Deoxygenation of Sugar Derivatives by the Wolff–Kishner Reaction [1]

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The Wolff–Kishner reaction converts 1,5-anhydro-4,6-*O*-benzylidene-2-deoxy-D-*erythro*-hex-3-ulose (1) into its 3-deoxygenated analogue (2) in high yield. In contrast, methyl 4,6-*O*-benzylidene-3-deoxy-β-D-*erythro*-hexopyranosid-2-ulose (3) and methyl 4,6-*O*-benzylidene-2-deoxy-α-D-*erythro*-hexopyranosid-3-ulose (10) afford complex mixtures of products, most of which appear to arise through elimination processes; the expected deoxygenated glycosides (5) and (11) were isolated in only moderate and low yields, respectively. A slightly modified procedure in the reaction with (10) provided the pyrazole derivative (14) as the only product in high yield.

INVESTIGATIONS in this laboratory have been concerned with the development of procedures for selective functional modification of sugars to afford regiospecifically oxidized [2] and deoxygenated [3,4] products, both for their utility in preparation of rare sugars [5] and for their application in structural alteration of complex carbohydrates and their conjugates, such as polysaccharides,[6] nucleosides,[7] and aminocyclitol antibiotics.[8]

The traditional Wolff–Kishner reaction [9–11] for converting a ketone group into a methylene group has never found wide application with carbohydrates; [12] this is understandable in view of the severe conditions (strong base and elevated temperature) of the classic reaction

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[10] W. Rausch, 'Reduction,' ed. R. L. Augustine, Dekker, New York, 1968, p. 171.

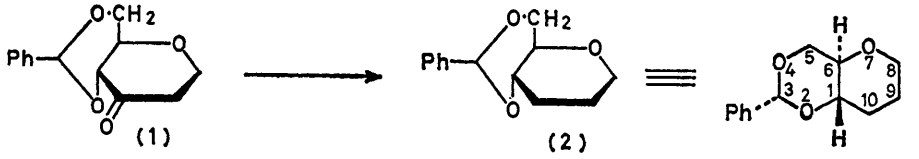
[11] H. O. House, 'Modern Synthetic Reactions,' Benjamin, Menlo Park, California, 1972, ch. 4.

[12] For one of the few applications in carbohydrate chemistry, see H. Paulsen and D. Stoye, *Chem. Ber.*, 1969, **102**, 3824.

procedure, the fragile nature of most carbohydrate derivatives, and the inaccessibility of suitable free-carbonyl sugar derivatives to earlier investigators. Now that the use of mild and specific oxidation methods is routine in the carbohydrate field,[2] it would be of value to have a procedure for the conversion of keto-sugars into the corresponding deoxy-derivatives. Under certain circumstances, such a procedure could be a useful alternative to the direct deoxygenation [4] of a secondary alcohol group.

Recent work [13] has shown the considerable synthetic potential of an adaptation of the reaction described by Klemer and Rodemeyer,[14] whereby α-deoxy-keto-sugar derivatives are obtained from vicinal benzylidene acetals by treatment with butyl-lithium. In principle, such deoxy-keto-derivatives might provide access, by way of a Wolff–Kishner reaction, to the corresponding vicinal dideoxy-sugars. Such a sequence would provide a net two-step conversion, in a pyranoid ring system, of a vicinal diol into the dideoxy-analogue, and might be a convenient alternative to the same net conversion effected [3] *via* a disulphonic ester that has proved particularly useful [8] in the field of aminocyclitol antibiotics.

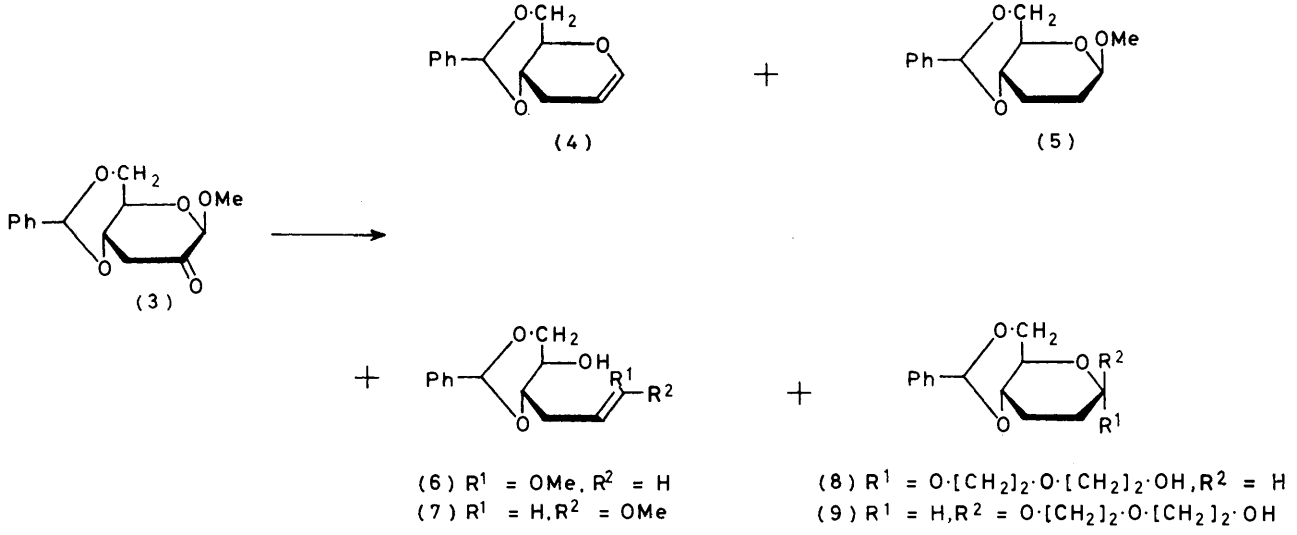
Three model carbohydrates [(1), (3), and (10)] were selected for study of the Wolff–Kishner reaction, and the reduction conditions used followed the relatively mild procedure of Lock.[15] Each compound was an α-deoxy-keto-derivative prepared from the benzylidene acetal of a vicinal diol by reaction with butyl-lithium. Thus methyl 2,3:4,6-di-*O*-benzylidene-β-D-allopyranoside gave methyl 4,6-*O*-benzylidene-3-deoxy-β-D-*erythro*-hexopyranosid-2-ulose [1,16] (3), methyl 2,3:4,6-di-*O*-benzylidene-α-D-mannopyranoside afforded methyl 4,6-*O*-benzylidene-2-deoxy-α-D-*erythro*-hexopyranosid-3-ulose [13] (10), and 1,5-anhydro-2,3:4,6-di-*O*-benzylidene-D-mannitol was converted into 4,6-*O*-benzylidene-D-*erythro*-3-hexulose [1,16] (1), all in high yields.



SCHEME 1

The ketose [16] (1) was heated at 100 °C with hydrazine hydrate in 2,2′-oxybis(ethanol), with subsequent addition of an excess of potassium hydroxide. One major product was formed (t.l.c.), which was isolated crystalline in 69% yield and shown to be the expected 3-deoxygenated 1,5-anhydrohexitol (2) (Scheme 1). Only minor proportions of side-products were formed, as indicated by t.l.c. This conversion thus demonstrates the practical feasibility of the Wolff–Kishner reaction, at least with the rather robust pyranose derivative (1) under the two-step conditions of Lock.[15] The structure (2) is fully supported by conventional analytical data, as well as by n.m.r. (Table 1) and mass (Table 2) spectra.

Similar treatment of the methyl glycosidulose [16] (3) (Scheme 2) afforded a complex mixture that was separated by column chromatography on silica gel. The first two components eluted were isolated crystalline in 24 and 19% yields and were identified by detailed spectroscopic (i.r. and n.m.r.; see Table 1) and mass



SCHEME 2

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[16] D. Horton and W. Weckerle, to be published.

spectrometric (Table 2) analyses as 1,5-anhydro-4,6-*O*-benzylidene-2,3-dideoxy-D-*erythro*-hex-1-enitol (4) and the 2-deoxygenated glycoside (5), respectively. These assignments were confirmed by the agreement of the physical constants with those reported for (4) [12] and (5) [12,17] prepared by different methods.

The third fraction (8%) proved to be a 1 : 4 mixture of geometric isomers, as concluded from the ^{1}H n.m.r. spectrum (Figure 1 and Table 1). The spectrum showed two singlets for methoxy-groups, together with two sets of signals for protons of a vinyl ether group; the latter exhibited coupling to protons at C-3, as demonstrated by double irradiation experiments. This information, together with the presence of an intact 1,3-dioxan ring (as evidenced by the benzylidene proton resonance at δ 5.52), and of a hydroxy-group (signal at δ 2.11 that disappeared upon addition of D_2O) suggested the open-chain structures (6) (*Z*-isomer) and (7) (*E*-isomer). A sample of (7) was obtained pure by recrystallizing the semi-solid mixture from hexane. Its mass spectrum ($M^{+\cdot}$ 250; see Table 2) and its elemental composition fully supported the structure.

The last fraction (20%) comprised an anomeric mixture of the 2-deoxygenated-2-(2-hydroxyethoxy)-ethyl glycosides (8) and (9), migrating as a single zone in t.l.c. The n.m.r. spectrum of the mixture (Table 1) closely resembled that of (5), displaying, in particular, the multi-line pattern at high field (δ 2.20—1.50) arising from the four protons at C-2 and C-3, but showed a complex multiplet and a broad singlet for the methylene

TABLE 1

100 MHz N.m.r. spectral data for compounds (2), (4)—(9), and (11)—(17)

Chemical shifts (δ) [b] [first-order couplings (Hz) in parentheses]

Compound [a]	H-1 ($J_{1,2a}$)	H-2e ($J_{1,2e}$)	H-2a ($J_{2a,3a}$) ($J_{2e,2a}$)	H-3e ($J_{2e,3e}$)	H-3a ($J_{2e,3a}$)	H-4 ($J_{3,4}$)	H-5 ($J_{4,5}$)	H-6 ($J_{5,6}$)	H-6′ ($J_{5,6'}$) ($J_{6,6'}$)	Aryl	PhC–H	1-OR	Others
(2)	3.99m	← 2.20—1.60m →				3.50m	3.30ddd (9.2)	4.24dd (4.5)	3.66t (10) (10.2)	7.60—7.27m	5.54s		3.88m (H-1a)
(4) [c]	6.32m	4.69m (6.3)	← 2.40—2.16m →			3.95m (2.1)	3.92—3.68m (7.8)	4.37dd (10.5)	3.92—3.68m (15.5)	7.60—7.25m	5.58s		
(5)	4.45dd (8.7)	← 2.20—1.50m →				← 3.64—3.18m →		4.27dd (4.5)	3.76t (10) (10.2)	7.65—7.20m	5.52s	346s	
(6) [d]	6.13d	4.70ddd (6.2)		(8)	(8)							3.65s	2.11 [e] (5-OH)
(7) [f]	6.50d	4.96ddd (12.5)	← 2.67—2.22m →	(7)	(7)	← 4.59—3.43m →				7.67—7.27m	5.52s	3.56s	2.11d (5.2) (5-OH)
(8) [g]	4.82m					← 4.15—3.30m →					5.54s		
(9)	4.59dd (8)	← 2.20—1.50m →				← 4.14—3.40m →		4.25dd (4.5)	3.85t (11) (10.5)	7.60—7.20m	5.50s	3.80—3.25m	2.77 [e] (OH)
(11)	4.65m	← 2.12—1.70m →				← 4.10—3.40m →				7.60—7.15m	5.53s	3.33s	
(12)	4.76dd (3.8)	2.18ddd (1.3)	1.71ddd (11.2) (13.4)		4.09m (5.2)	← 4.30—3.40m → (8)				7.60—7.20m	5.54s	3.30s	2.76d (2.8) (3-OH)
(13)	4.74dd (4)	2.32ddd (1.2)	1.70ddd (11.3) (12.8)		5.35ddd (5.5)	3.60t (8.8)	3.88m (~9)	4.23dd (3.4)	3.68t (9) (8.8)	7.55—7.15m	5.50s	3.29s	1.96s (3-OAc)
(14) [h]	7.60d	6.34d (1.8)				4.65d	3.89m (9)	4.24dd (4.3)	3.63t (10) (9.3)	7.55—7.20m	5.67s		12.75s [e] (NH) 5.16d [e] (5-OH)
(15) [h] and [i]	8.15d	6.52d (2.8)				4.86d	5.28m (9.5)	4.42dd (5.2)	3.72t (10) (10.7)	7.60—7.15m	5.64s		1.89s (NAc) 2.57s (OAc)
(16) [h]	[j]	6.33d (2)				4.92d	5.24m (9.5)		3.70t (10) (10.7)				1.83s (NAc)
(17) [h]	8.33d	6.68d (2.9)				5.11d	5.48m (9.6)	4.61dd (5.2)	3.87t (9.6) (10.6)	7.65—7.00m	5.73s		8.05—7.00m (OBz, NBz)

[a] In [^{2}H]chloroform except for (14), which was measured in [$^2H_6$]dimethyl sulphoxide. [b] d, doublet; m, multiplet; s, singlet; t, triplet. [c] $J_{3a,4}$ 7.8 Hz; $^4J_{1,3e} = {}^4J_{1,3a}$ = 2 Hz; $J_{2,3e}$ 3 (or 3.7) Hz; $J_{2,3a}$ 3.7 (or 3) Hz; $^4J_{2,4}$ 0.7 Hz. [d] Measured for a mixture of (6) and the *E*-isomer (7) (see Figure 1); the listed signals were found in addition to those of pure (7). From this spectrum, the product ratio was determined to be 4 : 1 in favour of (7). [e] Broadened signal. [f] $^4J_{1,3e} = {}^4J_{1,3a}$ = 1.2 Hz. [g] Taken from the n.m.r. spectrum of the anomeric mixture of products (8) and (9); the reported signals were found in addition to those of the pure β-anomer (9). The α : β ratios were determined to be 7 : 3 and 3 : 10 in the Wolff–Kishner reactions of (3) and (10), respectively. [h] To include these compounds in the Table, the numbering system of the parent sugar is retained (see Figure 2). [i] Inseparable mixture, the ratio being 4 : 1 in favour of (15) (see Figure 2). [j] Obscured by the aryl-proton signals.

[17] E. J. Hedgley, W. G. Overend, and R. A. Rennie, *J. Chem. Soc.*, 1963, 4701.

and hydroxy-protons of the aglycone, respectively, instead of the sharp singlet associated with the methoxy-group of (5). Additional resonances were present indicative of the α-anomer (8), the ratio being 3 : 7 in favour of (8). Mass spectrometry ($M^{+\cdot}$ 324; Table 2), i.r. spectroscopy, and the elemental composition of the crystalline β-anomer (9), which was isolated pure, provided additional evidence for the structure.

The reaction of methyl 4,6-*O*-benzylidene-2-deoxy-α-D-*erythro*-hexopyranosid-3-ulose [13] (10) with hydrazine hydrate and potassium hydroxide was performed in the same way as with (3). Separation of the resulting mixture of products on a column of silica gel yielded small proportions of the hex-1-enitol (4) and the 3-deoxygenated methyl glycoside (11) [corresponding to (5) in the foregoing reaction], together with a substantial proportion of a 3 : 10 mixture of (8) and (9). Compound (11) was identical with a product prepared earlier by an

TABLE 2

Electron-impact mass spectral data for compounds (2), (4)—(7), (9), and (11)—(17)

m/e of principal fragments [a] (% of base peak)

(2) [c]	(4)	(5)	(7)	(9)	(11) [d]	(12)	(13)	(14) [e]	(15) + (16) [f]	(17) [g]	Assignment [b]
221	219	251	251	325	251	267	309	247	331	455	$M + 1$
(0.6)	(8)	(0.5)	(0.05)	(1.2)	(0.9)	(13)	(3.3)	(0.03)	(0.13)	(0.06)	
220	218 *	250 *	250 *	324	250 *	266 *	308 *	246 *	330	454 *	$M^{+\cdot}$
(4.4)	(60)	(3.7)	(0.4)	(7)	(6.2)	(64)	(19)	(0.06)	(0.16)	(0.2)	
219	217	249	249	323	249	265	307	245	329	453	$M - 1$
(1.9)	(9)	(2)	(0.22)	(1.7)	(2.6)	(26)	(11.5)	(0.07)	(0.55)	(0.07)	
177	175 [6]	207 *,6	207	281	207 *,7	223	265	203 [4]	287 [6,9]	411 *,5	$M - \cdot CH_2CHO$
(0.04)	(0.15)	(5.8)	(0.7)	(0.01)	(5.2)	(5.7)	(0.3)	(9)	(5)	(0.07)	
		190		190	190	206	248 *				$M - HCO_2R$ [h]
		(0.1)		(1.7)	(0.05)	(0.3)	(29)				
		219	219 [8]	219	219 [9]	235	277				$M - RO\cdot$ [h]
		(0.2)	(1.2)	(7)	(3.2)	(14.5)	(0.3)				
		218	218 [7]	218	218	234 [5]	276				$M - ROH$ [h]
		(0.6)	(7)	(13.5)	(1.7)	(5)	(0.05)				
143	141	173	173	247	173	189	231	169	253	377	$M - Ph\cdot$
(0.36)	(1.5)	(0.2)	(0.08)	(0.1)	(0.3)	(1.5)	(0.8)	(0.1)	(0.1)	(0.02)	
97	95 *	127	127	201	127 [8]	143	185	123	207	331	$M - Ph\cdot - HCO_2H$
(5)	(7.2)	(0.8)	(1.7)	(0.4)	(0.9)	(0.5)	(0.1)	(1.5)	(0.03)	(0.005)	$M - H\cdot - PhCO_2H \sim -RO\cdot$ [h]
		96		96	96	112	154				
		(0.25)		(8)	(0.5)	(1.9)	(0.2)				
114 [4]	112 *,4,5	144	144	218	144	160	202	140 [5]	224	348 *	$M - PhCHO$
(13)	(37)	(1.1)	(0.5)	(13.5)	(0.9)	(1.1)	(0.25)	(4.3)	(0.5)	(1.6)	
84	82	114	114	188	114	130	172	110 *	194	318	$M - PhCHO - CH_2O$
(6.5)	(9.5)	(1.9)	(0.6)	(0.5)	(1.8)	(2.2)	(1.2)	(5.2)	(0.15)	(0.03)	
		83		83	83	99	141				$M - PhCHO - CH_2O - RO\cdot$
		(1.6)		(36)	(4)	(67)	(0.8)				
71 [4,5]	69 [4]	101 [4,5,6]	101 *,4	175 [4,6]	101 [5,6,7]	117 [4]	159 [4]	97 [4,5]	181 [8]	305 [6]	h_1
(100)	(7.2)	(100)	(10)	(75)	(100)	(76)	(51)	(100)	(4.8)	(6.2)	
149	149	149 [1]	149	149 [1]	149 [1,4]	149	149 [1]	149 [6]	149 [5,6]	149 [4]	h_2
(0.9)	(2.1)	(2.2)	(1.4)	(26)	(2.1)	(21)	(11)	(0.7)	(100)	(1)	
107	107 [2]	107	107 [2,6]	107	107 [2]	107	107 [2]	107 *,2	107 [2,5]	107	$PhCHOH^+$
(2.3)	(15)	(2.1)	(100)	(93)	(4)	(32)	(5.5)	(52)	(66)	(0.6)	
106	106	106	106	106	106	106	106	106 [6]	106	106	$PhCHO^{+\cdot}$
(4.7)	(11)	(3.4)	(8)	(33)	(11)	(20)	(6.1)	(3.6)	(6)	(8)	
105 [3]	105 [6]	105 [3]	105 [3]	105 [3]	105 [3]	105	105 [3]	105 [3]	105 [3]	105 [3,6]	$PhCO^+$
(11)	(65)	(11)	(27)	(100)	(20)	(84)	(43)	(7)	(20)	(100)	
91	91	91 [1]	95 [5]	91 [1]	91 [1]	91	91 [1]	91 *	91	91	$PhCH_2^+$
(3.4)	(7.8)	(8)	(10.5)	(36)	(8)	(23)	(35)	(5.8)	(12.2)	(2.7)	
79	79 [2]	79	79 [2]	79	79 [2]	79	79 [2]	79 [2]	79 [2]	79	$C_6H_7^+$
(5)	(8)	(2.2)	(26)	(16)	(3)	(10.5)	(10)	(19)	(4.3)	(3.7)	
77 [3]	77	77 [3]	77 [3]	77 [3]	77 [3]	77	77 [3]	77 [3]	77 [3]	77 [3]	Ph^+
(13)	(27)	(7)	(21)	(42)	(15)	(23.5)	(23)	(18)	(10)	(19)	
56 [5]	83 *,5	59 [4]	179 [5,6]	107 [4,5]	71 [4]	99 [4]	99 [4]		43	71 [4]	Others
(2.1)	(100)	(6.9)	(72)	(93)	(4.6)	(67)	(100)		(100)	(0.12)	
h_1 — Me·	DHP †	h_1 — keten		ROH_2^+	h_2 — C_6H_6	h_1 — H_2O	h_1 — HOAc		Ac+	h_2 — C_6H_6	
		69 [5]	59 [4]	89 [5]	59 [5]	179 *,5	43		139 [4,7,8]	122 [5]	
		(28)	(1.6)	(95)	(6.6)	(100)	(97)		(25)	(5)	
		h_1 — MeOH	h_1 — keten	ROH_2^+ — H_2O	h_1 — keten		Ac+		*N*-Ac of h_1 ion of (14)	$PhCO_2H^{+\cdot}$	
			189 [7]	157 [6]	69 [6]		248		270	332 [7,8]	
			(0.62)	(4.6)	(30)		(29)		(1.2)	(0.6)	
			218— ·CHO	h_1 — H_2O	h_1 — MeOH		M — HOAc		M — HOAc	M — $PhCO_2H$	
			200 [8]	45	86 [8]				97 [4]	161 [7]	
			(0.36)	(100)	(0.4)				(23.5)	(0.3)	
			219—		127—				= h_1 of (14)	PD‡	

TABLE 2 (*Continued*)

(2) [c]	(4)	(5)	(7)	(9)	(11) [d]	(12)	(13)	(14) [e]	(15) + (16) [f]	(17) [g]	Assignment [h]
			H_2O		MeO·						
					113[9]				111[7]		
					(5)				(1.5)		
					219—				139—		
					PhCHO				CO		
									227[9]	227[8]	
									(0.5)	(1.3)	
									287—	332—	
									HOAc	PhĊO	

[a] Prominent metastable fragments observed in the spectra are indicated by superscript arabic numbers; 1, 2, and 3 being used throughout for the decompositions 149 ⟶ 91 (calc. 55.58), 107 ⟶ 79 (calc. 58.33), and 105 ⟶ 77 (calc. 56.47); where $M^{+\cdot}$ is the parent ion, an asterisk is used. Deviations between observed and calculated values are less than ±0.1 mass units. [b] Fragment notations are based on plausible mechanistic steps and, in part, according to references § and ¶, but the possibility of isomeric structures is not excluded. [c] The metastable peak at 44.2 is compatible with both processes 4 and 5 (calc. 44.22 and 44.17, respectively). [d] The metastable peak at 58.3 may be attributed to process 2 (calc. 58.33) as well as 8 (calc. 58.24) and 9 (calc. 58.31). [e] The metastable peak at 46.4 is compatible with process 4 (calc. 46.35) as well as $M^{+\cdot}$ ⟶ $PhCHOH^+$ (calc. 46.54). [f] The fragment at 287 is formed either by loss of $\cdot CH_2CHO$ (cf. ref. ¶) or by expulsion of an acetyl radical. [g] The metastable peak at 36.2 is due to either process 5 (calc. 36.21) or 6 (calc. 36.15). [h] R = methyl for all compounds in question except (9) where R = 2-(2-hydroxyethoxy)ethyl.

† 3,4-Dihydropyrylium. ‡ 2-Phenyl-1,3-dioxinylium. § O. S. Chizhov, L. S. Golovkina, and N. S. Wulfson, *Carbohydrate Res.*, 1968, **6**, 138, 143; N. K. Kochetkov and O. S. Chizov, *Adv. Carbohydrate Chem.*, 1966, **21**, 39. ¶ J. Mitera, V. Kubelka, A. Zobáčová, and J. Jarý, *Coll. Czech. Chem. Comm.*, 1972, **37**, 3744.

independent route in this [5] and other [12,18] laboratories. T.l.c. of the mixture showed no zone attributable to the open-chain compounds (6) or (7), but two other products were detected in this instance. One of these was very minor (<1%), but was shown to be methyl 4,6-*O*-benzylidene-2-deoxy-α-D-*arabino*-hexopyranoside [19,20] (12), further characterized as its 3-acetate [20] (13).

The main product (24%) in this reaction, however, proved to have the unusual structure (14), as indicated by physical data and established by subsequent conversions. The n.m.r. spectrum of (14) (Table 1) showed well-separated one-proton signals for all but the phenyl protons. Five protons accounted for that part of the molecule forming the dioxan ring, as deduced from chemical shifts and verified by spin-decoupling experiments. A broadened doublet at δ 5.16, which disappeared on simple deuteriation, indicated a hydroxy-group at C-5 (confirmed by double irradiation), leaving only a pair of doublets at low field and a broad signal at δ 12.75 to be assigned. The elemental analysis, which

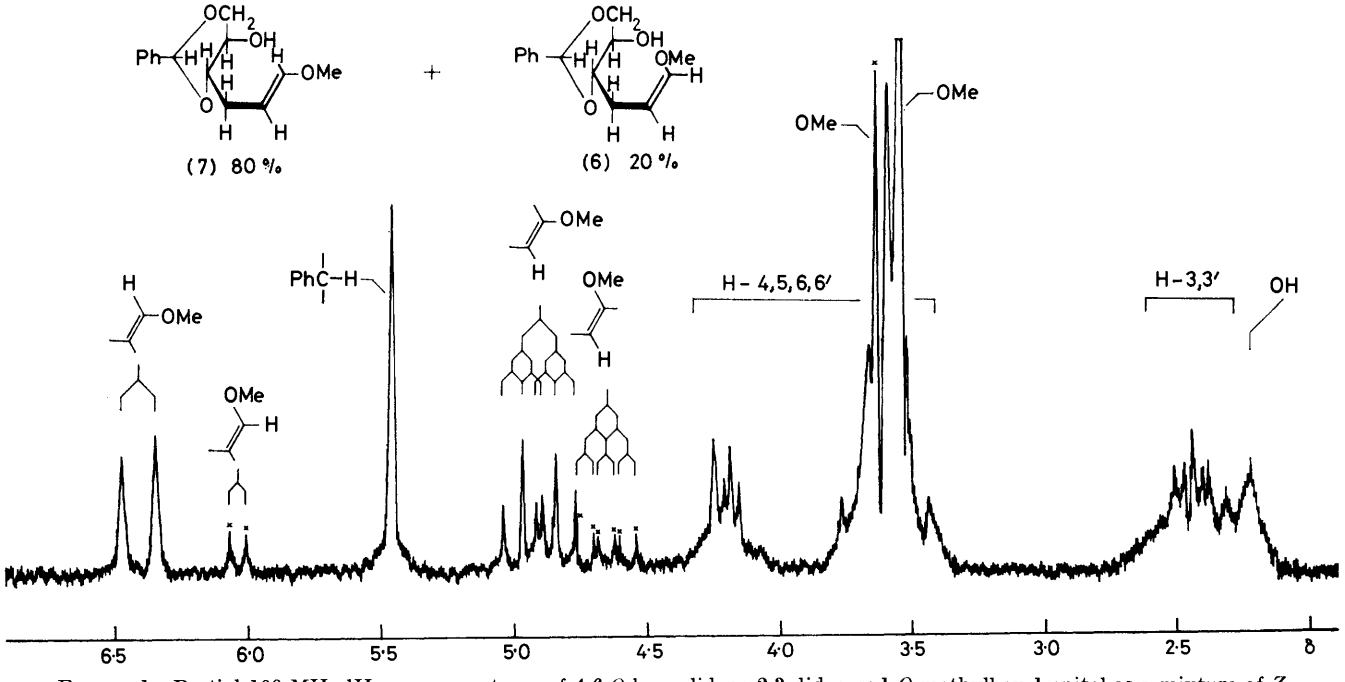


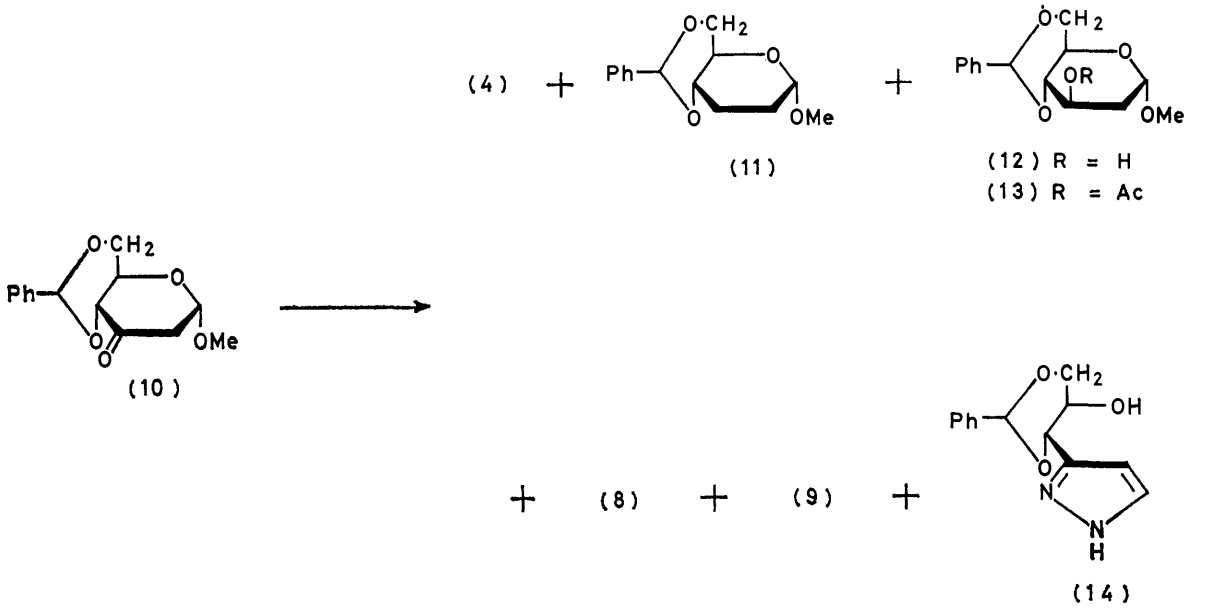
FIGURE 1 Partial 100 MHz ^1H n.m.r. spectrum of 4,6-*O*-benzylidene-2,3-dideoxy-1-*O*-methylhex-1-enitol as a mixture of *Z*- and *E*-isomers (6) and (7) in [^2H]chloroform; the well-separated signals for (6) are marked with an asterisk

[18] H. R. Bolliger and D. A. Prins, *Helv. Chim. Acta*, 1946, **29**, 1061.

[19] B. Flaherty, W. G. Overend, and N. R. Williams, *J. Chem. Soc.* (*C*), 1966, 398.

[20] B. Coxon, *Tetrahedron*, 1965, **21**, 3481.

revealed that nitrogen was present, together with mass spectrometric data, led to proposal of the pyrazole structure (14). Further evidence for this structure was by analysis of the ring-proton signals of the 1-acylpyrazole system, based on a study by Williams [21] with model 1-acylpyrazoles which showed that the 5-proton



SCHEME 3

provided by preparation of two derivatives. Conventional acetylation yielded a colourless, homogeneous (by t.l.c.) glass whose elemental composition and mass spectral data {*m/e* 330 ($M^{+\cdot}$) and 139 [*N*-acetyl-3-(hydroxymethyl)pyrazole cation]; see Table 2} indicated resonates at lowest field, the 3-proton at higher field, and the 4-proton at highest field. In addition, the coupling constants were 1.6 ($J_{3,4}$) and 2.9 Hz ($J_{4,5}$). On this basis, the major (80%) and presumably more stable component was identified as the 3-substituted

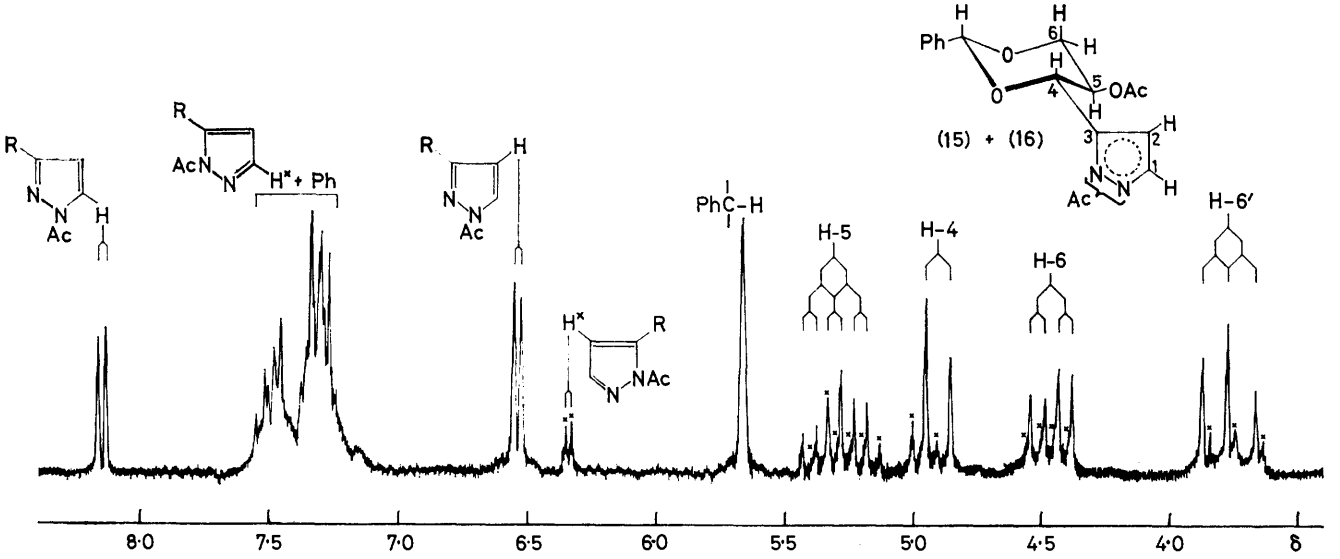


FIGURE 2 100 MHz ^{1}H n.m.r. spectrum of the mixture of 3- and 5-substituted *N*-acetylpyrazoles (15) and (16) in [^{2}H]chloroform; the signals for (16) are marked with an asterisk and the numbering for the protons corresponds to the atoms of the original sugar chain

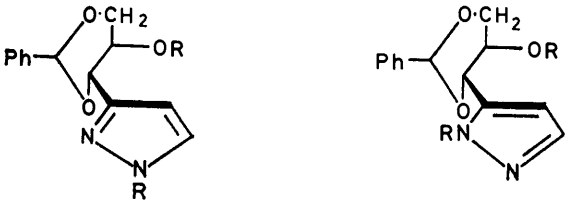
that it was an *NO*-diacetyl derivative. The n.m.r. spectrum (Figure 2 and Table 1) revealed the product to be a mixture of the 3- and 5-substituted * *N*-acetylpyrazoles (15) and (16). They could be readily identified isomer (15), the minor (20%) product being the 5-substituted one (16).

As the mixture of (15) and (16) did not crystallize and could not be separated, the dibenzoate of (14) was prepared in the hope of obtaining a crystalline derivative.

* Pyrazole ring numbering with N-1 as the acylated nitrogen atom.

[21] J. K. Williams, *J. Org. Chem.*, 1964, **29**, 1377.

The clear first-order n.m.r. spectrum (Table 1) indicated that only one isomer had been formed which, on the basis of Williams' work,[21] was identified as the 3-substituted pyrazole derivative (17). Mass spectral



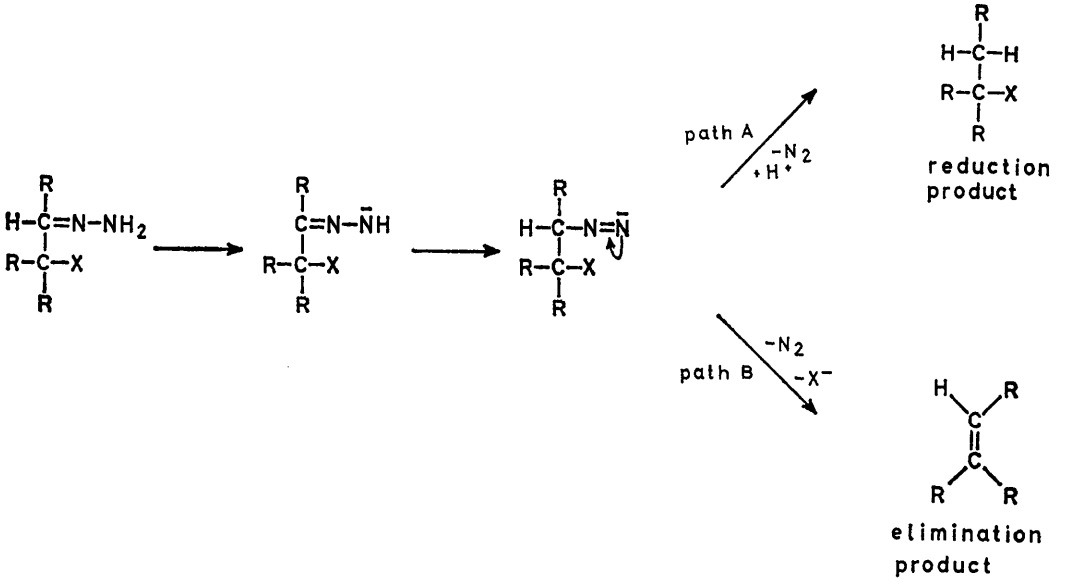
(15) R = Ac (16)
(17) R = Bz (18)

data ($M^{+\cdot}$ 454; Table 2) and elemental analysis confirmed the proposed gross structure. Although it was a pure isomer, it did not crystallize on trituration with a variety of solvents.

When the conditions in the foregoing reaction of (10) terminal in the rate-determining step. The di-imide anion thus formed is considered to be the common reaction intermediate for all the products observed. In the normal course of the reaction, the di-imide anion collapses in the presence of a proton source (solvent) to give a nitrogen molecule and the deoxygenated product (path A). However, compounds bearing a suitable α-substituent (X in Scheme 4) may follow an elimination–reduction pathway instead (path B).

On this basis, it may be readily understood why the alditol derivative (1) was successfully converted into the deoxygenated derivative (2), as compound (1) lacks any reasonable leaving group (the alkoxy-substituent at C-4 apparently does not act as such throughout the series) that would be necessary for the elimination reaction. The reaction with the methyl glycosiduloses (3) and (10), however, afforded the normal deoxygenation products (5) and (11) in only moderate and low yields, respectively.

In the reaction of (3), compounds (4), (6), and (7)



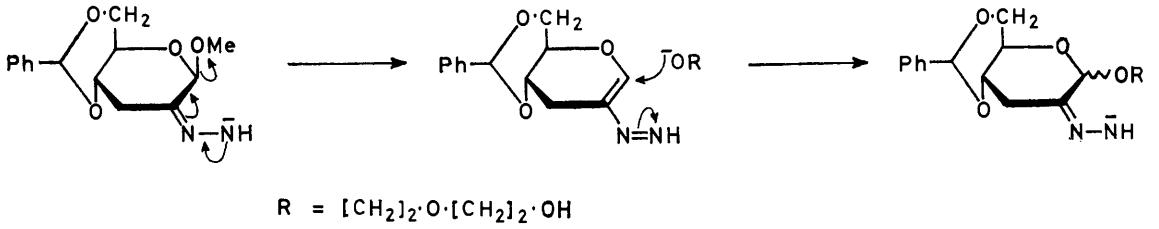
SCHEME 4

with hydrazine hydrate–potassium hydroxide were slightly modified (see Experimental section), the pyrazole derivative (14) was obtained in 64% yield as the only product. This reaction thus provides a feasible route to pyrazoles *C*-substituted by a carbohydrate chain, and is of potential synthetic interest in relation to the pyrazomycins and other *C*-nucleosides.[22]

In order to explain the aforementioned results, the mechanism of the Wolff–Kishner reaction needs to be considered briefly (Scheme 4). It is generally accepted [9-11] that the reaction involves initial removal of a proton from the β-nitrogen atom, followed by proton capture at the carbon terminal in the hydrazone anion, coupled with proton abstraction at the nitrogen evidently arise from the alternative elimination process. Loss of the aglycone methoxy-group leads to the glycal (4), and cleavage of the C(1)–O(5) bond results in the two isomeric enol ethers (6) and (7). Paulsen and Stoye [12] found (5) as the only product when they heated the hydrazone derivative of (3) (prepared from a dimesyl precursor) or the corresponding *N*-acetylhydrazone with hydrazine over a prolonged period. With the corresponding α-anomer, they observed both normal reduction and elimination of the glycosidic methoxy-group, the two reactions occurring to almost the same extent. On the basis of these results, they postulated the *trans*-diaxial arrangement of di-imide and the leaving group as a prerequisite for fragmentation. This hypothesis apparently does not hold true under the more vigorous conditions employed here, as the di-imide group in both

[22] S. Hanessian and A. G. Pernet, *Adv. Carbohydrate Chem. Biochem.*, 1976, **33**, 111.

equatorial and in axial disposition is *gauche* to the β-anomeric methoxy-group, and yet (4) is the preponderant product.[23] Similarly the fragmentation leading to cleavage of the ring must take place with both axially (≡ *gauche*) and equatorially (≡ *trans* relationship) exposed di-imide groups in order to produce both isomeric enol ethers (6) and (7), if a concerted mechanism is assumed. A possible intramolecular, cyclic transition state [24] involving the axial di-imide group and the ring oxygen atom could account for the preponderant formation of the *trans*-isomer (7).

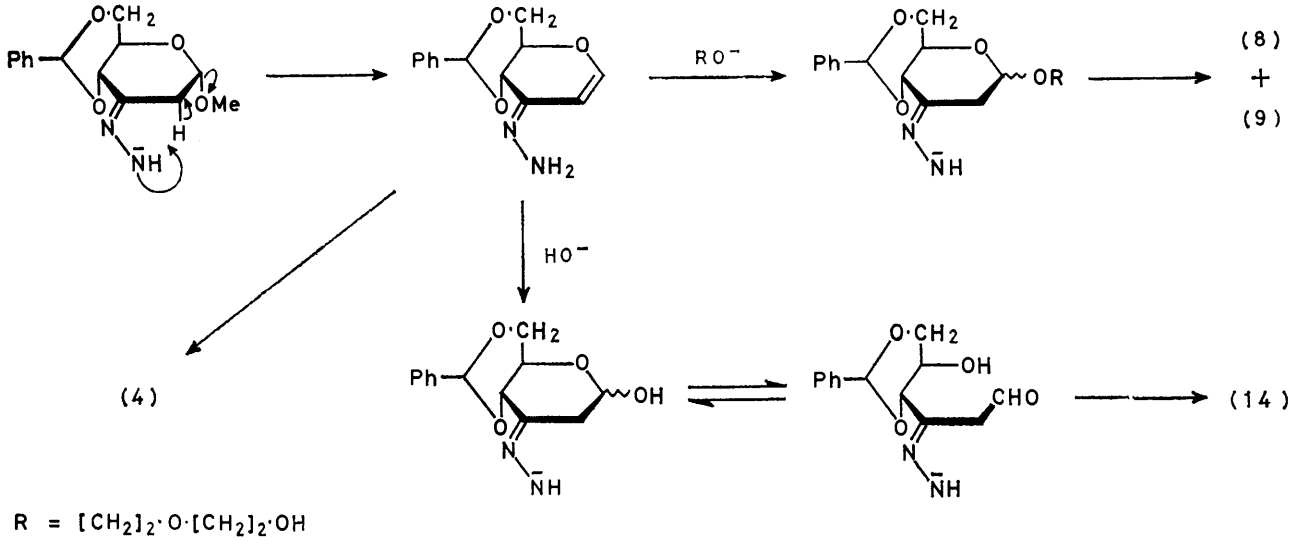


SCHEME 5

The anomers (8) and (9) observed in the reaction of (3) are considered to be normal deoxygenation products. composition of the hydrazone at this stage in a Wolff–Kishner manner affords the glycal (4), whereas nucleophilic attack by the alkoxide or hydroxide anion obviously leads to the anomeric 2-(2-hydroxyethoxy)-ethyl glycosides (8) and (9) and the pyrazole derivative (14), respectively.

The formation of small, though reproducible, amounts of the alcohol (12) in the reaction of (10) may be explained on the basis of a Meerwein–Ponndorf–Verley type of reduction, as reported for a semicarbazone,[26] although it is less probable [10] under the conditions of Lock [15] used here.

The foregoing results suggest that suitably protected glyculoses may generally be amenable to Wolff–Kishner reduction, but that complications may be expected when a glycosidic group is present. As a *C*-substituted pyrazole can be prepared in good yield from a 2-deoxyglycosid-3-ulose by adaptation of the Wolff–Kishner conditions, the results also offer the potential for access to *C*-nucleoside analogues of the pyrazomycin type.[22]



SCHEME 6

The transglycosylation is thought to take place prior to the rate-determining formation of the di-imide anion, by elimination of the glycosidic methoxy-group in the relatively long-lived [9] hydrazone anion, followed by nucleophilic attack by the 2-(2-hydroxyethoxy)ethanolate anion [25] (Scheme 5).

In the reaction of the glycosid-3-ulose (10), the formation of compounds (4), (8), (9), and (14) requires the rather unusual elimination of a β-substituent (methoxy-group), a possible mechanism for which is outlined in Scheme 6 starting with the hydrazone anion. The αβ-unsaturated hydrazone derivative is considered to be the common intermediate for all four products. De-

EXPERIMENTAL

Evaporations were performed under diminished pressure at a bath temperature below 50 °C. M.p.s were determined with a Thomas–Hoover apparatus. A Perkin-Elmer 141

[23] For another example of *cis* fragmentation in a related case see R. D. Guthrie and R. D. Wells, *Carbohydrate Res.*, 1972, **24**, 11.

[24] N. J. Leonard and S. Gelfand, *J. Amer. Chem. Soc.*, 1955, **77**, 3272.

[25] A similar mechanism for a phenylhydrazone has been postulated: P. M. Collins, S. Kumar, and W. G. Overend, *Carbohydrate Res.*, 1972, **22**, 187.

[26] F. Eisenlohr and R. Polenske, *Ber.*, 1924, **57**, 1639.

polarimeter and 1 dm tubes were used for measurement of specific rotations. I.r. spectra were taken on a Perkin-Elmer 457 grating spectrophotometer with solids dispersed in potassium bromide and syrups as films on sodium chloride discs. ^{1}H N.m.r. spectra (Table 1) were recorded at 100 MHz with a Varian HA-100 spectrometer (internal standard tetramethylsilane; spin-coupling values measured at a sweep width of 250 Hz). The assignment of hydroxy-proton resonances was confirmed in most instances by deuterium exchange. Integrations were consistent with peak assignments. T.l.c. was performed on precoated plates of Silica Gel 60 (Merck); zones were detected by u.v. light and by spraying with sulphuric acid and subsequent heating. Solvent volumes are v/v; light petroleum refers to the fraction boiling at 65—100 °C. Column chromatography was performed with silica gel (Merck 7734; 63—200 μm; 40 ml column volume per g of mixture separated). Yields are based on amounts of compounds actually isolated. Microanalyses were performed by W. N. Rond; satisfactory analytical data (±0.3% for C and H) were obtained for all compounds previously known. Mass spectra were recorded by C. R. Weisenberger with an A.E.I. MS9 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 °C. Data and probable assignments are presented in Table 2. *X*-Ray powder diffraction data give interplanar spacings (Å) for Cu-K_α 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); duplication of numbers indicates approximately equality in intensity.

1,5-*Anhydro*-4,6-O-*benzylidene*-2,3-*dideoxy*-D-erythro-*hexitol*{(1*S*,3*R*,6*R*)-3-*phenyl*-2,4,7-*trioxabicyclo*[4.4.0]*decane*} (2).—A mixture of 1,5-anhydro-4,6-*O*-benzylidene-2-deoxy-D-*erythro*-3-hexulose [16] (1) (500 mg, 2.13 mmol) and hydrazine hydrate (99%; 1 ml, 20.6 mmol) in 2,2′-oxybis(ethanol) (10 ml) was heated under reflux for 1 h at 100 °C. A solution of potassium hydroxide (1.1 g, 19.6 mmol) in 2,2′-oxybis(ethanol) (5 ml) was then added to the cooled mixture. The heating was continued for 2 h until the evolution of gas had ceased. The mixture was cooled in an ice–water bath and ammonium chloride (1.05 g) in ice–water (50 ml) was added with stirring. A crystalline precipitate was formed immediately and, after cooling and stirring for 30 min, was filtered off to give crude product (2). The product was dissolved in ether, decolourized with activated charcoal, and evaporated to give white, shiny crystals (236 mg, 50%). A second crop (90 mg, 19%) was obtained by extracting the aqueous mother liquor with dichloromethane (15, 10, and 10 ml) and, after conventional processing of the extract, column chromatography of the resultant syrupy residue with 4 : 1 ether–light petroleum as eluant. After recrystallization from hexane, *compound* (2) had m.p. 137—138°, $[\alpha]_D^{21}$ −3.4° (*c* 0.7 in chloroform); *X*-ray powder diffraction data: 11.18s, 8.42vw, 6.99m, 5.75m, 5.59w, 5.11vw, 4.77vs (1), 4.48s (3), 4.20s, 4.06w, 3.89vw, 3.73w, 3.66w, 3.53s (2), and 3.41m (Found: C, 70.65; H, 7.4. $C_{13}H_{16}O_3$ requires C, 70.9; H, 7.3%).

Wolff–Kishner Reaction with Methyl 4,6-O-*Benzylidene*-3-*deoxy*-β-D-erythro-*hexopyranosid*-2-*ulose* (3).—The glycoside [16] (3) (1.5 g, 5.68 mmol) in 2,2′-oxybis(ethanol) (30 ml) was treated with hydrazine hydrate (99%; 3 ml, 61.7 mmol) and subsequently with potassium hydroxide (3.3 g, 58.8 mmol) dissolved in 2,2′-oxybis(ethanol) (15 ml), as in the previous experiment. After addition of ammonium chloride (4.5 g) in water (75 ml) the mixture was extracted with dichloromethane (2 × 75 ml), and the combined extracts were washed with water, dried ($MgSO_4$), and evaporated. The syrupy residue (1.31 g) contained five major components according to t.l.c. (4 : 1 ether–light petroleum), R_F 0.69, 0.57, 0.44, 0.36, and 0.09. These were separated by column chromatography, first with the t.l.c. solvent and later with acetone as the eluant.

The fastest moving component (R_F 0.69; 300 mg, 24%) crystallized upon evaporation of the solution and was recrystallized from hexane to give 1,5-*anhydro*-4,6-O-*benzylidene*-2,3-*dideoxy*-D-erythro-*hex*-1-*enitol* (4), m.p. 110°, $[\alpha]_D^{22}$ +64.7° (*c* 0.7 in chloroform); $\nu_{max.}$ (KBr) 1 635, 1 240, and 1 085 (vinyl ether), 755, and 695 cm^{-1} (aryl); *X*-ray powder diffraction data: 10.97vw, 9.55s, 7.69s (3), 5.54vw, 5.18s, 4.88w, 4.79m, 4.57w, 4.30w, 4.20m, 3.99vs (1), 3.70s (2), 3.47w, and 3.37s. Although Fraser-Reid *et al.* described [27] a preparation of (4), no constants were given. However, Paulsen *et al.* reported [12] m.p. 110—112°, $[\alpha]_D$ +65.5° in chloroform for this compound.

The component having R_F 0.57 was obtained as a crystalline solid (266 mg, 19%) that was recrystallized from hexane to give *methyl* 4,6-O-*benzylidene*-2,3-*dideoxy*-β-D-erythro-*hexopyranoside* (5), m.p. 106°, $[\alpha]_D^{22}$ −56.8° (*c* 1 in chloroform); *X*-ray powder diffraction data: 8.19s (2), 6.73w, 5.21w, 4.88m (3), 4.67w, 4.25vw, 4.07s (1), 3.58m, 3.46vw, 3.36m, 3.07w, and 2.74w (lit.,[12] m.p. 106—107°, $[\alpha]_D$ −57.2° in chloroform; lit.,[17] $[\alpha]_D$ −58.8° in chloroform).

The third product, R_F 0.44, absorbed u.v. light strongly but did not char after spraying with sulphuric acid and subsequent heating. After concentrating the appropriate fractions, a yellow syrup was obtained that was still contaminated with the other components. As preparative t.l.c. failed to give a pure product with all solvent systems tried, no further attempts to elucidate the structure were made.

Evaporation of the fractions containing the product having R_F 0.36 gave semicrystalline material that was freed from faster-moving impurities by preparative t.l.c. with the same solvent system. The partially crystalline product (110 mg, 8%), which migrated as a single zone in t.l.c., was shown by n.m.r. spectroscopy (Table 1 and Figure 1) to be a 1 : 4 mixture of the *Z*- and *E*-isomers of 4,6-O-*benzylidene*-2,3-*dideoxy*-1-O-*methylhex*-1-*enitol* [(6) and (7), respectively]. After recrystallizing the mixture from hexane (7 ml) the pure *E*-isomer (7) was recovered (35 mg); m.p. 75—76°, $[\alpha]_D^{22}$ −29.8° (*c* 0.53 in chloroform); $\nu_{max.}$ (KBr) 3 420 (OH), 1 655, 1 235, and 1 070 (vinyl ether), and 765 and 705 cm^{-1} (aryl); *X*-ray powder diffraction data: 11.70vw, 9.40vw, 7.65vw, 6.13m, 5.71vw, 5.23m, 4.99m (2), 4.68m, 4.24s (1), 4.14w, 3.81m, and 3.66m (3) (Found: C, 67.05; H, 7.45. $C_{14}H_{18}O_4$ requires C, 67.2; H, 7.45%). Although Fraser-Reid and Radatus described [27] the preparation of (7) by an independent route, no constants were given.

Elution of the column with acetone gave a syrup (450 mg) containing the product having R_F 0.09 as the major component. It was rechromatographed on seven preparative t.l.c. plates (2 : 3 benzene–acetone) to give a slightly yellow syrup (360 mg, 20%) that was identified by n.m.r. spectroscopy (Table 1) as an anomeric mixture of 2-(2-hydroxy-

[27] B. Fraser-Reid and B. Radatus, *J. Amer. Chem. Soc.*, 1970, **92**, 6661.

ethoxy)ethyl 4,6-*O*-benzylidene-2,3-dideoxy-D-*erythro*-hexopyranosides [(8) and (9), respectively] in the ratio 7 : 3 in favour of the syrupy α-anomer (8). A small amount of the crystalline β-anomer (9) was isolated pure and was indistinguishable (m.p., optical rotation, and mass spectrometry) from a product described in the next section.

Wolff–Kishner Reaction with Methyl 4,6-O-*Benzylidene*-2-*deoxy*-α-D-erythro-*hexopyranosid*-3-*ulose* (10).—In a similar manner to the foregoing procedures, a mixture of the glycosidulose [13] (10) (4 g, 15.14 mmol) and hydrazine hydrate (99%; 8 ml, 164.6 mmol) in 2,2′-oxybis(ethanol) (50 ml) was heated for 1.5 h and, after addition of a solution of potassium hydroxide (8 g, 142.6 mmol) in 2,2′-oxybis(ethanol) (40 ml), for another 3 h until evolution of gas had ceased. Following addition of ammonium chloride (11 g) in water (250 ml), the mixture was extracted with dichloromethane (70, 50, and 50 ml), and the combined organic extracts were washed with water, dried ($MgSO_4$), and evaporated. The syrupy residue (2.47 g) was shown by t.l.c. (4 : 1 ether–light petroleum) to be a mixture of five major components, R_F 0.70, 0.61, 0.48, 0.29, and 0.08, which was fractionated by column chromatography on silica gel, first with the t.l.c. solvent and then with acetone as eluant.

The first compound eluted crystallized after evaporation to give 1,5-anhydro-4,6-*O*-benzylidene-2,3-dideoxy-D-*erythro*-hex-1-enitol (4) (70 mg, 2.1%), R_F 0.70, identical (m.p., optical rotation, and n.m.r. spectrum) with the corresponding product from the preceding experiment.

The second fraction, R_F 0.61, was found (by t.l.c.) to be contaminated with the next slower-moving component and therefore it was rechromatographed on four preparative t.l.c. plates to give methyl 4,6-*O*-benzylidene-2,3-dideoxy-α-D-*erythro*-hexopyranoside (11) (180 mg, 4.8%) indistinguishable from an authentic sample.[5] After recrystallization from hexane, compound (11) had m.p. 83—84°, $[\alpha]_D^{22}$ +117° (*c* 0.5 in chloroform); *X*-ray powder diffraction data: 11.94vw, 10.21vw, 8.11s (3), 5.55m, 4.33s (2), 4.09s (1), 3.74m, 3.58w, and 3.44m (lit.,[5] m.p. 82—84°, $[\alpha]_D$ +118 ± 1° in chloroform; lit.,[18] m.p. 82—83°, $[\alpha]_D$ +120.5 ± 2° in chloroform; lit.,[12] m.p. 83—85°, $[\alpha]_D$ +116.5° in chloroform).

As in the preceding experiment, the third component (R_F 0.48) absorbed u.v. light very strongly but did not char after spraying the t.l.c. plate with sulphuric acid and subsequently heating. Upon evaporation of the appropriate fractions, an impure yellow oil was obtained that could not be purified further and was therefore not characterized.

The component having R_F 0.29 crystallized on evaporation of the solution to give methyl 4,6-*O*-benzylidene-2-deoxy-α-D-*arabino*-hexopyranoside (12) (25 mg, 0.6%), m.p. 150—151° (from ether–light petroleum), $[\alpha]_D^{22}$ +99.2° (*c* 1 in chloroform), +98° (*c* 1 in acetone), and +83° (*c* 1.3 in ethanol); $\nu_{max.}$ (KBr) 3 400—3 250 (OH) and 740 and 695 cm^{-1} (aryl); *X*-ray powder diffraction data: 11.62s (3), 8.97w, 6.17s (2,2), 5.48m, 4.35s (2,2), 4.08vs (1), 3.72m, and 3.50s (lit.,[19] m.p. 151—152°, $[\alpha]_D$ +90° in acetone; lit.,[20] m.p. 149—150°, $[\alpha]_D$ +83.8° in ethanol).

The 3-acetate (13) was prepared from (12) by treatment with acetic anhydride–pyridine for 15 h at *ca.* 25 °C. Methanol was added with cooling, the mixture was concentrated, and pyridine and then toluene (two 10 ml portions each) were added to and evaporated from the residue. After recrystallization from ethanol, compound (13) had m.p. 130°, $[\alpha]_D^{21}$ +77° (*c* 1.7 in chloroform) {lit.,[20] m.p. 130—131° (subl.), $[\alpha]_D$ +79.1° in chloroform}; $\nu_{max.}$ (KBr) 1 725 (C=O) and 770 and 700 cm^{-1} (aryl); *X*-ray powder diffraction data: 14.36w, 10.10w, 9.16m (3), 6.53vw, 5.14s (1), 4.57m, 4.05s (2), 3.76m, 3.58vw, 3.26m, and 3.15m.

The last fraction, R_F 0.08, was obtained by elution with acetone. Evaporation gave a semi-crystalline residue (2 g) that was shown by t.l.c. (2 : 3 benzene–acetone) to be a mixture of two compounds, R_F 0.53 and 0.39. The two were readily separated by column chromatography on silica gel with 4 : 5 benzene–acetone as eluant.

The faster-moving component crystallized partially and was identified as an anomeric mixture of 2-(2-*hydroxyethoxy*)*ethyl* 4,6-O-*benzylidene*-2,3-*dideoxy*-D-erythro-*hexopyranosides* [(8) and (9)], in the ratio 10 : 3 (by n.m.r. spectroscopy) in favour of the β-anomer (see Table 1). The mixture (1 040 mg, 21.2%) was dissolved in warm ether (20 ml) and the resulting turbid mixture was filtered. Hexane (20 ml) was then added, and the crystals that formed were filtered off and dried to give the pure β-anomer (9) (recovery 520 mg); m.p. 99°, $[\alpha]_D^{22}$ −36° (*c* 1.31 in chloroform); $\nu_{max.}$ (KBr) 3 500—3 250 (OH) and 760 and 695 cm^{-1} (aryl); *X*-ray powder diffraction data: 10.16w, 8.30w, 5.82m, 5.26s (2), 4.70m (3,3), 4.47m (3,3), 4.27s (1), and 3.79w (Found: C, 62.75; H, 7.35. $C_{17}H_{24}O_6$ requires C, 62.95; H, 7.45%).

Evaporation of the mother liquor gave a syrup which contained mostly the α-anomer (8). However, compound (8) was not obtained free of (9) and therefore no further physical constants are given.

The slower-moving component crystallized when the appropriate fractions were combined and concentrated to give (2R,4S,5R)-5-*hydroxy*-2-*phenyl*-4-[*pyrazol*-3(5)-*yl*]-1,3-*dioxan* (14) (890 mg, 23.9%), m.p. 141—142° (from benzene), $[\alpha]_D^{21}$ −9.2° (*c* 1.37 in chloroform); $\nu_{max.}$ (KBr) 3 400—3 240 (OH, NH) and 750 and 695 cm^{-1} (aryl); *X*-ray powder diffraction data: 12.18m, 8.38vw, 7.49m, 6.21m, 5.88w, 5.08m (3,3), 4.70w, 4.34m (3,3), 4.10m (2), and 3.92s (1) (Found: C, 63.7; H, 5.95; N, 11.45. $C_{13}H_{14}N_2O_3$ requires C, 63.4; H, 5.75; N, 11.4%).

Modified Procedure for the Preparation of the Pyrazole Derivative (14).—A mixture of the ketone (10) (15 g, 56.8 mmol) and hydrazine hydrate (99%; 15 ml, 309 mmol) in 2,2′-oxybis(ethanol) (200 ml) was heated for 1.5 h to 110 °C. Water and hydrazine were then evaporated from the mixture at 20 mmHg while the temperature was maintained at *ca.* 135 °C. The mixture was then * cooled in an ice–water bath and a potassium hydroxide (10 g, 178 mmol) in 2,2′-oxybis(ethanol) (50 ml) was added. After another period of heating (3 h at 110 °C), the mixture was poured into ice–water (300 ml) containing ammonium chloride (15 g), and the aqueous phase was extracted with dichloromethane (3 × 100 ml). The combined extracts were washed with water, dried ($MgSO_4$), and evaporated to give a semi-crystalline residue (11.5 g). Recrystallization from benzene gave a first crop of (14) (3.5 g, 25%), m.p. 140—141°. T.l.c. of the mother liquor showed numerous components besides (14), some of them corresponding to products isolated in the preceding experiment, but none of them in appreciable yield. Evaporation and column chromatography of the residue as already described afforded another crop of (14) (5.5 g, 39.4%).

Acetylation of the Pyrazole Derivative (14).—Compound

* T.l.c. (2 : 3 benzene–acetone) of a sample showed that considerable amounts of (14) had already been formed at this stage.

(14) (500 mg, 2.03 mmol) was treated with 1 : 2 acetic anhydride–pyridine (9 ml) for 18 h at *ca.* 25 °C. Methanol (5 ml) was added with cooling and, after 1 h, the mixture was concentrated. Pyridine and then toluene (each 2 × 10 ml) were added to and evaporated from the residue. The resultant syrup was dissolved in ether (20 ml), and the solution decolourized with activated charcoal and evaporated. The product was kept over phosphorus pentaoxide, potassium hydroxide, and paraffin in a desiccator for several days to give a colourless glass, identified as a 4 : 1 mixture (by n.m.r.; see Table 1 and Figure 2) of (2*R*,4*S*,5*R*)-5-acetoxy-4-(1-acetylpyrazol-3-yl)- and -(1-acetylpyrazol-5-yl)-2-phenyl-1,3-dioxan [(15) and (16), respectively] (670 mg, 99%), migrating as a single narrow zone in t.l.c. (R_F 0.57; 4 : 1 ether–light petroleum ether); $[\alpha]_D^{22}$ −4.1° (*c* 1.7 in chloroform); $\nu_{max.}$ (film) 1 790—1 700 cm^{-1} (OAc, NAc) (Found: C, 61.55; H, 5.8; N, 8.25. Calc. for $C_{17}H_{18}N_2O_5$: C, 61.8; H, 5.5; N, 8.5%).

Benzoylation of the Pyrazole Derivative (14).—To the derivative (14) (500 mg, 2.03 mmol) in pyridine (6 ml) was added benzoyl chloride (1.2 ml, 10.4 mmol). After 18 h at *ca.* 25 °C, water (110 μl, 6 mmol) was added.[28] After 1 h more, the mixture was diluted with dichloromethane (60 ml), washed thrice with aqueous sodium hydrogen carbonate, dried ($MgSO_4$), and evaporated. Toluene (2 × 10 ml) was added to and evaporated from the residue. Processing as in the preceding experiment afforded a colourless glass consisting of (2R,4S,5R)-5-*benzoyloxy*-4-(1-*benzoylpyrazol*-3-*yl*)-2-*phenyl*-1,3-*dioxan* (17) (910 mg, 98.6%) as the only isomer present, according to its n.m.r. spectrum (Table 1); R_F 0.67 (t.l.c.; 4 : 1 ether–light petroleum); $[\alpha]_D^{22}$ −62.6° (*c* 2.34 in chloroform); $\nu_{max.}$ (film) 1 750—1 670 (OBz, NBz) and 1 595 and 1 580 cm^{-1} (monosubstituted phenyl) (Found: C, 71.35; H, 5.25; N, 5.85. $C_{27}H_{22}N_2O_5$ requires C, 71.35; H, 4.9; N, 6.15%).

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[28] A stoicheiometric amount of water is mandatory; see H. G. Fletcher, jun., *Methods Carbohydrate Chem.*, 1963, **2**, 234.