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Synthesis and properties of 5,6-dichlorobenzimidazole 2′→5′- and 3′→5′-nucleotide dimers and trimers*,†

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ABSTRACT

5,6-Dichloro-1-β-D-ribofuranosylbenzimidazole (**2**), synthesised by the fusion method, was used for the synthesis of 2′→5′- and 3′→5′-linked di- and tri-meric oligonucleotides. The protecting groups used were *p*-methoxytrityl for HO-5′, *tert*-butyldimethylsilyl for HO-2′,3′, and 2,5-dichlorophenyl and 2-(4-nitrophenyl)ethyl for the phosphate group. The internucleotidic linkages were established by the phosphotriester approach to give the fully protected 2′→5′ dimers (**15**, **17**, and **18**) and trimers (**27** and **28**), as well as the 3′→5′ dimers (**22** and **23**) and trimers (**31** and **32**). Deprotection involved a sequence of steps to afford the corresponding free oligonucleotides **21**, **26**, **30**, and **33** isolated as the triethylammonium salts in good yields. The new compounds were characterised by elemental analysis and by u.v. and ^{1}H-n.m.r. spectroscopy.

INTRODUCTION

The beginning of antiviral research is associated with 5,6-dichloro-1-β-D-ribofuranosylbenzimidazole[2–7] (DRB), which inhibits partially the synthesis of hnRNA and, to an even larger extent, the production of mRNA. Furthermore, DRB also triggers the production of interferon in human fibroblasts[8] and thus stimulates antiviral activity indirectly. These results have initiated the syntheses of halo-substituted benzimidazole nucleosides[9–12], including modifications of the sugar moiety[13] as well as the formation of a 3′→5′-nucleotide dimer[14] that carried benzimidazole and a thymine residue as a nucleo base. Since one mode of the action of interferon[15,16] is the induction of the enzyme 2′-5′A synthetase that is responsible[17] for the formation of pppA2′p5′A2′p5′A, a low-molecular-weight inhibitor of cell-free protein synthesis[18,19], we decided to combine some of the structural features of the bioactive molecules in a new type of oligomer by synthesising the 2′→5′- and 3′→5′-linked oligonucleotide trimers from DRB.

SYNTHESES AND DISCUSSION

Since all the syntheses were based on 5,6-dichloro-1-β-D-ribofuranosylbenzimidazole (**2**), an effective synthesis of **2** was developed first. The "heavy-metal" procedure[20], used in the condensation of 5,6-dichlorobenzimidazole mercurichloride with

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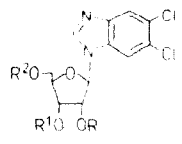
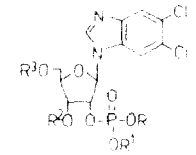
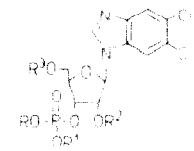
2,3,5-tri-*O*-benzoyl-D-ribofuranosyl chloride and which gave a yield of 68% of **2**, was substituted by the "fusion" method applied for the first time by Sato *et al.*[21] in the purine nucleoside series. Fusion of 5,6-dichlorobenzimidazole with 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose at 170–180° in the presence of a catalytic amount of *p*-toluenesulfonic acid for 1 h gave an α,β-mixture of the benzimidazole ribosides, from which **1** (51%) was isolated by chromatography. A simpler approach to DRB (**2**) was achieved when the above α,β-mixture was deacylated, since the resulting β-nucleoside crystallised (65%) from water. The yield was improved further when 1,2,3,5-tetra-*O*-acetyl-β-D-ribofuranose was used in the fusion reaction.

The next step was the *p*-methoxytritylation of **2** in pyridine to give **3** (81%) which, with *tert*-butyldimethylsilyl chloride under imidazole catalysis, afforded, as usual, a mixture of three compounds, which was fractionated by chromatography to give the 2'- (**4**), 3'- (**5**), and 2',3'-di-*O*-*tert*-butyldimethylsilyl (**6**) derivatives. The assignment of structures to **4** and **5** was based on ^{1}H-n.m.r. data. The spectra of solutions in $CDCl_3$ and $CDCl_3$–D_2O, respectively, defined the signals of *H*COH (H-2' in **5**, H-3' in **4**). Irradiation of H-1' only in **5** caused a sharpening of the multiplet for H-2 to a doublet. 5,6-Dichloro-1-(2,3-di-*O*-*tert*-butyldimethylsilyl-5-*O*-*p*-methoxytrityl-β-D-ribofuranosyl)benzimidazole (**6**) was detritylated with *p*-toluenesulfonic acid in CH_2Cl_2–MeOH to give **7** (82%). The conversion of **4** and **5** into the [2,5-dichlorophenyl 2-(4-nitrophenyl)ethyl]-phosphotriesters **8** and **12**, respectively, was based on known techniques that used 2,5-dichlorophenyl phosphorodichloridate and 1,2,4-triazole in the first step and then 2-(4-nitrophenyl)ethanol. Both **8** and **12** were converted into the *p*-nitrophenylethyl-phosphodiesters **10** and **13**, respectively, by the oximate method, which gave the triethylammonium salts in good yields. Treatment of **8** with acid gave 1-(3-*O*-*tert*-butyldimethylsilyl-β-D-ribofuranosyl)-5,6-dichlorobenzimidazole 2'-[2,5-dichlorophenyl] 2-(4-nitrophenyl)ethyl phosphate] (**9**, 82%).







	R	R^1	R^2
1	Bz	Bz	Bz
2	H	H	H
3	H	H	MeODTr
4	^{t}BuMe$_2$Si	H	MeODTr
5	H	^{t}BuMe$_2$Si	MeODTr
6	^{t}BuMe$_2$Si	^{t}BuMe$_2$Si	MeODTr
7	^{t}BuMe$_2$Si	^{t}BuMe$_2$Si	H

	R	R^1	R^2	R^3
8	2,5-$Cl_2C_6H_3$	Npe	^{t}BuMe$_2$Si	MeODTr
9	2,5-$Cl_2C_6H_3$	Npe	^{t}BuMe$_2$Si	H
10	$HNEt_3$	Npe	^{t}BuMe$_2$Si	MeODTr
11	2,5-$Cl_2C_6H_3$	$C_5H_5\overset{+}{N}H$	^{t}BuMe$_2$Si	MeODTr

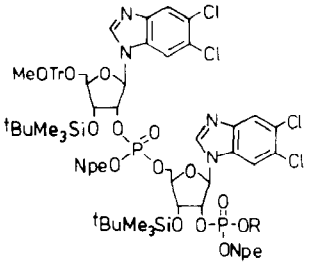
	R	R^1	R^2	R^3
12	2,5-$Cl_2C_6H_3$	Npe	^{t}BuMe$_2$Si	MeODTr
13	$HNEt_3$	Npe	^{t}BuMe$_2$Si	MeODTr
14	2,5-$Cl_2C_6H_3$	$C_5H_5\overset{+}{N}H$	^{t}BuMe$_2$Si	MeODTr

Npe = 2-(4-nitrophenyl)ethyl

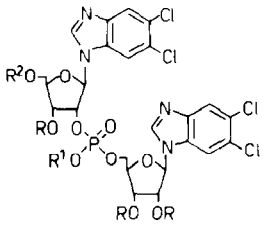
In the first chain-elongation reaction, the phosphodiester **10** was condensed with the phosphotriester **9**, using 2,4,6-tri-isopropylbenzenesulfonyl chloride and *N*-methyl-imidazole as catalysts, to give the dinucleoside diphosphotriester **15** (47%). Selective cleavage of the 2,5-dichlorophenoxy residue from the 2'-terminal phosphotriester

function by oximate then afforded **16**, which was condensed with 5,6-dichloro-1-(2,3-di-*O*-*tert*-butyldimethylsilyl-β-D-ribofuranosyl)benzimidazole (**7**) to give the fully protected trimer **27** (44%) by applying the phosphotriester methodology.

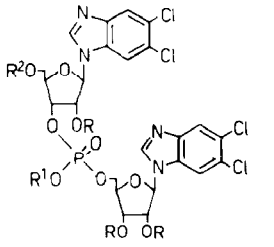
A second route to **27** involved building up the oligonucleotide chain from **7** towards the 5′-end. Condensation of **7** and **10** in the usual manner gave the dinucleoside monophosphotriester **17**, and detritylation to the HO-5′ component **19** and reaction with the phosphodiester **10** then yielded the trimer **27** (43%).



	R
15	2,5-$Cl_2C_6H_3$
16	$HNEt_3$



	R	R^1	R^2
17	$^tBuMe_2Si$	Npe	MeOTr
18	$^tBuMe_2Si$	2,5-$Cl_2C_6H_3$	MeOTr
19	$^tBuMe_2Si$	Npe	H
20	$^tBuMe_2Si$	2,5-$Cl_2C_6H_3$	H
21	H	$HNEt_3$	H

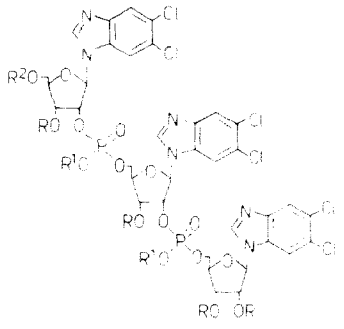


	R	R^1	R^2
22	$^tBuMe_2Si$	Npe	MeOTr
23	$^tBuMe_2Si$	2,5-$Cl_2C_6H_3$	MeOTr
24	$^tBuMe_2Si$	Npe	H
25	$^tBuMe_2Si$	2,5-$Cl_2C_6H_3$	H
26	H	$HNEt_3$	H

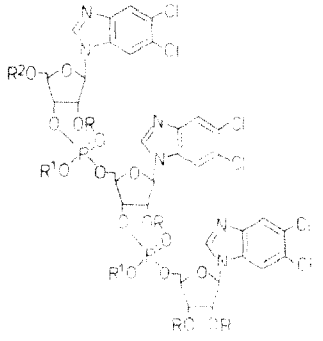
Since the yields of the trimer were not satisfactory, another approach was investigated. 1-(3-*O*-*tert*-Butyldimethylsilyl-5-*O*-*p*-methoxytrityl-β-D-ribofuranosyl)-5,6-dichlorobenzimidazole (**5**) was treated with 2,5-dichlorophenyl phosphorodichloridate–1,2,4-triazole at 0° to give, after hydrolytic work-up, the 2,5-dichlorophenyl-phosphodiester as its pyridinium salt (**11**). Crude **11** was condensed with **7**, using 2,4,6-tri-isopropylbenzenesulfonyl chloride and *N*-methylimidazole, to yield the dimer **18** (57%). Detritylation of **18** with *p*-toluenesulfonic acid in dichloromethane–methanol gave **20** (90%). Condensation of the HO-5′ component **20** with the phosphodiester **11** yielded the fully protected trinucleoside disphosphotriester **28** (55%).

In a series of analogous reactions, the di- and tri-meric 3′→5′-oligonucleotides were synthesised. 1-(2-*O*-*tert*-Butyldimethylsilyl-5-*O*-*p*-methoxytrityl-β-D-ribofuranosyl)-5,6-dichlorobenzimidazole (**4**) was either phosphorylated to give the [2,5-dichlorophenyl 2-(4-nitrophenyl)ethyl]-phosphotriester **12**, which was converted by oximate into the phosphodiester **13**, or the 2,5-dichlorophenyl-phosphodiester **14**, which was used as a crude product in the form of its pyridinium salt. The condensations of **13** and **14**, respectively, were mediated by 2,4,6-tri-isopropylbenzenesulfonyl chloride–*N*-methylimidazole in pyridine to give the fully protected dinucleoside-3′,5′-phosphotriesters **22** (50%) and **23** (62%), respectively. Detritrylation of **22** and **23** with acid gave **24** and **25**, respectively, which were condensed, as for **13** and **14**, to form the trimer **31** (64%) and the structural analogue **32** (68%), respectively. In general, the yields were

higher in the 3′,5′ than in the 2′,5′ series. The phosphotriester **28** was detritylated to give **29**, which demonstrated that the construction of longer oligonucleotides can be achieved by the same methodology.



	R	R¹	R²
27	^{t}BuMe$_2$Si	Npe	MeODTr
28	^{t}BuMe$_2$Si	2,5-Cl$_2$C$_6$H$_3$	MeODTr
29	^{t}BuMe$_2$Si	2,5-Cl$_2$C$_6$H$_3$	H
30	H	HNEt$_3$	H



	R	R¹	R²
31	^{t}BuMe$_2$Si	Npe	MeODTr
32	^{t}BuMe$_2$Si	2,5-Cl$_2$C$_6$H$_3$	MeODTr
33	H	HNEt$_3$	H

Finally, the removal of the various blocking groups was carried out by a sequence of reactions. Cleavage of the 2,5-dichlorophenyl groups by the oximate method[22] worked better if a 1:1:1 mixture of triethylamine–dioxane–water was used instead of 1,1,3,3-tetramethylguanidine in 1:1 dioxane–water. The resulting phosphodiesters were isolated by chromatography before removal of the silyl groups by tetrabutylammonium fluoride in tetrahydrofuran and the *p*-methoxytrityl group in aqueous 80% acetic acid. The 2′→5′- (**30**) and 3′→5′-trimers (**33**) were purified by chromatography on DEAE-Sephadex with a linear gradient of triethylammonium hydrogencarbonate buffer (pH 7.5). Taking into account the hypochromicity effects, the calculated yields of **30** and **33** were 64% and 57%, respectively. Deblocking of the dimers **18** and **23** was performed in an analogous manner and gave higher yields of **21** (86%) and **26** (88%).

The trimeric *p*-nitrophenylethyl phosphotriesters **27** and **31** could be deprotected in a one-pot procedure. Treatment with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), which cleaved the 2-(4-nitrophenyl)ethyl groups by β-elimination, was followed in sequence by tetrabutylammonium fluoride and aqueous acetic acid to remove the silyl and *p*-methoxytrityl groups. Purification on DEAE-Sephadex as above afforded **30** (92%) and **33** (75%).

The foregoing new compounds were characterised on the basis of elemental analysis and spectroscopic data. The u.v. spectra (Table 1) provided valuable information.

Each compound had λ_{max} at ~287 and ~297 nm characteristic of the 5,6-dichlorobenzimidazole chromophore. Introduction of the phosphodiester and phosphotriester moieties caused only an increase in the extinction coefficients. A comparison

TABLE I

U.v. data of 5,6-dichlorobenzimidazole nucleosides and nucleotides

Compound	λ_{max} *(nm)*						*log ε*					
1	215	228	[260][a]	277	285	296	4.34	4.04	[3.88]	3.70	3.72	3.65
2	213	254	[260]	[279]	287	296	4.20	3.75	[3.77]	[3.49]	3.66	3.67
3		252	260		285	294		3.89	3.85		3.73	3.66
4	[234]	253	[260]	281	287	297	[4.26]	3.88	[3.85]	3.65	3.70	3.70
5	[233]	253	[260]	281	287	297	[4.26]	3.87	[3.84]	3.65	3.69	3.68
6	[234]	254	[260]	281	286	296	[4.24]	3.86	[3.81]	3.63	3.69	3.69
7	214	255	260	[279]	286	295	4.66	3.77	3.77	[3.47]	3.62	3.64
8		[230]	261	[280]	[286]	297		[4.46]	4.17	[4.08]	[4.03]	3.89
9	211		259	[270]		[294]	4.74		4.16	[4.08]		[3.88]
10		[235]	263	[280]	[286]	297		[4.26]	4.15	[4.10]	[4.08]	3.97
12		[255]	262	[280]	[285]	297		[4.17]	4.21	[4.10]	[4.05]	3.92
13		[236]	263	[280]	286	296		[4.26]	4.18	[4.12]	4.10	4.00
15			262	[281]	[286]	297			4.46	[4.35]	[4.31]	4.17
16			261	[278]	[285]	296			4.37	[4.29]	[4.26]	4.17
17		[235]	261	[279]	286	297		[4.36]	4.32	[4.16]	4.15	4.06
18	[212]	253	[259]	[282]	287	297	[5.07]	4.11	[4.09]	[3.90]	3.95	3.94
19	213	[256]	261	278	286	296	4.97	[4.27]	4.29	4.13	4.15	4.07
20	213	256	259	[281]	287	297	4.96	4.07	4.07	[3.82]	3.93	3.93
22	[212]	[233]	261	[278]	286	297	[5.09]	[4.39]	4.33	[4.17]	4.17	4.09
23	[212]	255	[260]	[281]	288	297	[5.07]	4.12	[4.13]	[3.91]	3.97	3.97
24	214	[256]	261	279	286	296	4.99	[4.29]	4.31	4.13	4.15	4.08
25	214	256	260	[281]	288	297	4.99	4.09	4.09	[3.83]	3.94	3.94
27	[211]	[255]	261	[278]	286	297	[5.21]	[4.50]	4.52	[4.39]	4.37	4.26
28	[212]	253	[259]	[282]	287	297	[5.20]	4.25	[4.24]	[4.03]	4.08	4.08
29	212	254	[259]	[281]	287	297	5.12	4.22	[4.21]	[3.98]	4.07	4.08
31		[255]	260		285	295		[4.50]	4.56		4.40	4.28
32		254	[260]	[281]	287	297		4.35	[4.33]	[4.13]	4.17	4.13

[a] [ ] = Shoulder.

of the data for similarly substituted monomers, dimers, and trimers, such as **8**, **9**, **17**, **19**, and **27** or **8**, **9**, **18**, **20**, **28**, and **29**, reveals a high degree of additivity in the extinction coefficients, which indicates that there is little or no stacking in the fully protected compounds. The *p*-nitrophenylethyl phosphotriester series exhibit consistently higher extinction coefficients than the 2,5-dichlorophenyl analogues.

The ^{1}H-n.m.r. spectra (see Experimental) contained distinct signals for the various substituted nucleosides and for some of the monomeric nucleotides, whereas those of the dimers and trimers were complex due to the presence of mixtures of diastereomers that resulted from the chiral phosphotriester moieties. Information on the fine structure could not be deduced from these spectra, but the structures of the new compounds can be assigned on the basis of the unambiguous syntheses.

The purity of the fully deprotected DRB-dimers (**21** and **26**) and -trimers (**30** and **33**) was checked by reverse-phase h.p.l.c. on RP-18 with 0.1M ammonium acetate–acetonitrile (65:35). In general, the 2′→5′ oligomers had markedly shorter retention times than the 3′→5′ analogues. The 2′,5′-trimer **30** was even faster running than the 2′,5′-dimer **21**, which accords with the much stronger intramolecular stacking of **30** than in **21** and is also reflected in the respective hypochromicities of 37% and 21%.

EXPERIMENTAL

General. – T.l.c. was performed on Silica Gel F 1500 LS 254 and cellulose F 1440 (Schleicher & Schüll), preparative t.l.c. on Silica Gel 60 PF_{254} (plates 40 × 20 × 0.2 cm, Merck), and column chromatography on Silica Gel 60 (Merck, 0.063–0.2 mesh). P.c. was performed on sheets (58 × 60 cm) from Schleicher & Schüll. Medium pressure chromatography involved columns of type B (250 × 24 mm) or type C (400 × 39.5 mm) prepared[24] from silica gel LiChroPrep Si 60 (15–25 μ, Merck). The working pressure was 8–10 bar and detection was monitored by an Abimed UV detector. Ion-exchange chromatography was performed on DEAE Sephadex A-25 (Pharmacia). H.p.l.c. involved an SP 8000 B chromatograph (Spectra Physics), a LiChrosorb RP-18 column (Merck), a working pressure of 100 bar, and a mobile phase of 0.1M NH_4OAc–MeCN (65:35). Melting points (Büchi apparatus) were not corrected. U.v.–visible spectra were obtained with Uvikon 820 (Kontron) and Lambda 5 instruments (Perkin–Elmer): λ_{max} in nm (log ε); absorbance (o.d.) at 260 nm. ^{1}H-N.m.r. spectra (internal Me_4Si) were obtained with a Bruker WM-250 spectrometer. Elemental analyses were carried out in the microanalytical laboratory of Konstanz University.

5,6-Dichloro-1-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)benzimidazole (**1**). – A mixture of 5,6-dichlorobenzimidazole[25] (1.87 g, 10 mmol), 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose (6.05 g, 12 mmol), and *p*-toluenesulfonic acid (10 mg) was heated at 170–180° for 1 h at 20 Torr. A solution of the cooled melt in $CHCl_3$ (50 mL) was extracted with H_2O (2 × 20 mL), dried (Na_2SO_4), and filtered, and the solvent was evaporated. Column chromatography (20 × 2 cm) of the residue with 1,2-dichloroethane (50 mL), then with 1,2-dichloroethane–ethyl acetate (9:1), gave colorless amorphous **1** (3.2 g, 51%). ^{1}H-N.m.r. data ($CDCl_3$): δ 8.18 (s, 1 H, H-2), 8.1–7.9 (m, 6 H,

aromatic H), 7.85 (s, 1 H, H-7), 7.78 (s, 1 H, H-4), 7.61–7.33 (m, 9 H, aromatic H), 6.30 (d, 1 H, H-1'), 5.95 (m, 2 H, H-2',3'), 4.88 (m, 1 H, H-4'), 4.75 (m, 2 H, H-5'a,5'b).

Anal. Calc. for $C_{33}H_{24}Cl_2N_2O_7$ (631.5): C, 62.77; H, 3.83; N, 4.43. Found: C, 62.66; H, 3.83; N, 4.18.

*5,6-Dichloro-1-β-*D*-ribofuranosylbenzimidazole*[9] (DRB, **2**). — A mixture of 5,6-dichlorobenzimidazole (1.86 g, 10 mmol) and either 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose (6.05 g, 12 mmol) or 1,2,3,5-tetra-*O*-acetyl-β-D-ribofuranose (3.8 g, 12 mmol) was melted and worked-up by the above procedure. The product, isolated by chromatography, was stirred with methanolic 0.4M sodium methoxide (50 mL) overnight. The solvent was evaporated and the solution of the residue in H_2O (50 mL) was neutralised with AcOH. The precipitate was collected and recrystallised from H_2O (750 mL), to give **2** (1.78 g, 56%), m.p. 218°; lit.[9] m.p. 214–217°. ^{1}H-N.m.r. data [$(CD_3)_2SO$]: δ 8.57 (s, 1 H, H-2), 8.22 (s, 1 H, H-7), 7.96 (s, 1 H, H-4), 5.88 (d, 1 H, H-1'), 5.49 (d, 1 H, HO-2'), 5.23 (d, 1 H, HO-5'), 5.19 (d, 1 H, HO-3'), 4.31 (m, 1 H, H-2'), 4.11 (m, 1 H, H-3'), 3.99 (d, 1 H, H-4'), 3.66 (m, 2 H, H-5'a,5'b).

*5,6-Dichloro-1-(5-*O*-p-methoxytrityl-β-*D*-ribofuranosyl)benzimidazole* (**3**). — Dry pyridine (50 mL) was evaporated from **2** (3.19 g, 10 mmol), then *p*-methoxytrityl chloride (3.71 g, 12 mmol) and dry pyridine (50 mL) were added. The mixture was stirred overnight at room temperature, diluted with $CHCl_3$ (50 mL), and extracted with phosphate buffer (pH 7, 100 mL). The aqueous layer was extracted with $CHCl_3$ (2 × 20 mL), the combined $CHCl_3$ layers were dried (Na_2SO_4), the solvent was evaporated, and toluene was evaporated twice from the residue. Column (9 × 6 cm) chromatography with dichloroethane (1 L) followed by $CHCl_3$ gave amorphous **3** (5.13 g, 87%). A part of this material was purified further by chromatography to give pure **3**. ^{1}H-N.m.r. data ($CDCl_3$): δ 7.77 (s, 1 H, H-2), 7.68 (s, 1 H, H-7), 7.48–7.18 (m, 13 H, aromatic H), 6.80 (d, 2 H, *o*-H of MeOPh), 5.72 (d, 1 H, H-1'), 4.62 (m, 1 H, H-2'), 4.49 (m, 1 H, H-3'), 4.30 (s, 1 H, H-4'), 3.74 (s, 3 H, OCH_3), 3.47 (m, 2 H, H-5'a,5'b).

Anal. Calc. for $C_{32}H_{28}Cl_2N_2O_5$ (591.5): C, 64.98; H, 4.77; N, 4.73. Found: C, 64.96; H, 5.13; N, 4.56.

*1-(2-*O*-tert-Butyldimethylsilyl- and 1-(3-*O*-tert-butyldimethylsilyl-5-*O*-p-methoxytrityl-β-*D*-ribofuranosyl)-5,6-dichlorobenzimidazole* (**4** *and* **5**) *and 5,6-dichloro-1-(2,3-di-*O*-tert-butyldimethylsilyl-5-*O*-p-methoxytrityl-β-*D*-ribofuranosyl)benzimidazole* (**6**). — Dry pyridine (35 mL) was evaporated from a mixture of **3** (3.7 g, 6.25 mmol) and imidazole (1.02 g, 15 mmol). The residue was dissolved in dry pyridine (27 mL), *tert*-butyldimethylsilyl chloride (1.13 g, 7.5 mmol) was added, and the solution was stirred in a sealed flask for 18 h at room temperature. The mixture was diluted with MeOH (12 mL), then stirred for 15 min, $CHCl_3$ (50 mL) was added, and the mixture was extracted with phosphate buffer (pH 7, 25 mL). The organic layer was dried (Na_2SO_4) and filtered, the solvent was evaporated, and toluene (20 mL) was evaporated twice from the residue. Column (9 × 6 cm) chromatography with toluene (600 mL) and then toluene–ethyl acetate (9:1) gave **6**, and then a mixture of **4** + **5**.

Evaporation of the solvent from the first fraction yielded amorphous **6** (0.46 g, 9%). ^{1}H-N.m.r. data ($CDCl_3$): δ 8.11 (s, 1 H, H-2), 7.89 (s, 1 H, H-7), 7.82 (s, 1 H, H-4), 7.48–7.21 (m, 12 H, aromatic H), 6.83 (d, 2 H, *o*-H of MeOPh), 5.80 (d, 1 H, H-1'), 4.48 (t, 1 H, H-2'), 4.14 (m, 2 H, H-3',4'), 3.78 (s, 3 H, OCH_3), 3.56 (m, 1 H, H-5'a), 3.40 (m, 1 H, H-5'b), 0.88 (s, 9 H, ^{t}Bu), 0.73 (s, 9 H, ^{t}Bu), 0.06–0.07, −0.13, −0.58 (4 s, 12 H, 4 $SiCH_3$).

Anal. Calc. for $C_{44}H_{70}Cl_2N_2O_5Si_2$ (820.0): C, 64.44; H, 6.88; N, 3.42. Found: C, 64.24; H, 6.72; N, 3.44.

The mixture **4** + **5** was fractionated by low-pressure chromatography (10.5 bar; flow rate, 18 mL/min) on special silica-gel columns[24] (12,000 theoretical plates), using hexane–$CHCl_3$ (2:1). The faster running component **4** was obtained as an amorphous solid (0.88 g, 20%). ^{1}H-N.m.r. data ($CDCl_3$): δ 8.10 (s, 1 H, H-2), 7.88 (s, 1 H, H-7), 7.40 (s, 1 H, H-4), 7.44–7.20 (m, 12 H, aromatic H), 6.81 (d, 2 H, *o*-H of MeOPh), 5.78 (d, 1 H, H-1'), 4.66 (t, 1 H, H-2'), 4.28 (m, 2 H, H-3',4'), 3.78 (s, 3 H, OCH_3), 3.53 (m, 1 H, H-5'a), 3.41 (m, 1 H, H-5'b), 0.8 (s, 9 H, ^{t}Bu), −0.12, −0.35 (2 s, 6 H, 2 $SiCH_3$).

Anal. Calc. for $C_{38}H_{42}Cl_2N_2O_5Si$ (705.8): C, 64.67; H, 5.99; N, 3.96. Found: C, 64.50; H, 5.75; N, 3.90.

The slower moving fraction afforded amorphous **5** (1.54 g, 35%). ^{1}H-N.m.r. data ($CDCl_3$): δ 8.16 (s, 1 H, H-2), 7.87 (s, 1 H, H-7), 7.74 (s, 1 H, H-4), 7.41–7.18 (m, 12 H, aromatic H), 6.78 (d, 2 H, *o*-H of MeOPh), 5.73 (d, 1 H, H-1'), 4.41–4.34 (m, 2 H, H-2',3'), 4.16 (m, 1 H, H-4'), 3.78 (s, 3 H, OCH_3), 3.52 (m, 1 H, H-5'a), 3.29 (m, 1 H, H-5'b), 0.88 (s, 9 H, ^{t}Bu), 0.06, −0.03 (2 s, 6 H, 2 $SiCH_3$).

Anal. Calc. for $C_{38}H_{42}Cl_2N_2O_5Si$ (705.8): C, 64.67; H, 5.99; N, 3.96. Found: C, 64.46; H, 5.99; N, 3.89.

*5,6-Dichloro-1-(2,3-di-*O*-tert-butyldimethylsilyl-β-*D*-ribofuranosyl)benzimidazole* (**7**). – Compound **6** (0.565 g, 0.7 mmol) was stirred with 1% *p*-toluenesulfonic acid in CH_2Cl_2–MeOH (35 mL, 4:1) at room temperature for 1 h. The mixture was diluted with $CHCl_3$ (75 mL), extracted with phosphate buffer (pH 7, 2 × 75 mL), dried (Na_2SO_4), and filtered, and the solvent was evaporated. Column (14 × 3 cm) chromatography of the residue with dichloroethane (600 mL) followed by $CHCl_3$ (1 L) gave amorphous **7** (0.31 g, 82%). ^{1}H-N.m.r. data ($CDCl_3$): δ 8.38 (s, 1 H, H-2), 7.87 (s, 1 H, H-7), 7.80 (s, 1 H, H-4), 5.82 (d, 1 H, H-1'), 4.49 (m, 1 H, H-2'), 4.30 (m, 1 H, H-3'), 4.15 (s, 1 H, H-4'), 4.02 (m, 1 H, H-5'a), 3.88 (m, 1 H, H-5'b), 0.94, 0.85 (2 s, 18 H, 2 ^{t}Bu), 0.11 (s, 6 H, 2 $SiCH_3$), −0.11 (s, 3 H, $SiCH_3$), −0.52 (s, 3 H, $SiCH_3$).

Anal. Calc. for $C_{24}H_{40}Cl_2N_2O_4Si_2$ (547.7): C, 52.63; H, 7.36; N, 5.11. Found: C, 52.73; H, 7.53; N, 5.03.

*1-(3-*O*-tert-Butyldimethylsilyl-5-*O*-p-methoxytrityl-β-*D*-ribofuranosyl)-5,6-dichlorobenzimidazole 2'-[2,5-dichlorophenyl 2-(4-nitrophenyl)ethyl phosphate]* (**8**). – A solution of 1,2,4-triazole (0.22 g, 3.2 mmol) and 2,5-dichlorophenyl phosphorodichloridate (0.42 g, 1.5 mmol) in dry pyridine (4 mL) was stirred at room temperature for 10 min, then cooled to 0°, and a cold solution of **5** (0.705 g, 1 mmol) in dry pyridine (5 mL) was added dropwise with stirring. Stirring was continued for 30 min at 0° and 2-(4-nitrophenyl)ethanol (0.5 g, 3 mmol) was added. The mixture was stirred at room

temperature for 4 h, diluted with $CHCl_3$ (100 mL), and extracted with phosphate buffer (pH 7, 2 × 100 mL). The aqueous layer was treated with $CHCl_3$ (2 × 100 mL), the combined organic phases were dried (Na_2SO_4), the solvent was evaporated, and toluene was evaporated twice from the residue. Column (20 × 4 cm) chromatography with toluene (500 mL), toluene–ethyl acetate 9:1 (300 mL), and toluene–ethyl acetate (4:1) gave amorphous **8** (0.762 g, 71%). ^{1}H-N.m.r. data ($CDCl_3$): δ 8.22 and 8.15 (2 s, 1 H, H-2, diastereomers), 8.03 (d, 2 H, *o*-H of NO_2Ph), 7.80 (s, 1 H, H-7), 7.65 (s, 1 H, H-4), 7.43–6.95 (m, 34 H, aromatic H), 6.80 (d, 2 H, *o*-H of MeOPh), 6.12 and 6.04 (2 d, 1 H, H-1′), 5.19 (m, 1 H, H-2′), 4.53 (m, 1 H, H-3′), 4.30 (m, 1 H, H-4′), 4.19 (m, 2 H, CH_2), 3.75 (s, 3 H, OCH_3), 3.54 (m, 1 H, H-5′a), 3.33 (m, 1 H, H-5′b), 2.88 (m, 2 H, CH_2), 0.84 and 0.79 (2 s, 9 H, ^{t}Bu), 0.04, −0.01, −0.04, −0.06 (4 s, 6 H, 2 $SiCH_3$).

Anal. Calc. for $C_{52}H_{52}Cl_4N_3O_{10}PSi$ (1079.9): C, 57.83; H, 4.85; N, 3.89. Found: C, 57.84; H, 5.10; N, 3.69.

*1-(3-*O*-tert-Butyldimethylsilyl-β-*D*-ribofuranosyl)-5,6-dichlorobenzimidazole 2′-[2,5-dichlorophenyl 2-(4-nitrophenyl)ethyl phosphate]* (**9**). — A solution of **8** (0.324 g, 0.3 mmol) in 1% *p*-toluenesulfonic acid in CH_2Cl_2–MeOH (4:1, 12 mL) was kept at room temperature for 10 min, then diluted with $CHCl_3$ (75 mL), and extracted with phosphate buffer (pH 7, 2 × 75 mL). The organic layer was dried (Na_2SO_4) and the solvent was evaporated. Column (12 × 2 cm) chromatography of the residue with $CHCl_3$ gave amorphous **9** (0.192 g, 82%). ^{1}H-N.m.r. data ($CDCl_3$): δ 8.48 and 8.41 (2 s, 1 H, H-2, diastereomers), 8.03 (d, 2 H, *o*-H of NO_2Ph), 7.82 (s, 1 H, H-7), 7.77 (s, 1 H, H-4), 7.23–6.94 (m, 5 H, aromatic H), 6.11 and 6.08 (2 d, 1 H, H-1′), 5.22 (m, 1 H, H-2′), 4.62 (m, 1 H, H-3′), 4.30 (m, 1 H, H-4′), 4.20 (m, 2 H, CH_2), 4.05 (m, 1 H, H-5′a), 3.85 (m, 1 H, H-5′b), 2.85 (m, 2 H, CH_2), 0.91 and 0.88 (2 s, 9 H, ^{t}Bu), 0.09, 0.05 (2 s, 6 H, 2 $SiCH_3$).

Anal. Calc. for $C_{32}H_{36}Cl_4N_3O_9PSi$ (807.5): C, 47.60; H, 4.49; N, 5.20. Found: C, 47.83; H, 4.44; N, 5.21.

*1-(3-*O*-tert-Butyldimethylsilyl-5-*O*-p-methoxytrityl-β-*D*-ribofuranosyl)-5,6-dichlorobenzimidazole 2′-[2-(4-nitrophenyl)ethyl triethylammonium phosphate]* (**10**). — A solution of 4-nitrobenzaldoxime (0.5 g, 3 mmol) in dioxane (6 mL), H_2O (6 mL), and triethylamine (6 mL) was stirred for 20 min at room temperature. Compound **8** (0.324 g, 0.3 mmol) was added and stirring was continued for 1.5 h. The solvent was evaporated, and dry pyridine (15 mL) and toluene (3 × 20 mL) were evaporated from the residue. Column (10 × 2.5 cm) chromatography with $CHCl_3$ (200 mL), $CHCl_3$–MeOH (95:5, 100 mL), and $CHCl_3$–MeOH–Et_3N (95:5:5) gave amorphous **10** (0.257 g, 83%). ^{1}H-N.m.r. data ($CDCl_3$): δ 12.25 (bs, 1 H, NH), 8.34 (s, 1 H, H-2), 8.04 (s, 1 H, H-7), 8.00 (d, 2 H, *o*-H of NO_2Ph), 7.80 (s, 1 H, H-4), 7.44–7.14 (m, 14 H, aromatic H), 6.78 (d, 2 H, *o*-H of MeOPh), 6.14 (d, 1 H, H-1′), 4.88 (m, 1 H, H-2′), 4.44 (m, 1 H, H-3′), 4.23 (m, 1 H, H-4′), 3.90 (m, 2 H, CH_2), 3.76 (s, 3 H, OCH_3), 3.36 (m, 2 H, H-5′a), 2.92–2.77 (m, 8 H, CH_2 and 3 NCH_2), 1.17 (t, 9 H, 3 CH_3), 0.80 (s, 9 H, ^{t}Bu), 0.06, −0.03 (2 s, 6 H, 2 $SiCH_3$).

Anal. Calc. for $C_{52}H_{65}Cl_2N_4O_{10}PSi$ (1036.1): C, 60.28; H, 6.32; N, 5.40. Found: C, 59.55; H, 6.33; N, 5.53.

1-(3-O-tert-Butyldimethylsilyl-5-O-p-methoxytrityl-β-D-ribofuranosyl)-5,6-dichlorobenzimidazole 2'-[2,5-dichlorophenyl pyridinium phosphate] (**11**). — A solution of 1,2,4-triazole (0.352 g, 4.8 mmol) and 2,5-dichlorophenyl phosphorodichloridate (0.63 g, 2.25 mmol) in dry pyridine (3 mL) was stirred at room temperature for 10 min, then cooled to 0°, and a solution of **5** (0.53 g, 0.75 mmol) in dry pyridine (3 mL) was slowly added dropwise. Stirring was continued for 30 min, aqueous 90% pyridine (8 mL) was added, and the mixture was stirred for 15 min at 0°, diluted with $CHCl_3$ (75 mL), and extracted with phosphate buffer (pH 7). The aqueous layer was extracted twice with $CHCl_3$, the $CHCl_3$ phases were combined, extracted with phosphate buffer, dried (Na_2SO_4), and filtered, the solvent was evaporated, and dry pyridine (7 mL) was evaporated twice from the residue to give amorphous **11**, which was used in the following reactions.

1-(2-O-tert-Butyldimethylsilyl-5-O-p-methoxytrityl-β-D-ribofuranosyl)-5,6-dichlorobenzimidazole 3'-[2,5-dichlorophenyl 2-(4-nitrophenyl)ethyl phosphate] (**12**). — A solution of 1,2,4-triazole (0.573 g, 7.8 mmol) and 2,5-dichlorophenyl phosphorodichloridate (1.025 g, 3.66 mmol) in dry pyridine (10 mL) was stirred at room temperature for 10 min, then cooled to 0°, and a solution of **4** (1.723 g, 2.44 mmol) in dry pyridine (10 mL) was added dropwise followed, after stirring for 45 min, by 2-(4-nitrophenyl)ethanol (1.22 g, 7.32 mmol). The mixture was stirred at room temperature for 20 h, diluted with $CHCl_3$ (100 mL), and extracted with phosphate buffer (pH 7, 2 × 100 mL). The organic layer was dried (Na_2SO_4), the solvent was evaporated, and toluene (3 × 20 mL) was evaporated from the residue. Column (38 × 4 cm) chromatography with toluene–ethyl acetate (9:1) and rechromatography of a mixed fraction gave amorphous **12** (1.976 g, 75%). ^{1}H-N.m.r. data ($CDCl_3$): δ 8.08 (m, 3 H, H-2 and *o*-H of NO_2Ph), 7.88 (s, 1 H, H-7), 7.74 (s, 1 H, H-4'), 7.42–7.04 (m, 17 H, aromatic H), 6.80 (d, 2 H, *o*-H of MeOPh), 5.80 (m, 1 H, H-1'), 4.73 (m, 1 H, H-3'), 4.47–4.34 (m, 3 H, H-4' and CH_2), 3.74 (s, 3 H, OCH_3), 3.50 (m, 1 H, H-5'a), 3.36 (m, 1 H, H-5'b), 3.04 (m, 2 H, CH_2), 0.71, 0.67 (2 s, 9 H, ^{t}Bu), −0.11, −0.16, −0.40 (3 s, 6 H, 2 $SiCH_3$).

Anal. Calc. for $C_{55}H_{52}Cl_4N_3O_{10}PSi$ (1079.9): C, 57.83; H, 4.85; N, 3.89. Found: C, 57.41; H, 4.67; N, 3.86.

1-(2-O-tert-Butyldimethylsilyl-5-O-p-methoxytrityl-β-D-ribofuranosyl)-5,6-dichlorobenzimidazole 3'-[2-(4-nitrophenyl)ethyl triethylammonium phosphate] (**13**). — A mixture of dioxane (6 mL), H_2O (6 mL), triethylamine (6 mL), and 4-nitrobenzaldoxime (1.452 g, 8.8 mmol) was stirred at room temperature for 20 min. Compound **12** (0.95 g, 0.88 mmol) was added, stirring was continued for 6 h, the solvent was evaporated, and dry pyridine (2 × 30 mL) and toluene (2 × 20 mL) were evaporated from the residue. Column (20 × 3 cm) chromatography with $CHCl_3$ (400 mL) and $CHCl_3$–MeOH–Et_3N (90:5:5) gave amorphous **13** (0.738 g, 78%). ^{1}H-N.m.r. data ($CDCl_3$): δ 12.45 (bs, 1 H, NH), 8.10 (s, 1 H, H-2), 8.06 (d, 2 H, *o*-H of NO_2Ph), 7.84 (s, 1 H, H-7), 7.42–7.15 (m, 14 H, aromatic H), 6.76 (d, 2 H, *o*-H of MeOPh), 5.88 (d, 1 H, H-1'), 4.77 (m, 1 H, H-2'), 4.67 (m, 1 H, H-3'), 4.59 (m, 1 H, H-4'), 4.08 (m, 2 H, CH_2), 3.74 (s, 3 H, OCH_3), 3.42 (m, 2 H, H-5'a,5'b), 2.95 (m, 8 H, CH_2 and 3 NCH_2), 1.24 (t, 9 H, 3 CH_3), 0.72 (s, 9 H, ^{t}Bu), −0.05, −0.29 (2 s, 6 H, 2 $SiCH_3$).

Anal. Calc. for $C_{52}H_{65}Cl_2N_4O_{10}PSi{\cdot}2H_2O$ (1072.1): C, 58.25; H, 6.11; N, 5.22. Found: C, 57.78; H, 6.67; N, 5.48.

*1-(2-*O*-*tert*-Butyldimethylsilyl-5-*O*-*p*-methoxytrityl-β-*D*-ribofuranosyl)-5,6-dichlorobenzimidazole 3'-[2,5-dichlorphenyl pyridinium phosphate]* (**14**). — Using the procedure described above for the preparation of **11**, **4** (0.53 g, 0.75 mmol) was converted into crude **14**.

*1-(3-*O*-*tert*-Butyldimethylsilyl-5-*O*-*p*-methoxytrityl-β-*D*-ribofuranosyl)-5,6-dichlorobenzimidazolyl-(2'-{O^P-[2-(4-nitrophenyl)ethyl]}→5')-1-(3-*O*-*tert*-butyldimethylsilyl-β-*D*-ribofuranosyl)-5,6-dichlorobenzimidazole 2'-[2,5-dichlorophenyl 2-(4-nitrophenyl)ethyl phosphate]* (**15**). — Dry pyridine (2 × 2 mL) was evaporated from a mixture of **10** (0.208 g, 0.2 mmol) and **9** (0.14 g, 0.17 mmol). To a solution of the residue in dry pyridine (2 mL) were added *N*-methylimidazole (0.1 mL, 1.2 mmol) and 2,4,6-triisopropylbenzenesulfonyl chloride (0.12 g, 0.4 mmol). The mixture was stirred at room temperature for 24 h, diluted with $CHCl_3$ (50 mL), and extracted with phosphate buffer (pH 7). The aqueous layer was extracted with $CHCl_3$ (2 × 30 mL), the combined $CHCl_3$ extracts were dried (Na_2SO_4), the solvent was evaporated, and toluene was evaporated twice from the residue. Preparative t.l.c., with three irrigations with $CHCl_3$–MeOH (100:1), gave bands with R_F 0.25 and 0.35, which consisted of the two diastereomers. Extraction with $CHCl_3$–MeOH (7:1) gave amorphous **15** (0.14 g, 47%). ^{1}H-N.m.r. data ($CDCl_3$): δ 8.35–8.25 (m, 2 H, H-2), 8.10 and 7.90 (2 m, 4 H, *o*-H of NO_2Ph), 7.82–7.70 (m, 4 H, H-4,7), 7.63–6.92 (m, 19 H, aromatic H), 6.85–6.73 (m, 2 H, *o*-H of MeOPh), 6.18–5.92 (m, 2 H, H-1'), 5.18–4.88 (m, 2 H, H-2'), 4.52–4.43 (m, 2 H, H-3'), 4.41–4.28 (m, 2 H, H-4'), 4.14 (m, 4 H, 2 CH_2), 3.76 and 3.75 (2 s, 3 H, OCH_3), 3.55–3.20 (m, 4 H, H-5'a,5'b), 2.98–2.81 (m, 4 H, 2 CH_2), 0.89–0.76 (m, 18 H, ^{t}Bu), 0.1 to −0.12 (m, 12 H, 4 $SiCH_3$).

Anal. Calc. for $C_{78}H_{84}Cl_6N_6O_{18}P_2Si_2$ (1724.4): C, 54.33; H, 4.90; N, 4.87. Found: C, 53.87; H, 5.15; N, 4.87.

*1-(3-*O*-*tert*-Butyldimethylsilyl-5-*O*-*p*-methoxytrityl-β-*D*-ribofuranosyl)-5,6-dichlorobenzimidazolyl-(2'-{O^P-[2-(4-nitrophenyl)ethyl]}→5')-1-(3-*O*-*tert*-butyldimethylsilyl-β-*D*-ribofuranosyl)-5,6-dichlorobenzimidazole 2'-[2-(4-nitrophenyl)ethyl triethylammonium phosphate]* (**16**). — A mixture of dioxane (3 mL), H_2O (3 mL), triethylamine (3 mL), and 4-nitrobenzaldoxime (0.23 g, 1.38 mmol) was stirred for 20 min at room temperature. Compound **15** (0.21 g, 0.12 mmol) was added, stirring was continued for 2 h, the solvents were evaporated *in vacuo*, and dry pyridine (2 × 10 mL) and toluene (3 × 15 mL) were evaporated from the residue. Preparative t.l.c. (2 plates) with $CHCl_3$–MeOH–Et_3N (90:5:5), with extraction of the main band with the same solvent mixture (300 mL), gave amorphous **16** (0.165 g, 82%). ^{1}H-N.m.r. data ($CDCl_3$): δ 11.95 (bs, 1 H, NH), 8.34 and 8.24 (2 s, 2 H, H-2), 8.02 (d, 4 H, *o*-H of NO_2Ph), 7.95–7.72 (m, 4 H, H-4,7), 7.43–7.21 (m, 16 H, aromatic H), 6.77 (m, 2 H, *o*-H of MeOPh), 6.17–6.08 (m, 2 H, H-1'), 5.01 (m, 1 H, H-2'), 4.69 (m, 1 H, H-2'), 4.43 (m, 1 H, H-3'), 4.15 (m, 5 H, H-3' and OCH_2), 3.95 (m, 4 H, H-4',5'a), 3.74 (s, 3 H, OCH_3), 3.45 (m, 2 H, H-5'b), 2.99–2.82 (m, 10 H, 2 CH_2 and 3 NCH_2), 1.26 (pt, 9 H, 3 CH_3), 0.83–0.72 (m, 18 H, 2 ^{t}Bu), 0.03, −0.06, −0.15 (m, 12 H, 4 $SiCH_3$).

Anal. Calc. for $C_{78}H_{97}Cl_4N_5O_{18}P_2Si_2$ (1680.6): C, 55.74; H, 5.82; N, 5.83. Found: C, 55.26; H, 6.21; N, 5.91.

1-(3-O-tert-Butyldimethylsilyl-5-O-p-methoxytrityl-β-D-ribofuranosyl)-5,6-dichlorobenzimidazolyl-(2'-{O^P-[2-(4-nitrophenyl)ethyl]}→5')-5,6-dichloro-1-(2,3-di-O-tert-butyldimethylsilyl-β-D-ribofuranosyl)benzimidazole (**17**). — Dry pyridine (3 × 4 mL) was evaporated from a mixture of **10** (0.622 g, 0.6 mmol) and **7** (0.328 g, 0.6 mmol). To a solution of the residue in dry pyridine (4 mL) were added *N*-methylimidazole (0.28 mL, 3.6 mmol) and 2,4,6-tri-isopropylbenzenesulfonyl chloride (0.363 g, 1.2 mmol). The mixture was stirred at room temperature for 2 days, then treated with phosphate buffer (pH 7, 200 mL), and extracted with $CHCl_3$ (2 × 100 mL). The organic layers were again extracted with phosphate buffer (100 mL), dried (Na_2SO_4), and filtered, the solvent was evaporated, and toluene was evaporated thrice from the residue. Preparative t.l.c. (3 plates) with $CHCl_3$–MeOH (100:1) gave bands of the diastereomers with R_f 0.47 and 0.57, which were eluted with $CHCl_3$–MeOH (4:1) to give amorphous **17** (0.422 g, 48%). ^{1}H-N.m.r. data ($CDCl_3$): δ 8.20 (s, 1 H, H-2), 8.06 (d, 2 H, *o*-H of NO_2Ph), 8.02 (s, 1 H, H-2), 7.85 (s, 1 H, H-7), 7.81 (s, 2 H, H-4,7), 7.48 (s, 1 H, H-4), 7.37–7.19 (m, 14 H, aromatic H), 6.76 (d, 2 H, *o*-H of MeOPh), 6.13 (d, 1 H, H-1'), 5.69 (d, 1 H, H-1'), 5.04 (m, 1 H, H-2'), 4.43 (m, 1 H, H-2'), 4.25–3.89 (m, 6 H, H-3',4' and CH_2), 3.75 (s, 3 H, OCH_3), 3.48 (m, 4 H, H-5'a,5'b), 2.95 (t, 2 H, CH_2), 0.89–0.74 (m, 27 H, 3 ^{t}Bu), 0.04 to −0.15 (m, 18 H, 6 $SiCH_3$).

Anal. Calc. for $C_{70}H_{85}Cl_4N_5O_{13}PSi_2$ (1464.5): C, 57.41; H, 6.05; N, 4.78. Found: C, 57.46; H, 6.32; N, 4.80.

1-(3-O-tert-Butyldimethylsilyl-5-O-p-methoxytrityl-β-D-ribofuranosyl)-5,6-dichlorobenzimidazolyl-(2'-{O^P-(2,5-dichlorophenyl)}→5')-5,6-dichloro-1-(2,3-di-O-tert-butyldimethylsilyl-β-D-ribofuranosyl)benzimidazole (**18**). — Dry pyridine (2 × 6 mL) was evaporated from the residue of the preparation of **11** and **7** (0.35 g, 0.63 mmol). To a solution of the residue in dry pyridine (6.5 mL) were added *N*-methylimidazole (0.35 mL, 4.5 mmol) and 2,4,6-tri-isopropylbenzenesulfonyl chloride (0.454 g, 1.5 mmol). The mixture was stirred at room temperature for 20 h, then diluted with phosphate buffer (pH 7, 200 mL), and extracted with $CHCl_3$ (2 × 100 mL). The combined extracts were again treated with phosphate buffer, then dried (Na_2SO_4), the solvent was evaporated, and toluene (2 × 20 mL) was evaporated from the residue. Preparative t.l.c. (3 plates) with $CHCl_3$–MeOH (100:1) gave bands of the diastereomers with R_f 0.43 and 0.33, which were eluted with $CHCl_3$–MeOH (4:1) to give amorphous **18** (0.527 g, 87%). ^{1}H-N.m.r. data ($CDCl_3$): δ 8.22–8.01 (m, 2 H, H-2), 7.86–7.66 (m, 3 H, H-4,7,7), 7.50–7.05 (m, 14 H, H-4 and aromatic H), 6.79 (d, 2 H, *o*-H of MeOPh), 6.22 and 6.11 (2 d, 1 H, H-1'), 5.70 (m, 1 H, H-1'), 5.20 (m, 1 H, H-2'), 4.54 (m, 1 H, H-2'), 4.35–4.03 (m, 6 H, H-3',4',5'a), 3.78 and 3.75 (2 s, 3 H, OCH_3), 3.53–3.24 (m, 2 H, H-5'b), 0.98–0.71 (m, 27 H, 3 ^{t}Bu), 0.06 to −0.51 (m, 18 H, 6 $SiCH_3$).

Anal. Calc. for $C_{68}H_{83}Cl_6N_4O_{13}PSi_2$ (1460.4): C, 55.92; H, 5.73; N, 3.83. Found: C, 55.60; H, 5.70; N, 3.76.

1-(3-O-tert-Butyldimethylsilyl-β-D-ribofuranosyl)-5,6-dichlorobenzimidazolyl-(2'-{O^P-[2-(4-nitrophenyl)ethyl]}→5')-5,6-dichloro-1-(2,3-di-O-tert-butyldimethylsi-

*lyl-β-*D*-ribofuranosyl)benzimidazole* (**19**). — A 1% solution of *p*-toluenesulfonic acid in CH_2Cl_2–MeOH (4:1, 5 mL) was stirred with **17** (0.195 g, 0.133 mmol) at room temperature for 6 h. The mixture was diluted with $CHCl_3$ (50 mL), extracted with phosphate buffer (pH 7, 3 × 50 mL), dried (Na_2SO_4), and filtered, and the solvent was evaporated. Preparative t.l.c. of the residue with $CHCl_3$–MeOH (100:3, 2 developments) gave bands of the diastereomers with R_F 0.42 and 0.49. Elution with $CHCl_3$–MeOH (4:1) gave amorphous **19** (0.134 g, 84%). ^{1}H-N.m.r. data ($CDCl_3$): δ 8.41 and 8.29 (2 s, 1 H, H-2), 8.22 and 8.15 (2 s, 1 H, H-2), 8.08 and 7.98 (2 d, 2 H, *o*-H of NO_2Ph), 7.92–7.74 (m, 3 H, H-4,7,7), 7.52 (m, 1 H, H-4), 7.26 and 7.05 (2 d, 2 H, *o*-H of NO_2Ph), 6.06 (d, 1 H, H-1′), 5.74 (d, 1 H, H-1′), 5.07 and 4.94 (2 m, 1 H, H-2′), 4.57 (m, 1 H, H-2′), 4.24–3.70 (m, 13 H, H-3′,4′,5′a,5′b and HO-5′), 2.96 (2 t, 2 H, CH_2), 0.90–0.74 (m, 27 H, 3 ^{t}Bu), 0.09–0.05 (m, 12 H, $SiCH_3$), −0.14, −0.45 (2 s, 6 H, 2 $SiCH_3$).

Anal. Calc. for $C_{50}H_{72}Cl_4N_5O_{12}PSi_3$ (1192.2): C, 50.37; H, 6.09; N, 5.87. Found: C, 50.11; H, 6.16; N, 5.80.

*1-(3-*O*-*tert*-Butyldimethylsilyl-β-*D*-ribofuranosyl)-5,6-dichlorobenzimidazolyl-{2′-[O^P-(2,5-dichlorophenyl)]→5′}-5,6-dichloro-1-(2,3-di-*O*-tert-butyldimethylsilyl-β-*D*-ribofuranosyl)benzimidazole* (**20**). — Compound **18** (0.39 g, 0.27 mmol) was treated as in the preceding procedure. The crude product was subjected to column (12 × 2.5 cm) chromatography with $CHCl_3$ (500 mL) and then $CHCl_3$–MeOH (50:1), to give amorphous **20** (0.3 g, 95%). ^{1}H-N.m.r. data ($CDCl_3$): δ 8.31–8.17 (4 s, 2 H, H-2), 7.85–7.72 (s, 3 H, H-4,7,7), 7.51 (s, 1 H, H-4), 7.38–7.11 (m, 3 H, aromatic H), 6.14–6.06 (2 d, 1 H, H-1′), 5.71 (m, 1 H, H-1′), 5.32–5.12 (m, 1 H, H-2′), 4.72–4.62 (m, 1 H, H-2′), 4.28–3.78 (m, 8 H, H-3′,4′,5′a,5′b), 3.32 (bs, 1 H, HO-5′), 0.89–0.74 (m, 27 H, 3 ^{t}Bu), 0.10–0.08 (m, 12 H, 4 $SiCH_3$), −0.15, −0.47 (m, 6 H, 2 $SiCH_3$).

Anal. Calc. for $C_{48}H_{67}Cl_6N_4O_{10}PSi_3$ (1188.0): C, 48.52; H, 5.68; N, 4.71. Found: C, 48.60; H, 5.45; N, 4.60.

*1-(2-*O*-*tert*-Butyldimethylsilyl-5-*O*-p-methoxytrityl-β-*D*-ribofuranosyl-5,6-dichlorobenzimidazolyl-{2′-[O^P-2-(4-nitrophenyl)ethyl]→5′}-5,6-dichloro-1-(2,3-di-*O*-tert-butyldimethylsilyl-β-*D*-ribofuranosyl)benzimidazole* (**22**). — Dry pyridine (2 × 4 mL) was evaporated from a mixture of **13** (0.485 g, 0.468 mmol) and **7** (0.256 g, 0.468 mmol). To a solution of the residue in dry pyridine (4 mL) were added *N*-methylimidazole (0.22 mL, 2.8 mmol) and 2,4,6-tri-isopropylbenzenesulfonyl chloride (0.142 g, 0.47 mmol). The mixture was stirred at room temperature for 66 h, then treated with phosphate buffer (pH 7), and extracted with $CHCl_3$ (2 × 60 mL), the combined organic phases were dried (Na_2SO_4), the solvent was evaporated, and toluene was evaporated twice from the residue. Preparative t.l.c. (2 plates) with $CHCl_3$–MeOH (100:1, 2 developments) gave bands of the diastereomers with R_F 0.32 and 0.38, which were eluted with $CHCl_3$–MeOH (4:1) to give amorphous **22** (0.343 g, 50%). ^{1}H-N.m.r. data ($CDCl_3$): δ 8.15 and 8.12 (2 s, 2 H, H-2), 8.06 (d, 2 H, *o*-H of NO_2Ph), 7.88 and 7.86 (2 s, 2 H, H-7), 7.76 and 7.58 (2 s, 2 H, H-4), 7.41–7.18 (m, 14 H, aromatic H), 6.80 (d, 2 H, *o*-H of MeOPh), 5.83–5.74 (2 d, 2 H, H-1′), 4.86 (m, 1 H, H-2′), 4.70 (m, 1 H, H-2′), 4.45 (m, 1 H, H-3′), 4.33–4.03 (m, 7 H, H-3′,4′,5′a and CH_2), 3.75 (s, 3 H, OCH_3), 3.53–3.40 (m, 2 H, H-5′b), 3.04–2.86 (m, 2 H, CH_2), 0.96–0.69 (m, 27 H, 3 ^{t}Bu), 0.14–0.05 (m, 6 H, 2 $SiCH_3$), −0.08, −0.36 (2 s, 6 H, 2 $SiCH_3$).

Anal. Calc. for $C_{70}H_{88}Cl_4N_8O_{13}PSi_2$ (1464.5): C, 57.41; H, 6.05; N, 4.78. Found: C, 56.80; H, 6.30; N, 4.68.

1-(2-O-tert-Butyldimethylsilyl-5-O-p-methoxytrityl-β-D-ribofuranosyl)-5,6-dichlorobenzimidazolyl-{2'-[O^P-(2,5-dichlorophenyl)]→5'}-5,6-dichloro-1-(2,3-di-O-tert-butyldimethylsilyl-β-D-ribofuranosyl)benzimidazole (**23**). — Dry pyridine (2 × 6 mL) was evaporated from a mixture of crude **14** and **7** (0.411 g, 0.75 mmol). To a solution of the residue in dry pyridine (6 mL) were added tetrazole (0.315 g, 4.5 mmol) and 2,4,6-tri-isopropylbenzenesulfonyl chloride (0.454 g, 1.5 mmol). The mixture was stirred for 3 h at room temperature, then diluted with phosphate buffer (pH 7, 200 mL), and extracted with $CHCl_3$ (2 × 100 mL), the combined organic layers were dried (Na_2SO_4), the solvent was evaporated, and toluene (2 × 20 mL) was evaporated from the residue. Preparative t.l.c. (3 plates) with $CHCl_3$–MeOH (100:1) gave bands of the diastereomers with R_f 0.17 and 0.21. Elution with $CHCl_3$–MeOH (4:1, 300 mL) gave amorphous **23** (0.67 g, 62%). ^{1}H-N.m.r. data ($CDCl_3$): δ 8.23–8.08 (4 s, 2 H, H-2), 7.87 (m, 3 H, H-4,7,7), 7.53–7.07 (m, 16 H, H-4 and aromatic H), 5.94 (d, 1 H, H-1'), 5.78 (m, 1 H, H-1'), 5.11 (m, 1 H, H-2'), 4.78 (m, 1 H, H-2'), 4.53–4.15 (m, 6 H, H-3',4',5'a), 3.74 (s, 3 H, OCH_3), 3.57–3.26 (m, 2 H, H-5'b), 0.95–0.65 (m, 27 H, 3 ^{t}Bu), 0.13 to −0.54 (m, 18 H, 6 $SiCH_3$).

Anal. Calc. for $C_{68}H_{85}Cl_6N_4O_{11}PSi_2$ (1460.8): C, 55.92; H, 5.73; N, 3.83. Found: C, 55.66; H, 5.63; N, 3.84.

1-(2-O-tert-Butyldimethylsilyl-β-D-ribofuranosyl)-5,6-dichlorobenzimidazolyl-(2'-{O^P-[2-(4-nitrophenyl)ethyl]}→5')-5,6-dichloro-1-(2,3-di-O-tert-butyldimethylsilyl-β-D-ribofuranosyl)benzimidazole (**24**). — A solution of **22** (0.23 g, 0.157 mmol) in a 1% *p*-toluenesulfonic acid in CH_2Cl_2–MeOH (4:1, 5 mL) was stirred at room temperature for 6 h, diluted with $CHCl_3$ (50 mL), and then extracted with phosphate buffer (pH 7, 2 × 50 mL). The organic layer was dried (Na_2SO_4) and the solvent was evaporated. Preparative t.l.c. of the residue with $CHCl_3$–MeOH (50:1, 3 developments) and extraction of the main band with $CHCl_3$–MeOH (4:1) gave amorphous **24** (0.16 g, 85%). ^{1}H-N.m.r. data ($CDCl_3$): δ 8.28–8.23 (4 s, 2 H, H-2), 8.11 (m, 2 H, *o*-H of NO_2Ph), 7.85 (m, 3 H, H-4,7,7), 7.61 (s, 1 H, H-4), 7.34 (m, 2 H, *m*-H of NO_2Ph), 5.84–5.79 (m, 2 H, H-1'), 4.88 (m, 1 H, H-2'), 4.59 (m, 1 H, H-2'), 4.41–4.20 (m, 7 H, H-3',4', CH_2 and HO-5'), 3.90–3.77 (m, 4 H, H-5'a,5'b), 3.08 (t, 2 H, CH_2), 0.93–0.71 (m, 27 H, 3 ^{t}Bu), 0.11 to −0.44 (m, 18 H, 6 $SiCH_3$).

Anal. Calc. for $C_{50}H_{72}Cl_4N_5O_{12}PSi_2$ (1192.2): C, 50.37; H, 6.09; N, 5.87. Found: C, 50.10; H, 6.03; N, 5.71.

1-(2-O-tert-Butyldimethylsilyl-β-D-ribofuranosyl)-5,6-dichlorobenzimidazolyl-{2'-[O^P-(2,5-dichlorophenyl)]→5'}-5,6-dichloro-1-(2,3-di-O-tert-butyldimethylsilyl-β-D-ribofuranosyl)benzimidazole (**25**). — Compound **23** (0.23 g, 0.157 mmol) was treated as in the preceding procedure and gave, after the same work-up, amorphous **25** (0.164 g, 86%). ^{1}H-N.m.r. data ($CDCl_3$): δ 8.31–8.22 (s, 2 H, H-2), 7.92–7.85 (m, 2 H, H-7), 7.57–7.49 (m, 2 H, H-4), 7.39–7.09 (m, 3 H, aromatic H), 5.93 (d, 1 H, H-1'), 5.84–5.73 (m, 1 H, H-1'), 5.20 and 5.04 (2 m, 2 H, H-2'), 4.70–4.21 (m, 6 H, H-3',4',5'a,5'b), 4.03–3.86 (m, 2 H, H-5'a,5'b), 3.48 (bs, 1 H, HO-5'), 0.94–0.64 (m, 27 H, 3 ^{t}Bu), 0.12 to −0.49 (m, 18 H, 6 $SiCH_3$).

Anal. Calc. for $C_{48}H_{67}Cl_6N_4O_{10}PSi_3$ (1188.0): C, 48.52; H, 5.68; N, 4.71. Found: C, 48.34; H, 5.43; N, 4.62.

*1-(3-*O*-tert-Butyldimethylsilyl-5-*O*-p-methoxytrityl-β-*D*-ribofuranosyl)-5,6-dichlorobenzimidazolyl-(2'-{O^P-[2-(4-nitrophenyl)ethyl]}→5')-1-(3-*O*-tert-butyldimethylsilyl)-5,6-dichlorobenzimidazolyl-(2'-{O^P-[2-(4-nitrophenyl)ethyl]}→5')-5,6-dichloro-1-(2,3-di-*O*-tert-butyldimethylsilyl-β-*D*-ribofuranosyl)benzimidazole* (**27**). — Dry pyridine (3 × 2 mL) was evaporated from a mixture of **10** (0.131 g, 0.12 mmol) and **19** (0.095 g, 0.08 mmol). To a solution of the residue in dry pyridine (1 mL) were added *N*-methylimidazole (0.056 mL, 0.72 mmol) and 2,4,6-tri-isopropylbenzenesulfonyl chloride (0.073 g, 0.24 mmol), and then the mixture was stirred at room temperature with the exclusion of moisture for 25 h. More *N*-methylimidazole (0.03 mL) and sulfonyl chloride (0.037 g) were added and stirring was continued for 2 days. The mixture was diluted with phosphate buffer (pH 7, 50 mL), then extracted with $CHCl_3$ (3 × 50 mL), the combined organic phases were dried (Na_2SO_4), the solvent was evaporated, and toluene (2 × 10 mL) was evaporated from the residue. Preparative t.l.c. with $CHCl_3$–MeOH (50:1, 2 developments) gave bands of the diastereomeric trimers with R_F 0.35–0.45. Elution with $CHCl_3$–MeOH (4:1) gave amorphous **27** (0.072 g, 43%). ^{1}H-N.m.r. data ($CDCl_3$): δ 8.23–8.13 (m, 3 H, H-2), 8.07–7.95 (m, 4 H, *o*-H of NO_2Ph), 7.85–7.63 (m, 6 H, H-4,7), 7.59–6.73 (m, 18 H, aromatic H), 6.14–5.73 (m, 3 H, H-1'), 5.09–4.80 (m, 2 H, H-2'), 4.49–4.41 (m, 1 H, H-2'), 4.22–4.06 (m, 10 H, H-3',4',5'a and CH_2), 3.74 (s, 3 H, OCH_3), 3.50–3.21 (m, 2 H, H-5'b), 2.98–2.86 (m, 4 H, CH_2), 2.66–2.51 (m, 2 H, H-5'b), 0.90–0.74 (m, 36 H, 4 ^{t}Bu), 0.15 to −0.52 (m, 24 H, 8 $SiCH_3$).

Anal. Calc. for $C_{96}H_{120}Cl_6N_8O_{21}P_2Si_4$ (2109.1): C, 54.67; H, 5.73; N, 5.31. Found: C, 53.96; H, 5.76; N, 5.21.

*1-(3-*O*-tert-Butyldimethylsilyl-5-*O*-p-methoxytrityl-β-*D*-ribofuranosyl)-5,6-dichlorobenzimidazolyl-{2'-[O^P-(2,5-dichlorophenyl)]→5'}-2-(3-*O*-tert-butyldimethylsilyl-β-*D*-ribofuranosyl)-5,6-dichlorobenzimidazolyl-{2'-[O^P-(2,5-dichlorophenyl)]→5'}-5,6-dichloro-1-(2,3-di-*O*-tert-butyldimethylsilyl-β-*D*-ribofuranosyl)benzimidazole* (**28**). — Compound **11** was prepared from **5** (0.143 g, 0.2 mmol) with 1,2,4-triazole (0.095 g, 1.3 mmol) and 2,5-dichlorophenyl phosphorodichloridate (0.17 g, 0.6 mmol) according to the preceding procedure. Dry pyridine (2 × 5 mL) was evaporated from the crude product, to a solution of which in dry pyridine (2 mL) were added **20** (0.24 g, 0.2 mmol), tetrazole (0.085 g, 1.2 mmol), and 2,4,6-tri-isopropylbenzenesulfonyl chloride (0.122 g, 0.4 mmol). The mixture was stirred at room temperature for 24 h, diluted with $CHCl_3$ (50 mL), and extracted with phosphate buffer (pH 7, 100 mL). The aqueous phase was extracted again with $CHCl_3$ (50 mL), the combined organic layers were dried (Na_2SO_4), the solvent was evaporated, and toluene (10 mL) was evaporated from the residue. Preparative t.l.c. (2 plates) with $CHCl_3$–MeOH (50:1, 3 developments) gave two main bands with R_F 0.28 and 0.31. Elution with $CHCl_3$–MeOH (4:1, 300 mL) gave amorphous **28** (0.231 g, 54%). ^{1}H-N.m.r. data ($CDCl_3$): δ 8.21–8.04 (m, 3 H, H-2), 7.93–7.65 (m, 6 H, H-4,7), 7.59–7.00 (m, 15 H, aromatic H), 6.82–6.73 (2 H, *o*-H of MeOPh), 6.19–5.99 (4 d, 2 H, H-1'), 5.73–5.65 (2 d, 1 H, H-1'), 5.20–4.98 (m, 3 H, H-2'), 4.53–3.97 (m, 10 H, H-3',4',5'a), 3.74 (s, 3 H, OCH_3), 3.48 and 3.23 (2 m, 2 H, H-5'b), 0.89–0.72 (m, 36 H, 4 ^{t}Bu), 0.08 to −0.55 (m, 24 H, 8 $SiCH_3$).

Anal. Calc. for $C_{96}H_{100}Cl_{10}N_6O_{17}P_2Si_4$ (2100.7): C, 52.60; H, 5.27; N, 4.00. Found: C, 52.49; H, 5.28; N, 3.95.

1-(3-O-tert-Butyldimethylsilyl-β-D-ribofuranosyl)-5,6-dichlorobenzimidazolyl-{2'-[O^P-(2,5-dichlorophenyl)]→5'}-(3-O-tert-butyldimethylsilyl-β-D-ribofuranosyl)-5,6-dichlorobenzimidazolyl-{2'-[O^P-(2,5-dichlorophenyl)]→5'}-5,6-dichloro-1-(2,3-di-O-tert-butyldimethylsilyl-β-D-ribofuranosyl)benzimidazole (**29**). – Compound **28** (0.105 g, 0.05 mmol) was treated with 1% *p*-toluenesulfonic acid in CH_2Cl_2–MeOH (4:1, 5 mL) at room temperature for 5 h. The mixture was diluted with $CHCl_3$ (15 mL) and extracted with phosphate buffer (pH 7, 2 × 20 mL), the organic layer was dried (Na_2SO_4), and the solvent was evaporated. Preparative t.l.c. of the residue with $CHCl_3$–MeOH (95:5) gave main bands with R_f 0.44–0.53. Elution with $CHCl_3$–MeOH (4:1), evaporation of the solvent, and drying of the residue in high vacuum at 40° gave amorphous **29** (0.08 g, 87%). ^{1}H-N.m.r. data ($CDCl_3$): δ 8.29–8.07 (m, 3 H, H-2), 7.86–7.74 (m, 4 H, H-4,7), 7.61–7.40 (m, 2 H, H-4), 7.33–6.95 (15 H, aromatic H), 6.16–6.04 (m, 2 H, H-1'), 5.76 (d, 1 H, H-1'), 5.38 (m, 2 H, H-2'), 4.97 (m, 1 H, H-2'), 4.70 (bs, 1 H, HO-5'), 4.40–3.95 (m, 12 H, H-3',4',5'a,5'b), 0.91–0.72 (m, 36 H, 4 ^{t}Bu), 0.11 to –0.47 (m, 24 H, 8 $SiCH_3$).

Anal. Calc. for $C_{72}H_{94}Cl_{10}N_6O_{16}P_2Si_4$ (1844.4): C, 46.88; H, 5.13; N, 4.55. Found: C, 47.18; H, 5.02; N, 4.48.

1-(2-O-tert-Butyldimethylsilyl-5-O-p-methoxytrityl-β-D-ribofuranosyl)-5,6-dichlorobenzimidazolyl-(3'-{O^P-[2-(4-nitrophenyl)ethyl]}→5')-1-(2-O-tert-butyldimethylsilyl-β-D-ribofuranosyl)-5,6-dichlorobenzimidazolyl-(3'-{O^P-[2-(4-nitrophenyl)ethyl]}→5')-5,6-dichloro-1-(2,3-di-O-tert-butyldimethylsilyl-β-D-ribofuranosyl)benzimidazole (**31**). – Dry pyridine (3 × 2 mL) was evaporated from a mixture of **13** (0.16 g, 0.145 mmol) and **24** (0.125 g, 0.1 mmol). To a solution of the residue in dry pyridine (1 mL) were added *N*-methylimidazole (0.07 mL, 0.87 mmol) and 2,4,6-tri-isopropylbenzenesulfonyl chloride (0.088 g, 0.29 mmol). The mixture was stirred for 20 h, more *N*-methylimidazole (0.035 mL) and sulfonyl chloride (0.044 g) were added, and stirring was continued for 2 days. The mixture was diluted with $CHCl_3$ (50 mL) and extracted with phosphate buffer (pH 7, 100 mL), the aqueous phase was extracted with $CHCl_3$ (2 × 50 mL), and the combined organic layers were extracted with phosphate buffer. The $CHCl_3$ extract was dried (Na_2SO_4), the solvent was evaporated, and toluene (2 × 10 mL) was evaporated from the residue. Preparative t.l.c. with $CHCl_3$–MeOH (100:1, 2 developments) gave main bands with R_f 0.22–0.37. Elution with $CHCl_3$–MeOH (4:1) gave amorphous **31** (0.135 g, 64%). ^{1}H-N.m.r. data ($CDCl_3$): δ 8.37–8.20 (m, 3 H, H-2'), 8.17–7.97 (m, 4 H, *o*-H of NO_2Ph), 7.86 (m, 3 H, H-7), 7.73 (m, 1 H, H-4), 7.58 (m, 2 H, H-4), 7.43–7.16 (m, 16 H, aromatic H), 6.81 (d, 2 H, *o*-H of MeOPh), 6.02–5.72 (m, 3 H, H-1'), 4.85–4.72 (m, 3 H, H-2'), 4.48–4.12 (m, 10 H, H-3',4' and CH_2), 3.74 (s, 3 H, OCH_3), 3.51 and 3.29 (2 m, 6 H, H-5'a,5'b), 3.09–2.87 (m, 4 H, CH_2), 0.94–0.53 (m, 36 H, 4 ^{t}Bu), 0.11 to –0.47 (m, 24 H, 8 $SiCH_3$).

Anal. Calc. for $C_{90}H_{120}Cl_8N_8O_{21}P_2Si_4$ (2109.1): C, 54.67; H, 5.73; N, 5.31. Found: C, 54.58; H, 6.03; N, 5.52.

1-(2-O-tert-Butyldimethylsilyl-5-O-p-methoxytrityl-β-D-ribofuranosyl)-5,6-dichlorobenzimidazolyl-{3'-[O^P-(2,5-dichlorophenyl)]→5'}-1-(2-O-tert-butyldimethylsilyl-β-D-

*ribofuranosyl)-5,6-dichlorobenzimidazolyl-{3'-[O^{P}-(2,5-dichlorophenyl)]→5'}-5,6-dichloro-1-(2,3-di-*O*-tert-butyldimethylsilyl-β-D-ribofuranosyl)benzimidazole* (**32**). — Compound **14** was prepared, according to the preceding procedure, from **4** (0.106 g, 0.15 mmol), 1,2,4-triazole (0.071 g, 0.96 mmol), and 2,5-dichlorophenyl phosphorodichloridate (0.126 g, 0.45 mmol) in dry pyridine (7 mL). Dry pyridine (2 × 2 mL) was evaporated from a mixture of the crude product and **25** (0.178 g, 0.15 mmol). To a solution of the residue in dry pyridine (1.5 mL) were added tetrazole (0.063 g, 0.9 mmol) and 2,4,6-tri-isopropylbenzenesulfonyl chloride (0.091 mg, 0.3 mmol). The mixture was stirred at room temperature for 3 h, diluted with $CHCl_3$ (50 mL), and extracted with phosphate buffer (pH 7, 100 mL), the aqueous phase was extracted with $CHCl_3$, the combined $CHCl_3$ extracts were dried (Na_2SO_4), the solvent was evaporated, and toluene was evaporated from the residue. Preparative t.l.c. (2 plates with $CHCl_3$–MeOH (50:1, 2 developments) gave main bands with R_F 0.39–0.58. Elution with $CHCl_3$–MeOH (4:1, 300 mL), evaporation of the solvent, and drying of the residue in a high vacuum at 40° gave amorphous **32** (0.215 g, 68%). ^{1}H-N.m.r. data ($CDCl_3$): δ 8.28–8.07 (m, 3 H, H-2), 7.93–7.84 (m, 6 H, H-4,7), 7.53–6.80 (15 H, aromatic H), 6.04–5.73 (m, 3 H, H-1'), 5.18–5.01 (m, 3 H, H-2'), 4.76–4.16 (m, 10 H, H-3',4',5'a), 3.74 (s, 3 H, OCH_3), 3.53 (m, 2 H, H-5'b), 0.93–0.64 (m, 36 H, 4 ^{t}Bu), 0.10 to −0.46 (m, 24 H, 8 $SiCH_3$).

Anal. Calc. for $C_{92}H_{100}Cl_{10}N_6O_{17}P_2Si_4$ (2100.7): C, 52.60; H, 5.27; N, 4.80. Found: C, 52.26; H, 5.07; N, 3.96.

General procedure for total deblocking. — *(a) 2,5-Dichlorophenyl-phosphotriesters* (**18**, **23**, **28**, *and* **32**). A solution of 4-nitrobenzaldoxime (38 mg, 0.23 mmol) in dioxane (0.5 mL), H_2O (0.5 mL), and Et_3N (0.5 mL) was stirred for 20 min at room temperature. The fully protected dimer or trimer (10 μmol) was added, the mixture was stirred for 12 h, the solvent was evaporated, and dry pyridine and then toluene were evaporated from the residue. The residue was subjected to preparative t.l.c. (plate 20 × 20 × 0.2 cm) with $CHCl_3$–MeOH–Et_3N (9:1:1). The main band was eluted several times with the same solvent mixture (300 mL), the solvent was evaporated, and CH_2Cl_2 (six times) and dry pyridine (twice) were evaporated from the residue which was then stirred with M tetrabutylammonium fluoride in tetrahydrofuran (5 mL) for 24 h. After evaporation of the solvent and evaporation of toluene from the residue, detritylation was achieved by stirring in aqueous 80% AcOH (5 mL) for 12 h. The solvent was evaporated and water was evaporated from the residue until all AcOH was removed. A solution of the residue in H_2O (100 mL) was put on a column (60 × 1 cm) of DEAE-Sephadex A-25, which was eluted with a linear gradient of 0→0.5M triethylammonium hydrogencarbonate buffer (pH 7.5), and fractions of 200 drops were collected. The solvent was evaporated from the appropriate fractions and water was evaporated several times from the residue, an aqueous solution (50 mL) of which was lyophilised to give the amorphous triethylammonium salt.

(b) 2-(4-Nitrophenyl)ethyl-phosphotriesters (**27** *and* **31**). A solution of the fully protected oligonucleotide (10 μmol) in 0.5M 1,8-diazabicyclo[5.4.0]undecene in pyridine (10 mL) was stirred at room temperature for 24 h, then neutralised with M AcOH in pyridine (5 mL), and the solvent was evaporated. The residue was then treated as in *(a)*

with M tetrabutylammonium fluoride in tetrahydrofuran (8 mL) and aqueous 80% AcOH (8 mL). The product was purified by chromatography on DEAE-Sephadex and isolated by lyophilisation of an aqueous solution.

*5,6-Dichloro-1-β-*D*-ribofuranosylbenzimidazolyl-(2′→5′)-5,6-dichloro-1-β-*D*-ribofuranosylbenzimidazole* (**21**). — Compound **18** (14.6 mg, 10 μmol) was deblocked by method (*a*) to give **2** with 83 o.d. units (86%), taking into account a hypochromicity of 21%; R_f 0.46 (cellulose) in 1-BuOH–AcOH–H_2O (6:1:1), *T* (h.p.l.c.) 205 s (RP-18, 0.1M NH_4OAc–CH_3CN, 65:35).

*5,6-Dichloro-1-β-*D*-ribofuranosylbenzimidazolyl-(3′→5′)-5,6-dichloro-1-β-*D*-ribofuranosylbenzimidazole* (**26**). — Compound **23** (15 mg, 10 μmol) was deblocked by method (*a*) to give **26** with 80 o.d. units (88%), taking into account a hypochromicity of 26%; R_f 0.70 (cellulose) in 1-BuOH–AcOH–H_2O (8:1:1), *T* (h.p.l.c.) 255 s.

*5,6-Dichloro-1-β-*D*-ribofuranosylbenzimidazolyl-(2′→5′)-5,6-dichloro-1-β-*D*-ribofuranosylbenzimidazolyl-(2′→5′)-5,6-dichloro-1-β-*D*-ribofuranosylbenzimidazole* (**30**). Treatment of **28** (21 mg, 10 μmol) by method (*a*), or **27** (21 mg, 10 μmol) by method (*b*), gave 75 (65%) and 90 o.d. units (91%), respectively, of **30**, taking into account a hypochromicity of 37%; R_f 0.55 (cellulose) in 1-BuOH–AcOH–H_2O (6:1:3), *T* 176 s.

*5,6-Dichloro-1-β-*D*-ribofuranosylbenzimidazolyl-(3′→5′)-5,6-dichloro-1-β-*D*-ribofuranosylbenzimidazolyl-(3′→5′)-5,6-dichloro-1-β-*D*-ribofuranosylbenzimidazole* (**33**). Treatment of **32** (21 mg, 10 μmol) by method (*a*), or **31** (21 mg, 10 μmol) by method (*b*), gave 82 (57%) and 107 o.d. units (75%), respectively, of **33**, taking into account a hypochromicity of 22%; R_f 0.22 (cellulose) in 1-BuOH–AcOH–H_2O (6:1:3), *T* 285 s.

REFERENCES

1 R. Charubala, R. W. Sobol, R. J. Suhadolnik, and W. Pfleiderer, *Helv. Chim. Acta*, 74 (1991) in press.
2 P. B. Seghal, E. Derman, G. R. Molley, I. Tamm, and J. E. Darnell, *Science*, 194 (1976) 431–433.
3 P. B. Seghal, J. E. Darnell, and I. Tamm, *Cell*, 9 (1976) 437–480.
4 I. Tamm, R. Hand, and L. A. Caliguiri, *J. Cell Biol.*, 69 (1976) 229–240.
5 E. Egyhazi, B. Daneholt, J. E. Edström, B. Lambert, and U. Ringborg, *J. Cell Biol.*, 47 (1970) 516–520.
6 I. Tamm and P. B. Seghal, *Adv. Virus Res.*, 22 (1977) 187–258.
7 E. Egyhazi and D. Shugar, *FEBS Lett.*, 107 (1979) 431–435.
8 I. Tamm and P. B. Seghal, *Biochem. Pharmacol.*, 27 (1978) 2475–2483.
9 H. M. Kissman, R. G. Child, and M. J. Weiss, *J. Am. Chem. Soc.*, 79 (1957) 1185–1188.
10 Z. Kazimierczuk, R. Stolarski, L. Dudycz, and D. Shugar, *Z. Naturforsch., Teil C*, 36 (1981) 126–134.
11 Z. Kazimierczuk, L. Dudycz, R. Stolarski, and D. Shugar, *J. Carbohydr., Nucleosides, Nucleotides*, 8 (1981) 101–117.
12 Z. Kazimierczuk, R. Stolarski, L. Dudycz, and D. Shugar, *Nucleosides Nucleotides*, 1 (1982) 275–287.
13 Z. Kazimierczuk, R. Stolarski, L. Dudycz, and D. Shugar, *Z. Naturforsch., Teil C*, 35 (1980) 30–35.
14 D. L. Sweeney, J. E. Gearien, L. Bauer, and B. L. Currie, *J. Carbohydr., Nucleosides, Nucleotides*, 6 (1979) 387–409.
15 G. C. Sen, *Pharmac. Ther.*, 24 (1984) 235–257.
16 P. F. Torrence, *Mol. Aspects Med.*, 5 (1982) 129–171.
17 I. M. Kerr and R. E. Brown, *Proc. Natl. Acad. Sci. U.S.A.*, 75 (1978) 256–260.
18 R. M. Friedman, D. H. Merz, R. M. Esteban, D. R. Tovell, and I. M. Kerr, *J. Virol.*, 10 (1972) 1184–1198.
19 I. M. Kerr, R. M. Friedman, R. E. Brown, L. A. Ball, and J. C. Brown, *J. Virol.*, 13 (1974) 9–21.
20 K. A. Watanabe, D. H. Hollenberg, and J. J. Fox, *J. Carbohydr., Nucleosides, Nucleotides*, 1 (1974) 1–37.
21 T. Sato, T. Shimidate, and Y. Ishido, *Nippon Kagaku Zasshi*, 81 (1960) 1440–1442.

22 E. Uhlmann and W. Pfleiderer, *Helv. Chim. Acta*, 64 (1981) 1688–1703.
23 C. B. Reese and L. Zard, *Nucleic Acids Res.*, 9 (1981) 4611–4626.
24 D. Flockerzi, Diploma Thesis, University of Stuttgart, 1977.
25 F. Weygand, A. Wacker, and F. Wirth, *Z. Naturforsch., Teil B*, 6 (1951) 25–34.