Carbohydrate Research, 70 (1979) 59–73

SYNTHESIS OF TWO 3-AMINO-2,3-DIDEOXYHEXURONIC ACID DERIVATIVES*

DEREK HORTON, WOLFGANG WECKERLE, AND BÉAT WINTER
Department of Chemistry, The Ohio State University, Columbus, Ohio 43210 (U.S.A.)
(Received May 25th, 1978; accepted for publication, June 13th, 1978)

ABSTRACT

Methyl (methyl 3-acetamido-2,3-dideoxy-α-D-*ribo*-hexopyranosid)uronate was prepared from methyl 3-acetamido-4-*O*-benzoyl-6-bromo-2,3,6-trideoxy-α-D-*ribo*-hexopyranoside (**2**) by a sequence of reactions involving photodecomposition of the 6-azido-4-hydroxyl analog of **2**, followed by successive mild hydrolysis of the intermediate imine **8** (to afford the aldehyde **11**), oxidation, and esterification. In contrast, mild hydrolysis of the photoproduct (**6**) from the corresponding 6-azido-4-acetate proceeded with complete β-elimination to give, after oxidation and esterification, methyl (methyl 3-acetamido-2,3,4-trideoxy-α-D-*glycero*-hex-4-enopyranosid)uronate. The intermediate imines (**6** and **8**) and corresponding aldehydes (**9** and **11**) were characterized as their crystalline 1,3-diphenylimidazolidine analogs, and aldehyde **9** further as the oxime.

INTRODUCTION

A program[1,2] in this laboratory is concerned with the synthesis of various deoxy and amino sugars as potential replacements for daunosamine (3-amino-2,3,6-trideoxy-L-*lyxo*-hexose), the carbohydrate constituent of the antitumor antibiotics[3] daunorubicin and doxorubicin (adriamycin), in order to provide access to functional and/or configurational analogs of these anthracycline glycosides that might display better therapeutic indices than the parent drugs. Several such analogs prepared by us[1,4–7] and by others[8–12] have daunosamine replaced by acosamine[8] (3-amino-2,3,6-trideoxy-L-*arabino*-hexose) and ristosamine[9] (L-*ribo* stereochemistry) and their enantiomers[1,4,5], by 6-hydroxy[10,11] and 4-deoxy[12] analogs of daunosamine, and by digitoxose[6] (2,6-dideoxy-D-*ribo*-hexose) and its 5-epimer[6,7] (L-*lyxo* configuration); some of these products display significant activity against experimental tumors in mice.

We now report the synthesis of methyl (methyl 3-acetamido-2,3-dideoxy-α-D-*ribo*-hexopyranosid)uronate (**15**) and its β-elimination product **14**; these may be useful intermediates for synthesis of new anthracycline glycosides having daunos-

*For a preliminary report, see ref. 1.

amine replaced by a hexuronic acid moiety, as probes for ascertaining the effect of a 5'-carboxylic group on biological activity.

Aminohexuronic acids are relatively rare, and only a few are known to occur in Nature and/or have been prepared synthetically. The first examples reported, namely, 2-amino-2-deoxy-D-galacturonic acid[13] and its D-*gluco*[14] isomer, were synthesized by Heyns and his coworkers long before they were found[15,16] as constituents of polysaccharides from micro-organisms, as are the *manno*[17] and *gulo*[18] isomers. Ezoaminuroic acid (3-amino-3,4-dideoxy-D-*xylo*-hexuronic acid) has been isolated[19] from the ezomycins, a complex of antifungal antibiotics, and is the first naturally occurring 3-aminohexuronic acid. The chemical synthesis of this compound[20] and its D-*allo*[21] isomer was reported by Ogawa and Kinoshita and their coworkers, respectively. 4-Aminohexuronic acids were detected in the nucleoside antibiotics gougerotin[22a] and blasticidin S (ref. 22b), and their identity was established[23,24] by chemical synthesis. Finally, the 5-amino-5-deoxy-D-allofuranosiduronic acid moiety forms part of the polyoxins[22c], a group of antifungal, peptidic nucleosides. Chemical synthesis of derivatives of this aminohexuronic acid[25], as well as of some analogs[26], has been accomplished by a number of groups. Beyond that, however, only a few other derivatives of other aminohexuronic acids have been prepared[27]. In this report, we describe the synthesis of the 3-amino-3-deoxyhexuronic acid derivatives **15** and **14** by a route involving photolysis of primary azides, with subsequent, mild hydrolysis of the intermediate imines to give the corresponding aldehydes, which were then oxidized.

RESULTS AND DISCUSSION

The starting material in this series of reactions was methyl 3-acetamido-4-*O*-benzoyl-6-bromo-2,3,6-trideoxy-α-D-*ribo*-hexopyranoside (**2**), obtained[28] crystalline in 53.5% net yield in five steps from methyl α-D-mannopyranoside (**1**). Treatment of **2** with sodium azide in *N*,*N*-dimethylformamide afforded the crystalline 6-azide **3** in 88% yield; this product was fully characterized by analytical and spectroscopic data.

The photolysis of a primary azide, as in **3**, has been described before as an excellent synthetic route to ω-aldehydo derivatives of simple alkyl[29,30] and aryl[30,31] glycosides. Furthermore, the reaction has been exploited for the preparation of 6-aldehydo analogs of starch[32] and cellulose[33], and was subsequently extended to nucleosides[34]. The photolysis was also effective with secondary azides[35], to give the corresponding ketones, but the yields were mediocre. However, when compound **3**, dissolved in benzene (ether, or acetone) and blanketed with nitrogen, was irradiated with light from a medium-pressure, mercury-arc lamp, it failed to undergo a straightforward transformation but, instead, led invariably, after mild hydrolysis of the presumed aldimine intermediate, to a complex mixture of products; this result was attributed to the presence of the benzoyloxy group at C-4 and its conceivable participation in the reaction. Therefore, the 4-hydroxyl derivative **5** and the 4-acetate **7**

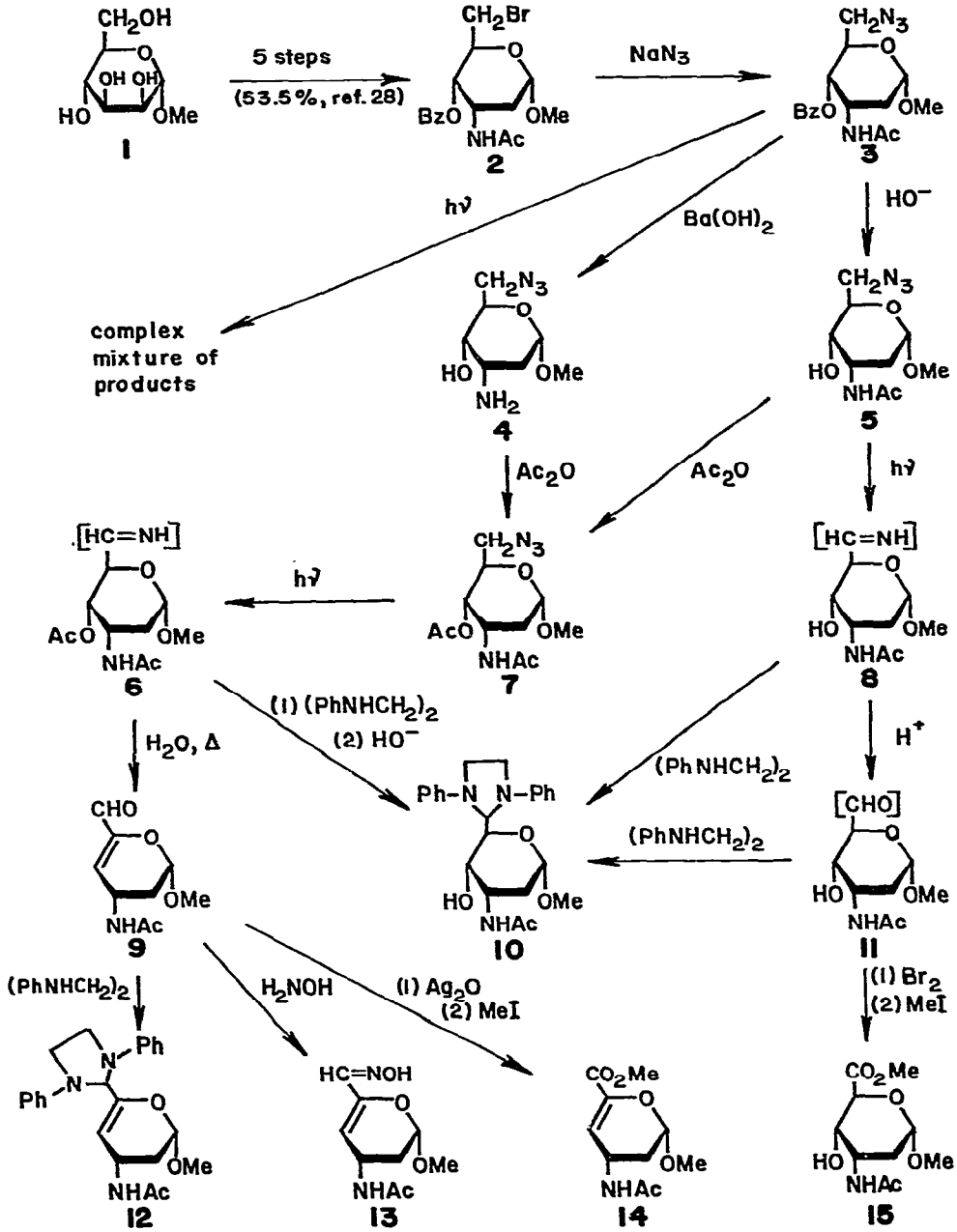
were envisaged as better substrates for the photolysis reaction, based on earlier experience with primary azides of unprotected and acetylated glycosides that could successfully be converted[29-33] into the respective aldehydes.

Conventional debenzoylation of **3** gave **5** in theoretical yield as an analytically pure syrup that failed to crystallize, and the crystalline acetate **7** was prepared from **3** *via* the fully deacylated, crystalline methyl glycoside **4** or, in better yield, from **5** by simple acetylation.

Irradiation of a solution of **5** in benzene under nitrogen with light from a mercury arc for 90 min at room temperature led to decomposition of all of the starting material (as shown by t.l.c.) and formation of an amorphous precipitate formulated as an oligomeric form of the expected imine **8**. It is generally considered[36] that photolysis of an azide proceeds *via* an intermediate nitrene ($R-CH_2N:$) that rearranges, by a 1,2-hydrogen shift, to give the corresponding imine. The elemental analysis of compound **8** gave somewhat variable values, but indicated the empirical formula $C_9H_{16}N_2O_4$, and the compound displayed i.r. absorption at 3420 cm^{-1} (N–H stretching vibration). There was no C=N band group in the 1630-cm^{-1} region, and the n.m.r. spectrum of **8** in chloroform-*d* was poorly resolved and clearly inconsistent with a monomeric structure[29,30]. Unambiguous evidence for the general imine structure **8** was provided, however, by the reactions exhibited by the product. Thus, the crystalline imidazolidine derivative **10** was conveniently prepared by treating **8** with 1,2-bis(anilino)ethane[37]. Furthermore, mild hydrolysis with anion-exchange resin, by the general procedure established in earlier work[29-34], afforded the aldehyde **11** as an amorphous material in high yield (83% from **5**); it migrated as a single zone in t.l.c., and gave positive reducing-sugar tests (aniline phthalate, Schiff reagent). The n.m.r. spectrum of **11** in chloroform-*d* showed extensive line-broadening, and the signal (δ 9.83) for the aldehyde proton accounted for less than 0.5 proton. These findings, and the low intensity of the carbonyl absorption band in the i.r. spectrum of **11**, are indicative of substantial intermolecular association[30,34,38] and, possibly, partial solvation.

Chemical evidence for the presence of the aldehydo group in **11** was provided by its conversion into the crystalline, readily identified, imidazolidine derivative **10**, and by its oxidation, with subsequent esterification, to give the aminohexuronate **15**. The results of detailed analysis of the excellent, first-order n.m.r. spectrum (see Table I) of **15** in chloroform-*d* eliminated the possibility that epimerization at C-5 had occurred at any of the reaction steps. The large value for $J_{4,5}$ (9.5 Hz) established the *trans*-diaxial disposition of H-4 and H-5, and the consistently small coupling-constants (1.8–3.8 Hz) between the protons at C-1–C-4 indicated their consecutive *gauche* orientation; these values are compatible only with the α-D-*ribo* configuration (in the $^4C_1$ conformation) assigned to **15**. Other spectral characteristics [i.r.: 1740 (ester C=O), 1640 and 1530 cm^{-1} (amide); mass spectrometry: 216 (M^+ — MeO·)] and its elemental composition entirely supported the structure indicated.

When a solution of the acetylated azide **7** in benzene was exposed to u.v. irradiation, the starting material completely disappeared after 90 min, as shown by



t.l.c. analysis. The i.r. spectrum [3430 (NH), 1745 (ester C=O), 1680 and 1520 cm^{-1} (amide)] of the tan solid obtained after evaporation of the solvent suggested that the 4-*O*-acetyl derivative (**6**) of **8** had been formed, again in a nonmonomeric form as manifested by absence of the characteristic C=N stretching absorption near 1630 cm^{-1}, and supported by extensive line-broadening in the n.m.r. spectrum of **6**

TABLE I

100-MHz, ^{1}H-N.M.R.-SPECTRAL DATA FOR COMPOUNDS 3–15

Compound[a]	*Chemical shifts (δ)[b] (first-order couplings, Hz, in parentheses)*											
	H-1 ($J_{1,2a}$)	*H-2e* ($J_{1,2e}$)	*H-2a* ($J_{2a,3}$)	*H-3* ($J_{2e,3}$)	*H-4* ($J_{3,4}$)	*H-5* ($J_{4,5}$)	*H-6* ($J_{5,6}$)	*H-6'* ($J_{5,6'}$)	*OMe-1*	*NH-3* ($J_{3,NH}$)	*NAc*	*Others*[a]
3[d]	4.90–4.75 m (4.0)	1.88 ddd (1.6)	2.14 m$_6$ (4.0)	4.90–4.75 m (3.1)	5.03 dd (4.0)	4.18 m (10.0)	← 3.44–3.37 m →		3.48 s	6.85 d (9.0)	1.92 s	8.05–7.30 m (aryl)
4[e]	4.76 m$_3$	← 2.10–1.95 m →		3.07 m	← 3.80–3.30 m ——→ (4.2)				3.36 s	2.63 bs	—	~3.50 b (OH)
5	4.77 dd (3.8)	1.86 ddd (1.8)	2.04 m$_6$ (3.8)	4.47 m$_6$ (3.2)	← 3.95–3.20 m ——→				3.42 s	7.00 d (8.0)	2.00 s	4.20 bs (OH)
6[f]	4.79 bs	← 2.15–1.80 m →		4.68 m	4.98 dd	3.93 m		—	3.39 s	6.80 d (9.0)	1.99 s	1.99 s (OAc)
7	4.82 dd	← 2.18–1.75 m →		← 4.80–4.60 m →		4.03 m$_5$ (10.0)	← 3.36 d → (4.5)	(4.5)	3.46 s	6.78 d (8.8)	1.98 s	1.98 s (OAc)
8[f]	4.73 bs	← 2.15–1.70 m →		← 4.60–3.20 m ——→				—	3.33 s	6.88 d (8.0)	1.96 s	
9	5.26 m$_3$	← 2.25–2.05 m →		4.79 m	6.04 d (5.5)	—	9.20 s	—	3.44 s	6.38 d (9.0)	1.93 s	
10	4.65 bs	← 1.90–1.60 m →		4.30 m	3.90–3.50 m	4.10 dd (10.2)	5.89 d (1.8)	—	3.03 s	~6.80[g]	1.93 s	7.40–6.60 m (aryl) ~4.10 (OH) 3.90–3.50 m (CH_2CH_2)
11[f]	4.80 bs	← 2.20–1.80 m →		← 4.70–3.40 m →			9.83 s	—	3.39 s	6.92 b	2.00 s	
12	4.88 bs	← 2.00–1.74 m →		4.56 m	5.35 d (6.0)	—	5.45 s	—	2.94 s	6.20 d (9.0)	1.84 s	7.40–6.60 m (aryl) 3.71 m (CH_2CH_2)
13[h]	5.12 bs	← 2.25–1.90 m →		4.92 m	5.46 d (4.6)	—	8.01 s	—	3.28 s	7.90 b	2.03 s	~4.90 (OH)
14	5.23 m$_3$	← 2.10–1.97 m →		4.70 m	6.17 d (6.0)	—	—	—	3.43 s	6.44 d (9.0)	1.90 s	3.76 s (CO_2Me)
15[i]	4.85 dd (3.2)	1.88 ddd (1.8)	2.22 m$_6$ (3.2)	4.51 m (3.8)	3.97 dd (3.8)	4.25 d (9.5)	—	—	3.36 s	6.86 d (9.0)	2.04 s	4.15 d (OH) (2.4) 3.67 s (CO_2Me)

[a]In chloroform-*d*, unless otherwise stated. [b]Signal multiplicities; b, broadened; d, doublet; m, multiplet; m$_x$, x-line pattern; s, singlet. [c]Assignments in parentheses. [d]$J_{2,2'}$ 15.5 Hz. [e]The partially obscured OH signal was detected in the δ 3.80–3.30 multiplet by deuterium exchange; $J_{3,4}$ was taken from a double-irradiation experiment. [f]In these spectra, extensive line-broadening was observed. [g]Obscured by aryl-proton signals. [h]In pyridine-d_5. [i]$J_{2,2'}$ 12.5 Hz.

in chloroform-*d*. However, the ready conversion of **6** into the imidazolidine derivative **10**, by treatment with 1,2-bis(anilino)ethane[37], followed by saponification, provided clear evidence for the latent aldehydo group in **6**.

When the "imine" **6** was boiled in aqueous solution for 90 min under reflux, the α,β-unsaturated aldehyde **9** was obtained exclusively. This result emphasizes the well-known[30,39,40] susceptibility of β-substituents in carbonyl sugar derivatives to α,β-elimination, even under extremely mild conditions.

Compound **9** was characterized by microanalysis, by chemical tests (aniline phthalate, Schiff reagent, potassium permanganate), and by its spectral (i.r., u.v., m.s., and n.m.r.) behavior. It is noteworthy that, in the n.m.r. spectrum (see Table I) of **9** in chloroform-*d*, the vinylic proton (H-4) signal (sharp doublet at δ 6.04) did not exhibit any long-range coupling, suggesting[40] that **9** adopts the $^2H_1$ conformation, which does not incorporate a "W" pathway for coupling between H-2 and H-4. In addition, the observed value of 5.5 Hz for $J_{3,4}$ is more consistent[40,41] with a *quasi*-equatorial ($^2H_1$ conformation) than a *quasi*-axial ($^1H_2$) disposition of the allylic proton (H-3). From the same observations on the spectra (see Table I) of the other dihydropyran (glycal) derivatives (**12**, **13**, and **14**) in this series, it was concluded that these compounds also favor the $^2H_1$ conformation, in agreement with earlier findings[40,42] that, among members of this class, the anomeric C–OR bond exhibits a pronounced tendency to assume a pseudo-axial orientation.

Treatment of the unsaturated aldehyde **9** with 1,2-bis(anilino)ethane[37] gave the dehydrated analog (**12**) of the 1,3-diphenylimidazolidine derivative **10**, crystalline and in high yield (84%). A characteristic feature in the n.m.r. spectra (see Table I) of both derivatives (**10** and **12**) is the anticipated, diamagnetic shift of the H-6 signal from its low-field position in the spectra of the aldehydes **11** and **9** to δ 5.89 and 5.45, respectively. Another feature common to **10** and **12** is present in their mass spectra, which show, as the base peak, the diphenylimidazolidinium cation (*m/e* 223) that arises by rupture of the C-4–C-5 bond.

Hydroxylamine readily converted the aldehyde **9** into the crystalline oxime **13**; the latter constitutes an immediate precursor of the corresponding 3,6-diamino-hex-4-enopyranoside, a structural analog of which (the 2,6-diamino isomer) exists[43] in Nature in glycosidic conjugation in the antibiotic sisomicin.

When the aldehyde **9**, in aqueous solution, was brought into reaction with silver oxide in the presence of barium hydroxide, and the product was treated with methyl iodide in *N,N*-dimethylformamide, a crystalline compound was obtained in good yield (80%) that was formulated as the 4,5-unsaturated 4-deoxyhexopyranuronate **14**, based on the evidence of microanalysis, i.r., u.v., and n.m.r. spectroscopy, and mass spectrometry. Its n.m.r. spectrum (see Table I) showed the signals anticipated for the two methyl and the acetyl groups, together with a low-field (δ 6.17) doublet for the vinylic proton (H-4) indicative[40,41] ($J_{3,4}$ 6 Hz; no long-range coupling) of the $^2H_1$ conformation for **14** (see foregoing discussions). The u.v. spectrum of **14** showed a strong (ε_{mM} 8.29) absorption at 241 nm, characteristic[39a] of an α,β-unsaturated acid component. The mass spectrum of **14** showed a distinctive molecular

ion (*m/e* 229) and the fragmentations anticipated from loss of MeOH, $\cdot CO_2Me$, and ·NHAc, together with fragments arising through[27a] retro-Diels–Alder decomposition.

Preliminary results indicated that catalytic hydrogenation[39a] of **14** proceeds with significant stereoselectivity, to give mainly the saturated *β*-L-*threo*-hexopyranuronate.

Uronic acids featuring the endocyclic, enol-acetal system present in **14** are encountered[39] as products of enzymic or base-catalyzed, *β*-eliminative degradation of polysaccharides containing uronic acid residues.

The foregoing reactions illustrate an extension to acetamido sugar derivatives of the azide photolysis procedure[29–35], providing, after oxidation and subsequent esterification, the crystalline methyl glycosiduronates **15** and **14** in 23 and 47% overall yields, respectively, from **2**.

EXPERIMENTAL

General methods. — Solvents were evaporated under diminished pressure at bath temperatures below 50°. T.l.c. was performed on precoated plates of Silica Gel 60 (E. Merck, Darmstadt); zones were detected by u.v. light, and by spraying with sulfuric acid and subsequent heating. Melting points were determined with a Thomas–Hoover apparatus and are uncorrected. A Perkin–Elmer Model 141 polarimeter and 1-dm tubes were used for measurement of specific rotations. I.r. spectra were recorded with a Perkin–Elmer Model 457 grating i.r. spectrophotometer (potassium bromide pellets, chloroform solutions, or films on sodium chloride discs). U.v. spectra were recorded with a Perkin–Elmer 202 spectrophotometer. ^{1}H-N.m.r. spectra were recorded at 100 MHz with a Varian HA-100 spectrometer; chemical shifts refer to an internal standard of tetramethylsilane (δ = 0.00) and are listed, together with spin-coupling values (Hz), in Table I. Mass spectra were recorded by C. R. Weisenberger with an AEI MS-9 double-focusing, high-resolution spectrometer operating at an ionizing potential of 70 eV and an accelerating potential of 8 kV; the source temperature (direct-inlet system) was 120°. Data, and probable assignments, for compounds **3**, **5**, **7**, and **15** are summarized in Table II. Microanalyses were performed by W. N. Rond. X-Ray powder diffraction data give interplanar spacings, Å, for CuKα radiation. The camera diameter was 114.59 mm. Relative intensities were estimated visually: m, moderate; s, strong; v, very; w, weak. The strongest lines are numbered (1, strongest).

*Methyl 3-acetamido-6-azido-4-O-benzoyl-2,3,6-trideoxy-α-*D-ribo*-hexopyranoside* (**3**). — A mixture of methyl 3-acetamido-4-*O*-benzoyl-6-bromo-2,3,6-trideoxy-*α*-D-*ribo*-hexopyranoside[28] (**2**; 12 g, 31.1 mmol) and sodium azide (6 g, 92.3 mmol) in *N*,*N*-dimethylformamide (120 ml) was stirred magnetically for 24 h at 60°, and then poured onto ice–water (500 ml). The precipitate that formed was collected and dried. Recrystallization from chloroform–hexane afforded pure **3**; yield 9.5 g (88%), m.p. 136–137°, $[\alpha]_D^{25}$ +86.6° (*c* 1.5, chloroform); $\nu_{max}^{CHCl_3}$ 3425 (NH), 2840 (OMe), 2100 (N_3), 1725 (ester C=O), 1675 and 1510 (amide), 1605 and 1588 cm^{-1} (mono-

TABLE II

MASS-SPECTRAL DATA FOR COMPOUNDS 3, 5, 7, AND 15

m/e *of principal fragments*[a] *(% of base peak)*									
Compound				*Assignment*[b]	*Compound*				*Assignment*[b]
3	5	7	15		3	5	7	15	
348 (—)	244 (0.2)	286 (—)	247 (—)	$M^{+\cdot}$	290 (0.2)	186 (0.4)	228 (0.1)	189 (—)	E_1^2
347 (0.01)				M − 1	58 (4)	58 (18)	58 (11)	58 (14)	E_1^1
316 (0.4)	212 (0.3)	254 (0.1)	215 (—)	A_1	129 (1.5)	129 (14)	129 (11)	129 (3.6)	F_1^1
194 (0.2)	194 (—)	194 (0.1)	197 (0.1)	A_2	114 (1)	114 (9.5)	114 (9)	114 (2.5)	F_2^1
138* (14)	138 (4.4)	138 (31)	138 (1)	A_3	128 (15)	128 (9)	128* (20)	128 (2.7)	F_1^2
226 (0.1)	226 (—)	226 (0.2)	229 (—)	B_1	86 (8)	86 (20)	86 (25)	86 (13)	G_1^1
183 (0.7)	183 (0.3)	183 (1)	186 (0.1)	B_2	72 (3)	72 (22)	72 (18)	72 (17)	G_1^2
317 (2)	213 (7.5)	255 (3)	216 (0.2)	C_1	—	86 (20)	—	86 (13)	H_1
258 (—)	154 (0.5)	196 (0.1)	157 (0.4)	C_2	43 (22)	43 (100)	43 (100)	43 (100)	Ac^+
136 (0.2)	136 (0.5)	136 (0.5)	139 (0.6)	C_3	292 (2.3)	188 (0.7)	230 (4)	188 (0.1)	$M - R^4$
263 (0.2)	159 (9)	201 (0.3)	159 (2)	D_1	170 (50)	170 (10)	170* (50)	170 (0.4)	$M - R^4 - R^3OH$
205 (0.3)	101 (16)	143 (1.5)	101 (9)	D_2	[c]	[d]	—	[e]	others
163 (—)	59 (35)	101 (6.5)	59 (40)	D_3					

[a]Prominent metastable fragments observed in the spectra are indicated by an asterisk at the daughter ion of the process involved; deviations between observed and calculated values are less than ±0.1 mass unit. [b]For details, see ref. 44. [c]*m/e* 122 (8%, $BzOH^{+\cdot}$), 105 (100, $PhCO^+$), and 77 (25, Ph^+). [d]*m/e* 158 (99%, $D_1 - H\cdot$) and 83 (46). [e]*m/e* 158* (7%, $D_1 - H\cdot$).

substituted phenyl); λ_{max}^{MeOH} 230 (ε_{mM} 13.00), 250 (3.5), 272 (1.70), and 280 nm (1.50); for m.s. data, see Table II; X-ray powder diffraction data: 12.26 m, 9.01 s (3), 7.93 s, 7.43 w, 7.07 w, 6.48 w, 5.55 m, 5.32 m, 4.91 s (1), 4.57 s (2), 3.98 m, 3.85 m, and 3.50 m.

Anal. Calc. for $C_{16}H_{20}N_4O_5$ (348.36): C, 55.16; H, 5.78; N, 16.08. Found: C, 55.26; H, 5.63; N, 15.81.

*Methyl 3-amino-6-azido-2,3,6-trideoxy-α-*D-ribo-*hexopyranoside* (**4**). — To a suspension of the peracylated glycoside **3** (2.07 g, 5.95 mmol) in water (50 ml) was added barium hydroxide octahydrate (20 g, 31.5 mmol), and the mixture was boiled for 24 h under reflux. Extraction with dichloromethane (five 50-ml portions), and evaporation of the dried (magnesium sulfate) extract, furnished crude **4**, which was recrystallized from carbon tetrachloride; yield 995 mg (83%), m.p. 113–114[9] (subl.), $[\alpha]_D^{25}$ +132° (*c* 1.2, chloroform); $\nu_{max}^{CHCl_3}$ 3425 and 3355 (NH_2), 2845 (OMe), and 2110 cm^{-1} (N_3); *m/e* (rel. intensity): 203 (1, M + 1), 171 (5.5, M — MeO·), 160 (50, M — ·N_3), 146 (1.6, M — ·CH_2N_3), 128 (9, 146 — H_2O or 160 — MeOH; m* at 102.4, calc. for 160 → 128: 102.40), 116 (14), 104 (26), 96 (1, 128 — MeOH; m* at 72.0, calc. 72.00), 86 (60), 72 (70), 59 (47), and 43 (100, Ac^+); X-ray powder diffraction data: 8.42 w, 7.40 s (2), 6.17 w, 5.57 w, 5.05 s (1), 4.67 s (3), 4.42 w, 4.19 w, 4.00 w, 3.69 m, 3.48 w, and 3.38 w.

Anal. Calc. for $C_7H_{14}N_4O_3$ (202.22): C, 41.57; H, 6.92; N, 27.70. Found: C, 41.45; H, 6.63; N, 27.69.

*Methyl 3-acetamido-6-azido-2,3,6-trideoxy-α-*D-ribo-*hexopyranoside* (**5**). — A mixture of the 4-benzoate **3** (8.9 g, 25.6 mmol) in methanol (80 ml) containing M aqueous sodium hydroxide (80 ml) was stirred for 12 h at 25°. The mixture was then extracted with dichloromethane (three 100-ml portions), and the combined extracts were washed with water, dried (magnesium sulfate), and evaporated, to give syrupy **5**; yield 6.1 g (98%). To secure analytical data, a sample was distilled *in vacuo* (bath temp. 190°, 0.3 mtorr); $[\alpha]_D^{23}$ −40.0° (*c* 1, chloroform); ν_{max}^{film} 3400 (broad, NH, OH), 2100 (N_3), 1655 and 1520 cm^{-1} (amide); for m.s. data, see Table II.

Anal. Calc. for $C_9H_{16}N_4O_4$ (244.25): C, 44.25; H, 6.60; N, 22.93. Found: C, 44.45; H, 6.58; N, 22.80.

*Photolysis of methyl 3-acetamido-4-*O*-acetyl-6-azido-2,3,6-trideoxy-α-*D-ribo-*hexopyranoside* (**7**) *to generate the imine* **6**. — Irradiation of a benzene solution (20 ml) of **7** (200 mg, 0.7 mmol), blanketed with nitrogen, with filtered (Pyrex filter) light from a medium-pressure mercury-lamp (450 W) for 90 min afforded, after evaporation of the solvent, compound **6** as a light-tan, amorphous powder; yield 170 mg (94%), m.p. 123–125° (dec.), $[\alpha]_D^{28}$ +84° (*c* 1.7, chloroform); $\nu_{max}^{CHCl_3}$ 3430 (NH), 2850 (OMe), 1745 (ester C=O), 1680 and 1520 cm^{-1} (amide). The 1630-cm^{-1} region of the i.r. spectrum of **6** did not show absorption assignable to C=N, and the n.m.r. spectrum (Table I) displayed considerable line-broadening; both observations are indicative of intermolecular association[29,30].

*Methyl 3-acetamido-4-*O*-acetyl-6-azido-2,3,6-trideoxy-α-*D-ribo-*hexopyranoside* (**7**). — *A. From* **5**. The syrupy 4-hydroxyl derivative **5** (6.61 g, 27.0 mmol) was treated with 1:2 acetic anhydride–pyridine (60 ml) for 10 h at 25°. Conventional processing

afforded crude, crystalline **7**; yield 7.2 g (98%). Recrystallization was effected from chloroform–hexane; m.p. 123°, $[\alpha]_D^{25}$ +74.1° (*c* 1.1, chloroform); $\nu_{max}^{CHCl_3}$ 3410 (NH), 2850 (OMe), 2110 (N_3), 1745 (ester C=O), 1680 and 1518 cm^{-1} (amide); for m.s. data, see Table II; X-ray powder diffraction data: 12.44 m, 8.88 s (3), 7.62 m, 6.17 s, 5.45 m, 4.83 s (1), 4.33 s (2), 3.88 m, and 2.11 m.

Anal. Calc. for $C_{11}H_{18}N_4O_5$ (286.29): C, 46.14; H, 6.33; N, 19.57. Found: C, 46.17; H, 6.28; N, 19.38.

B. From the unprotected glycoside **4**. Acetylation of **4** (610 mg, 3.0 mmol), essentially as described in the preceding paragraph for the partially protected **5**, furnished, after recrystallization from chloroform–hexane, pure **7**, identical in all respects with the foregoing sample; yield 540 mg (63%).

*Photolysis of methyl 3-acetamido-6-azido-2,3,6-trideoxy-α-*D*-ribo-hexopyranoside* (**5**) *to generate the imine* **8**. — A solution of **5** (1.70 g, 7.0 mmol) in benzene (250 ml), blanketed with nitrogen, was irradiated at 15° through a Pyrex filter with light from a medium-pressure mercury-lamp (450 W). A colorless material began to precipitate and, after 90 min, t.l.c. (9:1 chloroform–methanol) indicated that decomposition of the starting material (**5**) was complete. The solvent was evaporated, to afford a tan, amorphous product (**8**; 1.38 g, 91%) that gave an analysis agreeing approximately with that calculated for the empirical formula $C_9H_{16}N_2O_4$; m.p. 85–90° (dec.), $[\alpha]_D^{28}$ +34° (*c* 1.1, chloroform); $\nu_{max}^{CHCl_3}$ 3420 (amide NH), 3320 (imine NH), 2850 (OMe), 1660 and 1520 cm^{-1} (amide), no band in the 1630-cm^{-1} region (C=N). The n.m.r. spectrum (see Table I) of **8** showed extensive line-broadening that was inconsistent[29,30] with a monomeric structure.

*Methyl 3-acetamido-2,3,4-trideoxy-6-*aldehydo-*α-*D*-glycero-hex-4-enodialdo-1,5-pyranoside* (**9**). — A solution of the crude photoproduct **6** (170 mg, 0.66 mmol) in water (30 ml) was boiled for 90 min under reflux. Extraction with dichloromethane (three 20-ml portions), and evaporation of the dried (magnesium sulfate) extract, furnished crude **9**, which was purified by sublimation (80°/50 mtorr). Alternatively, the crude material was recrystallized from ethyl acetate–hexane; yield 80 mg (57% from **7**), m.p. 119–120°, $[\alpha]_D^{25}$ −148.2° (*c* 0.7, chloroform); $\nu_{max}^{CHCl_3}$ 3440 (NH), 2850 (OMe), 1705 (α,β-unsaturated C=O), 1670 and 1505 cm^{-1} (amide); *m/e* (rel. intensity): 199 (7, M^+), 170 (24, M − ·CHO), 167 (39, M − MeOH; m* at 140.1, calc. 140.15), 156 (7, M − Ac·; m* at 122.3, calc. 122.29), 128 (9, 170 − ketene; m* at 96.4, calc. 96.38), 125 (13, 167 − ketene; m* at 93.6, calc. 93.56), 112 and 58 (39 and 31, ions arising through retro-Diels–Alder decomposition[27a] of fragment 170; m* at 73.8, calc. for 170 → 112: 73.79), 111 (50, 170 − $AcNH_2$; m* at 62.0, calc. for M^+ → 111: 61.91), 96 (9, 125 − ·CHO), 70 (100, 112 − ketene), and 43 (60, Ac^+); X-ray powder diffraction data: 10.77 s (2), 8.11 w, 6.19 m, 5.86 w, 5.32 s (3), 5.09 w, 4.82 w, 4.41 m, and 4.10 s (1).

Anal. Calc. for $C_9H_{13}NO_4$ (199.21): C, 54.26; H, 6.57; N, 7.03. Found: C, 54.29; H, 6.74; N, 6.85.

In an alternative procedure, the intermediate imine **6** was not isolated, but was immediately converted, after complete (90 min) photodecomposition of the

azide **7** (2 g, 7.0 mmol), into the α,β-unsaturated aldehyde **9** by adding 19:1 water–acetic acid (200 ml) to the solution in benzene (250 ml). The turbid mixture was boiled for 2 h under reflux, the organic layer was separated, and the aqueous phase was extracted five more times with dichloromethane (100-ml portions). The organic phases were combined, dried (magnesium sulfate), and evaporated, to afford crude **8**, which was recrystallized from ethyl acetate–hexane; yield 950 mg (70%).

*Methyl 3-acetamido-2,3-dideoxy-5-C-(1,3-diphenylimidazolidin-2-yl)-α-*D*-ribo-pentopyranoside* (**10**). — *A. From the hexodialdopyranoside* **11**. To a solution of **11** (181 mg, 0.89 mmol) and 1,2-bis(anilino)ethane[37] (212 mg, 1.0 mmol) in methanol (5 ml) was added acetic acid (50%, 0.5 ml), and the mixture was boiled for 1 h under reflux. The solvent was then evaporated, the residue was taken up in ether, the suspension was filtered, and the filtrate was evaporated. Crystallization of the residue from ether in the cold afforded **10** as very fine, colorless needles; yield 198 mg (54%), m.p. 216–217°, $[\alpha]_D^{25}$ −84.5° (*c* 0.8, chloroform); $\nu_{max}^{CHCl_3}$ 3420 (NH), 2850 (OMe), 1655 and 1515 (amide), 1600, 1580, and 1510 cm^{-1} (phenyl); *m/e* (rel. intensity): 411 (1.1, M^+), 393 (0.25, M − H_2O), 380 (0.15, M − MeO·), 362 (0.05, M − $AcNH_2$), 223 (100, 1,3-diphenylimidazolidinyl cation: m* at 121.0, calc. for $M^+ \rightarrow$ 223: 121.00), 120 (3, *N*-phenylaziridinium cation; m* at 64.6, calc. for 223 → 120: 64.57), 77 (7, Ph^+), and 43 (2.2, Ac^+); X-ray powder diffraction data: 13.28 s (2), 11.94 w, 10.71 w, 9.71 w, 8.70 m (3), 8.00 w, 6.75 s (1), 5.96 w, 5.60 w, 5.26 w, 5.05 m, 4.82 m, and 4.62 m.

Anal. Calc. for $C_{23}H_{29}N_3O_4$ (411.53): C, 67.12; H, 7.10; N, 10.21. Found: C, 67.13; H, 7.16; N, 10.26.

B. From the imine **8**. To a solution of the crude photoproduct **8** (200 mg, 0.82 mmol) in 4:1 benzene–methanol (25 ml) were added 1,2-bis(anilino)ethane[37] (175 mg, 0.82 mmol) and acetic acid (1 ml). The solvent was removed after 16 h at 25°, and the residue was processed as described under section *A*, to afford crystalline **10**, indistinguishable from the foregoing sample; yield 141 mg (42%).

C. From the imine **6**. A mixture of the crude photoproduct **6** (200 mg, 0.7 mmol), 1,2-bis(anilino)ethane[37] (150 mg, 0.71 mmol), benzene (20 ml), and acetic acid (1 ml) was kept for 16 h at 25°, and then evaporated. Toluene (three 10-ml portions) was added to, and evaporated from, the residue, which was taken up in ether, the suspension filtered, and the filtrate evaporated. To a solution of the resulting syrup in methanol (10 ml) was added M aqueous sodium hydroxide (5 ml). The crystalline precipitate formed after 2 h was filtered off, and recrystallized from ether, to give **10**, identical in all respects with the foregoing sample; yield 188 mg (65%).

*Methyl 3-acetamido-2,3-dideoxy-6-*aldehydo-α-D-ribo-*hexodialdo-1,5-pyranoside* (**11**). — An aqueous solution of the product (**8**; 1.38 g, 6.38 mmol) from the photolysis experiment was treated with Amberlite IRC-50 (H^+) anion-exchange resin for 1 h at 23°. The suspension was filtered and the filtrate was evaporated, to afford the aldehyde **11** as an amorphous powder; yield 1.26 g (83% from **4**), $[\alpha]_D^{28}$ +39° (*c* 1.5, chloroform); $\nu_{max}^{CHCl_3}$ 3420 (NH), 2850 (OMe), 1740 (very weak, aldehyde C=O), 1660 and 1520 cm^{-1} (amide). This product gave positive reactions with the Schiff

reagent and with aniline phthalate, but its i.r. (small carbonyl absorption band) and n.m.r. (see Table I) spectra indicated that the aldehydo function was masked by intermolecular association[30,34,38]. As **11** was difficult to purify, an elemental analysis within acceptable limits was not obtained.

*Methyl 3-acetamido-2,3,4-trideoxy-5-C-(1,3-diphenylimidazolidin-2-yl)-α-*D*-glycero-pent-4-enopyranoside* (**12**). — 1,2-Bis(anilino)ethane[37] (116 mg, 0.55 mmol) was added to a solution of the unsaturated aldehyde **9** (100 mg, 0.5 mmol) in a mixture of methanol (5 ml), water (0.5 ml), and acetic acid (0.5 ml). After 18 h at 25° and 1 h of boiling under reflux, t.l.c. (1:1 chloroform–ether) indicated that the reaction was complete. Water was added to the hot mixture until the onset of turbidity and, after 18 h at 25°, the crystalline precipitate was collected, and recrystallized from ether, to give pure **12**; yield 164 mg (84%), m.p. 154–155°, $[\alpha]_D^{25}$ −88.0° (*c* 1.3, chloroform); $\nu_{max}^{CHCl_3}$ 3440 (NH), 2850 (OMe), 1660 and 1505 (amide), and 1600 and 1580 cm^{-1} (phenyl); *m/e* (rel. intensity): 393 (13, M⁺), 362 (0.25, M − MeO·), 334 (2, M − $AcNH_2$), 223 (100, 1,3-diphenylimidazolidinyl cation), 160 (11), 120 (5.8, *N*-phenylaziridinium cation), 104 (7, $PhN{=}CH^+$), 77 (16, Ph^+), and 43 (8, Ac^+); X-ray powder diffraction data: 14.02 m, 12.35 w, 6.94 s (1), 6.60 s (2), 5.82 w, 5.27 w, 4.96 s (3), 4.68 m, and 4.08 m.

Anal. Calc. for $C_{23}H_{27}N_3O_3$ (393.49): C, 70.21; H, 6.92; N, 10.68. Found: C, 70.45; H, 7.17; N, 10.45.

*Methyl 3-acetamido-2,3,4-trideoxy-6-*aldehydo-α-D-glycero-*hex-4-enodialdo-1,5-pyranoside 6-oxime* (**13**). — To a solution of the unsaturated aldehyde **9** (200 mg, 1 mmol) in water (1 ml) was added a solution of hydroxylamine hydrochloride (140 mg, 2 mmol) and sodium acetate (280 mg, 3.4 mmol) in water (1 ml). The oxime **13** precipitated almost immediately, and was collected; yield 193 mg (90%). Recrystallization from water gave an analytical sample: m.p. 225–227° (dec.), $[\alpha]_D^{27}$ −139° (*c* 0.9, methanol); ν_{max}^{KBr} 3280 (broad; NH, OH), 2840 (OMe), and 1640 and 1560 cm^{-1} (amide); *m/e* (rel. intensity): 214 (0.75, M⁺), 197 (15, M − ·OH), 182 (7, M − MeOH), 165 (80, 182 − ·OH; m* at 149.6, calc. 149.59), 156 and 58 (2.2 and 70, ions arising through retro-Diels–Alder decomposition[27a]), 139 (34, M − MeO· − ·CH=NOH), 124 (33, M − MeO· − $AcNH_2$), 123 (25, 165 − ketene; m* at 91.7, calc. 91.69), 111 (24, M − ·CH=NOH − $AcNH_2$), 97 (38), 70 (55), and 43 (100, Ac^+); X-ray powder diffraction data: 11.11 vs (1), 6.12 s, 5.60 m, 5.37 m, 4.96 w, 4.74 s (3), 4.36 s, 4.21 w, and 3.90 vs (2).

Anal. Calc. for $C_9H_{14}N_2O_4$ (214.22): C, 50.46; H, 6.59; N, 13.08. Found: C, 50.58; H, 6.50; N, 12.89.

*Methyl (methyl 3-acetamido-2,3,4-trideoxy-α-*D*-glycero-hex-4-enopyranosid)-uronate* (**14**). — A mixture of the α,β-unsaturated aldehyde **9** (100 mg, 0.5 mmol), silver oxide (140 mg, 0.6 mmol), and barium hydroxide octahydrate (95 mg, 0.3 mmol) in water (2 ml) was stirred for 1 h at 25°. T.l.c. (9:1 chloroform–methanol) then revealed that **9** had all reacted. The suspension was filtered, and the filtrate was evaporated, to afford a colorless solid that was treated with methyl iodide (0.2 ml, 455 mg, 3.2 mmol) in *N,N*-dimethylformamide (2 ml) for 20 h at 25°; the product

(**14**) was then detected as a u.v.-absorbing zone (R_F 0.73) in t.l.c. (9:1 chloroform–methanol). The mixture was poured onto ice–water (50 ml), and extracted with chloroform (three 10-ml portions). Evaporation of the dried (magnesium sulfate) extract afforded crude **14**; yield 92 mg (80%). By recrystallization from ether–hexane, compound **14** was obtained as colorless needles, m.p. 111–112°, $[\alpha]_D^{25}$ −111.3° (*c* 1.2, chloroform); $\nu_{max}^{CHCl_3}$ 3440 (NH), 2850 (OMe), 1733 (ester C=O), 1665 and 1503 cm^{-1} (amide); λ_{max}^{EtOH} 241 nm (ε_{mM} 8.29); *m/e* (rel. intensity): 229 (3, M^+), 198 (7, M − ·OMe), 197 (41, M − MeOH; m* at 169.5, calc. 169.47), 186 (8, M − Ac·), 182 (39, 197 − Me·), 170 (3.5, M − ·CO_2Me), 139 (26, 170 − MeO·), 112 and 58 (100 and 50, ions arising through retro-Diels–Alder decomposition[27a] of fragment 170), 111 (65, 170 − $AcNH_2$), 96 (14, 170 − MeOH − ketene), 70 (100, 112 − ketene; m* at 44.8, calc. 43.75), and 43 (56, Ac^+); X-ray powder diffraction data: 12.62 w, 8.75 m, 7.79 m (3), 6.10 w, 5.53 s (2), 5.08 w, 4.83 w, 4.36 s (1), 4.01 w, 3.80 w, 3.57 w, and 2.42 w.

Anal. Calc. for $C_{10}H_{15}NO_5$ (229.23): C, 52.39; H, 6.59; N, 6.11. Found: C, 52.18; H, 6.77; N, 5.91.

*Methyl (methyl 3-acetamido-2,3-dideoxy-α-*D*-ribo-hexopyranosid)uronate* (**15**).—To a mixture of the crude aldehyde **11** [from 200 mg (0.82 mmol) of the azide **7**] and barium carbonate (500 mg, 2.5 mmol) with water (10 ml) was added bromine (0.3 ml, 5.4 mmol) with stirring. The bromine remaining after 1 h at ~25° was removed by bubbling nitrogen through the solution. The inorganic material was filtered off, and the filtrate was evaporated, to give the crude barium uronate as a pale-yellow solid. A solution of this material in *N,N*-dimethylformamide (5 ml) was treated with methyl iodide (0.5 ml, 1.14 g, 12.5 mmol) for 20 h at 25°. The mixture was then poured into ice–water (50 ml), and the product was extracted with chloroform (three 50-ml portions). The dried (magnesium sulfate) extract was evaporated, to give a yellow solid (100 mg) that was twice recrystallized from ethyl acetate–hexane, to afford **15** as fine, colorless needles; yield 65 mg (32%), m.p. 146–147°, $[\alpha]_D^{25}$ +35.5° (*c* 1.6, chloroform); ν_{max}^{KBr} 3390, 3250 (NH, OH), 1740 (ester C=O), 1640 and 1530 cm^{-1} (amide); for m.s. data, see Table II; X-ray powder diffraction data: 8.62 w, 8.04 w, 7.46 s (1), 6.55 w, 5.79 s (2), 5.15 m, 4.85 m, 4.59 m, 4.19 m, 4.04 s (3), 3.87 s, and 3.59 s.

Anal. Calc. for $C_{10}H_{17}NO_6$ (247.25): C, 48.57; H, 6.93; N, 5.66. Found: C, 48.78; H, 6.83; N, 5.90.

ACKNOWLEDGMENT

This work was supported, in part, by Contract No. NO1-CM-57015 (The Ohio State University Research Foundation Project 784226) from the Division of Cancer Treatment, National Cancer Institute, National Institutes of Health, Department of Health, Education, and Welfare, Bethesda, Md. 20014.

REFERENCES

1 D. HORTON, T.-M. CHEUNG, R. J. SORENSON, W. WECKERLE, AND B. WINTER, *Abstr. Pap. Chem. Inst. Can., Am. Chem. Soc. Joint. Conf., 2nd,* (1977) CARB-39.
2 T.-M. CHEUNG, D. HORTON, R. J. SORENSON, AND W. WECKERLE, *Carbohydr. Res.*, 63 (1978) 77–89, and earlier papers, cited therein.
3 A. DI MARCO AND F. ARCAMONE, *Arzneim.-Forsch.*, 25 (1975) 368–375; S. K. CARTER, *J. Natl. Cancer Inst.*, 55 (1975) 1265–1274; A. DI MARCO, F. ARCAMONE, AND F. ZUNINO, in J. W. CORCORAN AND F. E. HAHN (Eds.), *Antibiotics*, Vol. III, Springer Verlag, New York, 1975, pp. 101–128.
4 E.-F. FUCHS, D. HORTON, W. WECKERLE, AND B. WINTER, *J. Antibiot.*, in press.
5 D. HORTON, R. G. NICKOL, W. WECKERLE, AND E. WINTER-MIHALY, unpublished results.
6 E.-F. FUCHS, D. HORTON, W. WECKERLE, AND E. WINTER-MIHALY, *J. Med. Chem.*, in press.
7 E.-F. FUCHS, D. HORTON, AND W. WECKERLE, *Carbohydr. Res.*, 57 (1977) c36–c39.
8 F. ARCAMONE, S. PENCO, A. VIGEVANI, S. REDAELLI, G. FRANCHI, A. DI MARCO, A. M. CASAZZA, T. DASDIA, F. FORMELLI, A. NECCO, AND C. SORANZO, *J. Med. Chem.*, 18 (1975) 703–707.
9 F. ARCAMONE, A. BARGIOTTI, G. CASSINELLI, S. PENCO, AND S. HANESSIAN, *Carbohydr. Res.*, 46 (1976) c3–c5.
10 F. ARCAMONE, A. BARGIOTTI, G. CASSINELLI, S. REDAELLI, S. HANESSIAN, A. DI MARCO, A. M. CASAZZA, T. DASDIA, A. NECCO, P. REGGIANI, AND R. SUPINO, *J. Med. Chem.*, 19 (1976) 733–734.
11 A. BARGIOTTI, G. CASSINELLI, G. FRANCHI, B. GIOIA, E. LAZZARI, S. REDAELLI, A. VIGEVANI, F. ARCAMONE, AND S. HANESSIAN, *Carbohydr. Res.*, 58 (1977) 353–361, and references cited therein.
12 F. ARCAMONE, S. PENCO, S. REDAELLI, AND S. HANESSIAN, *J. Med. Chem.*, 19 (1976) 1424–1425.
13 K. HEYNS AND M. BECK, *Chem. Ber.*, 90 (1957) 2443–2447.
14 K. HEYNS AND H. PAULSEN, *Chem. Ber.*, 88 (1955) 188–195.
15 K. HEYNS, G. KIESSLING, W. LINDENBERG, H. PAULSEN, AND M. E. WEBSTER, *Chem. Ber.*, 92 (1959) 2435–2438.
16 A. R. WILLIAMSON AND S. ZAMENHOF, *J. Biol. Chem.*, 238 (1963) 2255–2258; S. HANESSIAN AND T. H. HASKELL, *ibid.*, 239 (1964) 2758–2764.
17 H. R. PERKINS, *Biochem. J.*, 86 (1963) 475–483.
18 M. TORII, K. SAKAKIBARA, AND K. KURODA, *Eur. J. Biochem.*, 37 (1973) 401–405; R. REISTAD, *Carbohydr. Res.*, 36 (1974) 420–423.
19 K. SAKATA, A. SAKURAI, AND S. TAMURA, *Tetrahedron Lett.*, (1975) 3191–3194, and earlier papers, cited therein.
20 T. OGAWA, M. AKATSU, AND M. MATSUI, *Carbohydr. Res.*, 44 (1975) c22–c24.
21 A. TSUJI, T. KINOSHITA, AND M. MAEDA, *Chem. Pharm. Bull.*, 16 (1968) 539–543.
22 R. J. SUHADOLNIK, *Nucleoside Antibiotics*, Wiley–Interscience, New York, 1970, (*a*) pp. 172–189; (*b*) pp. 189–203; (*c*) pp. 218–234.
23 K. A. WATANABE, E. A. FALCO, AND J. J. FOX, *J. Am. Chem. Soc.*, 94 (1972) 3272–3274; F. W. LICHTENTHALER, T. MORINO, W. WINTERFELDT, AND Y. SANEMITSU, *Tetrahedron Lett.*, (1975) 3527–3530, and references cited therein.
24 R. S. GOODY, K. A. WATANABE, AND J. J. FOX, *Tetrahedron Lett.*, (1970) 293–296.
25 N. P. DOMADARAN, G. H. JONES, AND J. G. MOFFATT, *J. Am. Chem. Soc.*, 93 (1971) 3812–3813; T. NAKA, T. HASHIZUME, AND M. NISHIMURA, *Tetrahedron Lett.*, (1971) 85–98; H. OHRUI, H. KUZUHARA, AND S. EMOTO, *ibid.*, (1971) 4267–4270.
26 H. PAULSEN AND E. MÄCKEL, *Chem. Ber.*, 106 (1973) 1525–1536; K. OCHI AND K. OKUI, *Chem. Pharm. Bull.*, 22 (1974) 2223–2230; A. ROSENTHAL AND A. J. BRINK, *Carbohydr. Res.*, 46 (1976) 289–292, and references cited therein.
27 See, for example, (*a*) J. KISS AND F. BURKHARDT, *Helv. Chim. Acta*, 52 (1969) 2622–2636; (*b*) T. M. K. CHIU, K. A. WATANABE, AND J. J. FOX, *Carbohydr. Res.*, 32 (1974) 211–216.
28 D. HORTON AND W. WECKERLE, *Carbohydr. Res.*, 44 (1975) 227–240.
29 D. HORTON, A. E. LUETZOW, AND J. C. WEASE, *Carbohydr. Res.*, 8 (1968) 366–367; D. M. CLODE, R. HEMS, D. HORTON, A. E. LUETZOW, AND H. SHOJI, *Abstr. Pap. Am. Chem. Soc. Meet.*, 157 (1969) CARB-5; R. L. WHISTLER AND A. K. M. ANISUZZAMAN, *J. Org. Chem.*, 34 (1969) 3823–3824.
30 A. E. LUETZOW, Ph.D. Dissertation, The Ohio State University, 1971; *Diss. Abstr. Int. B*, 32 (3) (1971) 1455.

31 D. M. CLODE, D. HORTON, E. K. JUST, A. E. LUETZOW, AND K. D. PHILIPS, *Abstr. Pap. Chem. Inst. Can., Am. Chem. Soc. Joint Conf., 1st*, (1970) CARB-21.
32 D. M. CLODE AND D. HORTON, *Carbohydr. Res.*, 17 (1971) 365–373.
33 D. M. CLODE AND D. HORTON, *Carbohydr. Res.*, 19 (1971) 329–337; D. HORTON, A. E. LUETZOW, AND O. THEANDER, *ibid.*, 26 (1973) 1–19.
34 D. C. BAKER AND D. HORTON, *Carbohydr. Res.*, 21 (1972) 393–405.
35 D. M. CLODE AND D. HORTON, *Carbohydr. Res.*, 14 (1970) 405–408; R. L. WHISTLER AND L. W. DONER, *J. Org. Chem.*, 35 (1970) 3562–3563.
36 D. H. R. BARTON AND L. R. MORGAN, JR., *J. Chem. Soc.*, (1962) 622–631; R. A. ABRAMOVITCH AND B. A. DAVIS, *Chem. Rev.*, 64 (1964) 149–185; R. M. MORIARTY AND M. RAHMAN, *Tetrahedron*, 21 (1965) 2877–2891; W. LWOWSKI, *Angew. Chem.*, 79 (1967) 922–931; *Angew. Chem. Int. Ed. Engl.*, 6 (1967) 897–906.
37 H. W. WANZLICK AND W. LÖCHEL, *Chem. Ber.*, 86 (1953) 1463–1466; L. F. FIESER AND M. FIESER, *Reagents for Organic Synthesis*, Wiley, New York, 1967, p. 187.
38 R. S. SCHAFFER AND H. S. ISBELL, *J. Am. Chem. Soc.*, 79 (1957) 3864–3866; M. L. WOLFROM, W. VON BEBENBURG, AND A. THOMPSON, *J. Org. Chem.*, 26 (1961) 4151–4153; T. D. INCH, *Carbohydr. Res.*, 5 (1967) 53–61; D. HORTON AND F. O. SWANSON, *ibid.*, 14 (1970) 159–171.
39 (a) J. KISS, *Adv. Carbohydr. Chem. Biochem.*, 29 (1974) 229–303; (b) B. LINDBERG, J. LÖNNGREN, AND S. SVENSSON, *ibid.*, 31 (1975) 185–240.
40 D. M. MACKIE AND A. S. PERLIN, *Carbohydr. Res.*, 24 (1972) 67–85, and references cited therein.
41 R. J. FERRIER, *Adv. Carbohydr. Chem. Biochem.*, 24 (1969) 199–266.
42 P. L. DURETTE AND D. HORTON, *Adv. Carbohydr. Chem. Biochem.*, 26 (1971) 49–125.
43 D. J. COOPER, R. S. JARET, AND H. REIMANN, *J. Chem. Soc., Chem. Commun.*, (1971) 285–286; H. REIMANN AND R. S. JARET, *Infection (Munich)*, 4 (Suppl. 4) (1976) 289–291.
44 D. HORTON, R. J. SORENSON, AND W. WECKERLE, *Carbohydr. Res.*, 58 (1977) 125–138.