Carbohydrate Research, 110 (1982) 43–54
Elsevier Scientific Publishing Company, Amsterdam – Printed in The Netherlands

SYNTHESIS OF NITROGEN-15-LABELED AMINO SUGAR DERIVATIVES BY ADDITION OF PHTHALIMIDE-^{15}N TO A CARBOHYDRATE EPOXIDE*

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(Received May 11th, 1982; accepted for publication, May 29th, 1982)

ABSTRACT

Derivatives of methyl 2-amino-2-deoxy-α-D-altropyranoside-*2*-^{15}N and methyl 3-amino-3-deoxy-α-D-glucopyranoside-*3*-^{15}N have been synthesized by addition of phthalimide-^{15}N to methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-allopyranoside. The structures of the phthalimido derivatives that resulted have been proved chemically, by conversion into known aminodeoxy derivatives, and spectroscopically, by ^{1}H- and ^{13}C-n.m.r. spectroscopy. ^{1}H-N.m.r. spectroscopy at 360 MHz also allowed definition of the configurations and conformations of the labeled and unlabeled phthalimido derivatives, and the measurement of vicinal ^{1}H–^{15}N coupling-constants that are characteristic of ^{1}H–^{15}N dihedral angles of ~60°.

INTRODUCTION

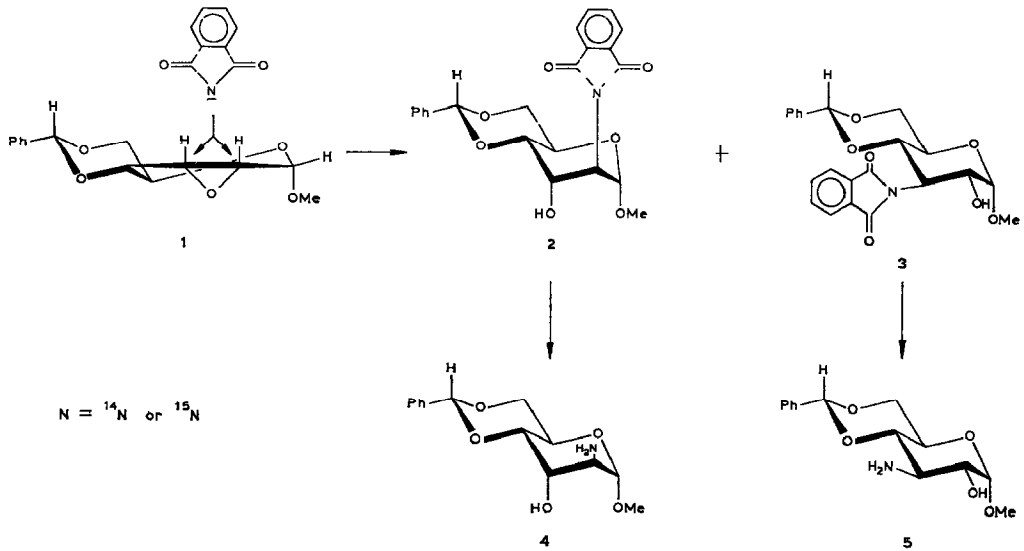
In connection with studies of the possible dependence of vicinal ^{15}N–proton coupling-constants on the dihedral angle of the ^{15}N and proton nuclei, ^{15}N-labeled derivatives of amino sugars were required in which the ^{15}N nucleus would possess a definite, fixed, stereochemical orientation. Definition of such an angular dependence for amino sugars would provide guidance for the projected use of proton-coupled, ^{15}N-n.m.r. spectra in the structural, configurational, and conformational analysis of aminoglycoside antibiotics and amino sugar derivatives. A suitably rigid, molecular framework for this study exists in the *trans*-fused methyl 4,6-*O*-benzylidene-α-D-hexopyranoside derivatives, many of which have been shown previously[1,2] by proton-n.m.r. spectroscopy to adopt the $^{4}C_{1}$(D) conformation almost exclusively.

In the synthesis of several ^{15}N-labeled, ω-amino-ω-deoxy sugar derivatives reported previously[2–7], potassium phthalimide-^{15}N was used as a convenient source of the ^{15}N isotope, especially because labeled ammonia and azide ion are less suitable for this purpose. Methods were therefore sought for the synthesis of methyl 4,6-*O*-benzylidenedeoxyphthalimido-α-D-hexopyranoside derivatives from the methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-hexopyranosides.

*Presented at the IXth International Symposium on Carbohydrate Chemistry, London, England, April 14, 1978.

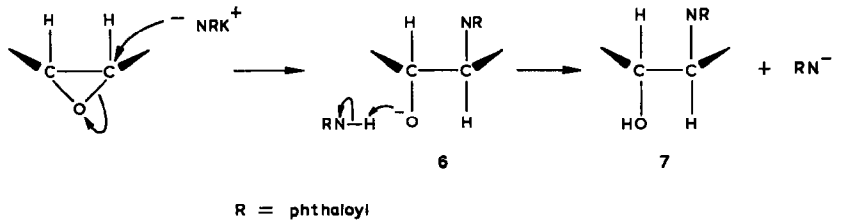
RESULTS AND DISCUSSION

Synthesis. — The attempted reaction of solutions of methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-allopyranoside (**1**) in hexamethylphosphoric triamide (HMP) with potassium phthalimide alone at 150° led to extensive degradation of the reactants, and no useful product could be isolated. However, when this reaction was conducted in the presence of 1.2 molecular equivalents of phthalimide, together with ~0.3 equivalent of its potassium salt, compound **1** reacted slowly, to give a mixture of products from which, by fractional recrystallization, were isolated methyl 4,6-*O*-benzylidene-2-deoxy-2-phthalimido-α-D-altropyranoside (**2**) in 44% yield, and methyl 4,6-*O*-benzylidene-3-deoxy-3-phthalimido-α-D-glucopyranoside (**3**) in 15% yield*. Repetition of the synthesis with phthalimide-^{15}N and its potassium salt led to the corresponding ^{15}N-labeled products **2**-^{15}N and **3**-^{15}N in similar yields.



We consider that this reaction proceeds by rearside attack of the phthalimide ion on the epoxide ring, with formation of intermediate alkoxide ions (for example, **6**). It seems possible that, if free phthalimide is not present in the reaction mixture, the phthalimido rings of such intermediates as **6** are cleaved by the nucleophilic attack of other alkoxide anions, so that phthalimido-substituted products are not isolated. In the presence of phthalimide, an anion such as **6** may be expected to be neutralized by detachment of a proton from a phthalimide molecule, with formation of such relatively stable, hydroxyphthalimido products as **7**, and regeneration of the phthalimide ion. Therefore, the net reaction involves addition of the elements of

*Compare with the reaction product of **1** with 1,3-dithian-2-yl-lithium which, on acetylation, afforded[8] only the 2-substituted α-D-*altro* derivative in 30% yield.



phthalimide to the epoxide[9]. The phthalimide anion appears to play a catalytic role, although, in practice, quantities greater than catalytic were used.

The structures of **2** and **3** were proved chemically by hydrazinolysis to the corresponding, known 2-amino (**4**) and 3-amino (**5**) derivatives, and were confirmed by ^{13}C-n.m.r. spectroscopy. Proton-n.m.r. studies at 360 MHz indicated the structures, configurations, and conformations of **2** and **3**.

In accordance with the Fürst–Plattner rule[10], the 2,3-diaxial-addition product **2** is the preponderant product (44%) of the reaction of **1** with phthalimide. However, the relative proportion (yield, 15%) of the 2,3-diequatorial product **3** is substantially

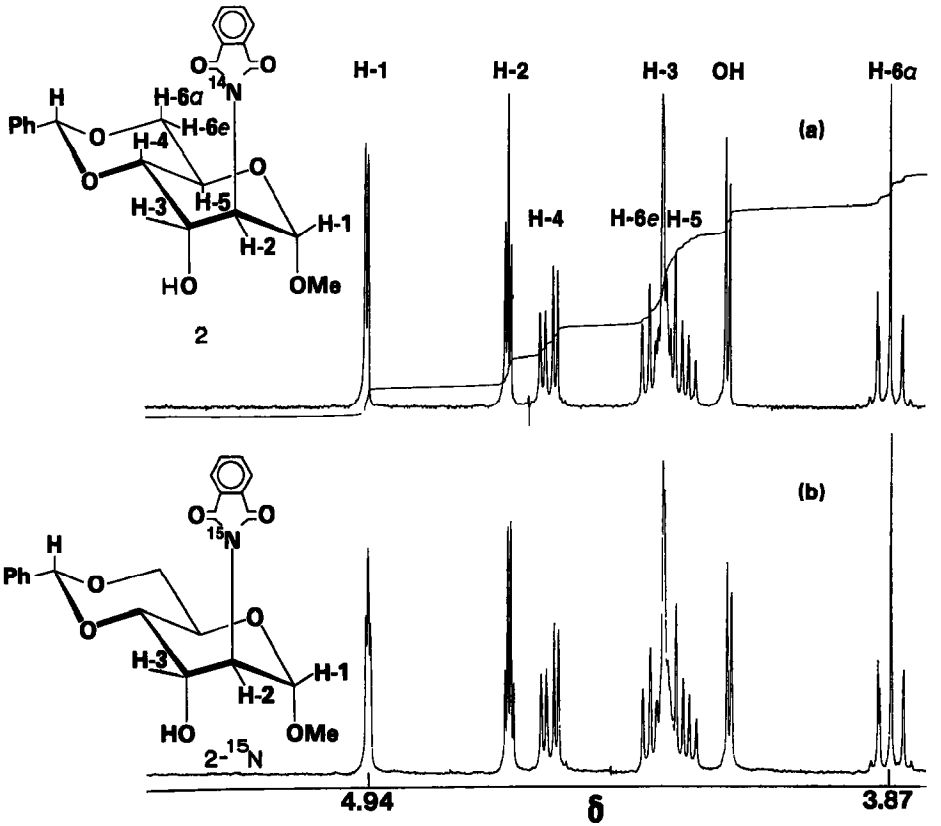


Fig. 1. Partial proton-n.m.r. spectra of solutions in acetone-d_6 at 360 MHz: (a) methyl 4,6-*O*-benzylidene-2-deoxy-2-phthalimido-α-D-altropyranoside (**2**), and (b) its ^{15}N-labeled derivative (**2**-^{15}N).

greater than that previously reported[11] for reactions of **1** with azide ion, which yielded a product ratio of 2-azidoaltroside:3-azidoglucoside of 15:1. The smaller relative yield of the 2-deoxy-2-phthalimidoaltroside derivative **2** may be attributed to the development of some conformational instability in the transition state leading to **2**, as a consequence of erection of the bulky phthalimido substituent into an axial orientation. The non-chair conformation adopted by methyl 4,6-*O*-benzylidene-2-deoxy-2-(pentachlorophenyl)-α-D-altropyranoside[12] may be compared here.

Proton-n.m.r. spectroscopy. — At 360 MHz, the proton-n.m.r. spectra (see Fig. 1) of **2** and **2**-^{15}N were sufficiently well dispersed that all of the proton coupling-constants possible could be measured, with the exception of $^3J_{3,^{15}N}$, which was obscured by overlap of the H-3 multiplet with the H-5 and H-6*e* signals. Coupling of H-3 with the hydroxyl proton also contributed to the complexity of the H-3 multiplet. Introduction of the ^{15}N isotope into compound **2** caused the appearance of additional couplings, $^3J_{1,^{15}N}$ 1.5 and $^2J_{2,^{15}N}$ 2.1 Hz, in the H-1 and H-2 signals, respectively (see Fig. 1b), thus indicating that the nitrogen atom is located at C-2.

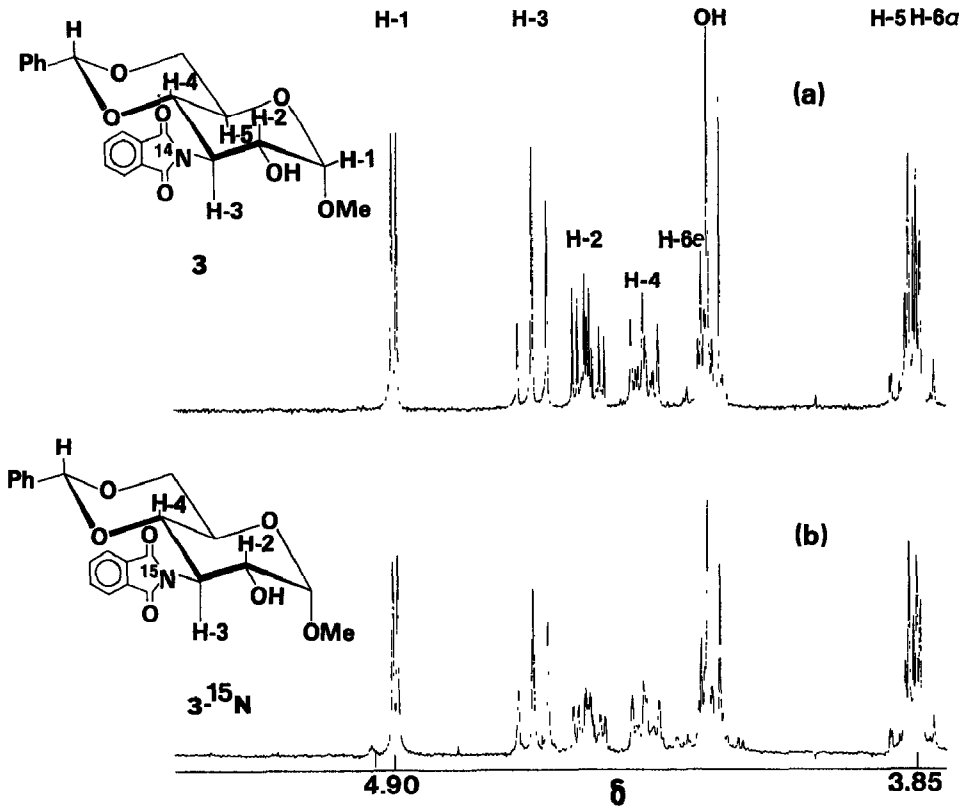


Fig. 2. Partial proton-n.m.r. spectra of solutions in acetone-d_6 at 360 MHz: (a) methyl 4,6-*O*-benzylidene-3-deoxy-3-phthalimido-α-D-glucopyranoside (**3**), and (b) its ^{15}N-labeled derivative (**3**-^{15}N).

TABLE I

PROTON CHEMICAL SHIFTS[a] AND COUPLING CONSTANTS (Hz) OF METHYL 4,6-*O*-BENZYLIDENEDEOXYPHTHALIMIDO-α-D-HEXOPYRANOSIDE DERIVATIVES

Derivative	*Position*							*OMe*	*OH*	*PhCH*	*Ph*		*Phthalimido*
	1	*2*	*3*	*4*	*5*	*6*					*2(6)*	*3(5) 4*	
2	4.94d[b]	4.65t	4.34[c]	4.57q	4.30s[c]	3.87s (6*a*)	4.36q[c] (6*e*)	3.34	4.20d	5.76	7.53m	← 7.36m →	7.88m
	$J_{1,2}$ 2.0	$J_{2,3}$ 2.2	$J_{3,4}$ 3.9	$J_{4,5}$ 9.5	$J_{5,6e}$ 5.2	$J_{5,6a}$ 9.8	$J_{6e,6a}$ 9.8	—	$J_{3,OH}$ 3.4	—	—	—	—
2-^{15}N	4.94t	4.65q	4.33[c]	4.57q	4.30s[c]	3.87s (6*a*)	4.36q[c] (6*e*)	3.34	4.20d	5.76	7.53m	← 7.36m →	7.88m
	$J_{1,2}$ 1.9	$J_{2,3}$ 2.1	$J_{3,4}$ 3.7	$J_{4,5}$ 9.5	$J_{5,6e}$ 5.1	$J_{5,6a}$ 9.8	$J_{6e,6a}$ 9.8	—	$J_{3,OH}$ 3.4	—	—	—	—
	$J_{1,^{15}N}$ 1.5	$J_{2,^{15}N}$ 2.1	$J_{3,^{15}N}$[d]										
3	4.90d	4.51o	4.63t	4.40o	3.87m[c]	3.85m[c] (6*a*)	4.28m[c] (6*e*)	3.50	4.27d	5.59	7.36m	← 7.29m →	7.84m
	$J_{1,2}$ 3.6	$J_{2,3}$ 10.5	$J_{3,4}$ 10.5	$J_{4,5}$ 8.7	$J_{5,6e}$ 5.0	$J_{5,6a}$ 10.4	$J_{6e,6a}$ −10.4	—	$J_{2,OH}$ 8.7	—	—	—	—
3-^{15}N	4.90d	4.51hd	4.63t	4.40o[c]	3.87m	3.85m[c] (6*a*)	4.28m[c] (6*e*)	3.50	4.26d	5.59	7.35m	← 7.26m →	7.84m
	$J_{1,2}$ 3.6	$J_{2,3}$ 10.5	$J_{3,4}$ 10.5	$J_{4,5}$ 8.7	$J_{5,6e}$ 5.5	$J_{5,6a}$ 10.1	$J_{6e,6a}$ −10.2		$J_{2,OH}$ 8.8	—	—	—	—
		$J_{2,^{15}N}$ 0.9	$J_{3,^{15}N}$ <0.5	$J_{4,^{15}N}$ <0.5									

[a]In p.p.m. from internal tetramethylsilane, in $(CD_3)_2SO$ at 360 MHz. [b]Signal multiplicities: d, doublet; hd, hexadecet; m, multiplet; o, octet; q, quartet; s, sextet; t, triplet. All peak areas computed were consistent with the structures assigned. [c]Incompletely resolved. [d]Obscured. [e]Broadened.

TABLE II

CARBON-13 CHEMICAL SHIFTS[a] AND COUPLING CONSTANTS (Hz) OF METHYL 4,6-*O*-BENZYLIDENEDEOXYPHTHALIMIDO-α-D-HEXOPYRANOSIDE DERIVATIVES

Derivative	*Position*						*OMe*	*PhCH*	*Ph*				*Phthalimido*			
	1	*2*	*3*	*4*	*5*	*6*			*1*	*2(6)*	*3(5)*	*4*	*1(6)*	*2(5)*	*3(4)*	*C=O*
2	99.5	55.6	58.0	76.2	67.6	69.4	55.4	101.9	137.4	126.2	128.2	129.1	131.5	123.5	134.3	167.6
	$^1J_{^{13}CH}$ 171	150	151	147	151	144	143	160	—	161	162	160	—	164	163	—
2-^{15}N	99.5	55.6d[b,c]	58.0	76.2	67.6	69.4	55.3	101.9	137.3	126.2	128.2	129.1	131.5d	123.5	134.3	167.6d
	$J_{C-2,^{15}N}$ 9.8												$J_{C-1(C-6),^{15}N}$ 7.3			$J_{C=O,^{15}N}$ 12.2
3	99.9	64.2	54.1	75.2	68.1	68.9	55.4	101.7	137.2	126.3	128.1	129.0	131.9	123.4	133.9	168.6
													131.6	123.1		
	$^1J_{^{13}CH}$ 172	152	146	—[c]	151	148	142	162	—	164	161	160	—	165	167	—
3-^{15}N	99.7	64.2	54.1d	75.1	68.2	68.9	55.5	101.7	137.1	126.3	128.1	129.0	132.0d[c]	123.5	133.9	168.6d
			$J_{C-3,^{15}N}$ 9.8										131.6d[c]	123.2		$J_{C=O,^{15}N}$ 12.2
													$J_{C-1(C-6),^{15}N}$ 8.5			

[a]In p.p.m. from internal tetramethylsilane, in $CDCl_3$ at 22.6 MHz. [b]d, doublet. [c]Not fully resolved.

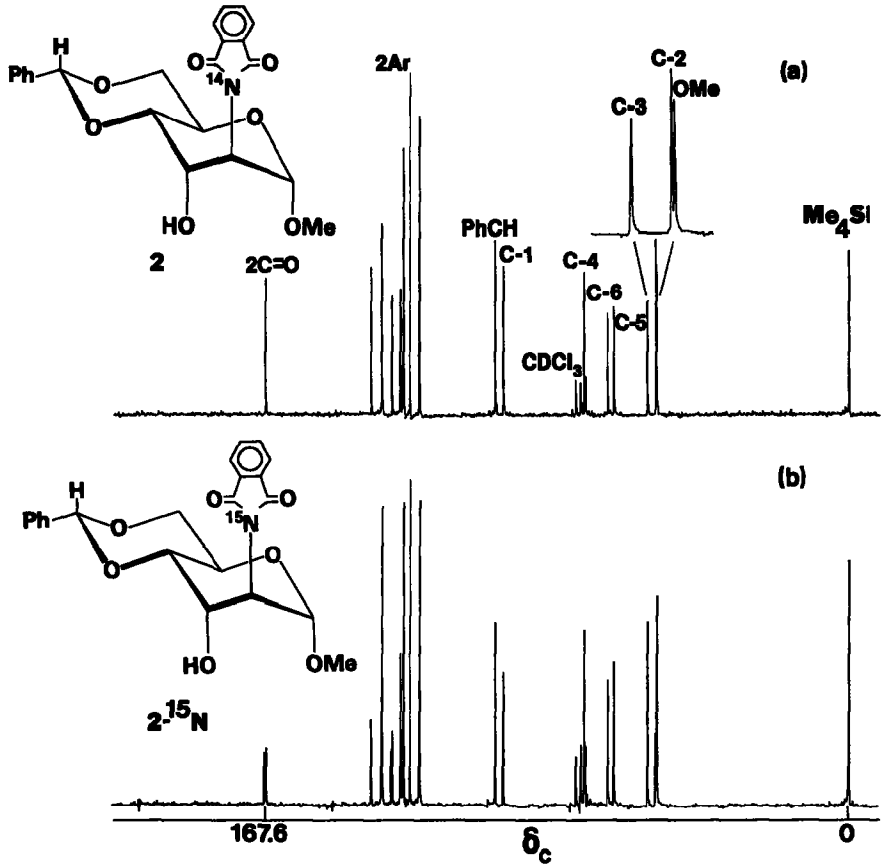


Fig. 3. ^{13}C-N.m.r. spectra of solutions in chloroform-*d* at 22.6 MHz: (a) methyl 4,6-*O*-benzylidene-2-deoxy-2-phthalimido-α-D-altropyranoside (**2**), and (b) its ^{15}N-labeled derivative (**2**-^{15}N).

The magnitude of $J_{3,OH}$ (3.4 Hz) indicates the location of the hydroxyl group at C-3. Small values of $J_{1,2}$, $J_{2,3}$, and $J_{3,4}$ (see data for **2** in Table I) are characteristic of α-D-altropyranosides in the $^4C_1$(D) conformation[2,13], and consequently, **2** may be assigned this configuration and conformation.

A complete set of proton chemical shifts and coupling constants (see Table I) was obtained from the 360-MHz, proton-n.m.r. spectra (see Fig. 2) of **3** and **3**-^{15}N. Again, the magnitude of $J_{2,OH}$ (8.7 Hz) indicates that the hydroxyl group resides at C-2, and, therefore, by elimination, the nitrogen atom must be located at C-3. This structural assignment is consistent with the value $^3J_{2,^{15}N}$ 0.9 Hz observed for **3**-^{15}N, although couplings of the ^{15}N nucleus with H-3 and H-4 were not resolved. The magnitudes of the vicinal proton–proton coupling-constants for **3** and **3**-^{15}N allow assignment of the α-D-*gluco* configuration and $^4C_1$(D) conformation[2,13,14].

Carbon-13 n.m.r. spectroscopy. — The ^{13}C-n.m.r. spectra* of **2** and **2**-^{15}N

*For a previous study of the ^{13}C-n.m.r. spectra of simple, *trans*-fused methyl 4,6-*O*-benzylidene-D-glycopyranoside derivatives, see ref. 15.

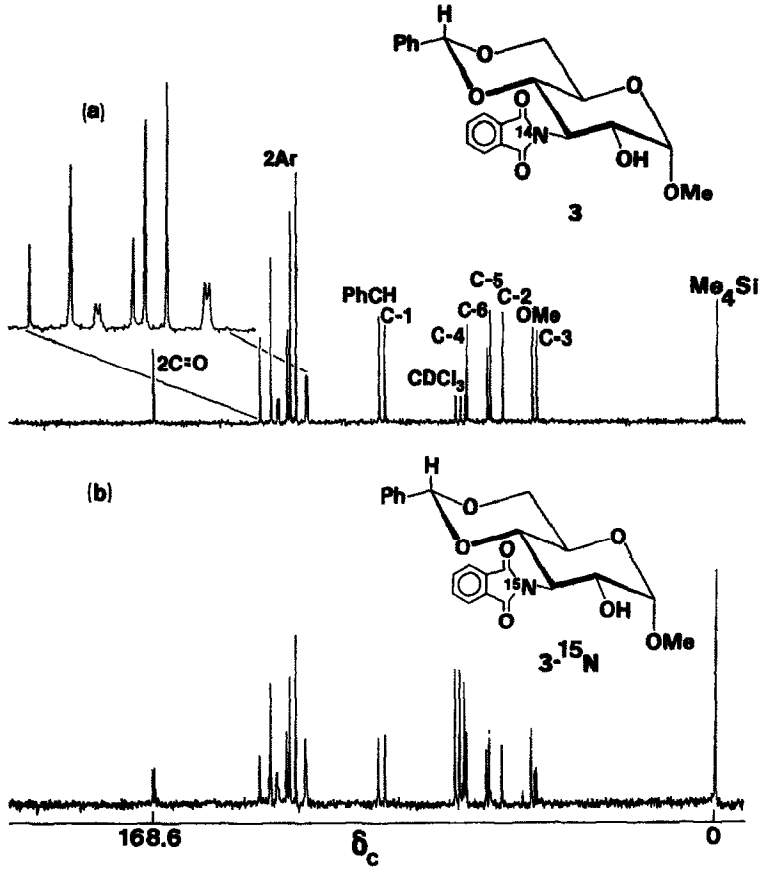


Fig. 4. ^{13}C-N.m.r. spectra of solutions in chloroform-*d* at 22.6 MHz: (a) methyl 4,6-*O*-benzylidene-3-deoxy-3-phthalimido-α-D-glucopyranoside (**3**), and (b) its ^{15}N-labeled derivative (**3**-^{15}*N*).

(see Fig. 3) display resolved, ^{13}C resonances for all single ^{13}C nuclei or pairs of position-equivalent, aromatic ^{13}C nuclei. The methoxyl ^{13}C resonance is slightly overlapped by the C-2 resonance at high field, the chemical shift of the latter resonance being consistent with the shifts found previously[7,16] for other derivatives containing ^{13}C nuclei bonded to the nitrogen atoms of phthalimido groups. Detailed assignments of the ^{13}C chemical shifts and coupling constants of **2**, **2**-^{15}*N*, **3**, and **3**-^{15}*N*, given in Table II, were confirmed by selective proton-decoupling, and analysis of ^{13}C–^{1}H and ^{13}C–^{15}N spin-coupling patterns. The location of the ^{15}N isotope in **2**-^{15}*N* is indicated by the appearance of additional splittings in the C-2, C=O, and phthalimido C-1 (C-6) resonances ($J_{C\text{-}2,^{15}N}$ 9.8, $J_{C=O,^{15}N}$ 12.2, and $J_{C\text{-}1(C\text{-}6),^{15}N}$ 7.3 Hz, respectively).

Similar results (see Table II) were obtained from the ^{13}C-n.m.r. spectra (see Fig. 4) of **3** and **3**-^{15}*N*, except that the C-3 resonance of **3**-^{15}*N* was now split by coupling ($J_{C\text{-}3,^{15}N}$ 9.8 Hz) with ^{15}N. The ^{13}C-n.m.r. spectra of **3** and **3**-^{15}*N* seem

to be unique, in that C-1 and C-6 of the phthalimido group are non-equivalent, as are also C-2 and C-5 of this group (see Fig. 4a, expansion of 2Ar region). This non-equivalence (which amounts to 0.3 p.p.m. in each case) could be due either to the asymmetry of neighboring carbon atoms or to a favored orientation[17] of the phthalimido group.

The substituents attached to C-2–C-6 of the sugar chains of the phthalimido derivatives have similar electronegativities and, hence, the values of $^1J_{^{13}CH}$ for these ^{13}C nuclei are also similar, and fall within the range of 144–152 Hz (see Table II). Only C-1 (which has more electronegative substituents) shows a significantly larger value, $^1J_{^{13}CH}$ 171–172 Hz (see refs. 7 and 18). The values of $^1J_{^{13}CH}$ for the benzylic and aromatic ^{13}C nuclei are all similar, and fall within the range of 160–167 Hz. The values of the ^{13}C–^{15}N coupling-constants found for **2**-^{15}N and **3**-^{15}N are similar to those previously reported for ω-deoxy-ω-phthalimidoaldose derivatives[7,16].

In summary, the values of the vicinal proton–^{15}N coupling constants reported herein (range, $^3J_{HCCN}$ <0.5–1.5 Hz) appear to be appropriate for proton–^{15}N dihedral angles of ~60°, as determined by the chair conformations found for the phthalimido derivatives.

EXPERIMENTAL*

General. — Reactions were monitored by thin-layer chromatography (t.l.c.) on silica gel G (Analtech). The plates were developed either in 97:3 dichloromethane–methanol (compounds **1**–**3**) or in 4:1 (v/v) dichloromethane–methanol (derivatives **4** and **5**), with detection either by charring with aqueous, 10% sulfuric acid or by heating with ninhydrin (derivatives **4** and **5**). Optical rotations were measured for solutions in chloroform by means of a Perkin–Elmer polarimeter, model 141.

Proton-n.m.r. spectra were recorded (*a*) in the pulse-Fourier-transform (F.t.) mode at 360 MHz by use of a Bruker Instruments spectrometer, model WH-360, with a spectral width of 4 kHz and a 32,768-point data-set (digital resolution of transform, 0.24 Hz/point), (*b*) in the F.t. or continuous-wave (c.w.) mode at 220 MHz, using a Varian Associates HR-220 spectrometer, or (*c*) in the c.w. mode at 60 MHz with a Varian A-60 instrument. ^{13}C-N.m.r. spectra were obtained in the F.t. mode at 22.6 MHz by using a Bruker HFX-11 spectrometer with a 45° pulse (3 μs), a repetition time of 5 s, a spectral width of 5 kHz, and 8,192-point data-set, and field-frequency stabilization on solvent-deuterium. All spectra were obtained by using 5-mm sample-tubes. Solutions for proton-n.m.r. spectroscopy at 360 MHz contained 20 mg of solute in 0.5 mL of acetone-d_6, and those for ^{13}C-n.m.r. spectroscopy, 44–175 mg of solute in 0.3–0.6 mL of chloroform-*d*.

*Certain commercial equipment, instruments, or materials are herein identified in order to specify adequately the experimental procedure. Such identification does not imply recommendation or endorsement by the National Bureau of Standards, nor does it imply that the materials or equipment identified are necessarily the best available for the purpose.

Spectral assignments and simulation. — Comparison of proton-n.m.r. spectra measured at different frequencies (60, 220, and 360 MHz) assisted the spectral analysis. However, the detailed assignments for the proton-n.m.r. spectra of **2** and **3** were confirmed by homonuclear, spin-decoupling experiments at 360 MHz in which each of the protons (H-1–H-5, H-6*e*, H-6*a*, and OH) was irradiated in turn. By using the estimated values $J_{5,6e}$ 5.2, $J_{5,6a}$ 9.8, and $J_{6e,6a}$ −9.8 Hz, the complex, eight-spin system of **3** was partially simulated as a seven-spin sub-system comprised of H-2–H-5, H-6*e*, H-6*a*, and OH by means of the ITRCAL program for the Nicolet Instrument Corporation minicomputer, model BNC-12. Good agreement was obtained between the experimental and theoretical spectra.

The ^{13}C assignments for compounds **2** and **3** were indicated by a series of proton-decoupling experiments in which H-1–H-5, H-6*e*, and the benzylic and methoxyl protons were selectively irradiated at ~90 MHz. Further evidence for the assignments was obtained by off-resonance, proton decoupling, and from proton-coupled, ^{13}C-n.m.r. spectra acquired with retention of the nuclear Overhauser effect by gated irradiation of the protons at 90 MHz, during the period (4 s) between data acquisitions. For derivatives **2**-^{15}N and **3**-^{15}N, the splittings of ^{13}C signals caused by the ^{15}N isotope indicated the assignments for C-2 and C-3, respectively.

Reaction of methyl 2,3-anhydro-4,6-O-benzylidene-α-D-allopyranoside (**1**) *with phthalimide.* — A mixture of **1** (5.02 g), phthalimide (3.40 g, 1.22 mol. equiv.), and potassium phthalimide (1.00 g, 0.28 mol. equiv.) was dried at 60° under vacuum, treated with dry HMP (90 mL), and the resulting suspension heated and stirred for 27 h at 152°. The mixture was cooled to 0°, poured into ice–water (3 L), and the milky solution that resulted was nucleated with **2** and **3** and stored in a refrigerator. The pale-yellow precipitate that separated was filtered off, air-dried, and dissolved in dichloromethane. The cooled solution deposited fine needles of phthalimide, 0.27 g, m.p. 235–236°. The yellow mother-liquors were decolorized (charcoal on Celite), evaporated to ~10 mL, diluted with ethanol, and nucleated with **2**. Crystallization of the solution at 2° yielded two crops of methyl 4,6-*O*-benzylidene-2-deoxy-2-phthalimido-α-D-altropyranoside (**2**) as thick rods; 3.1 g, m.p. 177–178°, and 0.32 g, m.p. 150–160° (total yield 44%). T.l.c. indicated the presence of a trace of **1** in the first crop of **2**, and a minor proportion of **1** in the second crop. Two recrystallizations of the combined crops from ethanol–dichloromethane afforded chromatographically pure **2** (2.7 g), m.p. 178–179°, $[\alpha]_D^{20}$ +2.6° (*c* 6.80); ν_{max}^{Nujol} 3550m (OH), 1775m and 1710s (fused lactam ring C=O), and 1605w cm^{-1} (Ar).

Anal. Calc. for $C_{22}H_{21}NO_7$: C, 64.22; H, 5.15; N, 3.41. Found: C, 64.31; H, 5.34; N, 3.32.

Crystallization of the mother liquors from ethanol (~10 mL) yielded two crops of crude methyl 4,6-*O*-benzylidene-3-deoxy-3-phthalimido-α-D-glucopyranoside (**3**) as thick needles, 1.2 g (15%). Two recrystallizations of the combined crops from ethanol gave chromatographically pure **3**, m.p. 165–166°, $[\alpha]_D^{20}$ +47.1° (*c* 5.97); ν_{max}^{Nujol} 3500w sh (free OH), 3400m (H-bonded OH), 1760m and 1700s (fused lactam ring C=O), and 1600w cm^{-1} (Ar).

Anal. Calc. for $C_{22}H_{21}NO_7$: C, 64.22; H, 5.15; N, 3.41. Found: C, 64.17; H, 5.40; N, 3.35.

Similar processing of a mixture of **1** (2.51 g), phthalimide-^{15}N (1.67 g, 1.19 mol. equiv.), potassium phthalimide-^{15}N (0.50 g, 0.28 mol. equiv.), and HMP (50 mL) yielded (*a*) two crops of methyl 4,6-*O*-benzylidene-2-deoxy-2-phthalimido-α-D-altropyranoside-2-^{15}N (**2**-^{15}N), 1.49 g (38%), m.p. 178–178.5°, $[\alpha]_D^{20}$ +2.4° (*c*, 5.26) and 35 mg (0.9%), m.p. 175–177°, and (*b*) two crops of crude methyl 4,6-*O*-benzylidene-3-deoxy-3-phthalimido-α-D-glucopyranoside-3-^{15}N (**3**-^{15}N), 219 mg (5.6%), m.p. 145–150° and 265 mg (6.8%), m.p. 146–153°. Three recrystallizations of the last two (combined) crops from ethanol afforded pure **3**-^{15}N as needles, m.p. 165.5–166°, $[\alpha]_D^{20}$ +45.9° (*c*, 1.28).

*Methyl 2-amino-4,6-*O*-benzylidene-2-deoxy-α-*D*-altropyranoside* (**4**). — A mixture of compound **2** (1.02 g), 85% hydrazine hydrate solution (0.35 mL, 2.5 mol. equiv.), and ethanol (20 mL) was stirred for 2 h at room temperature, and then boiled under reflux for a further 2 h. The suspension that resulted was cooled, and evaporated to dryness, and the colorless, solid residue was treated with cold, 5% potassium hydroxide solution (35 mL) and potassium carbonate (3.5 g). This mixture was extracted with dichloromethane (3 × 20 mL); the extracts were combined, dried (potassium carbonate), and evaporated to a colorless syrup (693 mg, 99%). Crystallization of the syrup from ethanol yielded two crops of **4** as very fine needles, 416 mg (60%); m.p. 169°, $[\alpha]_D$ +107.0° (*c* 2.08), and 96 mg (14%), m.p. 168°; lit.[19] m.p. 168°, $[\alpha]_D^{18}$ +104.7° (*c*, 1.35). In t.l.c., amine **4** appeared as a single, dark-red spot when heated with ninhydrin.

*Methyl 3-amino-4,6-*O*-benzylidene-3-deoxy-α-*D*-glucopyranoside* (**5**). — A mixture of compound **3** (351 mg), 85% hydrazine hydrate solution (0.15 mL), and 1-butanol (35 mL) was boiled under reflux for 64 h. The clear solution was cooled, and evaporated to a solid residue that was dried at 52° under vacuum and then treated with 5% potassium hydroxide solution (20 mL). The resulting suspension was extracted with dichloromethane (4 × 15 mL), and the extracts were combined, washed with water (25 mL), dried (Na_2SO_4), and evaporated to a colorless solid that was recrystallized from ethanol–pentane to give very fine needles of **5**, 191 mg (80%); m.p. 188° (dec., with sublimation), undepressed on admixture with authentic material, $[\alpha]_D^{20}$ +101.7° (*c*, 1.49); lit.[1] m.p. 184.5–186° (dec., sublimed), $[\alpha]_D^{20}$ +102°. In t.l.c., the amine **5** displayed a reddish brown spot when detected by heating with ninhydrin.

ACKNOWLEDGMENTS

Thanks are due Dr. Cheri Fisk of the National Institutes of Health and Dr. B. L. Hawkins (formerly of Bruker Instruments) for proton-n.m.r. spectra at 220 and 360 MHz, respectively.

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