 3 H), 3.76 (s, 3 H), 4.04 (dd, 1 H, *J* = 5.1, 12.6 Hz), 4.14 (dd, 1 H, *J* = 3.0, 12.6 Hz, 4.85 (ddd, 1 H, *J* = 4.0, 7.0, 8.5 Hz), 5.06 (ddd, 1 H, *J* = 3.0, 5.1, 8.1 Hz), 5.31 (dd, 1 H, *J* = 2.7, 8.2 Hz), 5.35 (dd, 1 H, *J* = 2.8, 7.0 Hz), 6.13 (d, 1 H, *J* = 8.5 Hz), 7.31 (d, 1 H, *J* = 4.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.42, 20.50, 20.52, 20.60, 22.99, 48.56, 61.58, 61.73, 67.80, 68.17, 69.37, 145.02, 169.62, 169.67, 169.81, 169.92, 170.35. Anal. Calcd for $C_{17}H_{26}N_2O_{10}$ (418.40): C, 48.80; H, 6.26; N, 6.70. Found: C, 48.43; H, 6.53; N, 6.59.

2-Acetamido-2-deoxy-3,4,5,6-tetra-*O*-benzoyl-D-mannose Methyloxime (10). To a 250-mL round-bottom flask were added **4** (3.00 g, 13.56 mmol), methoxyamine hydrochloride (1.36 g, 16.27 mmol), and 100 mL of pyridine. The reaction was stirred under N_2 for 12 h, at which point the starting material was no longer visible by thin-layer chromatography (*n*-BuOH:AcOH:H_2O 5:3:2). Benzoyl chloride (9.15 g, 65.0 mmol, 1.2 equiv) was added over a period of 5 min at room temperature. After 2 h, the reaction mixture was transferred to a 500-mL separatory funnel, and 225 mL of ethyl acetate was added. The organic layer was washed repeatedly with a saturated solution of $CuSO_4$ (150 mL per wash) until the aqueous layer remained light blue. The organic layer was then washed twice with a brine solution (100 mL), dried over $NaSO_4$, and concentrated by rotary evaporation. Purification by column chromatography on silica gel (2:1 hexanes:ethyl acetate) yielded **10** as a clear syrup (3.80 g, 42%): IR (NaCl) 3300, 3060, 2960, 2940, 1730, 1660, 1530, 1310, 1250, 1100 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.94 (s, 3 H), 3.65 (s, 3 H), 4.62 (dd, 1 H, *J* = 6.4, 12.3 Hz), 4.90 (dd, 1 H, *J* = 3.2, 12.3 Hz), 5.13 (ddd, 1 H, *J* = 4.8, 7.8, 8.0 Hz), 5.81 (ddd, 1 H, *J* = 3.2, 6.4, 9.3 Hz), 5.98 (t, 1 H, *J* = 5.4 Hz), 6.08 (dd, 1 H, *J* = 5.4, 5.9 Hz), 6.51 (d, 1 H, *J* = 7.8 Hz), 7.3–7.8 (m, 13 H), 7.9 (m, 8 H); ^{13}C NMR (100 MHz,

(17) Whistler, R.; BeMiller, J. *Methods in Carbohydrate Chemistry*; Academic Press; New York, 1976; Vol. 7. The procedure was modified by replacing sulfuric acid with *p*-toluenesulfonic acid.

$CDCl_3$) δ 23.00, 50.46, 61.77, 62.31, 70.23, 70.27, 71.30, 128.29, 128.31, 128.37, 128.52, 128.79, 128.96, 129.11, 129.37, 129.69, 129.78, 129.85, 133.08, 133.29, 133.39, 133.60, 144.81, 165.25, 165.51, 165.60, 166.00, 169.75. Anal. Calcd for $C_{37}H_{34}N_2O_{10}$ (666.683): C, 66.66; H, 5.14; N, 4.20. Found: C, 66.61; H, 5.16; N, 4.13.

2-Acetamido-2-deoxy-3:4,5:6-diisopropylidene-D-glucose Methyloxime (12). To a 250-mL round-bottom flask were added **5** (3.00 g, 13.56 mmol), methoxyamine hydrochloride (1.36 g, 16.27 mmol), and 60 mL of pyridine. The reaction was stirred for 12 h at which point the starting material was no longer visible by thin-layer chromatography (*n*-BuOH:AcOH:H_2O 5:3:2). The reaction was then concentrated by rotary evaporation, and toluene (3 × 100 mL) was used to azeotrope off any remaining pyridine to yield a clear syrup. To this reaction mixture were added 2,2-dimethoxypropane (100 mL) and *p*-toluenesulfonic acid (0.505 g, 0.2 equiv). The reaction mixture was refluxed for 5 h and allowed to cool to room temperature. Filtration followed by rotary evaporation gave a yellow syrup. This material was then dissolved in 150 mL of ethyl acetate and transfered to a 500-mL separatory funnel. The organic layer was washed twice with a brine solution (100 mL), dried over $MgSO_4$, and concentrated by rotary evaporation. Purification by column chromatography on silica gel (2:1 hexanes:ethyl acetate) yielded **12** as a clear syrup (2.78 g, 62%): IR (NaCl) 3300, 2990, 2940, 2890, 1650, 1530, 1370, 1250, 1215, 1160, 1070 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 1.27 (s, 6 H), 1.30 (s, 3 H), 1.37 (s, 3 H), 1.95 (s, 3 H), 3.60 (t, 1 H, *J* = 8.1 Hz), 3.75 (s, 3 H), 3.90 (dd, 1 H, *J* = 4.7, 8.5 Hz), 3.96 (m, 1 H), 4.06 (m, 1 H), 4.08 (dd, 1 H, *J* = 2.5, 5.2 Hz), 4.96 (ddd, 1 H, *J* = 2.6, 4.3, 9.2 Hz), 6.33, (d, 1 H, *J* = 9.2 Hz), 7.30 (d, 1 H, *J* = 4.3 Hz); ^{13}C NMR (100 MHz, CDCl3) δ 23.04, 25.07, 26.33, 26.67, 26.68, 48.18, 61.59, 67.48, 76.63, 77.48, 79.80, 109.41, 109.91, 146.92, 169.40. Anal. Calcd for $C_{15}H_{26}N_2O_6$ (330.38): C, 54.53; H, 7.93; N, 8.48. Found: C, 54.46; H, 8.01; N, 8.39.

Procedure for the Ozonolysis of Oximes to Aldehydes. 2-Acetamido-2-deoxy-3,4,5,6-tetra-*O*-acetyl-*aldehydo*-D-mannose (16). To a 1-L Erlenmeyer flask were added **9** (3.00 g, 7.17 mmol) and 600 mL of CH_2Cl_2. The reaction was cooled to −78 °C, and ozone as bubbled through the reaction mixture for 1 h. The saturated ozone solution was allowed to stand for an additional 10 h, at which time the starting material was no longer visible by TLC (1:1 ethyl acetate:hexanes). Excess ozone was removed by purging the system with N_2. Dimethyl sulfide (6.0 mL, 81.6 mmol) was added to the reaction at −78 °C, and the reaction mixture was allowed to warm to room temperature (4 h). The reaction was transfered to a 1-L separatory funnel and washed twice with a brine–bicarbonate solution (1:1 v/v, 200 mL). The organic layer was dried over $NaSO_4$ and concentrated in vacuo to yield **16** as a colorless syrup (2.60 g, 93%, >95% purity). Compound **16** was unstable to silica gel and could not be further purified. The major impurity, DMSO, could be removed under high vacuum (48 h). IR (NaCl) 3350 (br), 2980, 1740, 1670, 1540, 1370, 1210, 1050 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 2.03 (s, 3 H), 2.04 (s, 6 H), 2.06 (s, 3 H), 2.13 (s, 3 H), 4.11 (dd, 1 H, *J* = 5.6, 12.6 Hz), 4.25 (dd, 1 H, *J* = 2.9, 12.6 Hz), 4.75 (d, 1 H, *J* = 5.5 Hz), 5.12 (ddd, 1 H, *J* = 2.9, 5.5, 8.0 Hz), 5.44 (dd, 1 H, *J* = 3.4, 5.5 Hz), 5.48 (dd, 1 H, *J* = 3.4, 7.7 Hz), 9.55 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.50, 20.65, 20.73, 20.76, 22.82, 58.38, 61.64, 68.48, 68.93, 69.82, 169.88, 170.16, 170.59, 196.10; mass spectrum (FAB^+) 390 (MH^+, 80%), 160 (base).

Compounds **13**, **14**, **15**, **17**, **18**, and **19** were prepared from their corresponding oximes according to the procedure described above. Spectral data for these compounds are provided below.[6,13]

2,3,4,5,6-Penta-*O*-acetyl-*aldehydo*-D-glucose (13): yield 87%; IR (NaCl) 3460, 2940, 1740, 1430, 1370, 1230, 1030 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 2.06 (s, 3 H), 2.07 (s, 6 H), 2.12 (s, 3 H), 2.21 (s, 3 H), 4.10 (dd, 1 H, *J* = 5.5, 12.4 Hz), 4.28 (dd, 1 H, *J* = 3.2, 12.4 Hz), 5.13 (m, 1 H), 5.27 (d, *J* = 5.1 Hz), 5.50 (dd, 1 H, *J* = 3.6, 7.6 Hz), 5.5. (dd, 1 H, *J* = 3.6, 5.0 Hz), 9.52 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.22, 20.37, 20.42, 20.59, 20.67, 61.59, 68.10, 68.19, 68.33, 74.97, 169.25, 169.41, 169.59, 169.72, 170.53, 193.80.

2,3,4,5-Tetra-*O*-acetyl-*aldehydo*-D-arabinose (14): yield 90%; IR (NaCl) 3460, 2940, 1740, 1430, 1370, 1230, 1030 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 2.08 (s, 6 H), 2.09 (s, 3 H), 2.21 (s, 3 H), 4.19 (dd, 1 H, *J* = 4.5, 12.6 Hz), 4.32 (dd, 1 H, *J* = 2.6, 12.6 Hz), 5.27 (m, 1 H), 5.39 (d, 1 H, *J* = 2.1 Hz), 5.68 (dd, 1 H, *J* = 2.1, 9 Hz), 9.48 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.19, 20.36, 20.55, 20.59, 61.38, 67.13, 67.92, 75.77, 110.43, 169.41, 169.50, 169.78, 170.44, 193.79.

2,3,4,5,6-Penta-*O*-acetyl-*aldehydo*-D-mannose (15): yield 92%; IR (NaCl) 3520, 3030, 1775, 1765, 1470, 1460, 1390, 1240, 1060 cm^{-1}; ^1H NMR (500 MHz) δ 2.03 (s, 3 H), 2.05 (s, 3 H), 2.10 (s, 3 H), 2.16 (s, 3 H), 4.11 (dd, 1 H, *J* = 4.8, 12.6 Hz), 4.20 (dd, 1 H, *J* = 2.6, 12.6 Hz), 5.01 (dd, 1 H, *J* = 1.0, 7.8 Hz), 5.13 (ddd, 1 H, *J* = 2.6, 4.8, 9.0 Hz), 5.44 (dd, 1 H, *J* = 2.2, 9.0 Hz), 5.47 (dd, 1 H, *J* = 2.2, 7.7 Hz), 9.40 (d, 1 H, *J* = 1.0 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 20.34, 20.44, 20.54, 20.60, 20.71, 61.71, 67.21, 67.47, 67.62, 74.14, 169.51, 169.58, 169.71, 169.82, 170.50, 195.19.

2-Acetamido-2-deoxy-3,4,5,6-tetra-*O*-benzoyl-*aldehydo*-D-mannose (17): yield 99%; IR (NaCl) 3360, 3060, 2960, 1720, 1670, 1520, 1315, 1260, 1180, 1100, 1020 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 2.00 (s, 3 H), 4.66 (dd, 1 H, *J* = 6.2, 12.4 Hz), 4.91 (dd, 1 H, *J* = 3.2, 12.3 Hz), 5.12 (dd, 1 H, *J* = 3.5, 6.9 Hz), 5.84 (m, 1 H), 6.03 (t, 1 H), 6.20 (t, 1 H, *J* = 5.7 Hz), 6.63 (d, 1 H, *J* = 6.6 Hz), 7.3–7.6 (7, 12 H), 7.85–8.05 (m, 8 H), 9.81 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.72, 59.80, 62.25, 70.22, 70.62, 71.11, 128.33, 128.38, 128.44, 128.65, 129.00, 129.33, 129.71, 129.76, 129.79, 129.85, 133.14, 133.41, 133.61, 133.85, 165.34, 165.42, 165.68, 166.02, 170.38, 195.48.

2-Acetamido-2-deoxy-3,4,5,6-tetra-*O*-acetyl-*aldehydo*-D-glucose (18): yield 85%; IR (NaCl) 3350 (br), 2980, 1740, 1670, 1540, 1370, 1210, 1050 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 2.05 (s, 3 H), 2.06 (s, 3 H), 2.07 (s, 3 H), 2.11 (s, 3 H), 2.14 (s, 3 H), 4.10 (dd, 1 H, *J* = 4.9, 12.5 Hz), 4.23 (dd, 1 H, *J* = 3.0, 12.5 Hz), 4.88 (t, 1 H, *J* = 6.0 Hz), 5.16 (ddd, 1 H, *J* = 3.0, 5.0, 8.1 Hz), 5.38 (dd, 1 H, *J* = 3.1, 8.4 Hz), 5.71 (dd, 1 H, *J* = 3.1, 6.0 Hz), 6.25 (d, 1 H, *J* = 12 Hz), 9.67 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.27, 20.40, 20.51, 20.77, 22.67, 57.72, 60.16, 61.43, 67.92, 68.65, 169.19, 169.58, 169.82, 170.29, 170.98, 196.32.

2-Acetamido-2-deoxy-3:4,5:6-diisopropylidene-*aldehydo*-D-glucose (19): yield 90%; IR (NaCl) 3430, 3350, 1735, 1680, 1500, 1370, 1060 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 1.32 (s, 3 H), 1.34 (s, 3 H), 1.36 (s, 3 H), 1.42 (s, 3 H), 2.08 (s, 3 H), 3.65 (t, 1 H, *J* = 8.1 Hz), 3.96 (dd, 1 H, *J* = 4.4, 8.7 Hz), 4.07 (ddd, 1 H, *J* = 4.4, 6.3, 8.0 Hz), 4.13 (dd, 1 H, *J* = 6.3, 8.7 Hz), 4.49 (dd, 1 H, 1.9, 8.0 Hz), 4.99 (dd, 1 H, *J* = 1.9, 9.0 Hz), 6.24 (d, 1 H, *J* = 8.8 Hz), 9.64 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.96, 25.01, 26.36, 26.65, 40.72, 58.24, 67.53, 76.68, 77.38, 109.91, 110.13, 170.13, 197.73.

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Restricted Rotation and Torsional Isomerism in Tamoxifen Derivatives

Silvio E. Biali,*[†] Menahem Kaftory,[‡] and Zvi Rappoport*[†]

Department of Organic Chemistry, The Hebrew University of Jerusalem, Jerusalem 91904, Israel, and Department of Chemistry, Technion-Israel Institute of Technology, Haifa 32000, Israel

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Introduction. In recent years there has been an increased interest in the molecular structure of the anti-

[†] The Hebrew University of Jerusalem.
[‡] Technion-Israel Institute of Technology.

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