Synthesis of Homo-*C*-nucleosides using Pyrimidinylmethylenephosphoranes

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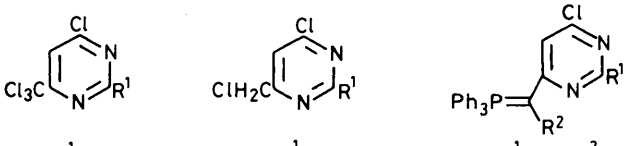
The direct synthesis of homo-*C*-nucleosides from pyrimidinylmethylenephosphoranes and protected D-ribose is described. Reaction of 2,3-*O*-isopropylidene-5-*O*-trityl-D-ribose (9) with pyrimidinylmethylenephosphoranes (5)—(8) gave protected α- and β-homo-*C*-nucleosides (14)—(21) and pyrimidinylolefins (10)—(13) in good yields. The ratio of α- and β-nucleosides depended on the properties of phosphoranes. Treatment of compounds (10)—(13) with base such as triethylamine or 1,8-diazabicyclo-[5.4.0]undec-7-ene (DBU) gave ring-closed products (14)—(21) in quantitative yields. Deprotection of compounds (14)—(21) with hydrochloric acid in either dioxan–water or methanol gave homo-*C*-nucleosides (22)—(32).

Previously, we have reported that reaction of 6-trichloromethylpyrimidines (1) and (2) with triphenylphosphine gives phosphoranes such as pyrimidin-6-ylchloromethylenetriphenylphosphoranes (7) and (8), which undergo a Wittig reaction with aldehydes to give pyrimidinylolefins.[1] Since such phosphoranes can be easily obtained by our reported procedure, we have continued our studies. The present paper reports the reaction of the phosphoranes (5)—(8) with 2,3-*O*-isopropylidene-5-*O*-trityl-D-ribofuranose (9) to afford the homo-*C*-nucleosides (14)—(21). Since Holy [2] reported the biological activity of homonucleotides, several papers concerning the synthesis of homo-*C*-nucleosides have been reported. For instance, Gensler *et al.*[3] reported the stereocontrolled synthesis of homo-*C*-nucleosides using a chiral bicyclic lactone. Such stereoselective syntheses have been also reported by Noyori *et al.*[4–6] 4-D-Ribofuranosyl-3-oxobutanoate was reported to serve as a precursor for the synthesis of homo-*C*-nucleosides.[7] On the other hand, a stable ylide such as methoxycarbonylmethylenetriphenylphosphorane reacted with the protected ribose (9) to give a *C*-glycoside.[8] We have applied this reaction to the synthesis of homo-*C*-nucleosides. Following the procedure reported previously,[1] the phosphoranes (7) and (8) were prepared by the reaction of 6-trichloromethylpyrimidines (1) and (2) and two molar equivalents of triphenylphosphine. The phosphoranes (5) and (6) were prepared by the reaction of triphenylphosphine with chloromethylpyrimidines (3) and (4) obtained from the phosphoranes (7) and (8), followed by treatment with alkali.

When a solution of the protected D-ribose (9) and the phosphorane (5) in acetonitrile was heated under reflux, a viscous oil was obtained the purification of which by silica-gel column chromatography gave the homo-*C*-nucleosides (14) and (15) and the olefins *Z*-(10) and *E*-(10) in yields of 64, 14, 6, and 7%, respectively. The configurations at the anomeric position of compounds (14) and (15) were determined by ^{13}C n.m.r. spectroscopy. Namely, in the ^{13}C n.m.r. spectrum of compound (14), signals due to two methyl carbons of the isopropylidene group are observed at δ 25.66 and 27.53, within the range strongly indicative of the β configuration (25.5 ± 0.2 and 27.5 ± 0.2), whereas those of compound (15) are observed at δ 25.01 and 26.30, clearly in the α range (24.9 ± 0.3 and 26.3 ± 0.2).[8] The configurations of compounds *Z*-(10) and *E*-(10) were elucidated from the coupling constants of the olefinic protons. The *J* value of 12 Hz is consistent with the coupling constant of the *Z*-isomer *Z*-(10), whereas the larger coupling constant of 16 Hz is ascribed to the signals of olefinic protons for the *E*-isomer, *E*-(10).



(1) R^1 = H
(2) R^1 = Me

(1) R^1 = H
(2) R^1 = Me

(5) R^1 = H, R^2 = H
(6) R^1 = Me, R^2 = H
(7) R^1 = H, R^2 = Cl
(8) R^1 = Me, R^2 = Cl

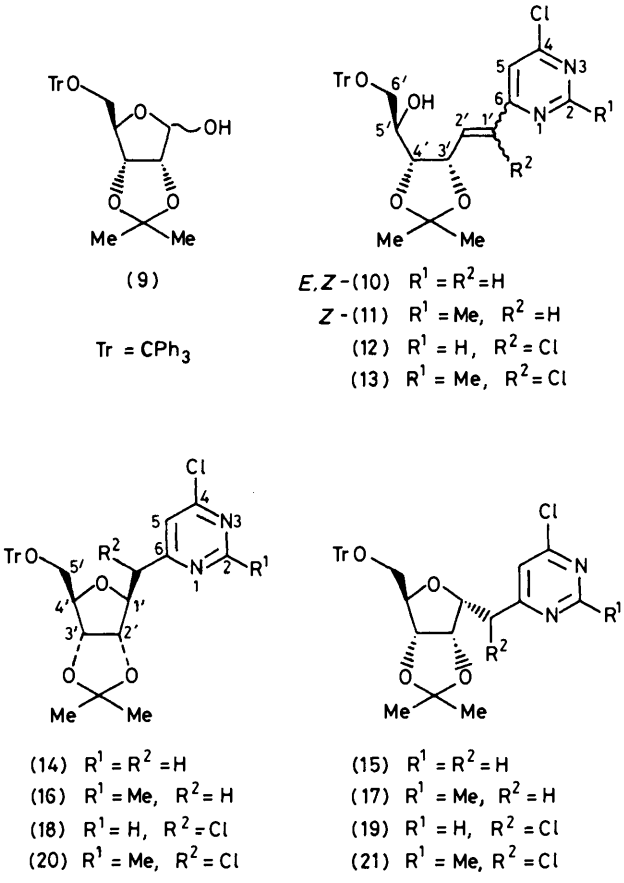
Scheme 1.

Similarly, the reaction of the phosphorane (6) with protected D-ribose afforded a 63% yield of the β-homo-*C*-nucleoside (16) together with a trace of the α-anomer and a 24% yield of the *Z*-olefin, *Z*-(11). The *E*-olefin was not detected in this reaction. The configurations of (16) and *Z*-(11) were also elucidated from the chemical shifts of the methyl carbons of the isopropylidene group and the coupling constants of the olefinic protons, respectively (see Table 3).

Next, the reaction of chloropyrimidinylmethylenephosphorane (7) with protected D-ribose (9) under similar conditions was carried out. Purification of the mixture obtained by silica-gel column chromatography, followed by high performance liquid chromatography (h.p.l.c.) gave the β-homo-*C*-nucleoside (18), the α-anomer (19), and the olefin (12) in yields of 29, 43, and 11%, respectively.

The configurations † of compounds (18) and (19) were determined by comparison of their ^1H n.m.r. spectra with those of the analogous compounds (20) and (21); that is, in the ^1H n.m.r. spectrum of compound (19) the signals due to methylene protons at the 5'-position are observed at δ 3.16 (1 H, dd, *J* 11, 4 Hz) and 3.34 (1 H, dd, *J* 11, 4 Hz) as a double doublet, respectively. On the other hand, a signal due to the methylene protons of compound (18) is observed at δ 3.32 (2 H, d, *J* 4 Hz) as a doublet. The configuration (*E* or *Z*) of the olefin (12) could not be determined. Similar reaction of the phosphorane (8) with protected D-ribose (9) afforded β-homo-*C*-nucleoside (20), the α-anomer (21), and the olefin (13) in yields of 29, 43, and 17%, respectively. The structure of compound (20) was confirmed by *X*-ray crystallography. The

† The configurations could not be determined by ^{13}C n.m.r. spectroscopy (see Table 2).



Scheme 2.

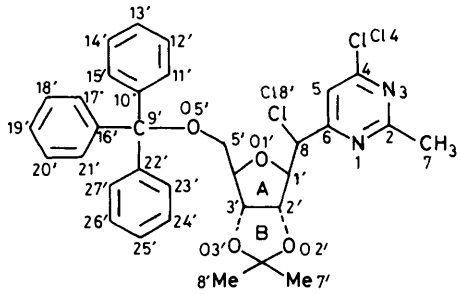
molecular shape and the atomic numbering are shown in the Figure.

The ^{1}H n.m.r. spectrum of compound (20) shows a doublet signal due to the methylene protons at δ 3.21 (2 H, d, *J* 4 Hz), whereas that of compound (21) presents two double doublets due to the methylene protons at δ 3.14 (1 H, dd, *J* 11, 4 Hz) and 3.34 (1 H, dd, *J* 11, 3 Hz). The configuration of the olefin (13) could not be determined. The ^{1}H n.m.r. and ^{13}C n.m.r. spectral data for the olefins (10)—(13) and the homo-*C*-nucleosides (14)—(21) are summarized in Tables 1—3.

Results for ring closure of the olefins (10)—(13) to the homo-*C*-nucleosides (14)—(21) in the presence of basic catalysts are summarized in Table 4. Thus, compound *Z*-(10) when treated with triethylamine in acetonitrile for 10 h afforded the β-homo-*C*-nucleoside (14) in quantitative yield. In the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) the reaction was complete within 10 min to afford compound (14) as the sole product. On the other hand, the *E*-form, *E*-(10), under similar conditions, was transformed to a mixture of the α- and β-homo-*C*-nucleosides (14) and (15).

Similar treatment of compound *Z*-(11) gave a mixture of α- and β-homo-*C*-nucleosides (16) and (17). However, compound *Z*-(11), after 2 months at room temperature in the absence of solvent and catalyst, was converted into β-homo-*C*-nucleoside (16) in quantitative yield. The 1-chloro-olefin (12) and (13), on treatment with triethylamine in acetonitrile, was converted into the α,β-homo-*C*-nucleosides (18) and (19) and α,β-(20) and (21), respectively. The α : β ratios are shown in Table 4.

Epimerization of the homo-*C*-nucleosides (14)—(21) was absent in the presence of triethylamine or DBU. Moffatt *et al.*[8] investigated the ring closure of 4,5,7-tri-*O*-benzyl-2,3-dideoxy-D-*ribo*-hept-2-enonate, prepared by the reaction of 2,3,5-tri-*O*-benzyl-D-ribofuranose with methoxycarbonylmethylene-triphenylphosphorane, to furanose *C*-glycoside, and reported that the *Z*-form gave only the β-glycoside whereas the *E*-form



(20)

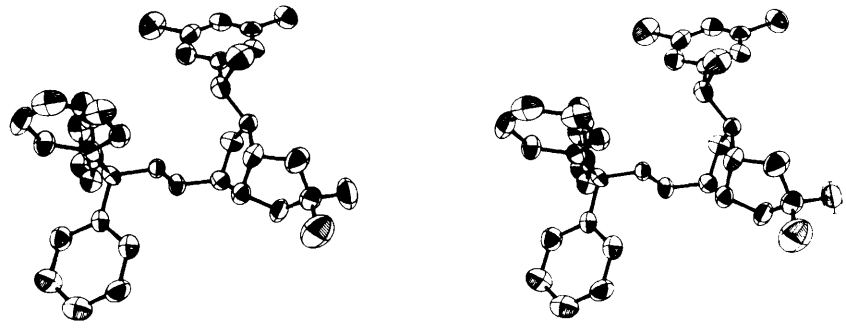


Figure. Stereoscopic view of (20). For the sake of clarity, hydrogenatoms have been omitted.

Table 1. ^{1}H N.m.r. spectra of pyrimidinylolefins (10)—(13) [a]

Compound	1′-H	2′-H	3′-H	4′-H	5′-H	6′-H	>CMe$_2$	Others
(*E*)-(10)	6.64 (1 H, dd, $J_{1',2}$ 16 and $J_{1',3'}$ 2)	7.3 (1 H, m)	4.95 (1 H, m)	4.29 (1 H, dd, $J_{3',4'}$ 6 and $J_{4',5'}$ 9)	3.66 (1 H, m)	3.37 (2 H, d, $J_{5',6'}$ 5)	1.40, 1.44 (each 3 H, s)	2.58 (1 H, d, *J* 5, OH), 7.3 (16 H, m, Tr and ring 5-H), 8.89 (1 H, d, *J* 1.5, ring 2-H)
(*Z*)-(10)	6.47 (1 H, d, $J_{1',2'}$ 12)	6.15 (1 H, dd, $J_{1',2'}$ 12 and $J_{2',3'}$ 8.5)	5.60 (1 H, dd, $J_{2',3'}$ 8.5 and $J_{3',4'}$ 6)	4.52 (1 H, dd, $J_{3',4'}$ 6 and $J_{4',5'}$ 8)	3.78 (1 H, m)	3.32 (2 H, m)	1.37, 1.43 (each 3 H, s)	3.78 (1 H, br, OH), 7.3 (16 H, m, Tr and ring 5-H), 8.96 (1 H, d, *J* 1.5, ring 2-H)
(*Z*)-(11)	6.42 (1 H, d, $J_{1',2'}$ 12)	6.07 (1 H, dd, $J_{1',2'}$ 12 and $J_{2',3}$ 8.5)	5.49 (1 H, dd, $J_{2',3'}$ 8.5 and $J_{3',4'}$ 6)	4.26 (1 H, dd, $J_{3',4'}$ 6 and $J_{4',5'}$ 8.5)	3.78 (1 H, m)	3.32 (2 H, m)	1.34, 1.42 (each 3 H, s)	2.70 (3 H, s, ring Me), 7.04 (1 H, s, ring 5-H), 7.3 (15 H, m, Tr)
(12)		7.3 (1 H, m)	5.30 (1 H, dd, $J_{2',3'}$ 9 and $J_{3',4'}$ 6)	4.34 (1 H, dd, $J_{3',4'}$ 6 and $J_{4',5'}$ 8)	3.79 (1 H, m)	3.30 (2 H, d, $J_{5',6'}$ 5)	1.39, 1.42 (each 3 H, s)	2.42 (1 H, d, *J* 5, OH), 7.3 (15 H, m, Tr), 7.67 (1 H, d, *J* 1.5, ring 5-H), 8.87 (1 H, d, *J* 1.5, ring 2-H)
(13)		7.3 (1 H, m)	5.29 (1 H, dd, $J_{2',3'}$ 9 and $J_{3',4'}$ 6)	4.35 (1 H, dd, $J_{3',4'}$ 6 and $J_{4',5'}$ 8)	3.78 (1 H, m)	3.31 (2 H, d, $J_{5',6'}$ 5)	1.39, 1.42 (each 3 H, s)	2.42 (1 H, d, *J* 5, OH), 2.68 (3 H, s, ring Me), 7.3 (16 H, m, Tr and ring 5-H)

[a] 100 MHz N.m.r. spectra in $CDCl_3$ solutions, δ downfield from internal $SiMe_4$, *J* in Hz.

Table 2. ^{1}H N.m.r. spectra of protected homo-*C*-nucleosides (14)—(21) [a]

Compound	Ring-CH_2 or CHCl: Ha	Ring-CH_2 or CHCl: Hb	1′,2′,3′, and 4′-H	5′-Ha	5′-Hb	>CMe$_2$	Others
(14)	3.16 (2 H, m)		4.1—4.6 (4 H, m)	3.16 (2 H, m)		1.36, 1.54 (each 3 H, s)	7.3 (16 H, m, Tr and ring 5-H), 8.92 (1 H, d, *J* 1.5, ring 2-H)
(15)	3.14 (2 H, m)		4.1—4.7 (4 H, m)	3.14 (2 H, m)		1.35, 1.54 (each 3 H, s)	7.3 (16 H, m, Tr and ring 5-H), 8.93 (1 H, d, *J* 1.5, ring 2-H)
(16)	2.94 (1 H, dd, $J_{Ha,Hb}$ 15 and $J_{Ha,1'}$ 8)	3.10 (1 H, dd, $J_{Ha,Hb}$ 15 and $J_{Hb,1'}$ 4)	4.1—4.6 (4 H, m)	3.14 (1 H, dd, $J_{5a',5b'}$ 10 and $J_{4',5a}$ 4)	3.33 (1 H, dd, $J_{5a',5b'}$ 10 and $J_{4',5b'}$ 4)	1.33, 1.52 (each 3 H, s)	2.67 (3 H, s, ring Me), 7.10 (1 H, s, ring (5-H), 7.3 (15, m, Tr)
(17)	3.15 (2 H, m)		4.2—4.7 (4 H, m)	3.15 (2 H, m)		1.35, 1.53 (each 3 H, s)	2.62 (3 H, s, ring Me), 7.3 (16 H, m, Tr and ring 5-H)
(18)	4.2—5.0 (1 H, m)		4.2—5.0 (4 H, m)	3.22 (2 H, d, $J_{4',5'}$ 4)		1.38, 1.55 (each 3 H, s)	7.3 (16 H, m, Tr and ring 5-H), 8.97 (1 H, d, *J* 1.5, ring 2-H)
(19)	5.13 (1 H, d, $J_{Ha,1'}$ 4)		4.1—4.9 (4 H, m)	3.16 (1 H, dd, $J_{5a',5b'}$ 11 and $J_{4',5a'}$ 4)	3.34 (1 H, dd, $J_{5a',5b'}$ 11 and $J_{4',5b'}$ 4)	1.32, 1.50 (each 3 H, s)	7.3 (15 H, m, Tr), 7.67 (1 H, d, *J* 1.5, ring 5-H), 8.93 (1 H, d, *J* 1.5, ring 2-H)
(20)	5.06 (1 H, d, $J_{Ha,1'}$ 4)		4.2—4.9 (4 H, m)	3.21 (2 H, d, $J_{4',5'}$ 6)		1.36, 1.54 (each 3 H, s)	2.68 (3 H, s, ring Me), 7.06 (1 H, s, ring 5-H), 7.3 (15 H, m, Tr)
(21)	5.07 (1 H, d, $J_{Ha,1'}$ 4)		4.1—4.9 (4 H, m)	3.14 (1 H, dd, $J_{5a',5b'}$ 11 and $J_{4',5a'}$ 4)	3.34 (1 H, dd, $J_{5a',5b'}$ 11 and $J_{4',5b'}$ 3)	1.32, 1.50 (each 3 H, s)	2.70 (3 H, s, ring Me), 7.06 (1 H, s, ring 5-H), 7.3 (15 H, m, Tr)

[a] See the corresponding footnote in Table 1.

Table 3. ^{13}C N.m.r. spectra of protected homo-*C*-nucleosides (14)—(21) [a]

Compound	Ring c	1′-, 2′-, 3′-, and 4′-C	5′-C	2-, 4-, and 6-C	5-C	Isopropylidene Me	Isopropylidene Me	Isopropylidene C
(14)	41.57	82.19, 82.78, 83.49, 84.36	64.05	158.52 (2-C), 161.16, 168.79	121.70	25.66	27.53	114.31
(15)	37.93	80.26, 82.02, 83.37	64.70	158.40 (2-C), 160.98, 169.79	121.65	25.01	26.30	112.37
(16)	41.74	82.19, 82.84, 83.49, 84.48	64.05	160.80, 168.62	118.24	25.66	27.48	114.25
(17)	38.04	80.55, 82.19, 83.49	64.88	160.87, 169.67	118.30	25.13	26.36	112.43
(18)	59.94	82.26, 83.28, 84.55, 86.63	64.13	158.67 (2-C), 161.93, 167.19	120.85	25.58	27.44	114.03
(19)	61.88	81.72, 82.13, 84.07, 85.48	63.64	158.22 (2-C), 162.15, 167.56	120.88	25.66	27.48	114.49
(20)	60.24	82.13, 83.19, 84.43, 86.48	64.11	161.51, 167.03, 169.14	117.30	25.54	27.36	113.95
(21)	62.12	81.61, 82.25, 84.07, 85.42	63.58	161.74, 167.44, 168.62	117.42	25.66	27.48	114.37

[a] 25 MHz N.m.r. spectra in $CDCl_3$ solutions, δ downfield from internal $SiMe_4$; ^{13}C–^{1}H attachments confirmed by off-resonance experiments.

Table 4. Ring closure of the pyrimidinylolefins (10)—(13) to protected homo-*C*-nucleosides (14)—(21) [a]

Olefin No.	Olefin R^1	Olefin R^2	Catalyst	Reaction time	Product No.	Product R^1	Product R^2	Ratio [b] β (Retention time, min)	Ratio [b] α (Retention time, min)
(*Z*)-(10)			Et_3N	10 hr	(14)			100 (7)	0 [c]
			DBU	10 min	(14)			100	0
	H	H				H	H		
(*E*)-(10)			Et_3N	20 hr	(14), (15)			18	82 (5)
			DBU	10 min	(14), (15)			42	58
(*Z*)-(11)	Me	H	Et_3N	50 hr	(16), (17)			4 (13)	96 [c] (6)
			DBU	10 min	(16), (17)	H	Me	14	86
			neat	2 months	(16)			100	0
(12)	H	Cl	Et_3N	10 min	(18), (19)	H	Cl	64 (14)	36 [d] (18)
(13)	Me	Cl	Et_3N	10 min	(20), (21)	Me	Cl	69 (14)	31 [d] (18)

[a] The ring closure proceeded in almost quantitative yield. [b] The ratio was determined by high performance liquid chromatography (h.p.l.c.) under the conditions as follows: Waters Associate instrument (M 6000 pump: U6K injector), detector: UV 254 nm. [c] Packing: μ Porasil, column: 3.9 mm × 30 cm, solvent: cyclohexane–dioxan (19 :1), flow rate: 2 ml/min. [d] Packing: μ Bondapak C_{18}, column: 3.9 mm × 30 cm, solvent: MeOH–H_2O (4 :1), flow rate: 2 ml/min.

afforded a mixture of α- and β-compounds. We found, however, that the *Z*-form was converted into both α- and β-compounds.

Next, the deprotection of the homo-*C*-nucleosides (14)—(21) was carried out. Compound (14) was treated with hydrochloric acid in aqueous dioxan for 30 min to give the crystalline homo-*C*-nucleoside (22) in 80% yield; a trace of the 4-hydroxy-derivative (23) was also obtained. When the treatment of compound (14) was prolonged (6 h), compounds (22) and (23) were obtained in 77 and 16% yields, respectively.

Similar treatment of compound (16) gave the homo-*C*-nucleoside (24) and the 4-hydroxy-derivative (25) in 80 and 14% yields, respectively. Use of methanol instead of aqueous dioxan as a solvent gave rise to the crystalline 4-methoxy-derivative (26) in 96% yield.

In contrast, the protected homo-*C*-nucleosides (18) and (19) (ratio = 2 : 3) when treated with hydrochloric acid in a aqueous dioxan gave compounds α,β-(27) and α,β-(28) in 30 and 40% yields, respectively.

Since the α- and β-homo-*C*-nucleosides of α,β-(27) or α,β-(28) were difficult to separate, the α : β ratio remained obscure. Similar treatment of a mixture of the protected homo-*C*-nucleosides (20) and (21) (ratio 2 : 3), followed by purification by silica-gel column chromatography gave the crystalline β-4-hydroxy-derivative (29) and its α-anomer (30) in 25 and 38% yields, respectively.

When methanol was used as a solvent, the β-4-methoxy-derivative (31) and its α-anomer (32) were obtained in 34 and 54% yields, respectively. Epimerization was not observed under the conditions used for the deprotection.

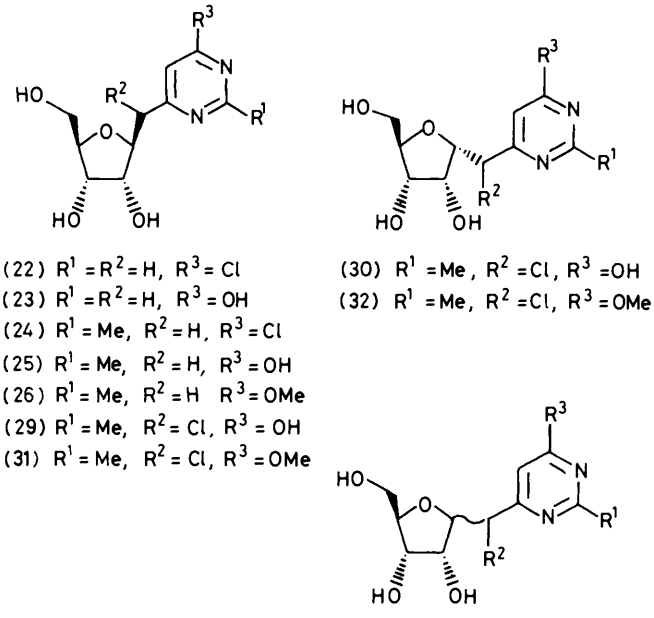
Experimental

M.p.s were determined on a Yanaco model MP. ^{1}H N.m.r. and ^{13}C n.m.r. spectra were recorded on a JEOL JNM FX-100 spectrometer. Mass spectra were taken with a Hitachi model M-52 and high resolution mass spectra were taken with a JMS OIS G-2. U.v. spectra were taken with a Beckman DB-G grating spectrophotometer. High performance liquid chromatography (h.p.l.c.) was carried out on a Waters Associate instrument (M 6000 pump; U6K injector) using a 254 nm u.v. detector. Wakogel (C-200) was employed for silica gel column chromatography.

4-Chloro-6-chloromethylpyrimidine (3).—A solution of [chloro(6-chloropyrimidin-4-yl)methylene]triphenylphosphorane (7) [1] (21.2 g, 50 mmol) and D-glucose (9 g, 50 mmol) in absolute methanol (150 ml) was refluxed for 1.5 h. The solvent was evaporated under reduced pressure, and hexane was added to the resulting residue. The crystals which separated (triphenylphosphine oxide) were filtered off. The filtrate was evaporated under reduced pressure to give an oil,

Table 5. Deprotection of protected homo-*C*-nucleosides (14)—(21) with 10% hydrochloric acid

Protected component				Products			
No.	g (mmol)	Solvent (ml)	Reaction time (h)	No.	Solvent for column Chloroform–methanol	Yield (g) [%]	M.p. (°C) [Solvent for recrystallization]
(14)	0.54 (1)	Dioxan–water (1 :1) (8)	0.5	(22)	15 :1	0.21 [80]	121 [Chloroform]
				(23)	6 :1	Trace	Foam
(16)	0.56 (1)	Dioxan–water (1 :1) (8)	0.5	(24)	15 :1	0.22 [80]	144 [Chloroform]
	0.56 (1)	Methanol (8)	6	(25)	6 :1	0.04 [14]	179 [Acetone–ethanol]
				(26)		0.26 [96]	148 [Chloroform]
(18) and (19) (2 :3)	2.90 (5)	Dioxan–water (2 :1) (80)	6	α,β-(27)	19 :1	0.44 [30]	Foam
				α,β-(28)	9 :1	0.56 [40]	Foam
(20) and (21) (2 :3)	3.00 (5)	Dioxan–water (1 :1) (40)	3	(29)	9 :1	0.36 [25]	167—168 [Acetone]
	3.00 (5)	Methanol (40)		(30)	9 :1	0.55 [38]	119—126
			3	(31)	19 :1	0.52 [34]	103—104 [Ether]
				(32)	19 :1	0.84 [55]	112—113 [Ether]



Scheme 3.

which was purified by distillation under reduced pressure to give the product (3) (4.3 g, 53%), b.p. 52 °C at 2 mmHg (Found: C, 36.6; H, 2.45; Cl, 43.25; N, 16.9. $C_5H_4Cl_2N_2$ requires C, 36.85; H, 2.45; Cl, 43.5; N, 17.2%); δ ($CDCl_3$) 4.60 (2 H, s, 6-CH_2Cl), 7.60 (1 H, s, 5-H), and 8.93 (1 H, s, 2-H).

4-Chloro-6-chloromethyl-2-methylpyrimidine (4).—Following the procedure described above, reaction of [chloro(6-chloro-2-methylpyrimidin-4-yl)methylene]triphenylphosphorane (8) [1] (21.8 g, 50 mmol) with D-glucose (9 g, 50 mmol) gave the product (4) as an oil (8.4 g, 95%), b.p. 58—59 °C at 3 mmHg (Found: C, 40.7; H, 3.5; Cl, 40.45; N, 16.1. $C_6H_6Cl_2N_2$ requires C, 40.7; H, 3.4; Cl, 40.05; N, 15.8%); δ ($CDCl_3$) 2.69 (3 H, s, 2-CH_3), 4.53 (2 H, s, 6-CH_2Cl), and 7.36 (1 H, s, 5-H).

(6-Chloropyrimidin-4-yl)methylenetriphenylphosphorane (5).—A solution of compound (3) (4.1 g, 25 mmol) and triphenylphosphine (6.6 g, 25 mmol) in dry benzene (150 ml) was refluxed for 70 h. The mixture was poured into water, and the aqueous layer was made alkaline with potassium carbonate. The crystals which separated were extracted with benzene. The benzene solution was dried (Na_2SO_4), and evaporated to give the product (5) as pale yellow prisms (5.6 g, 58%), m.p. 207—208 °C (decomp.) (Found: C, 71.3; H, 4.75; Cl, 9.1; N, 7.5. $C_{23}H_{18}ClN_2P$ requires C, 71.05; H, 4.65; Cl, 9.1; N, 7.2%); δ ($CDCl_3$) 6.43 (1 H, s, P=CH) and 7.3—7.8 (17 H, m, ring-H); *m/e* 388 (M^+) and 353 (M^+ − Cl).

(6-Chloro-2-methylpyrimidin-4-yl)methylenetriphenylphosphorane (6).—A solution of compound (4) (5.3 g, 30 mmol) and triphenylphosphine (7.9 g, 30 mmol) in dry benzene (180 ml) was refluxed for 50 h. Work-up as above gave compound (6) as pale yellow prisms (5.7 g, 47%), m.p. 166 °C (Found: C, 71.0; H, 4.9; Cl, 9.3; N, 6.7. $C_{24}H_{20}ClN_2P$ requires C, 71.55; H, 5.00; Cl, 8.8; N, 6.95%); δ ($CDCl_3$) 1.92 (3 H, s, CH_3), 6.25 (1 H, s, P=CH), and 7.3—7.8 (16 H, m, ring-H); *m/e* 402 (M^+) and 367 (M^+ − Cl).

Reaction of the Phosphorane (5) *with* 2,3-O-*Isopropylidene*-5-O-*trityl*-D-*ribofuranose* (9).—A solution of the phosphorane (5) (2.57 g, 6.6 mmol) and compound (9) [9] (2.60 g, 6 mmol) in acetonitrile (20 ml) was refluxed for 2 h. The solvent was evaporated under reduced pressure, and the residue was subjected to silica gel (250 g) column chromatography. Elution with hexane–ethyl acetate (9 : 1) gave 4-chloro-6-

Table 6. ^{1}H N.m.r. spectra of the homo-*C*-nucleosides (22)—(32) [a]

Compound	Ring-CH_2 or CHCl: Ha	Ring-CH_2 or CHCl: Hb	1′, 2′, 3′, and 4′-H	5′-Ha	5′-Hb	Others
(22)	2.88 (1 H, dd, $J_{Ha,Hb}$ 14 and $J_{Ha,1'}$ 8)	3.02 (1 H, dd, $J_{Ha,Hb}$ 14 and $J_{Hb,1'}$ 4)	3.7—4.1 (4 H, m)	3.42 (2 H, m)		4.7 (3 H, m, OH), 7.65 (1 H, s, ring 5-H), 9.95 (1 H, s, ring 2-H)
(23)	2.68 (2 H, m)		3.6—3.9 (4 H, m)	3.44 (2 H, m)		4.7 (3 H, br, OH), 6.21 (1 H, s, ring 5-H), 8.12 (1 H, s, ring 2-H), 11.8 (1 H, br, NH)
(24)	2.82 (1 H, dd, $J_{Ha,Hb}$ 14 and $J_{Ha,1'}$ 8)	3.00 (1 H, dd, $J_{Ha,Hb}$ 14 and $J_{Hb,1'}$ 4)	3.7—4.1 (4 H, m)	3.41 (2 H, m)		2.60 (3 H, s, ring Me), 4.8 (3 H, m, OH), 7.43 (1 H, s, ring 5-H)
(25)	2.60 (2 H, m)		3.6—4.0 (4 H, m)	3.43 (2 H, m)		2.27 (3 H, s, ring Me), 4.7 (3 H, m, OH), 6.04 (1 H, s, ring 5-H), 12.2 (1 H, br, NH)
(26)	2.71 (1 H, dd, $J_{Ha,Hb}$ 14 and $J_{Ha,1'}$ 8)	2.90 (1 H, dd, $J_{Ha,Hb}$ 14 and $J_{Hb,1'}$ 4)	3.6—4.0 (4 H, m)	3.44 (2 H, m)		2.49 (3 H, s, ring Me), 3.88 (3 H, s, OMe), 4.8 (3 H, m, OH), 6.63 (1 H, s, ring 5-H)
α,β-(27)	5.08 and 5.21 (1 H, 2d, $J_{Ha,1'}$ 8 and $J_{Ha,1'}$ 5)		3.7—4.3 (4 H, m)	3.40 (2 H, m)		4.2—5.2 (3 H, br, OH), 7.87 (1 H, s, ring 5-H), 9.09 (1 H, s, ring 2-H)
α,β-(28)	4.76 and 4.88 (1 H, 2d, $J_{Ha,1'}$ 8 and $J_{Ha,1'}$ 4)		3.6—4.1 (4 H, m)	3.42 (2 H, m)		4.0—5.2 (3 H, br, OH), 6.46 and 6.52 (1 H, 2s, ring 5-H), 8.21 (1 H, s, ring 2-H), 11.8 (1 H, br, NH)
(29)	4.67 (1 H, d, $J_{Ha,1'}$ 7)		3.7—4.3 (4 H, m)	3.46 (2 H, m)		2.34 (3 H, s, ring Me), 4.3—5.0 (3 H, br, OH), 6.32 (1 H, s, ring 5-H), 12.4 (1 H, br, NH)
(30)	4.79 (1 H, d, $J_{Ha,1'}$ 5)		3.7—4.1 (4 H, m)	3.34 (2 H, m)		2.30 (3 H, s, ring Me), 4.3—4.9 (3 H, br, OH), 6.32 (1 H, s, ring 5-H), 12.4 (1 H, br, NH)
(31)	4.94 (1 H, d, $J_{Ha,1'}$ 5.5)		4.0—4.3 (4 H, m)	3.64 (1 H, dd, $J_{5a',5b'}$ 12 and $J_{4',5a'}$ 3)	3.82 (1 H, dd, $J_{5a',5b'}$ 12 and $J_{4',5b'}$ 3)	2.60 (3 H, s, ring Me),[b] 3.98 (3 H, s, OMe), 3.0—4.0 (3 H, br, OH), 6.73 (1 H, s, ring 5-H)
(32)	4.98 (1 H, d, $J_{Ha,1'}$ 3)		3.9—4.3 (4 H, m)	3.67 (2 H, m)		2.55 (3 H, s, ring Me),[b] 3.93 (3 H, s, OMe), 3.5—4.3 (3 H, br, OH), 6.81 (1 H, s, ring 5-H)

[a] 100 MHz N.m.r. spectra in $(CD_3)_2SO$ solutions, δ downfield from internal 3-(trimethylsilyl)propanesulphonic acid sodium salt (DSS), *J* in Hz. [b] In $CDCl_3$ solutions ($SiMe_4$).

Table 7. ^{13}C N.m.r. spectra of homo-*C*-nucleosides (22)—(32)

Compound	Ring C	1′, 2′, 3′, and 4′-C	5′-C	2, 4, and 6-C	5-C	Solvent (Internal standard)
(22)	42.10	72.51, 76.21, 82.31, 86.24	63.23	159.22 (2′-C), 162.28, 171.31	123.17	CD_3OD ($SiMe_4$)
(23)	41.57	72.51, 76.21, 82.19, 86.07	63.29	150.47 (2′-C), 165.33, 165.97	114.78	CD_3OD ($SiMe_4$)
(24)	42.10	72.46, 76.21, 82.40, 86.20	63.15	162.03, 171.28	119.68	CD_3OD ($SiMe_4$)
(25)	40.45	71.78, 75.29, 81.62, 84.69	62.33	161.29, 164.90, 167.29	111.20	D_2O (*p*-dioxan)
(26)	*a*	70.98, 74.45, 80.79, 84.48	61.88	166.56, 168.08, 169.26	103.86	$(CD_3)_2SO$ [b]
α,β-(27)	61.18	72.21, 72.68, 73.62, 73.92	62.70	159.04 (2′-C), 159.34 (2′-C)	122.06	CD_3OD ($SiMe_4$)
	62.41	85.13, 86.19, 86.77	63.29	162.75, 162.98, 168.91, 169.43	122.35	
α,β-(28)	61.53	72.16, 72.74, 73.80, 73.98	62.94	150.59 (2′-C), 150.83 (2′-C)	115.01	CD_3OD ($SiMe_4$)
	63.11	84.90, 85.95, 86.54	63.35	164.32, 164.68, 164.92	115.60	
(29)	61.65	72.04, 74.09, 84.90, 86.89	62.82	161.04, 164.92, 165.39	112.19	CD_3OD ($SiMe_4$)
(30)	63.23	72.68, 73.74, 84.83, 85.95	63.23	160.80, 165.09, 165.44	111.78	CD_3OD ($SiMe_4$)
(31)	60.35	70.63, 73.15, 84.36, 85.54	61.35	165.44, 167.26, 170.66	103.08	$CDCl_3$ ($SiMe_4$)
(32)	62.15	71.51, 72.68, 83.90, 84.48	62.53	165.42, 167.61, 170.43	104.09	$CDCl_3$ ($SiMe_4$)

[a] Signal was overlapped with that of $(CD_3)_2SO$. [b] Carbon signal (39.50) of $(CD_3)_2SO$ was used as internal standard.

(2′,3′-*O*-isopropylidene-5′-*O*-trityl-α-D-ribofuranosyl)methylpyrimidine (15) as a foam (0.46 g, 14%), 4-chloro-6-(2′,3′-*O*-isopropylidene-5′-*O*-trityl-β-D-ribofuranosylmethyl)pyrimidine (14) as a foam (2.1 g, 64%), and *Z*-4-chloro-6-(1′,2′-dideoxy-5-hydroxy-3′,4′-*O*-isopropylidene-6′-*O*-trityl-D-*ribo*-hex-1′-enyl)pyrimidine *Z*-(10) as a foam (0.2 g, 6%). Subsequent elution with hexane–ethyl acetate (4 : 1) gave *E*-4-chloro-6-(1′,2′-dideoxy-5′-hydroxy-3′,4′-*O*-isopropylidene-6′-*O*-trityl-D-ribo-hex-1′-enyl)pyrimidine *E*-(10) as a foam (0.23 g, 7%). Compound (14) (Found: 70.8; H, 5.8; Cl, 6.50; N, 5.05. $C_{32}H_{31}ClN_2O_4$ requires C, 70.8; H, 5.75; Cl, 6.5; N, 5.15%); $\lambda_{max.}$ (MeOH) 250 nm (log ε 3.79). Compound (15) (Found: 71.7; H, 6.5; Cl, 6.1; N, 4.45. $C_{32}H_{31}ClN_2O_4 \cdot \frac{1}{2}C_6H_{14}$ requires C, 71.7; H, 6.55; Cl, 6.05; N, 4.8%). Compound (10Z) (Found: C, 70.8; H, 5.85; N, 5.0; Cl, 6.65. $C_{32}H_{31}ClN_2O_4$ requires C, 70.8; H, 5.75; Cl, 6.55; N, 5.15%); $\lambda_{max.}$ (MeOH) 276 nm (log ε 4.09). Compound (10E) (Found: C, 67.8; H, 5.9; Cl, 5.75; N, 4.75. $C_{32}H_{31}ClN_2O_4 \cdot 1\frac{1}{2}H_2O$ requires C, 67.4; H, 5.75; Cl, 6.2; N, 4.9%).

Reaction of the Phosphorane (6) *with the Protected* D-*Ribose* (9).—A solution of the phosphorane (6) (2.65 g, 6.6 mmol) and compound (9) (2.60 g, 6 mmol) in acetonitrile (20 ml) was refluxed for 2 h. The solvent was evaporated under reduced pressure, and the residue was subjected to silica gel (150 g) column chromatography. Elution with hexane–ethyl acetate (9 : 1) gave 4-chloro-6-(2′,3′-*O*-isopropylidene-5′-*O*-trityl-α-D-ribofuranosylmethyl)-2-methylpyrimidine (17) (trace) as prisms (from hexane), m.p. 114—115 °C (Found: C, 71.4; H, 6.15; Cl, 6.3; N, 4.9. $C_{33}H_{32}ClN_2O_4$ requires C, 71.15; H, 5.95; Cl, 6.35; N, 5.0%), 4-chloro-6-(2′,3′-*O*-isopropylidene-5′-*O*-trityl-β-D-ribofuranosylmethyl)-2-methylpyrimidine (16) (2.1 g, 63%) as prisms (from ether), m.p. 151—152 °C (Found: C, 71.1; H, 5.85; Cl, 6.5; N, 4.75. $C_{33}H_{32}ClN_2O_4$ requires C, 71.15; H, 5.95; Cl, 6.35; N, 5.0%), and *Z*-4-chloro-6-(1′,2′-dideoxy-5′-hydroxy-3′,4′-*O*-isopropylidene-6′-*O*-trityl-D-*ribo*-hex-1′-enyl)-2-methylpyrimidine *Z*-(11) (0.8 g, 24%) as a foam (Found: C, 70.65; H, 6.2; Cl, 6.0; N, 4.7. $C_{33}H_{32}ClN_2O_4$ requires C, 71.15; H, 5.95; Cl, 6.35; N, 5.0%).

Reaction of the Phosphorane (7) *with the Protected* D-*Ribose* (9).—A solution of the phosphorane (7) (4.7 g, 11 mmol) and compound (9) (4.3 g, 10 mmol) in acetonitrile (40 ml) was refluxed for 10 h. The solvent was evaporated under reduced pressure, and the residue was submitted to silica gel (200 g) column chromatography. Elution with hexane–ethyl acetate (19 : 1) gave 4-chloro-6-[2′,3′-*O*-isopropylidene-5′-*O*-trityl-α- and β-D-ribofuranosyl(chloro)methyl]pyrimidines (18) and (19) (ratio = 2 : 3) (4.15 g, 72%) as a foam. Subsequent elution with hexane–ethyl acetate (9 : 1) gave 4-chloro-6-(1′-chloro-1′,2′-dideoxy-5′-hydroxy-3′,4′-*O*-isopropylidene-6′-*O*-trityl-D-*ribo*-hex-1′-enyl)pyrimidine (12) (0.63 g, 11%) as a foam (Found: C, 64.95; H, 5.35; Cl, 11.85; N, 4.45. $C_{32}H_{30}Cl_2N_2O_4 \cdot H_2O$ requires C, 64.55; H, 5.4; Cl, 11.9; N. 4.7%); $\lambda_{max.}$ (MeOH) 277 nm (log ε 4.22). Compounds (18) and (19) were separated one from the other by high performance liquid chromatography (h.p.l.c.) (packing, μ-Bondapak C_{18}; column, 7.8 mm × 30 cm; solvent, MeOH–H_2O (4 : 1); flow rate, 4 ml/min; retention time, β = 42 min, α = 58 min). Compound (18) was a foam (Found: C, 66.35; H, 5.35; Cl, 12.1; N, 4.8. $C_{32}H_{30}Cl_2N_2O_4$ requires C, 66.55; H, 5.25; Cl, 12.3; N, 4.85%); $\lambda_{max.}$ (MeOH) 253 nm (log ε 3.80). Compound (19) was a foam (Found: C, 66.45; H, 5.2; Cl, 12.4; N, 4.65. $C_{32}H_{30}Cl_2N_2O_4$ requires C, 66.55; H, 5.25; Cl, 12.3; N, 4.85%).

Reaction of the Phosphorane (8) *with the Protected* D-*Ribose* (9).—A solution of the phosphorane (8) (9.6 g, 22 mmol) and compound (9) (8.6 g, 20 mmol) in acetonitrile (80 ml) was refluxed for 9 h. The solvent was evaporated under reduced pressure, and the residue was subjected to silica gel (400 g) column chromatography. Elution with hexane–ethyl acetate (19 : 1) gave 4-chloro-6-[2′,3′-*O*-isopropylidene-5′-*O*-trityl-α- and β-D-ribofuranosyl(chloro)methyl]-2-methylpyrimidines (20) and (21) (ratio 2 : 3) (8.52 g, 72%) as a foam. Subsequent elution with hexane–ethyl acetate (9 : 1) gave 4-chloro-6-(1′-chloro-1′,2′-dideoxy-5′-hydroxy-3′,4′-*O*-isopropylidene-6′-*O*-trityl-D-*ribo*-hex-1′-enyl)-2-methylpyrimidine (13) (2.0 g, 17%) as a foam (Found: C, 66.5; H, 5.7; Cl, 11.75; N, 4.4. $C_{33}H_{32}Cl_2N_2O_4$ requires C, 67.0; H, 5.45; Cl, 12.0; N, 4.75%). Compounds (20) and (21) were separated by h.p.l.c. [packing, μ-Bondapak C_{18}; column, 7.8 mm × 30 cm; solvent, MeOH–H_2O (4 : 1); flow rate, 4 ml/min; retention time, (21) = 42 min, (20) = 58 min]; compound (20) was obtained as colourless prisms (from methanol), m.p. 142 °C (Found: C, 67.15; H, 5.4; Cl, 12.05; N, 4.6. $C_{33}H_{32}Cl_2N_2O_4$ requires C, 67.0; H, 5.45; Cl, 12.0; N, 4.75%); compound (21),* had m.p. 132—134 °C (Found: C, 66.7; H, 5.35; Cl, 11.9; N, 4.45. $C_{33}H_{32}Cl_2N_2O_4$ requires C, 67.0; H, 5.45; Cl, 12.0; N, 4.75%).

General Procedure for Ring Closure of the Olefins (10)—(13) *to Homo-C-nucleosides* (14)—(21).—*Method* 1. A solution of the olefin (10)—(13) (0.2 mmol) and triethylamine (0.1 g, 1 mmol) or 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) (0.15 g, 1 mmol) in acetonitrile (1 ml) was set aside at room temperature. The solvent was evaporated under reduced pressure to give the homo-*C*-nucleoside (14)—(21) in a quantitative yield. The ratio of the α and β isomers was determined by h.p.l.c. under the conditions shown in Table 4.

Method 2. The olefin *Z*-(11) (0.28 g, 0.5 mmol) was kept at room temperature for 2 months to give compound (16) (0.28 g, 100%).

General Procedure for Deprotection of Protected Homo-C-nucleosides (14)—(21) *with* 10% *Hydrochloric Acid.*—A solution of the protected homo-*C*-nucleoside (14)—(21) (1 or 5 mmol) in a 10% solution of hydrochloric acid in dioxan–water (or methanol) (1 : 1) or (8—80 ml) was set aside at room temperature. The solvent was evaporated under reduced pressure, and the resulting residue was washed with ether to remove trityl alcohol. The ether-insoluble residue was dissolved in methanol–water (1 : 1) (10—50 ml), and the solution was treated with Amberlite IR-45 (OH^-). The resin was filtered off, and the filtrate was evaporated under reduced pressure to give a residue, which was subjected to silica gel (15—120 g) column chromatography. Elution with the appropriate solvent gave the homo-*C*-nucleoside (22)—(32); the results are summarized in Table 5. Compound (22) (Found: C, 46.05; H, 4.85; Cl, 13.4; N, 10.5. $C_{10}H_{13}ClN_2O_4$ requires C, 46.1; H, 5.05; Cl, 13.6; N, 10.75%); compound (23) (Found: $M^+ + 1$, 243.0969. $C_{10}H_{15}N_2O_5$ requires 243.0980); compound (24) (Found: C, 47,95; H, 5.5; Cl, 13.0; N, 10.1. $C_{11}H_{15}ClN_2O_4$ requires C, 48.1; H, 5.5; Cl, 12.9; N, 10.2%); compound (25) (Found: C, 49.85; H, 6.1; N, 10.35. $C_{11}H_{16}N_2O_5 \cdot \frac{1}{2}H_2O$ requires C, 49.8; H, 6.45; N, 10.55%); compound (26) (Found: C, 47.25; H, 5.85; N, 9.2. $C_{12}H_{18}N_2O_5 \cdot \frac{1}{3}CHCl_3$ requires C, 47.55; H, 5.95; N, 8.95%); compound (27 α, β) (Found: $M^+ + 1$, 295.0126. $C_{10}H_{13}ClClN_2O_4$ requires 295.0251. Found: $M^+ + 3$, 297.0217. $C_{10}H_{13}Cl^{37}Cl-N_2O_4$ requires 297.0222. Found: $M^+ + 5$, 299.0154. $C_{10}H_{13}-{}^{37}Cl^{37}ClN_2O_4$ requires 299.0112. Found: $M^+ - Cl$, 259.0472. $C_{10}H_{12}ClN_2O_4$ requires 259.0485. Found: $M^+ + 2 - Cl$,

* Since compound (21) was transformed into (20) during recrystallization from methanol the latter is, thermodynamically, the more stable.

Table 8. Fractional atomic co-ordinates ($\times 10^4$), with estimated standard deviations in parentheses

Atom	*x*	*y*	*z*
Cl(4)	214(2)	1 809(2)	8 836(4)
Cl(8)	3 470(2)	3 328(1)	6 866(3)
O(1′)	1 566(4)	3 203(3)	3 945(7)
O(2′)	3 191(5)	4 168(3)	3 256(9)
O(3′)	2 297(5)	3 934(3)	1 331(8)
O(5′)	2 472(4)	2 109(2)	2 917(7)
N(1)	1 527(5)	3 528(3)	7 615(8)
N(3)	455(5)	2 974(4)	8 961(9)
C(2)	859(6)	3 491(4)	8 578(10)
C(4)	738(6)	2 480(5)	8 364(12)
C(5)	1 413(6)	2 448(4)	7 394(12)
C(6)	1 803(5)	3 000(4)	7 068(10)
C(7)	511(7)	4 078(5)	9 202(14)
C(8)	2 531(6)	3 039(4)	5 934(11)
C(1′)	2 296(5)	3 459(4)	4 625(10)
C(2′)	2 988(6)	3 535(4)	3 420(12)
C(3′)	2 528(6)	3 356(4)	1 989(11)
C(4)	1 710(5)	3 031(4)	2 429(10)
C(5′)	1 720(5)	2 355(4)	2 237(10)
C(6′)	2 895(6)	4 371(4)	1 839(12)
C(7′)	3 631(9)	4 433(7)	769(18)
C(8′)	2 409(11)	4 960(5)	1 975(17)
C(9′)	2 592(5)	1 461(4)	2 659(9)
C(10′)	2 825(5)	1 338(4)	1 103(11)
C(11′)	2 724(6)	764(4)	356(12)
C(12′)	3 019(6)	654(5)	−1 092(12)
C(13′)	3 395(6)	1 113(5)	−1 924(12)
C(14′)	3 506(6)	1 678(4)	−1 287(11)
C(15′)	3 226(6)	1 788(4)	175(11)
C(16′)	3 407(5)	1 283(4)	3 534(10)
C(17′)	3 619(5)	680(4)	3 772(11)
C(18′)	4 366(6)	515(4)	4 503(12)
C(19′)	4 916(6)	968(5)	5 022(12)
C(20′)	4 704(6)	1 572(5)	4 790(11)
C(21′)	3 965(5)	1 735(4)	4 066(11)
C(22′)	1 811(5)	1 117(3)	3 267(11)
C(23′)	1 129(6)	964(4)	2 335(12)
C(24′)	381(6)	718(5)	2 930(14)
C(25′)	295(6)	644(5)	4 460(15)
C(26′)	975(7)	788(5)	5 388(13)
C(27′)	1 720(6)	1 027(4)	4 777(11)

261.0439. $C_{10}H_{12}{}^{37}ClN_2O_4$ requires 261.0455), compound (28α, β) (Found: $M^+ + 1$, 277.0557. $C_{10}H_{14}ClN_2O_5$ requires 277.0590. Found: $M^+ + 3$, 279.0547. $C_{10}H_{14}{}^{37}ClN_2O_5$ rcquires 279.0461. Found: $M^+ - Cl$, 241.0813. $C_{10}H_{14}N_2O_5$ requires 241.0824); compound (29) (Found: C, 45.35; H, 5.25; Cl, 11.95; N, 9.4. $C_{11}H_{15}ClO_5N_2$ requires C, 45.45; H, 5.2; Cl, 12.2; N, 9.65%), compound (30) (Found: C, 45.65; H, 5.25; Cl, 11.95; N, 9.6. $C_{11}H_{15}ClO_5N_2$ requires C, 45.45; H, 5.2; Cl, 12.2; N, 9.65%), compound (31) (Found: C, 47.55; H, 5.55; Cl, 11.75; N, 8.9. $C_{12}H_{17}ClN_2O_5$ requires C, 47.3; H, 5.6; Cl, 11.65; N, 9.2%); and compound (32) (Found: C, 47.5; H, 5.85; Cl, 11.45; N, 8.95. $C_{12}H_{17}ClN_2O_5$ requires C, 47.3; H, 5.6; Cl, 11.65; N, 9.2%).

X-Ray Crystal Determination of (20).—A crystal of dimensions 0.6 × 0.4 × 0.2 mm obtained from methanol, was used for the intensity measurements. Intensity data were obtained on a four-circle automatic diffractometer, equipped with graphite-monochromated Cu-K_α radiation, and using the θ.2θ scan technique (2θ < 127°). Of the 2 843 unique reflections, 2 040 were significant ($|F_o| > 2.5\ \sigma\ |F_o|$). Data were corrected for Lorentz and polarization effects but not for absorption.

Crystal data. $C_{33}H_{32}Cl_2N_2O_4$, $M = 591.5$. Orthorhombic, $a = 15.623$ (3), $b = 21.914$ (4), $c = 8.898$ (2) Å, $Z = 4$, $D_c = 1.245$ g/cm^3, space group $P2_12_12_1$.

The structure was solved by direct methods using MULTAN.[10] The positional and thermal parameters were refined by block diagonal least-squares methods. The positions of all hydrogen atoms were located from a difference Fourier synthesis. The final discrepancy index *R* is 0.070. The positional parameters for non-hydrogen atoms are listed in Table 8 and correspond to the absolute configuration. Thermal

Table 9. Bond lengths (Å) and angles (°), with estimated standard deviations in parentheses

Cl(4)–C(4)	1.735(11)	C(6′)–C(7′)	1.499(18)
Cl(8)–C(8)	1.800(9)	C(6′)–C(8′)	1.501(16)
O(1′)–C(1′)	1.408(10)	C(9′)–C(10′)	1.533(13)
O(1′)–C(4′)	1.419(11)	C(9′)–C(16′)	1.542(12)
O(2′)–C(2′)	1.432(11)	C(9′)–C(22′)	1.532(11)
O(2′)–C(6′)	1.415(13)	C(10′)–C(11′)	1.396(12)
O(3′)–C(3′)	1.440(11)	C(10′)–C(15′)	1.386(12)
O(3′)–C(6′)	1.414(12)	C(11′)–C(12′)	1.390(15)
O(5′)–C(5′)	1.427(10)	C(12′)–C(13′)	1.380(15)
O(5′)–C(9′)	1.450(9)	C(13′)–C(14′)	1.372(15)
N(1)–C(2)	1.352(12)	C(14′)–C(15′)	1.395(14)
N(1)–C(6)	1.327(11)	C(16′)–C(17′)	1.378(12)
N(3)–C(2)	1.341(13)	C(16′)–C(21′)	1.402(12)
N(3)–C(4)	1.284(13)	C(17′)–C(18′)	1.384(13)
C(2)–C(7)	1.503(15)	C(18′)–C(19′)	1.391(14)
C(4)–C(5)	1.364(14)	C(19′)–C(20′)	1.380(16)
C(5)–C(6)	1.385(13)	C(20′)–C(21′)	1.370(13)
C(6)–C(8)	1.523(13)	C(22′)–C(23′)	1.391(13)
C(8)–C(1′)	1.528(13)	C(22′)–C(27′)	1.366(13)
C(1′)–C(2′)	1.531(13)	C(23′)–C(24′)	1.392(14)
C(2′)–C(3′)	1.514(14)	C(24′)–C(25′)	1.378(18)
C(3′)–C(4′)	1.515(12)	C(25′)–C(26′)	1.382(15)
C(4′)–C(5′)	1.491(12)	C(26′)–C(27′)	1.387(14)

C(1′)–O(1′)–C(4′)	112.7(4)	O(2′)–C(6′)–O(3′)	106.7(5)
C(2′)–O(2′)–C(6′)	108.9(5)	O(3′)–C(6′)–C(7′)	111.4(9)
C(3′)–O(3′)–C(6′)	107.5(5)	O(3′)–C(6′)–C(8′)	105.9(5)
C(5′)–O(5′)–C(9′)	114.2(4)	C(7′)–C(6′)–C(8′)	111.2(6)
C(2)–N(1)–C(6)	115.5(4)	O(5′)–C(9′)–C(16′)	105.9(4)
C(2)–N(3)–C(4)	116.4(8)	O(5′)–C(9′)–C(22′)	108.8(4)
N(1)–C(2)–C(7)	117.5(5)	O(5′)–C(9′)C(10′)	110.7(5)
N(1)–C(2)–N(3)	125.1(7)	C(10′)–C(9′)–C(16′)	104.0(4)
N(3)–C(2)–C(7)	117.3(7)	C(10′)–C(9′)–C(22′)	116.1(5)
Cl(4)–C(4)–C(5)	118.3(4)	C(16′)–C(9′)–C(22′)	110.8(5)
Cl(4)–C(4)–N(3)	116.8(7)	C(9′)–C(10′)–C(15′)	119.8(6)
N(3)–C(4)–C(5)	124.9(7)	C(9′)–C(10′)–C(11′)	122.1(7)
C(4)–C(5)–C(6)	115.3(6)	C(11′)–C(10′)–C(15′)	117.8(10)
N(1)–C(6)–C(5)	122.7(8)	C(10′)–C(11′)–C(12′)	120.5(8)
N(1)–C(6)–C(8)	115.9(5)	C(11′)–C(12′)–C(13′)	120.8(7)
C(5)–C(6)–C(8)	121.2(6)	C(12′)–C(13′)–C(14′)	119.3(12)
C(6)–C(8)–C(1′)	111.1(4)	C(13′)–C(14′)–C(15′)	120.2(8)
Cl(8)–C(8)–C(1′)	109.6(3)	C(10′)–C(15′)–C(14′)	121.3(6)
Cl(8)–C(8)–C(6)	108.8(6)	C(9′)–C(16′)–C(17′)	121.2(5)
O(1′)–C(1′)–C(8)	106.4(4)	C(9′)–C(16′)–C(21′)	120.4(4)
O(1′)–C(1′)–C(2′)	108.3(7)	C(17′)–C(16′)–C(21′)	118.4(7)
C(8)–C(1′)–C(2′)	115.5(4)	C(16′)–C(17′)–C(18′)	121.8(6)
O(2′)–C(2′)–C(1′)	109.5(5)	C(17′)–C(18′)–C(19′)	119.3(5)
O(2′)–C(2′)–C(3′)	105.6(7)	C(18′)–C(19′)–C(20′)	119.1(8)
C(1′)–C(2′)–C(3′)	103.0(4)	C(19′)–C(20′)–C(21′)	121.5(7)
O(3′)–C(3′)–C(4′)	107.9(4)	C(16′)–C(21′)–C(20′)	119.9(4)
O(3′)–C(3′)–C(2′)	103.5(4)	C(9′)–C(22′)–C(23′)	121.2(10)
C(2′)–C(3′)–C(4′)	107.8(7)	C(9′)–C(22′)–C(27′)	120.1(7)
O(1′)–C(4′)–C(3′)	104.7(5)	C(23′)–C(22′)–C(27′)	118.1(6)
O(1′)–C(4′)–C(5′)	112.0(6)	C(22′)–C(23′)–C(24′)	120.7(13)
C(3′)–C(4′)–C(5′)	115.4(5)	C(23′)–C(24′)–C(25′)	120.2(10)
O(5′)–C(5′)–C(4′)	109.7(5)	C(24′)–C(25′)–C(26′)	119.2(8)
O(2′)–C(6′)–C(7′)	110.1(5)	C(25′)–C(26′)–C(27′)	119.8(13)
O(2′)–C(6′)–C(8′)	111.3(9)	C(22′)–C(27′)–C(26′)	121.9(9)

parameters for the non-hydrogen atoms, fractional co-ordinates and isotropic thermal parameters for hydrogen atoms, bond lengths involving hydrogen atoms, and observed and calculated structure factors are in a Supplementary Publication [Sup. No. 23390 (16 pages)].*

Crystal and Molecular Structure of (20).—The structure and the stereochemistry of (20) were confirmed by *X*-ray analysis; Figure 1 shows the molecular shape, while bond distances and angles are given in Table 9.

The two five-membered rings are *cis*-fused to each other, and close to envelope conformations, C(3′) (ring A) being 0.276 Å and O(3′) (ring B) 0.393 Å out of the least-squares planes formed by the other four atoms. The angle at the A/B ring junction is 61.5°. The O(2′), O(3′), C(8), and C(5′) atoms deviate by −1.091, −1.517, 1.224, and 1.414 Å, respectively, from the least-squares plane through the five atoms of ring A. The torsion angles O(1′)–C(4′)–C(5′)–O(4′) and C(3′)–C(4′)–C(5′)–O(4′) are −70.0 and 49.7°, respectively, corresponding to a *gauche-gauche* (−*g*,*g*) conformation about the C(4′)–C(5′) bond. Thus, the situation of the five-membered ring A is comparable to the most common conformation found in the ribose of nucleosides and nucleotides.[11] The conformation about the C(8)–C(1′) bond is staggered with torsion angles C(6)–C(8)–C(1′)–O(1′) and Cl(8)–C(8)–C(1′)–C(2′) of −60.2 and 59.2°, respectively. The hydrogen atoms on C(8) and C(1′) are *trans* to each other. The observed interatomic bond distances and angles between non-hydrogen atoms are in good agreement with the expected values. There are no particularly short intermolecular contacts, the shortest being O(1′) and C(14′) at 3.157 Å.

* For details of the Supplementary publications scheme, see Notice to Authors No. 7, *J. Chem. Soc., Perkin Trans 1*, 1981, Index issue.

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