

Studies on Sugar Nitro-olefins. Part 7.¹ Synthesis of 3-(Alditol-1-yl)-1,2,3,5,6,7-hexahydro- and -1,5,6,7-tetrahydro-indol-4-ones. X-Ray Molecular Structure of (3S)-3-(1,2,3,4,5-Penta-O-acetyl-D-galacto-pentitol-1-yl)-1,2,3,5,6,7-hexahydroindol-4-one

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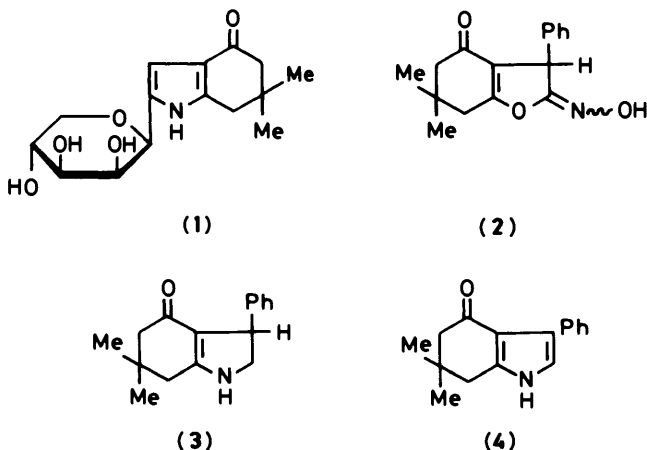
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Raney nickel reduction of (3*R*)-2-hydroxyimino-3-(1,2,3,4,5-penta-*O*-acetyl-*D*-galacto- or -*D*-gluco-pentitol-1-yl)-3,5,6,7-tetrahydrobenzofuran-4(2*H*)-ones (5) gives (3*S*)-3-(1,2,3,4,5-penta-*O*-acetyl-*D*-galacto- or -*D*-gluco-pentitol-1-yl)-1,2,3,5,6,7-hexahydroindol-4-ones (6) in high yields. Deacetylation of compounds (6) with catalytic sodium methoxide in methanol affords the corresponding (pentitol-1-yl)indolones (7). Compounds (6) can be transformed into the 3-(1,2,3,4,5-penta-*O*-acetyl-*D*-galacto- or -*D*-gluco-pentitol-1-yl)-1,5,6,7-tetrahydroindol-4-ones (8) by treatment with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone. The structure of (3*S*)-3-(1,2,3,4,5-penta-*O*-acetyl-*D*-galacto-pentitol-1-yl)-1,2,3,5,6,7-hexahydroindol-4-one (6a) was confirmed by an X-ray structure determination.

C-Glycosyl derivatives of 1,5,6,7-tetrahydroindol-4-ones [e.g. compound (1)] have attracted interest because of their biological (antimitotic) activity.² These compounds are the product of the acid-catalysed dehydration³ of the corresponding 2- or 3-*C*-(alditol-1-yl)indol-4-ones, which in turn are obtained in low yields by reaction of the rather inaccessible 2-amino-2-deoxyaldoheptoses, or 1-amino-1-deoxyheptuloses, with cyclohexane-1,3-diones.⁴ We report here simple procedures for the synthesis of the acetylated 3-(pentitol-1-yl)-1,2,3,5,6,7-hexahydroindol-4-ones (6) and 3-(pentitol-1-yl)-1,5,6,7-tetrahydroindol-4-ones (8) from the readily accessible 3,4,5,6,7-penta-*O*-acetyl-1,2-dideoxy-1-nitrohept-1-enitols through the previously described¹ benzofuranone oximes (5). It is known⁵ that 2-hydroxyimino-6,6-dimethyl-3-phenyl-3,5,6,7-tetrahydrobenzofuran-4(2*H*)-one (2) can be easily converted into the hexahydro-(3) and tetrahydroindol-4-ones (4).



The reduction of the benzofuranone oximes (5) with hydrogen and Raney nickel, as described⁵ for the conversion of compound (2) into (3), gave the (3*S*)-1,2,3,5,6,7-hexahydroindol-4-ones (6) as the only products, which were isolated in

high yields. Their deacetylation (catalytic MeONa in methanol) afforded almost quantitative yields of the 3-(pentitol-1-yl)-1,2,3,5,6,7-hexahydroindol-4-ones (7). Yields, physical constants, and analytical data of compounds (6) and (7) are in Table 1. Compound (6c) was obtained as an unstable syrup that could not be crystallized or purified, but the corresponding pentitol (7e) was crystalline. Compound (6d) and its deacetylated derivative (7d) were unstable and could not be purified; (6d) was characterized as the corresponding 1,5,6,7-tetrahydroindol-4-one (8d) (see below).

Compounds (6) and (7) had λ_{\max} at ca. 305 nm ($\log \epsilon$ 4.3) quite close to that of model compound (3) (Table 2); the calculated value using additive spectral increments⁶ is λ_{\max} 301 nm. Their i.r. spectra (Table 2) were also similar to that of (3) and showed in the double-bond region the three characteristic bands⁷ of *N*-monosubstituted aminoenones having the *E,s-trans* alignment. The n.m.r. spectra of compounds (3) and (6a and b) (Table 3) were also similar and consistent with the assigned structures. The NH proton appeared as a broad singlet at δ 4.34–4.80 p.p.m. 2-*H*_a, 2-*H*_b, and 3-*H* gave rise to a ABX system and the couplings $J_{2a,3}$ (2.4–4.6 Hz) and $J_{2b,3}$ (9.4–10.7 Hz) indicated⁸ that 2-*H*_a and 2-*H*_b are *trans* and *cis*, respectively, to 3-*H*. This proton appeared as a double doublet in compound (6a) due to the additional coupling ($J_{3,1'}$, ~ 0.8 Hz) with 1'-*H*. In compound (6b) $J_{3,1'}$ was still smaller and only caused some broadening of the 3-*H* double doublet. An antiperiplanar arrangement of 2'-*H* and 3'-*H* was deduced from the coupling $J_{2',3'}$ (9.6–10.3 Hz), and the $J_{1',2'}$ (1.7–2.3 Hz) and $J_{3',4'}$ (1.7–1.9 Hz) values indicated protons in the *gauche* disposition.⁹ These couplings showed that C-3 and the carbon atoms of the *D*-galacto-pentitolyl chain of compounds (6a) and (6b) in solution adopt a nearly planar zigzag conformation, as was also observed in the parent benzofuranone oximes (5a) and (5b).¹ The (3*S*)-configuration was assigned considering that the parent compounds have the (*R*-configuration at C-3).^{1,10} The large chemical shift ($\Delta\delta_C \sim 60$ p.p.m.) between the C-8 and C-9 is a consequence of the strong electron delocalization inside the aminoenone system contained in fragment (A) which tends to keep the five-membered ring, the

Table 1. Physical constants and analytical data of compounds (6), (7), and (8)

Compound (Formula)	Yield (%)	Solvent	M.p. (°C) (decomp.)	R_F^a	$[\alpha]_D^{20}$ ^b	Found (%) (Required)		
						C	H	N
(6a) (C ₂₃ H ₃₁ NO ₁₁)	97	MeOH	183—185	0.10 ^c	-155.3 ^d	55.6 (55.5)	6.4 (6.3)	3.3 (2.8)
(6b) (C ₂₅ H ₃₅ NO ₁₁)	85	MeOH	197—198	0.34 ^c	-132.6 ^d	56.8 (57.1)	6.75 (6.7)	2.6 (2.7)
(7a) (C ₁₃ H ₂₁ NO ₆)	90	MeOH	236—237		-192.5 ^e	54.45 (54.3)	7.45 (7.4)	4.5 (4.9)
(7b) (C ₁₅ H ₂₅ NO ₆ ·H ₂ O)	88		172—174 ^f		-117.3 ^e	53.9 (54.0)	7.7 (8.2)	4.2 (4.2)
(7c) (C ₁₃ H ₂₁ NO ₆)	92 ^g	MeOH	186—187		-169.4 ^g	54.2 (54.3)	7.2 (7.4)	4.7 (4.9)
(8a) (C ₂₃ H ₂₉ NO ₁₁)	59	EtOH	177—178	0.61 ^h	+70.2 ^d	55.8 (55.75)	6.2 (5.9)	2.6 (2.8)
(8b) (C ₂₅ H ₃₃ NO ₁₁)	52	EtOH	161—162	0.64 ^c	+75.1 ^d	57.5 (57.35)	6.6 (6.35)	2.9 (2.7)
(8c) (C ₂₃ H ₂₉ NO ₁₁)	42 ^g	MeOH	146—147	0.66 ⁱ	+130.0 ^g	55.4 (55.75)	5.7 (5.9)	3.0 (2.8)
(8d) (C ₂₅ H ₃₃ NO ₁₁)	40 ^l	MeOH	162—163	0.25 ^j	+128.3 ^e	57.55 (57.35)	6.4 (6.35)	2.45 (2.7)

^a T.l.c. on silica gel. ^b Compounds (6) and (8) in acetone, compounds (7) in water. ^c Developer diethyl ether-acetone (6:1). ^d At 26 °C. ^e At 25 °C. ^f Purified by preparative layer chromatography (p.l.c.) [methanol-chloroform (7:1), R_F 0.70]. ^g At 22 °C. ^h Developer diethyl ether-acetone (4:1). ⁱ Developer diethyl ether-acetone (3:1). ^j Developer diethyl ether-hexane (7:1). ^k Calculated from the starting oxime (5c). ^l Calculated from the starting oxime (5d).

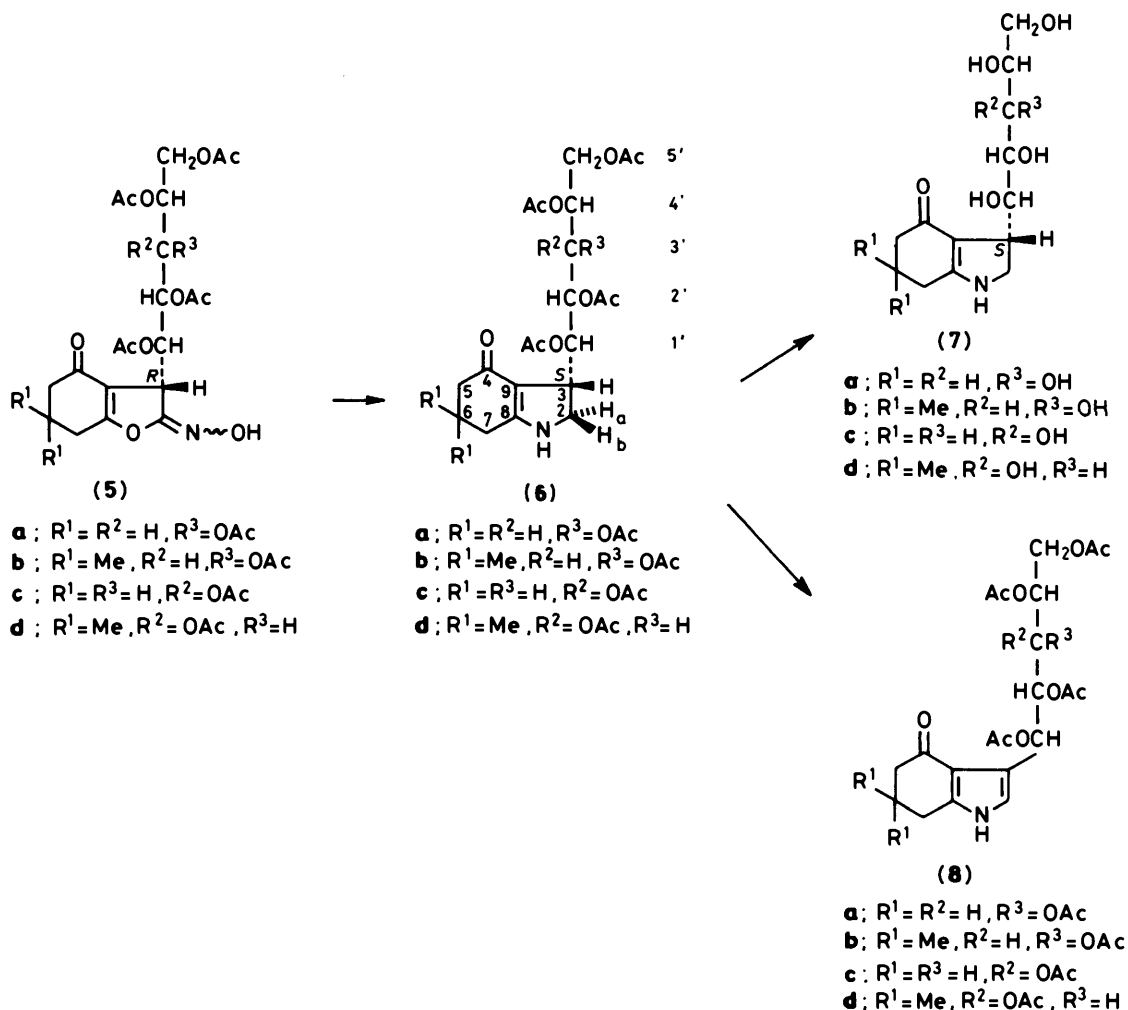


Table 2. U.v. and i.r. spectral data of compounds (3), (6), and (7)

Compound	$\lambda_{\max.}(\text{nm})^a$ (log ϵ)	Phase	$\nu_{\max.}(\text{cm}^{-1})$						
			OH	NH	OAc	C=O	C=C-NH		
(3)	310 (4.14)	KBr		3 210m			1 590s	1 555m	1 520vs
		CHCl ₃		3 440m			1 585s br		1 495s
(6a)	304 (4.31)	KBr		3 210m	1 750vs		1 594s	1 564sh	1 519vs
		CHCl ₃		3 450m	1 745vs		1 590s br		1 500ms
(6b)	306 (4.28)	KBr		3 180wm	1 750vs		1 590ms	1 570sh	1 510s
		CHCl ₃		3 450m	1 745vs		1 595s br		1 500ms
(6c)		film		3 200m	1 740s		1 580s br		1 510s br
(6d)		CHCl ₃		3 450w	1 745vs		1 600s br		1 495m
(7a)	304 (4.30)	KBr	3 430s	3 180ms			1 585m	1 555ms	1 510s br
(7b)	305 (4.28)	KBr	3 380s	3 210s			1 585ms	1 550sh	1 520s br
(7c)	307 (4.32)	KBr	3 420s	3 180m			1 580m	1 560m	1 510s br

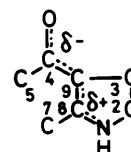
^a Compounds (3) and (6) in ethanol, compounds (7) in water.

Table 3. N.m.r. spectral data^a for compounds (3) and (6) (J -values in Hz)

	Compounds		
	(3) ^b	(6a)	(6b)
NH	4.80br s	4.39br s	4.34br s
2-H _a	4.36dd	3.47dd	3.50dd
	$J_{2a,3}$ 4.6,	$J_{2a,3}$ 2.4,	$J_{2a,3}$ 3.0,
	$J_{2a,2b}$ -10.9	$J_{2a,2b}$ -10.9	$J_{2a,2b}$ -11.0
2-H _b	4.03dd	3.39dd	3.45dd
	$J_{2b,3}$ 10.5	$J_{2b,3}$ 9.4	$J_{2b,3}$ 10.7
3-H	3.51dd	3.74ddd	3.80br dd
		$J_{3,1}$ ~ 0.8	$J_{3,1}$ ~ 0.2
5-H _a	2.19m	2.2m	2.07m
5-H _b	2.19m	2.2m	2.07m
6-H _a	1.13s ^c	1.9m	1.00s ^c
6-H _b	1.11s ^c	1.9m	0.96s ^c
7-H _a	2.28m	2.2m	2.07m
7-H _b	2.28m	2.2m	2.07m
1'-H		5.66dd	5.78br d
		$J_{1,2}$ 2.3	$J_{1,2}$ 1.7
2'-H		5.41dd	5.45dd
		$J_{2,3}$ 10.3	$J_{2,3}$ 9.6
3'-H		5.19dd	5.20dd
		$J_{3,4}$ 1.9	$J_{3,4}$ 1.7
4'-H		5.20ddd	5.21ddd
		$J_{4,5a}$ 4.2,	$J_{4,5a}$ 4.2,
		$J_{4,5b}$ 8.0	$J_{4,5b}$ 8.0
5'-H _a		4.23dd	4.27dd
		$J_{5a,5b}$ -11.7	$J_{5a,5b}$ -11.7
5'-H _b		3.73dd	3.75dd
OAc		2.04s, 2.02s, 2.02s,	2.07s, 2.07s, 2.05s,
		1.94s, 1.91s	1.98s, 1.94s
C-2	55.9t	46.1t	50.7t
C-3	50.7d	41.7d	41.6d
C-4	190.9s	191.7s	190.5s
C-5	37.8t	23.9t	37.8t
C-6	34.3s	22.4t	33.8s
C-7	43.9t	36.2t	46.3t
C-8	167.7s	169.0s	167.8s
C-9	117.7s	108.6s	106.9s
6-Me ₂	29.2q,		29.0q,
	28.5q		28.3q
OAc		170.5s, 170.5s, 170.2s,	170.4s, 170.4s, 170.2s,
(1'-5')		169.7s, 169.6s	169.6s, 169.3s
		21.0q, 20.6q, 20.6q,	20.9q, 20.7q, 20.7q,
		20.6q, 20.6q	20.6q, 20.6q
C-1'-C-5'		71.2d, 69.1d, 68.4d,	71.3d, 68.9d, 68.4d,
		68.1d, 62.7t	68.2d, 62.7t

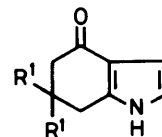
^a In CDCl₃; ¹H and ¹³C n.m.r. spectral data at 360 and 20.1 MHz, respectively, unless otherwise indicated. ^b ¹H and ¹³C n.m.r. spectral data at 200 and 50.3 MHz respectively. ^c 6-Me protons.

C=O group, and the C-5 and C-7 atoms in a plane; this value of $\Delta\delta_c$ is still larger than the one observed (~40 Hz) for the benzofuranone oximes (5)¹ as could be expected. The coupling $J_{3,1}$ (0—1 Hz) suggested a predominant *gauche* disposition between 3-H and 1'-H. The X-ray analysis of compound (6a) (see below) confirmed the above results.



(A)

Oxidation of the polyols (7) with sodium metaperiodate took place with splitting of the alditolyl chain and aromatization of the five-membered ring, giving rise to the known^{4a} 1,5,6,7-tetrahydroindol-4-ones (9). The best yields (>70%) were obtained by using 6 mol of oxidant per mol of alditol (7); the



(9)

a: R¹ = H
b: R¹ = Me

analytical oxidation indicated the consumption of 6 mol of metaperiodate per mol of (7), and the formation of 1 mol of formaldehyde and 3 mol of formic acid.

Oxidation of the hexahydroindol-4-ones (6) with an equimolecular amount of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) afforded the corresponding tetrahydroindol-4-ones (8) in 40—60% yield. Physical constants and analytical data of these compounds appear in Table 1. They gave a positive pyrrole test with the Ehrlich reagent under the same conditions as reference compound (4) did. The u.v. spectra (Table 4) of compounds (8) were very similar to that of compound (4), and so were their i.r. absorptions (Table 4). The lower frequencies for the $\nu(\text{N-H})$ and $\nu(\text{C=O})$ vibrations in the solid state is attributable to the strong intermolecular association of these

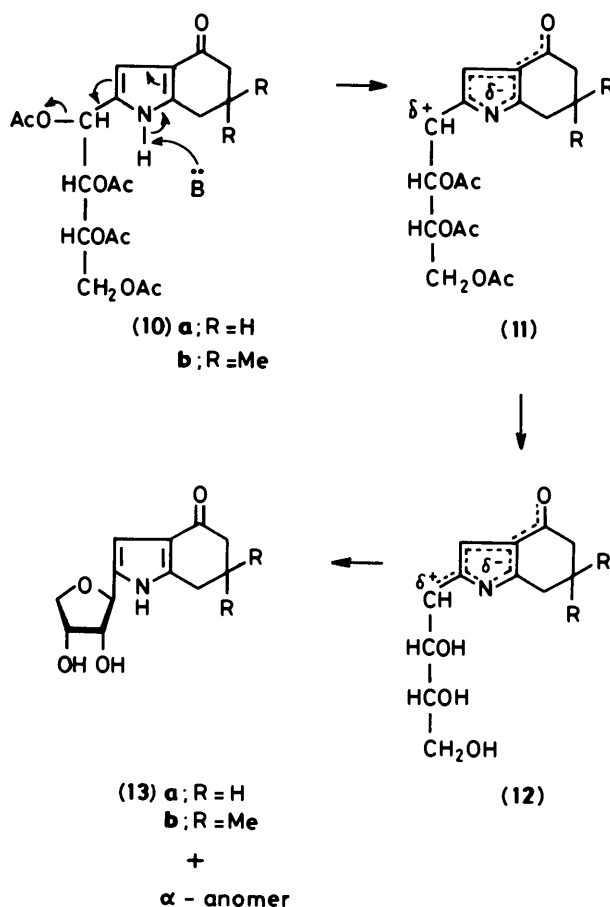
Table 4. U.v. and i.r. spectral data of compounds (4) and (8)

Compound	λ_{\max} . (nm) ^a (log ϵ)	ν_{\max} . (cm ⁻¹)					
		Phase	NH	=CH	OAc	C=O	Pyrrrole
(4)	245 (3.84), 265 (3.97)	KBr	3 270m	3 120w		1 640s	1 605w, 1 470m
(8a)	241 (3.97), 270 (3.85)	KBr	3 200w	3 110w	1 752vs	1 625ms	1 585w, 1 485m
		CHCl ₃	3 460m, 3 280w		1 750vs	1 660s	1 575w, 1 475ms
(8b)	244 (3.87), 275 (3.74)	KBr	3 200w	3 150w, 3 120w	1 760vs	1 630m	1 590w, 1 480m
		CHCl ₃	3 460m, 3 260w		1 750vs	1 660s	1 580w, 1 475m
(8c)	241 (3.82), 269 (3.77)	KBr	3 270mw	3 130w	1 750vs	1 640s	1 580w, 1 475ms
		CHCl ₃	3 460m, 3 280w		1 750vs	1 660ms	1 600w, 1 470m
(8d)	242 (3.81), 270 (3.70)	KBr	3 280m	3 120w	1 745vs	1 640s	1 600w sh, 1 470m
		CHCl ₃	3 460mw, 3 280w		1 745vs	1 660s	1 600w, 1 470m

^a In ethanol.

strongly polarized molecules. These u.v. and i.r. spectra were very similar to those reported for similar 1,5,6,7-tetrahydro-2-(tetritol-1-yl)indol-4-ones.^{4a} The n.m.r. spectra of compounds (8), presented together with those of compound (4) in Table 5, were also consistent with the assigned structure. The *J*-values observed for the protons of the *D-galacto* alditol chain of compounds (8a) and (8b) were almost the same as those measured for (6a) and (6b), and indicated the planar zigzag conformation of the chain. The couplings $J_{1,2}$ and $J_{2,3}$ for the *D-gluco* derivatives (8c and d) were of intermediate magnitude, corresponding to mixtures of conformational states.

Attempts to deacetylate compounds (8) with a catalytic amount of sodium methoxide in methanol were unsuccessful; approximately 1.0 mol of base per mol of compound (8) was required to complete the reaction, and mixtures of several Ehrlich-positive products with very similar chromatographic mobilities resulted. Likewise, the deacetylation of the 2-(1,2,3,4-tetra-*O*-acetyl-*D-arabino*-tetritol-1-yl)-1,5,6,7-tetrahydroindol-4-ones (10) required an excess (1.1 mol) of base, and the products were the known^{4a} 2-(β -*D-erythro*-furanosyl)-1,5,6,7-tetrahydroindol-4-ones (13) (isolated in yields > 50%). The formation of a by-product having a very similar R_F -value was observed, and a similar mixture was obtained when the parent 1,5,6,7-tetrahydro-2-(*D-arabino*-tetritol-1-yl)pyrroles, yielding anomeric mixtures of the corresponding *C-erythro*-furanosyl glycosides.¹¹ As *N*-substituted 3-(polyacetoxyalkyl)pyrroles undergo the Zemplén deacetylation in the usual way,¹² the behaviour of compounds (8) and (10) is considered to be due to the possibility of elimination of acetic acid, existing in the *N*-unsubstituted compounds, as shown in the Scheme for compounds (10). Removal of the NH proton by the base, and release of AcO⁻ from C-1', yield the resonance-stabilized intermediates (11), which is catalytically deacetylated to yield compounds (12). Intramolecular nucleophilic attack by O-4 on the electron-deficient C-1' then yields products (13) with predominant inversion of configuration.¹³ The similar reaction of compounds (8) would afford more complex α,β -anomeric mixtures of *C*-furanosyl and *C*-pyranosyl glycosides.¹⁴ An analogous deacetylation reaction with concomitant dehydration has been observed in acetylated sugar formazans,¹⁵ and the base-



Scheme.

catalysed dehydration of 2-(*D-arabino*-tetritol-1-yl)-1,5,6,7-tetrahydroindol-4-one to yield the furan (13a), most likely by a mechanism similar to that of the Scheme, has been reported.^{4a}

X-Ray Structure of (3S)-3-(1,2,3,4,5-Penta-*O*-acetyl-*D*-galacto-

Table 5. N.m.r. spectral data^a for compounds (4) and (8)

	Compounds				
	(4) ^b	(8a)	(8b)	(8c)	(8d)
NH	11.39br s	8.95br s	9.03br s	8.74br s	9.04br s
2-H	6.95br s	6.49br d	$J_{1,2}$ 2.3 6.50br d	$J_{1,2}$ 2.2 6.62br d	$J_{1,2}$ 2.0 6.63d
5-H _a	2.27s	2.45m	$J_{1,2}$ 0.9 2.30s	$J_{1,2}$ 0.5 2.40m	2.28s
5-H _b	2.27s	2.45m	2.30s	2.40m	2.28s
6-H _a	1.05s ^c	2.0m	1.09s ^c	2.1m	1.06s ^c
6-H _b	1.05s ^c	2.0m	1.07s ^c	2.1m	1.05s ^c
7-H _a	2.68s	2.74m	2.60s	2.75m	2.60s
7-H _b	2.68s	2.74m	2.60s	2.75m	2.60s
1'-H		6.49br d	6.47br	6.53dd	6.48d
2'-H		$J_{1,2}$ 1.9 5.66dd	$J_{1,2}$ 1.9 5.69dd	$J_{1,2}$ 5.7 5.82dd	$J_{1,2}$ 5.7 5.86dd
3'-H		$J_{2,3}$ 9.7 5.47dd	$J_{2,3}$ 9.8 5.47dd	$J_{2,3}$ 5.2 5.25dd	$J_{2,3}$ 5.6 5.23dd
4'-H		$J_{3,4}$ 1.9 5.32m	$J_{3,4}$ 1.9 5.32m	$J_{3,4}$ 10.3 5.15m	$J_{3,4}$ 11.1 5.11m
5'-H _a		$J_{4,5a}$ 4.7 $J_{4,5b}$ 7.5 4.33dd	$J_{4,5a}$ 4.8, $J_{4,5b}$ 7.6 4.33dd	$J_{4,5a}$ 2.8, $J_{4,5b}$ 6.9 4.44dd	$J_{4,5a}$ 3.0, $J_{4,5b}$ 6.7 4.40dd
5'-H _b		$J_{5a,5b}$ -11.6 3.87dd	$J_{5a,5b}$ -11.6 3.87dd	$J_{5a,5b}$ -12.2 4.24dd	$J_{5a,5b}$ -12.2 4.20dd
OAc		2.14s, 2.10s, 2.01s, 2.01s, 1.86s	2.14s, 2.10s, 2.01s, 2.00s, 1.84s	2.07s, 2.07s, 2.04s, 2.01s, 1.98s	2.03s, 2.03s, 2.01s, 1.97s, 1.94s
C-2	117.6d	116.2d	116.3d	117.6d	114.5d
C-3	122.8s	119.2s	119.6s	118.3s	116.2s
C-4	191.8s	184.4s	193.8s	184.8s	191.6s
C-5	36.4t	23.7t	36.9t	23.7t	34.9t
C-6	34.6s	22.6t	35.8s	22.8t	33.7s
C-7	53.1t	38.1t	52.5t	38.3t	50.6t
C-8	143.6s	143.8s	142.7s	143.4s	141.0s
C-9	114.7s	117.2s	116.5s	117.6s	115.9s
6-Me ₂	27.8q, 27.8q		29.1q, 27.9q		26.8q, 26.0q
OAc (1'-5')		170.2s, 170.2s, 170.0s, 169.7s, 168.7s	170.5s, 170.5s, 170.2s, 169.8s, 168.7s	170.4s, 169.9s, 169.8s, 169.8s, 168.5s	168.4s, 168.0s, 167.8s, 167.7s, 167.5s
		20.7q, 20.3q, 20.3q, 20.3q, 20.3q	20.9q, 20.7q, 20.6q, 20.6q, 20.4q	20.8q, 20.6q, 20.6q, 20.5q, 20.4q	18.9q, 18.7q, 18.7q, 18.6q, 18.5q
C-1'-C-5'		69.4d, 68.4d, 68.2d, 67.8d, 62.3t	69.6d, 68.6d, 68.4d, 68.1d, 62.5t	71.7d, 69.9d, 69.7d, 68.9d, 61.9t	69.7d, 67.9d, 67.7d, 67.0d, 59.9t

^a In CDCl₃; ¹H and ¹³C n.m.r. spectral data at 80 and 20.1 MHz, respectively, unless otherwise indicated. ^b In [²H₆]-Me₂SO. ^c 6-Me protons.

pentitol-1-yl)-1,2,3,5,6,7-hexahydroindol-4-one (6a).—In order to confirm the stereochemistry of compound (6a), an X-ray crystallographic study on this product was undertaken. Figure 1 shows a projection of the molecule; the Newman projections corresponding to the C(3)–C(11) bond, and the C–C bonds of the sugar chain, are shown in Figure 2. These data demonstrate that the chirality at C(3) is *S*, and that C(3) and the carbons of the sugar chain are coplanar [maximum deviation from the mean plane 0.024(9)Å]. The five-membered ring is nearly planar, with each atom deviating less than 0.026(12)Å from the best plane. C(11) is out of the plane by -1.076 Å, and the H(3)–C(3)–C(11)–H(11) torsional angle is -79°, consistent with the ¹H n.m.r. coupling constant. The cyclohexene ring conformation is nearly half-chair, Cremer and Pople's puckering parameters¹⁶ for the sequence C(4)–C(5)–C(6)–C(7)–C(8)–C(9) being $\theta = 61(1)$, $\phi = 125(1)^\circ$, and $Q = 0.43(1)$ Å. The C(5), C(9), C(8), and C(7) atoms are in a plane [maximum deviation 0.034(12) Å], and C(6) is out of this plane by

+0.606(13) Å. The angle between this plane and the one of the five-membered ring is 3.7(5)°. The distribution of bond lengths indicates extensive electron delocalization in the fragment O(4), C(4), C(9), C(8), N(1). The fact that the nitrogen atom is coplanar with the three atoms bonded to it and that the sum of its bond angles is 359.8° indicates that the state of hybridization of the nitrogen is *sp*².

Experimental

M.p.s were determined with a Büchi apparatus and are uncorrected. Optical rotations were measured with a Perkin-Elmer 241 MC polarimeter. I.r. spectra were taken with a Perkin-Elmer 299 spectrophotometer. Solutions were dried with MgSO₄ or Na₂SO₄, and evaporated under reduced pressure below 40 °C. Analytical samples were dried over P₂O₅ *in vacuo*. Analytical periodate oxidations were carried out as described.¹⁷ Other general methods were as in ref. 1.

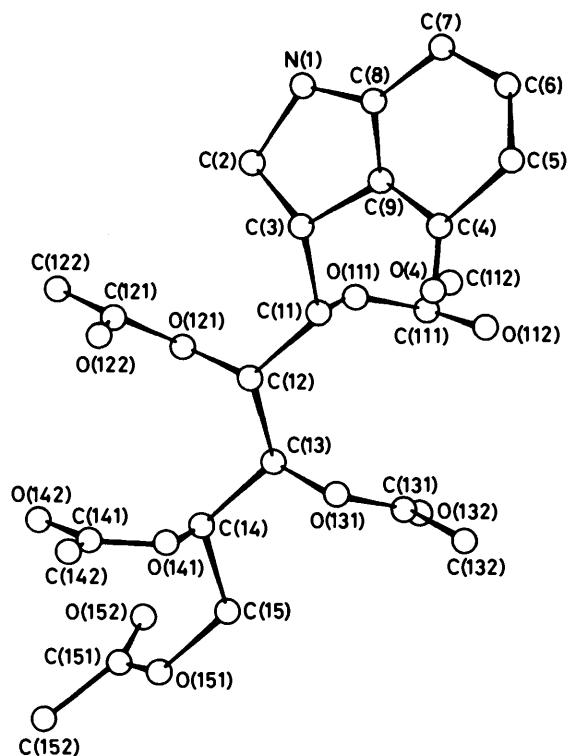


Figure 1. A projection of the molecule of compound (6a) on the plane ac , with the crystallographic numbering scheme used

(3*S*)-3-(1,2,3,4,5-Penta-*O*-acetylpenitol-1-yl)-1,2,3,5,6,7-hexahydroindol-4-ones (6).—Raney nickel (0.40 g) was added to a solution of an oxime (5) (0.95 mmol) in warm EtOH (50 ml). The mixture was placed in a Gerhard hydrogenation unit with hydrogen at 3 atm and heated (60–70 °C) until the complete transformation (t.l.c.) of the starting material (6–7 h). The catalyst was filtered off, and the filtrate was evaporated to yield chromatographically pure compound (6). Compounds (6a) and (6b) were crystallized from Et₂O–hexane (9:1), and then recrystallized from MeOH. Compounds (6c) and (6d) were unstable, and could not be crystallized or purified; they were used in subsequent transformations immediately after being prepared. Yields, physical constants, and analytical data of these compounds are in Table 1; their u.v. and i.r. spectra are summarized in Table 2, and their ¹H and ¹³C n.m.r. spectral data appear in Table 3.

O-Deacetylation of Compounds (6).—A solution of a compound (6a–c) (1.90 mmol) in MeOH (18 ml) was stirred overnight with methanolic 0.2M-sodium methoxide (1.50 ml, 0.30 mmol). Compounds (7a) and (7c) precipitated as amorphous solids which were filtered off and crystallized from MeOH. In the deacetylation of compound (6b) a jelly-like suspension resulted, which was diluted with water and made neutral with Amberlite IR-120(H⁺) resin. The solution was concentrated and the residue was purified by preparative t.l.c. (p.l.c.) [MeOH–CHCl₃ (7:1), *R_F* 0.70], to afford compound (7b). Yields, physical constants, and analytical data for compounds (7) appear in Table 1; their u.v. and i.r. spectra are in Table 2.

Periodate Oxidation of Compounds (7).—A stirred, ice-cooled solution of a compound (7a–c) (1.67 mmol) in water (10 ml) was treated with a solution of sodium metaperiodate (2.14 g, 10.02 mmol) in water (35 ml). After a few minutes, the aqueous

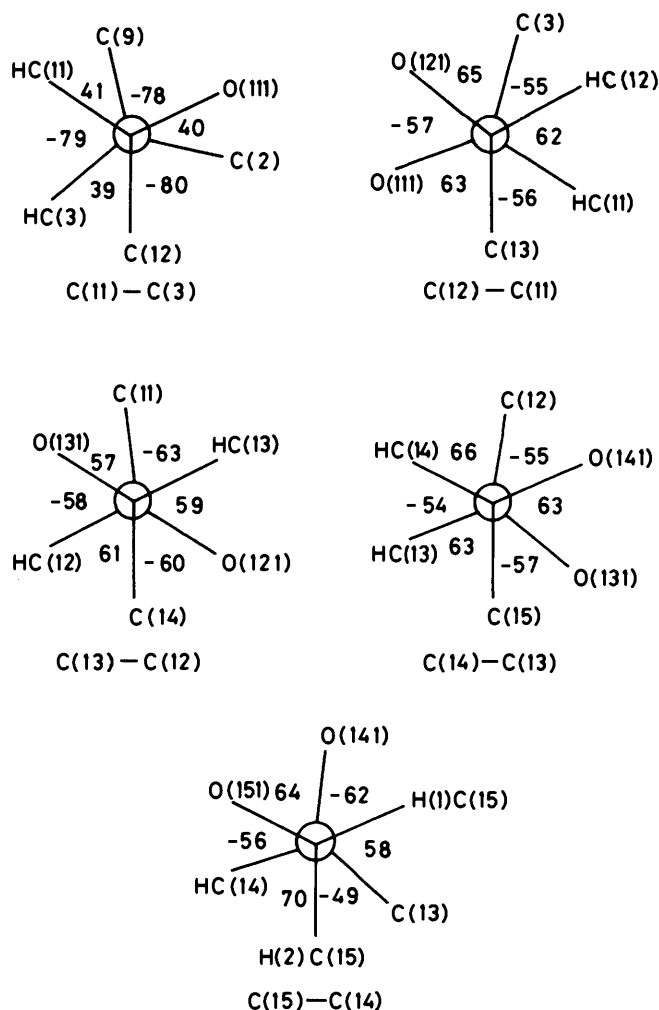


Figure 2. Newman projections corresponding to the C(3)–C(11) bond, and the C–C bonds of the sugar chain

solution was thoroughly extracted with dichloromethane. The extracts were washed with water, dried, and concentrated to afford the 3-unsubstituted indolones (9). Compounds (7a) and (7c) gave compound (9a) (~75%), m.p. and mixed m.p. 184–186 °C (from MeOH); ν_{\max} (KBr) 3 180 and 1 622 cm⁻¹; δ_{H} (360 MHz) 9.39 (s, 1 H), 6.70 (t, 1 H), 6.53 (t, 1 H), 2.84 (t, 2 H), 2.49 (t, 2 H), and 2.15 (m, 2 H); [lit.,¹¹ m.p. 185–187 °C; ν_{\max} (KBr) 3 180 and 1 620 cm⁻¹]. Compound (7b) afforded compound (9b) (71%), m.p. and mixed m.p. 178–180 °C (from MeOH); ν_{\max} (KBr) 3 180 and 1 650 cm⁻¹; [lit.,¹¹ m.p. 179–181 °C; ν_{\max} (KBr) 3 160 and 1 640 cm⁻¹].

3-(1,2,3,4,5-Penta-*O*-acetylpenitol-1-yl)-1,5,6,7-tetrahydroindol-4-ones (8).—A warm solution of a compound (6) (2.11 mmol) in 1,4-dioxane (15 ml) was treated with DDQ (1.12 g, 2.11 mmol) in 1,4-dioxane (15 ml). The reaction mixture was stirred until the complete transformation (t.l.c.) of the starting material (1–2.5 h). The precipitate was filtered off and the filtrate was concentrated, diluted with Et₂O, and then passed through a short column of silica gel, which was thoroughly eluted with Et₂O–acetone (4:1). Concentration of the combined eluates gave the corresponding oxidized product (8). Compounds (8a) and (8b) were crystallized from Et₂O–hexane (4:1), and then from EtOH. Compound (8c) was purified by p.l.c. [Et₂O–acetone (3:1)], and then crystallized from MeOH. Compound (8d) was purified by column chromatography

Table 6. Atomic co-ordinates for non-hydrogen atoms, with standard deviations in parentheses

Atom	x	y	z
N(1)	0.405 2(10)	-0.315 5(11)	0.339 6(8)
C(2)	0.224 7(13)	-0.229 1(15)	0.427 8(10)
C(3)	0.100 8(12)	-0.278 9(11)	0.358 6(8)
C(4)	0.195 4(13)	-0.473 1(12)	0.133 6(10)
C(5)	0.361 9(16)	-0.571 6(14)	0.011 9(12)
C(6)	0.518 5(16)	-0.520 7(15)	-0.008 1(13)
C(7)	0.569 3(15)	-0.497 3(13)	0.121 6(14)
C(8)	0.404 2(13)	-0.398 0(11)	0.231 7(10)
C(9)	0.229 7(12)	-0.382 5(11)	0.232 6(9)
C(11)	-0.048 7(11)	-0.149 0(10)	0.327 7(8)
C(12)	-0.213 3(12)	-0.073 9(11)	0.450 5(8)
C(13)	-0.367 1(12)	0.043 4(10)	0.412 2(8)
C(14)	-0.534 7(13)	0.111 1(12)	0.537 2(9)
C(15)	-0.692 8(13)	0.219 6(14)	0.499 6(10)
C(111)	0.031 4(14)	-0.004 3(13)	0.147 6(10)
C(112)	0.080 0(16)	0.137 5(16)	0.115 9(4)
O(111)	0.013 9(8)	-0.024 4(6)	0.278 4(5)
O(112)	0.008 6(16)	-0.091 5(14)	0.066 3(8)
C(121)	-0.165 0(15)	-0.053 3(15)	0.674 2(9)
C(122)	-0.132 1(16)	0.043 5(16)	0.772 5(13)
O(121)	-0.172 9(8)	0.007 3(7)	0.556 0(5)
O(122)	-0.181 5(13)	-0.179 2(10)	0.693 0(7)
C(131)	-0.411 1(15)	0.026 2(14)	0.194 0(11)
C(132)	-0.420 2(11)	-0.089 7(16)	0.087 4(13)
O(131)	-0.406 1(8)	-0.036 3(7)	0.309 8(5)
O(132)	-0.399 6(16)	0.148 3(10)	0.179 4(9)
C(141)	-0.604 0(14)	-0.019 5(12)	0.731 2(9)
C(142)	-0.636 9(16)	-0.161 4(16)	0.772 7(13)
O(141)	-0.581 6(7)	-0.016 1(7)	0.594 7(5)
O(142)	-0.596 3(12)	0.077 0(10)	0.807 0(6)
C(151)	-0.842 1(15)	0.416 3(16)	0.685 4(12)
C(152)	-1.003 0(16)	0.482 2(16)	0.812 5(13)
O(151)	-0.840 0(8)	0.288 5(8)	0.621 1(6)
O(152)	-0.737 5(15)	0.475 7(13)	0.649 2(11)
O(4)	0.043 6(10)	-0.479 5(9)	0.141 1(9)
O(350)*	0.762 5(11)	-0.428 2(11)	0.365 8(9)

* Of water molecule

[Et₂O-hexane (7:1), *R_F* 0.25], and subsequent crystallization from MeOH. Yields, physical constants, and analytical data of these compounds appear in Table 1; their u.v. and i.r. spectral data are in Table 4, and their n.m.r. spectra are summarized in Table 5.

O-Deacetylation of Compounds (10) and (8).—A suspension of compound (10a)^{4a} (0.47 mmol) in MeOH (2 ml) was stirred with methanolic 0.2 M-sodium methoxide (2.4 ml, 0.48 mmol). After 1 h, t.l.c. [dichloromethane-MeOH (7:1)] revealed the absence of starting material (10a), and the formation of the furan (13a) (*R_F* 0.30) and a second product (*R_F* 0.40). The solution was carefully neutralized with Amberlite IR-120(H⁺) resin, and then concentrated to afford compound (13a) (55%), m.p. 233–235 °C (from MeOH); λ_{max}^O 243 and 280 nm (log ε 3.86 and 3.85); ν_{max} (KBr) 3 470, 3 200, 1 610, 1 595, and 1 495 cm⁻¹; [lit.^{4a} m.p. 233–235 °C; λ_{max}^O 243 and 281 nm (log ε 3.98 and 3.96); ν_{max} (KBr) 3 470, 3 200, 1 620, 1 580, and 1 490 cm⁻¹].

The deacetylation of compound (10b)¹⁸ in the same way afforded a syrupy residue, which was purified by column chromatography [dichloromethane-MeOH (7:1)]. The crystalline mixture of the furan (13b) and its α-anomer obtained had m.p. 167–169 °C; λ_{max}^O 246 and 287 nm (log ε 3.45 and 3.46); ν_{max} (KBr) 3 440, 3 290, 1 630, 1 575, and 1 485 cm⁻¹; [lit.¹¹ m.p. 167–169 °C; λ_{max}^O 246 and 286 nm (log ε 3.71 and 3.69); ν_{max} (KBr) 3 420, 3 270, 1 620, 1 575, and 1 475 cm⁻¹].

Similar treatment of compound (8a) afforded a mixture (t.l.c.)

Table 7. Bond distances (Å) and bond angles (°)

N(1)–C(2)	1.461(10)	C(14)–C(15)	1.514(14)
N(1)–C(8)	1.307(14)	C(14)–O(141)	1.441(13)
C(2)–C(3)	1.547(17)	C(15)–O(151)	1.434(9)
C(3)–C(9)	1.486(10)	C(111)–C(112)	1.500(20)
C(3)–C(11)	1.524(12)	C(111)–O(111)	1.326(11)
C(4)–C(5)	1.566(12)	C(111)–O(112)	1.214(17)
C(4)–C(9)	1.416(16)	C(121)–C(122)	1.440(20)
C(4)–O(4)	1.255(14)	C(121)–O(121)	1.352(11)
C(5)–C(6)	1.479(20)	C(121)–O(122)	1.220(17)
C(6)–C(7)	1.509(21)	C(131)–C(132)	1.516(19)
C(7)–C(8)	1.502(12)	C(131)–O(131)	1.334(13)
C(8)–C(9)	1.398(15)	O(132)–C(131)	1.164(17)
C(11)–C(12)	1.523(9)	C(141)–C(142)	1.467(19)
C(11)–O(111)	1.453(11)	C(141)–O(141)	1.353(10)
C(12)–C(13)	1.527(12)	C(141)–O(142)	1.174(14)
C(12)–O(121)	1.445(12)	C(151)–O(152)	1.153(20)
C(13)–C(14)	1.542(10)	C(151)–C(152)	1.523(14)
C(13)–O(131)	1.406(12)	C(151)–O(151)	1.308(16)
H(1)–N(1)–C(2)	124.0(5)	C(12)–C(13)–C(14)	111.6(7)
H(1)–N(1)–C(8)	123.0(6)	C(14)–C(13)–O(131)	109.7(7)
C(2)–N(1)–C(8)	112.1(9)	C(13)–C(14)–O(141)	108.5(7)
N(1)–C(2)–C(3)	104.5(8)	C(13)–C(14)–C(15)	112.5(7)
C(2)–C(3)–C(11)	116.9(8)	C(15)–C(14)–O(141)	109.0(8)
C(2)–C(3)–C(9)	102.3(8)	C(14)–C(15)–O(151)	110.1(8)
C(9)–C(3)–C(11)	112.8(6)	O(111)–C(111)–O(112)	122.7(9)
C(9)–C(3)–O(4)	123.7(9)	C(112)–C(111)–O(112)	125.6(9)
C(5)–C(4)–O(4)	120.4(9)	C(112)–C(111)–O(111)	111.6(9)
C(5)–C(4)–C(9)	115.8(9)	C(11)–O(111)–C(111)	118.0(7)
C(4)–C(5)–C(6)	114.6(9)	O(121)–C(121)–O(122)	122.4(8)
C(5)–C(6)–C(7)	114.3(9)	C(122)–C(121)–O(122)	124.1(9)
C(6)–C(7)–C(8)	108.4(9)	C(12)–C(121)–O(121)	113.4(9)
N(1)–C(8)–C(7)	124.3(9)	C(12)–O(121)–C(121)	119.4(7)
C(7)–C(8)–C(9)	124.4(9)	O(132)–C(131)–O(131)	122.9(9)
N(1)–C(8)–C(9)	111.1(8)	O(132)–C(131)–C(132)	127.3(9)
C(13)–C(8)–C(8)	121.4(8)	C(132)–C(131)–O(131)	109.5(9)
C(3)–C(9)–C(8)	109.7(8)	C(13)–O(131)–C(131)	117.5(7)
C(3)–C(9)–C(4)	128.3(9)	C(141)–C(141)–O(142)	124.9(9)
C(3)–C(11)–O(111)	110.6(7)	C(142)–C(141)–O(142)	123.9(9)
C(3)–C(11)–C(12)	114.5(6)	C(142)–C(141)–O(141)	111.1(9)
C(12)–C(11)–O(111)	106.5(6)	C(14)–O(141)–C(141)	117.2(7)
C(11)–C(12)–O(121)	111.3(7)	C(152)–C(151)–O(151)	112.3(9)
C(11)–C(12)–C(13)	112.9(6)	O(152)–C(151)–O(151)	124.4(9)
C(13)–C(12)–O(121)	107.2(7)	O(152)–C(151)–C(152)	123.2(9)
C(12)–C(13)–O(131)	107.0(7)	C(15)–O(151)–C(151)	115.6(8)

of four products giving a positive Ehrlich test. The solution was neutralized with Amberlite IR-120(H⁺) and concentrated, to afford a syrupy residue which could not be purified.

Crystal Data for Compound (6a).—The compound crystallized with one molecule of water, C₂₃H₃₁NO₁₁·H₂O, *M_r* = 515.5. Triclinic, space group *P*1 with *a* = 8.254(2), *b* = 9.153(2), *c* = 10.160(2) Å, *α* = 92.46(2), *β* = 74.94(1), *γ* = 71.25(1)°, *V* = 695.1(2) Å³, *Z* = 1, *D_m* = 1.22 (measured by flotation), *D_c* = 1.23 g cm⁻³, μ(Mo-*K_α*) = 0.093 mm⁻¹, *F*(000) = 274. Data were measured at room temperature on an Enraf-Nonius CAD-4 diffractometer, with Mo-*K_α* radiation, λ = 0.710 69 Å (graphite monochromator). Unit-cell parameters were obtained from least-squares refinement of *θ* values of 25 reflections in the range 2 < *h* < 10, -12 < *k* < 12, 0 < *l* < 12) were measured in the 2θ < 60° range, ω-2θ mode. Two standard reflections (031 and 031) monitored every 100 reflections showed only statical fluctuations. 1 332 Observed reflections [*I* > 2σ(*I_o*)] were used for structure determination; corrections were made for Lorentz and polarization factors;

absorption and extinction were ignored. The structure was solved by direct methods using MULTAN80,¹⁹ and refined by full-matrix least-squares on F with anisotropic thermal parameters for all non-H atoms ($w^{-1} = \sigma^2$). H atoms (excluding H of water), located at geometric positions and checked on difference Fourier maps, were fixed during refinement with an isotropic temperature factor equal to that of the non-hydrogen atom attached to it. Final residuals were $R = 0.090$, $R_w = 0.092$. The rather high R -factors and e.s.d.s as well as discrepancies at low $\sin\theta$ between $|F_o|$ and $|F_c|$ seem to be due to extinction problems, resulting from the poor quality of the crystals. A final difference Fourier synthesis showed $\Delta\rho = \pm 0.3 \text{ e \AA}^{-3}$. Atomic scattering factors were taken from International Tables for X-ray Crystallography.²⁰ The absolute configuration was assumed on the basis of the compound used in the synthesis. The XRAY system²¹ was used for the structure refinement.

Table 6 lists the fractional atomic co-ordinates of non-hydrogen atoms. Table 7 gives the bond lengths and valence angles. The values of bond angles H(1)–N(1)–C(2) and H(1)–N(1)–C(8), containing hydrogen, have a standard deviation ten times larger than those not involving hydrogen. The packing is governed by two intermolecular hydrogen bonds between the oxygen O(350) of the water molecule and the O(4) and N(1) atoms [O(350) \cdots O(4) 2.696(10) Å, N(1) \cdots O(350) 2.882(12) Å]. Tables of hydrogen co-ordinates, least-squares planes, possible hydrogen bonds, certain intermolecular contacts, dihedral angles, and puckering co-ordinates are available as Supplementary Publication [SUP No. 56663 (10 pp.)].*

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* For details of the Supplementary Publications Scheme see 'Instructions for Authors,' *J. Chem. Soc., Perkin Trans. 1*, 1987, Issue 1, section 4.0. Thermal parameters have been deposited at the Cambridge Crystallographic Data Centre.

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