Additional Reactions of Sugar Oximes, Nitrile Oxides and Hydroximolactones

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Reaction of sugar oximes with dimethyl acetylenedicarboxylate gave chiral isoxazolines bearing a sugar moiety. Sugar nitrile oxides reacted with 1,3-dipolarophiles to afford the corresponding isoxazoles bearing a sugar moiety. Sugar hydroximolactones underwent a tandem Michael addition–1,3-dipolar cycloaddition by reaction with Michael acceptors to give the corresponding spiro sugar isoxazolidines. An X-ray crystallographic structure determination of (3*S*,5*R*,7*R*,8*R*,9*R*)-3-acetyl-8,9-isopropylidenedioxy-1-(3-oxobutyl)-7-trityloxymethyl-2,6-dioxa-1-azaspiro[4.4]nonane has been performed.

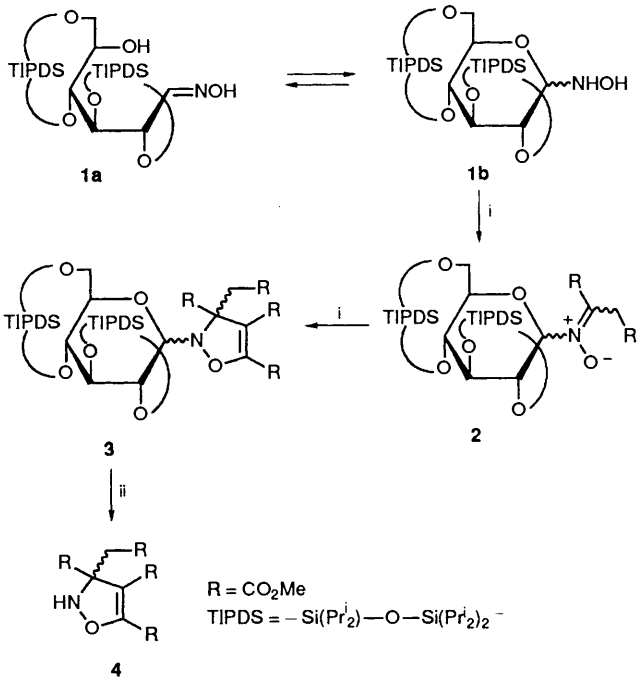
Recently, considerable attention has been given to unnatural nucleosides ever since the appearance of Acyclovir, Ribavirin, and AZT as potential antiviral agents.[1] As part of our study directed towards the synthesis of pharmaceutically important compounds,[2] we intended to develop the synthesis of new type of nucleosides. From this viewpoint we studied the reactions of sugar oximes. In this paper we report some of their reactions: (1) Reaction of sugar oximes with dimethyl acetylenedicarboxylate. (2) 1,3-Dipolar cycloaddition with sugar nitrile oxides. (3) Reaction of sugar hydroximolactones.

Results and Discussion

1. *Reaction of Sugar Oximes with Dimethyl Acetylenedicarboxylate.*—The asymmetric synthesis of isoxazolines by utilizing sugars as chiral auxiliaries has been investigated extensively by Vasella and co-workers.[3] We intended to synthesize a chiral isoxazoline glucoside starting from 2,3;4,6-di-*O*-(tetraisopropyldisiloxane-1,3-diyl)-D-glucose oxime **1** and dimethyl acetylenedicarboxylate (DMAD). Compound **1** was allowed to react with DMAD *via* a nitrone intermediate **2** to give the corresponding tetraisopropyldisiloxanediyl (TIPDS)-protected isoxazoline glucoside **3** in 87% yield (α/β 3/7). Furthermore, the α and β isomers could each be separated into two isomers epimeric at C-3 of the isoxazoline. The main products consisted of α and β glucosides in 20 and 53% yield, respectively. The α-glucoside was treated with 5% HCl–MeOH to afford the corresponding isoxazoline derivative **4** as the (−)-form {$[\alpha]_D$ −147° (*c* 0.48, $CHCl_3$)} in 51% yield, while the β-glucoside gave the (+)-form of compound **4** {$[\alpha]_D$ +147° (*c* 0.48, $CHCl_3$)} in 61% yield (Scheme 1). Compound **3** could be easily deprotected by treatment with tetrabutylammonium fluoride. Thus, the chiral isoxazoline glucosides can be synthesized by the present procedure.

Next, D-ribose was employed in this reaction as a chiral auxiliary. 2,3-*O*-Isopropylidene-5-*O*-trityl-D-ribose oxime **5** was treated with DMAD in the same way as before. An expected 2,3-*O*-isopropylidene-5-*O*-tritylribofuranosyl isoxazoline **7** was obtained in 98% yield (α riboside: 52 and 5.5%; β riboside: 27 and 13.5%) *via* the corresponding nitrone **6**. The main α and β ribosides had the specific rotatory powers of +113° (*c* 0.50, $CHCl_3$) and −44° (*c* 0.52, $CHCl_3$), respectively.

Interestingly, the α and β ribosides were detritylated by $FeCl_3$ to give the same 2-(2,3-*O*-isopropylidene-β-D-ribosyl)-3,4,5-tris(methoxycarbonyl)-3-methoxycarbonylmethyl-2,3-dihydroisoxazole **8** in 79% yield based on the β-form. Compound **8** was then treated with 5% HCl–MeOH to afford the (−)-form of compound **4** in 69% yield (Scheme 2). This fact shows that the

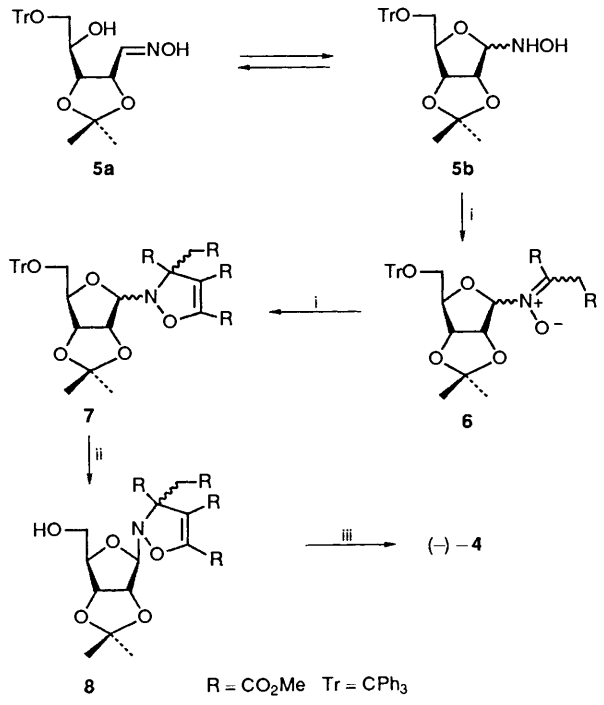


Scheme 1 *Reagents:* i, DMAD; ii, HCl, MeOH

α-riboside **7α** changes to the β riboside **7β** in the detritylation step and that the carbon-3 atoms in the isoxazoline ring of compounds **7α** and **7β** have the same stereochemistry. Judging from the isolated products, the higher α-selection (α/β 3/2) of oxime **5** compared with that of oxime **1** (α/β 3/7) seems to stem mainly from the effect of bulky 5-*O*-trityl group. The mechanism of chiral induction is unclear because the absolute configurations of products **4** are not known for certain.

The isoxazolines **4** obtained in this reaction are stable in $CHCl_3$ solution at room temperature for a week and can be stored in a freezer without decomposition for several months. Glucoside **3** and ribosides **7** and **8** are very stable compounds. The structure of compounds **3**, **7** and **8** was determined by their coupling constants and NOE NMR data. In the above two reactions, starting compounds **1** and **5** were found to exist in both oxime forms (**1a** and **5a**) and hydroxylamine forms (**1b** and **5b**) by ^1H NMR data.

2. 1,3-*Dipolar Cycloaddition with Sugar Nitrile Oxides.*[4]—In connection with our recent studies[5] on the synthesis of acyclonucleosides which have received considerable attention as anti-



Scheme 2 *Reagents:* i, DMAD; ii, $FeCl_3$; iii, HCl, MeOH

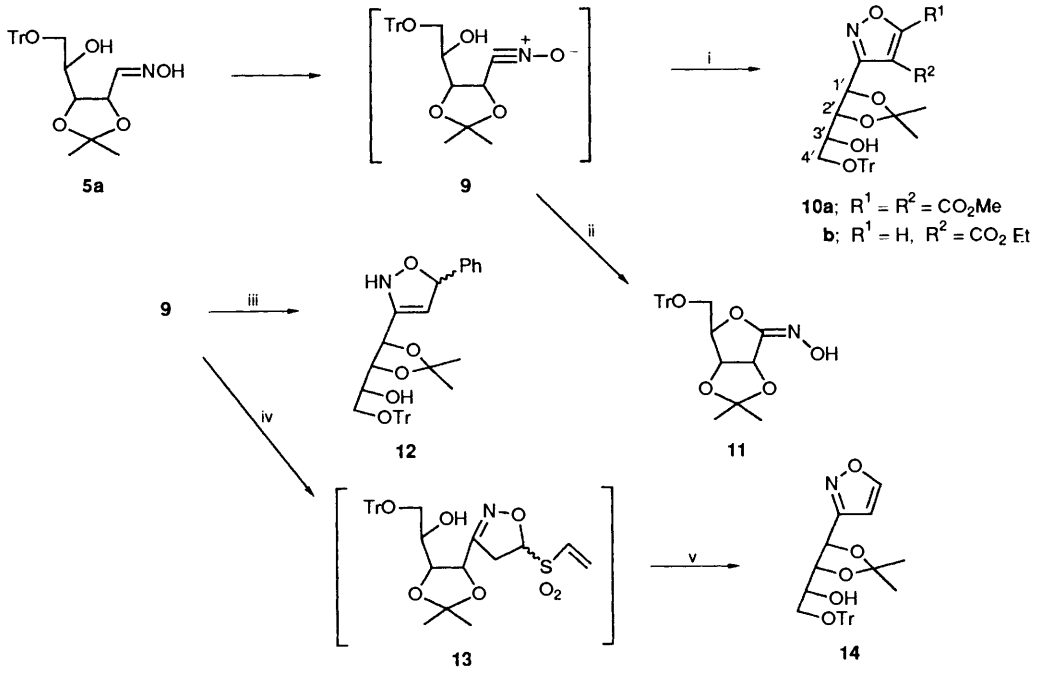
viral drugs,[6] we carried out the generation of a ribose nitrile oxide **9** which would afford the corresponding acyclonucleosides by the reaction with various 1,3-dipolarophiles.

A mixture of 2,3-*O*-isopropylidene-5-*O*-trityl-D-ribose oxime **5a** and DMAD was allowed to react with 5% aq. NaOCl in the presence of triethylamine to give the corresponding isoxazole **10a** in 86% yield. Similarly, the reaction of oxime **5a** with ethyl propiolate gave the corresponding isoxazole **10b** in 37% yield. From this experiment, we found that the intermediate nitrile oxide **9** was stable at 0 °C and changed gradually at room temperature into (*E*)-2,3-*O*-isopropylidene-5-*O*-trityl-D-ribonohydroximo-1,4-lactone **11**. The reaction of compound **9** with styrene afforded the corresponding isoxazoline **12** in a regioselective manner.

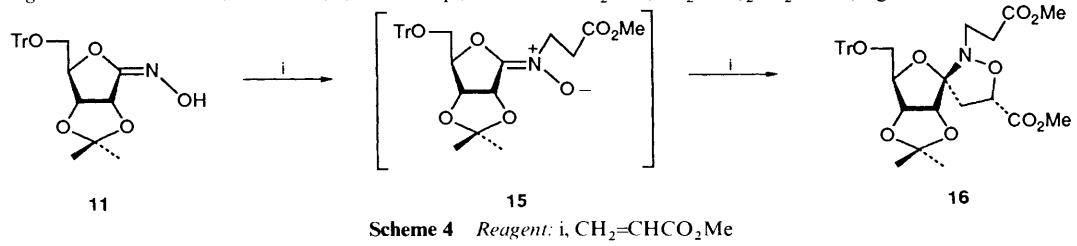
Sugar-substituted isoxazole **14** could be also synthesized (Scheme 3), by the reaction of compound **9** with divinyl sulphone followed by treatment with Na/Hg in 37% yield as a foam. On treatment with 5% HCl, compound **14** was easily deprotected.

3. *Reaction of Sugar Hydroximolactones.*—3.1. *Tandem Michael addition–1,3-dipolar cycloaddition.* A mixture of compound **11**, methyl acrylate, and dry toluene was heated at 120 °C in a sealed tube to give (3*S*,5*R*)-8,9-isopropylidenedioxy-3-methoxycarbonyl-1-[2′-(methoxycarbonyl)ethyl]-7-(trityloxymethyl)-2,6-dioxa-1-azaspiro[4.4]nonane **16** in 80% yield as a white powder. This reaction is considered to proceed as follows. A sugar nitrone **15** is first formed by the attack of the oxime nitrogen atom on methyl acrylate in a Michael addition manner, and then reacts with another molecule of methyl acrylate *via* 1,3-dipolar cycloaddition (Scheme 4). Such a type of oxime reaction has recently been investigated extensively by Grigg and co-workers.[7] This work is the first application of Grigg's reaction to the synthesis of sugar isoxazolidines.

Similarly, the reaction of compound **11** with methyl vinyl ketone gave the corresponding spiro sugar isoxazolidine **17** in 48% yield together with its (3*R*)-isomer (37%). Furthermore,



Scheme 3 *Reagents and conditions:* i, $R^1C{\equiv}CR^2$; ii, room temp.; iii, $PhCH{=}CH_2$; iv, $(CH_2{=}CH)_2SO_2$; v, Na/Hg



Scheme 4 *Reagent:* i, $CH_2{=}CHCO_2Me$

Table 1 Tandem Michael addition–1,3-dipolar cycloaddition of compound **24**[a]– equation (1)

Solvent	Yield (%)	Product proportions (**25**:**26**:others[b])
Toluene	65	44:21:0
Acetonitrile	59	46:23:31
None	72	31:31:38

[a] A mixture of **24** (0.2 mmol), methyl acrylate (4 mmol) and solvent (0.3 cm^3) was heated in sealed tube (volume 5 cm^3) at 120 °C for 13.5 h under a N_2 atmosphere. [b] More than two isomers were observed by NMR spectroscopy.

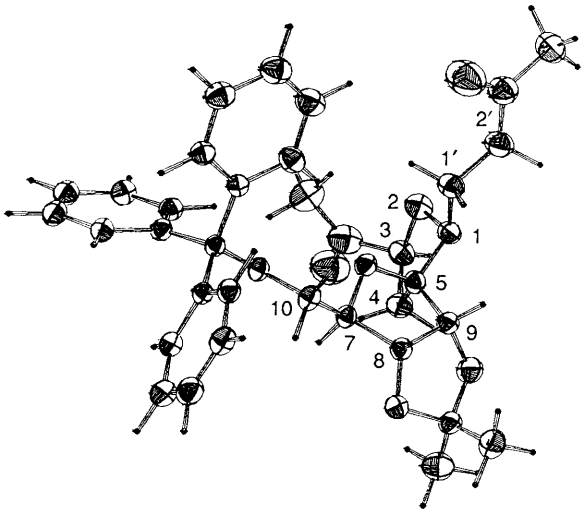
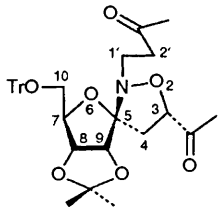


Fig. 1 ORTEP drawing of compound **17** showing 50% probability ellipsoids for all non-hydrogen atoms

the stereostructure of compound **17** was determined by X-ray diffraction (Fig. 1).

In a preliminary report[2c] the stereochemistry at the 3-position in compound **17** was incorrectly determined by NOE data. Compound **11** reacted with acrylonitrile to give the corresponding isoxazolidine **18** in 48% yield. The diastereoisomers of the product **18** were not separated.



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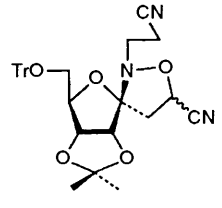

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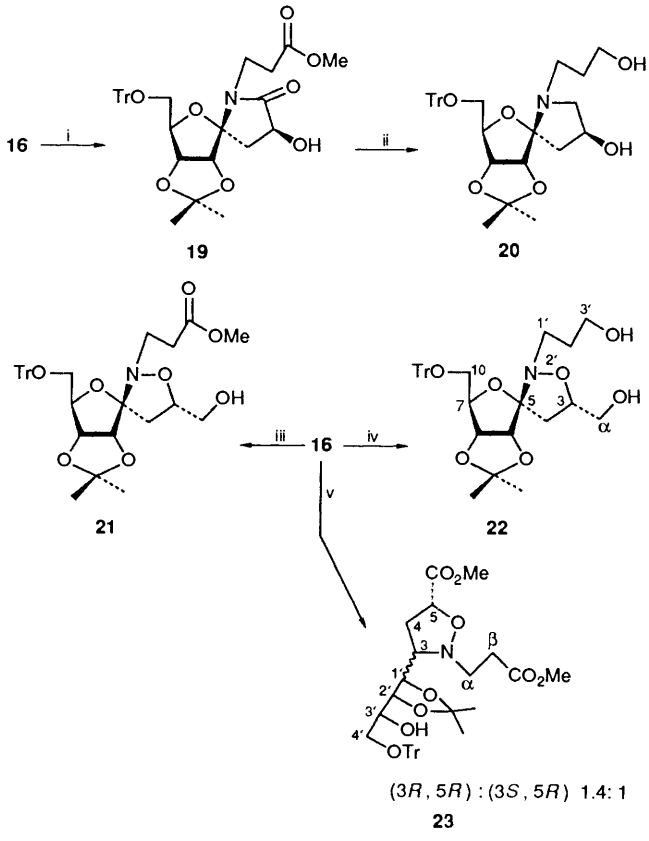
To show the utility of the spiro sugar isoxazolidines thus formed, compound **16** was treated with Raney nickel in refluxing methanol to afford (5*R*,8*S*)-8-hydroxy-3,4-isopropylidenedioxy-6-[2′-(methoxycarbonyl)ethyl]-7-oxo-2-trityloxymethyl-1-oxa-6-azaspiro[4.4]nonane **19** in 70% yield. Furthermore, treatment of compound **19** with $LiAlH_4$ in refluxing tetrahydrofuran (THF) gave (5*R*,8*S*)-8-hydroxy-6-(3′-hydroxypropyl)-3,4-isopropylidenedioxy-2-trityloxymethyl-1-oxa-6-azaspiro[4.4]nonane **20** in 40% yield. Compound **20** is a synthetic precursor of hydroxylated pyrrolidines possessing galactosidase inhibition activity.[8]

The reactions of compound **16** with some other reductants were examined. Compound **16** reacted with $NaBH_4$ in EtOH to give the corresponding spiro isoxazolidine **21** in 58% yield. On treatment of compound **16** with $LiAlH_4$, the corresponding spiro isoxazolidine **22** was isolated in 94% yield. Treatment of compound **16** with $NaBH_3CN$ in a mixed solution of EtOH and AcOH resulted in the formation of the ring-opened sugar isoxazolidine **23** in 75% yield as a mixture of diastereoisomers, which could be separated by preparative TLC (PLC) on silica gel, and their stereostructures were determined by NOESY measurements (Scheme 5). This result can be explained by the fact that O-6 is protonated more easily than is N-1.

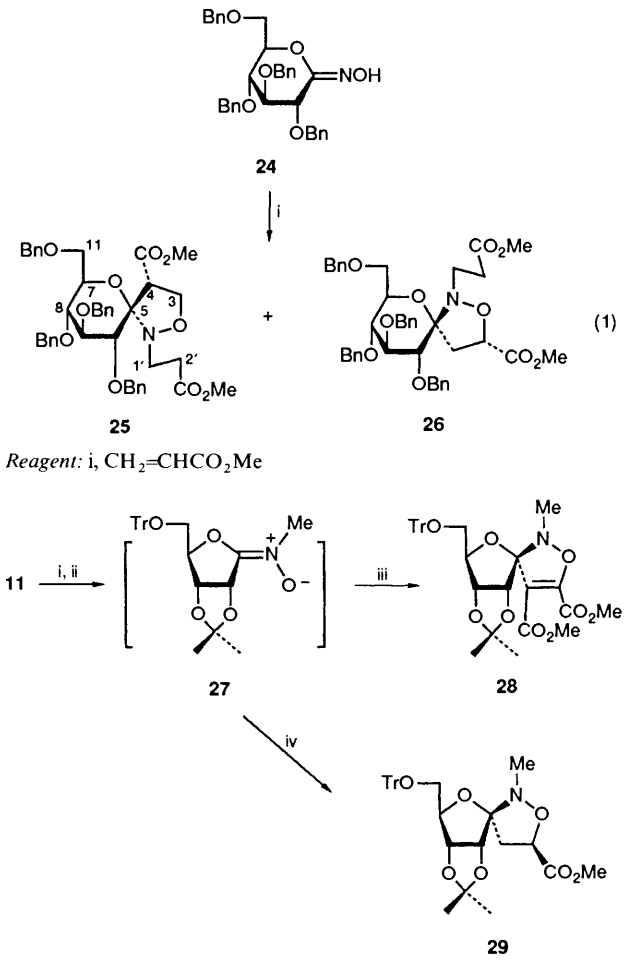


Scheme 5 *Reagents and conditions:* i, RaNi, MeOH, heat; ii, $LiAlH_4$, THF, heat; iii, $NaBH_4$, EtOH, room temp.; iv, $LiAlH_4$, THF, room temp.; v, $NaBH_3CN$, EtOH–AcOH, room temp.

The reaction was extended to the glucose lactoxime **24**.[9] Various reaction conditions for the reaction of compound **24** with methyl acrylate were examined. The results are summarized in Table 1. Note that reaction of compound **24** in toluene gave no by-products.

3.2. *Tandem alkylation–1,3-dipolar cycloaddition.* Compound **11** was allowed to react with methyl trifluoromethanesulphonate (MeOTf) and then the reaction mixture containing the intermediate **27** was treated with DMAD followed by the addition of triethylamine to give the corresponding isoxazoline **28** in a completely stereoselective manner (Scheme 6).

On the other hand, when methyl acrylate was used as a 1,3-dipolarophile, three stereoisomers were obtained and the stereostructure of the main product **29** (49% yield) was determined by



Scheme 6 *Reagents:* i, MeOTf; ii, Et_3N; iii, DMAD; iv, CH_2=$CHCO_2Me$

NOESY measurements. Therefore methyl trifluoromethanesulphonate was found to be a very useful *N*-alkylating reagent for generation of nitrones from oximes.

Experimental

Microanalyses were performed with a Perkin-Elmer 240 elemental analyser at the Chemical Analysis Center of Chiba University. IR spectra, for neat specimens unless otherwise stated, were recorded on a Hitachi 215 spectrometer. Mass spectra were obtained on Hitachi RMU 7M and JNM-BX-300 instruments. ^1H and ^{13}C NMR spectra, for $CDCl_3$ solutions, were recorded on JEOL MH-100, JNM-FX-270, JNM-GSX-400 and JNM-GSX-500 spectrometers. *J*-Values are given in Hz. Carbon signals were assigned by DEPT or INEPT data. 2D ^1H NMR (COSY and NOESY) data were measured with JNM-GSX-400 and JNM-GSX-500 spectrometers. Wakogel C-200 was used for low-pressure liquid chromatography (LPLC) and Wakogel B-5F was used for PLC.

2,3;4,6-*Di*-O-(*tetraisopropyldisiloxane*-1,3-*diyl*)-D-*glucose Oxime* **1**.—A mixture of D-glucose (900 mg, 5 mmol), dry pyridine (25 cm^3), and 1,3-dichloro-1,1,3,3-tetraisopropyldisiloxane (3.2 cm^3, 10 mmol) was stirred at −30 °C for 30 min under nitrogen and was then kept in a freezer overnight. The reaction mixture was evaporated, water was added, and the mixture was extracted with AcOEt. The extract was washed successively with 0.1 mol dm^{-3} HCl (2 × 20 cm^3) and then with saturated aq. $NaHCO_3$ (20 cm^3). After being dried with Na_2SO_4, the extract was evaporated to give a syrupy material. A mixture of the material obtained above, NH_2OH·HCl (1.7 g, 25 mmol), pyridine (15 cm^3), and EtOH (15 cm^3) was refluxed for 5 h. The reaction mixture was treated by the same way as mentioned above. Purification was performed by LPLC [Wakogel C-300; $CHCl_3$–AcOEt (15:1)]: First eluent (α-anomer of **1b**); second eluent (**1a**); third eluent (β-anomer of **1b**). Total overall yield was 51%. Compound **1** existed in CH_2Cl_2 as an equilibrium mixture (**1bα**:**1a**:**1bβ** 3:2:7) after storage for one week.

1a: Foam; δ_H 0.91–1.14 (56 H, m, Pr^i × 8), 1.62 (1 H, s, 5′-OH), 3.80–4.20 (5 H, m, 3′-, 4′- and 5′- and 6′-H_2), 4.64 (1 H, m, 2′-H), 7.27 (1 H, d, $J_{1',2'}$ 8.3, 1′-H) and 7.89 (1 H, br s, NOH); δ_C 11.7–17.7 (Pr^i), 62.6 (C-6′), 68.9, 72.6, 74.2 and 79.4 (C-2′, -3′, -4′ and -5′) and 149.3 (C-1′) (Found: C, 52.9; H, 9.5; N, 2.1. $C_{30}H_{65}NO_8Si_4$ requires C, 53.0; H, 9.6; N, 2.1%); *m/z* (FAB) 681 $(M + 1)^+$.

1bα: Foam; δ_H 4.88 (1 H, d, $J_{1',2'}$ 5.0, 1′-H); the other peaks appeared almost at the same field as those of compound **1a**; δ_C 11.7–17.7 (Pr^i), 61.1 (C-6′), 70.1, 71.4, 74.0 and 77.8 (C-2′, -3′, -4′ and -5′) and 89.7 (C-1′).

1bβ: Foam; δ_H 0.88–1.11 (56 H, m, Pr^i × 8), 3.21 (1 H, m, 5′-H), 3.57 (1 H, m, 2′-H), 3.77 (1 H, m, 3′-H), 3.85 (1 H, m, 4′-H), 4.00 and 4.11 (2 H, m, 6′-H_2) and 4.17 (1 H, d, $J_{1',2'}$ 8.8, 1′-H); δ_C 11.7–17.7 (Pr^i), 60.9 (C-6′), 60.9 73.3, 78.1 and 80.6 (C-2′, -3′, -4′ and -5′) and 93.2 (C-1′).

A Precursor of the Intermediary Nitrone **2**.—A mixture of oxime **1** (111 mg, 0.16 mmol), DMAD (0.023 cm^3, 0.19 mmol), and CH_2Cl_2 (0.1 cm^3) was stirred for 18 min at room temperature. Purification was carried out in the same way as described in the preparation of compound **3** below [PLC: $CHCl_3$–AcOEt (30:1)]; foam (81%); ν/cm^{-1} 3400 (OH), 2900 and 2850 (CH) and 1730 (CO); δ_H 0.87–1.14 (56 H, br s, Pr^i), 1.72 (1 H, br, OH), 3.94 (6 H, s, Me), 3.26 (1 H, m, 5′-H), 3.75–4.20 (5 H, m, 2′-, 3′-, 4′- and 6′-H_2), 4.58 (1 H, d, $J_{1',2'}$ 8.9, 1′-H) and 5.83 (1 H, s, =CH).

2-[2′,3′;4′,6′-*Di*-O-(*tetraisopropyldisiloxane*-1,3-*diyl*)-D-*glucosyl*]-3,4,5-*tris*(*methoxycarbonyl*)-3-*methoxycarbonylmethyl*-2,3-*dihydroisoxazole* **3**.—A mixture of compound **1** (183 mg, 0.27 mmol), DMAD (0.42 cm^3, 3.4 mmol), and CH_2Cl_2 (0.35 cm^3) was stirred for 10 h at room temperature. The reaction mixture was evaporated to give a pasty material, which was treated by LPLC [Wakogel C-300; $CHCl_3$–AcOEt (40:1)]. First eluent contained excess of DMAD and second eluent was further purified by PLC on silica gel [$CHCl_3$–AcOEt (40:1)] to give compound **3** as a foam in 87% yield (α/β 3/7). The α-anomer of compound **3** was then separated into two isomers by PLC [$CHCl_3$–AcOEt (40:1)], while the β-anomer was treated in the same way to give two isomers [$CHCl_3$–AcOEt (30:1)]. *Main α-anomer*: 20%; foam (Found: C, 52.4; H, 8.1; N, 1.7. $C_{42}H_{77}NO_{16}Si_4$ requires C, 52.2; H, 8.0; N, 1.5%); *m/z* (FAB) 965 $(M + 1)^+$; ν/cm^{-1} 2850 and 2900 (CH) and 1720 and 1740 (CO); δ_H 0.89–1.10 (56 H, m, Pr^i × 8), 3.25 and 3.29 (2 H, d, J_{gem} 16, CH_2), 3.65 (1 H, m, 5′-H), 3.65, 3.76, 3.79 and 3.84 (3 H × 4, s, Me × 4), 3.75–3.84 (2 H, m, 3′- and 6′-H), 3.92 (1 H, dd, J_{gem} 13, $J_{5',6'}$ 2, 6′-H), 3.98 (1 H, dd, $J_{1',2'}$ 6.6, $J_{2',3'}$ 9.1, 2′-H), 4.24 (1 H, dd, $J_{3',4'} = J_{4',5'}$ = 8.8, 4′-H) and 5.01 (1 H, d, $J_{1',2'}$ 6.6, 1′-H); NOE C(1′)–H ⟷ C(4′)–H.

Minor α-anomer: 6%; foam; *m/z* (FAB) 965 $(M + 1)^+$; δ_H 0.88–1.08 (56 H, m, Pr^i × 8), 3.24 and 3.31 (2 H, d, J_{gem} 15.9, CH_2), 3.66, 3.74 3.75 and 3.85 (3 H × 4, s, Me × 4), 3.79–3.87 (3 H, m, 3′-, 5′- and 6′-H), 3.90 (1 H, dd, $J_{1',2'}$ 5.8, $J_{2',3'}$ 9.6, 2′-H), 4.03 (1 H, m, J_{gem} 11.5, 6′-H), 4.21 (1 H, m, 4′-H) and 4.99 (1 H, d, $J_{1',2'}$ 5.8, 1′-H); NOE C(1′)–H ⟷ C(4′)–H.

Main β-anomer: 53%; foam; *m/z* (FAB) 965 $(M + 1)^+$; ν/cm^{-1} 2850 and 2930 (CH) and 1730 (CO); δ_H 0.91–1.10 (56 H, m, Pr^i × 8), 2.96 (1 H, m, 5′-H), 3.02 and 3.20 (2 H, d, J_{gem} 16.1,

CH_2), 3.60, 3.74, 3.78 and 3.89 (3 H × 4, s, Me × 4), 3.70–3.80 (3 H, m, 3′-, 4′- and 6′-H), 3.83 (1 H, dd, $J_{1',2'} = J_{2',3'} = 8.8$, 2′-H), 3.99 (1 H, m, J_{gem} 12.4, 6′-H), 4.35 (1 H, d, $J_{1',2'}$ 8.8, 1′-H); NOE C(1′)–H ⟷ C(5′)–H.

Minor β-anomer: 8%; foam; *m/z* (FAB) 965 $(M + 1)^+$; δ_H 0.90–1.12 (56 H, m, Pr^i × 8), 3.07 (1 H, m, 5′-H), 3.35 (2 H, s, CH_2), 3.68, 3.73, 3.74 and 3.87 (3 H × 4, s, Me × 4), 3.70 (1 H, dd, $J_{2',3'} = J_{3',4'} = 8.2$, 3′-H), 3.79 (1 H, dd, $J_{3',4'}$ 8.9, $J_{2',3'}$ 8.2, 4′-H), 3.79 (1 H, dd, $J_{1',2'}$ 8.5, $J_{2',3'}$ 8.2, 2′-H) and 3.02 and 3.20 (1 H × 2, dd, J_{gem} 12.4, $J_{5',6'}$ 1.6, 6′-H_2); NOE C(1′)–H ⟷ C(5′)–H.

Deprotection of Compound **3**.—A mixture of compound **3** (241 mg, 0.25 mmol), toluene (10 cm^3), and tetrabutylammonium fluoride (1 mol dm^{-3} THF solution, 1 cm^3) was stirred at room temperature for 30 min. The resulting mixture was added to water and then extracted with AcOEt. The extract was purified by HPLC [Nucleosil $5NH_2$; eluent: MeCN–water (6:4)] to give *deprotected compound* **3** in 80% yield (Found: C, 45.2; H, 5.3; N, 3.0. $C_{18}H_{25}NO_{14}$ requires C, 45.1; H, 5.3; N, 2.9%); *m/z* (FAB) 480 $(M + 1)^+$.

3,4,5-*Tris*(*methoxycarbonyl*)-3-*methoxycarbonylmethyl*-2,3-*dihydroisoxazole* **4**.—A mixture of the main β-anomer of compound **3** (270 mg, 0.29 mmol), diethyl ether (2 cm^3) and 5% HCl–MeOH (20 cm^3) was stirred for 7 h at 40 °C. The reaction mixture was evaporated, the residue was added to water (20 cm^3), and the mixture was adjusted to pH 9 with saturated aq. Na_2CO_3, and extracted with CH_2Cl_2. The extract was performed by the usual PLC work-up [$CHCl_3$–AcOEt (30:1)] to afford compound **4** as the (+)-form in 61% yield. In a similar way, the (−)-form of compound **4** was derived in 51% yield from the main α-anomer of compound **3**.

(−)-*Form* of **4**: Oil (51%) (Found: C, 45.6; H, 5.0; N, 4.5. $C_{12}H_{15}NO_9$ requires C, 45.4; H, 4.8; N, 4.4%); *m/z* (FAB) 318 $(M + 1)^+$; $[\alpha]_D$ −147° (*c* 0.48, $CHCl_3$); ν/cm^{-1} 3230 (NH), 2950 and 2980 (CH) and 1740 and 1720 (CO); δ_H 2.88 and 3.56 (2 H, d, J_{gem} 17.1, CH_2), 3.69, 3.73, 3.83 and 3.88 (3 H × 4, s, Me × 4) and 8.30 (1 H, s, NH); δ_C 40.09 (CH_2), 52.11, 52.18, 53.42 and 53.81 (Me × 4), 72.58 (C-3), 108.03 (C-4), 155.27 (C-5) and 158.51, 161.78, 170.53 and 170.59 (CO × 4).

(+)-Form of **4**: Oil (51%); *m/z* (FAB) 318 $(M + 1)^+$; $[\alpha]_D$ +147° (*c* 0.46, $CHCl_3$).

2,3,-O-*Isopropylidene*-5-O-*trityl*-D-*ribose Oxime* **5**.[10]—The preparative method was modified as follows: A mixture of D-ribose (3 g, 20 mmol), dimethylformamide (DMF) (37.5 cm^3), 2,2-dimethoxypropane (7.5 cm^3), and TsOH·$2H_2O$ (4.5 mg) was stirred at room temperature overnight. The reaction mixture was evaporated under 60 °C to remove DMF. The obtained oil was dissolved in CH_2Cl_2 (30 cm^3). A mixture of the resulting CH_2Cl_2 solution, trityl chloride (8.4 g, 30 mmol) and small amount of 4-(dimethylamino)pyridine was refluxed overnight. The reaction mixture was poured into water (30 cm^3) and extracted with CH_2Cl_2 (3 × 20 cm^3). The combined extract was dried over Na_2SO_4 and then rotary evaporated to give a brown syrupy material, which was purified by LPLC on silica gel [diethyl ether–hexane (1:1)] (60%).

Next, ethanol (10 cm^3) containing NaOEt (5 mmol) was treated with NH_2OH·HCl (0.35 g, 5 mmol) under nitrogen. The mixture was stirred, cooled, and filtered through a glass filter at 0 °C. The filtrate was added with the above ethanolic NH_2OH solution and a small amount of molecular sieves 4 Å. The resultant mixture was stirred under nitrogen overnight and then purified by LPLC [AcOEt–hexane (2:3)] to give compound **5** in 98% yield as a foam.

Intermediary Nitrone **6**.—The above reaction was stopped after 30 min. Usual work-up was performed: foam; ν/cm^{-1} 3040 (Ar, CH), 2900 (CH), and 1740 and 1710 (CO); δ_H 3.06 and 3.57 (2 H, dd, J_{gem} 10, $J_{4,5} = J_{4,5'} = 3$, CH_2), 3.71 (3 H, s, Me), 3.78 (2 H, s, CH_2CO_2Me), 3.87 (3 H, s, Me), 4.75 (1 H, dd, $J_{2,3}$ 5.4, $J_{3,4}$ 2.7, 3-H), 4.88 (1 H, m, 4-H), 5.27 (1 H, dd, $J_{1,2} = J_{2,3} =$ 5.4, 2-H), 7.00 (1 H, d, $J_{1,2}$ 5.4, 1-H).

2-(2,3,-O-*Isopropylidene*-5-O-*trityl*-D-*ribosyl*)-3,4,5-*tris*-(*methoxycarbonyl*)-3-*methoxycarbonylmethyl*-2,3-*dihydroisoxazole* **7**.—A mixture of compound **5** (224 mg, 0.5 mmol), DMAD (0.99 cm^3, 8 mmol), and CH_2Cl_2 (0.4 cm^3) was stirred for 72 h to give a pasty material in 98% yield. Usual purification with PLC on silica gel [AcOH–$CHCl_3$ (1:30)] was performed; the products were the main α riboside of compound **7** (52%), the minor α riboside (5.5%), the main β riboside (27%), and the minor β riboside (13.5%).

Main α riboside of compound **7**: Foam (Found: C, 64.2; H, 5.7; N, 2.0. $C_{39}H_{41}NO_{13}$ requires C, 64.0; H, 5.7; N, 1.9%); *m/z* (FAB) 732 $(M + 1)^+$; ν/cm^{-1} 3060 (Ar, CH), 2930 and 2850 (CH) and 1720–1740 (CO); δ_H 1.30, 1.53 (3 H × 2, s, Me × 2), 3.03 (1 H, dd, J_{gem} 10.3, $J_{4',5'}$ 2.9, 5′-H), 3.30 (2 H, s, CH_2CO_2Me), 3.40 (1 H, dd, J_{gem} 10.3, $J_{4',5'}$ 3.1, 5′-H), 3.56, 3.68, 3.76 and 3.87 (3 H × 4, s, CO_2Me × 4), 4.24 (1 H, m, 4′-H), 4.56 (1 H, m, 3′-H), 4.88 (1 H, m, 2′-H), 5.56 (1 H, d, $J_{1',2'}$ 5.1, 1′-H) and 7.21–7.48 (15 H, m, Ph × 3); NOE C(1′)–H ⟷ C(3′)–H, C(1′)–H ⟷ C(5′)–H; δ_C 24.9 and 25.5 (CMe_2), 38.6 (C-6), 51.8, 51.9, 52.9 and 53.5 (CO_2Me), 65.1 (C-5′), 75.9 (C-3), 80.6, 81.7 and 81.8 (C-2′, -3′ and -4′), 87.5 (Ph_3C), 90.5 (C-1′), 109.4 (C-4), 114.0 (Me_2C), 143.4 (*ipso*-C of Ph), 152.2 (C-5) and 158.2, 162.2, 169.3 and 169.4 (CO).

Main β riboside of compound **7**: Foam (Found: C, 63.8; H, 5.5; N, 2.2%); *m/z* (FAB) 732 $(M + 1)^+$; ν/cm^{-1} 3060 (Ar, CH), 2930 and 2850 (CH) and 1710, 1720, 1730 and 1740 (CO); δ_H 1.31 and 1.49 (3 H × 2, s, CMe_2), 3.01 and 3.12 (2 H, d, J_{gem} 16.1, CH_2), 3.22 (1 H, dd, J_{gem} 9.6, $J_{4',5'}$ 7.29, 5′-H), 3.27 (1 H, dd, J_{gem} 9.6, $J_{4',5'}$ 5.5, 5′-H), 3.51, 3.71, 3.72 and 3.73 (3 H × 4, s, CO_2Me × 4), 4.18 (1 H, m, 4′-H), 4.51 (1 H, m, 3′-H), 4.78 (1 H, m, 2′-H), 5.06 (1 H, d, $J_{1',2'}$ 1.4, 1′-H), 7.21–7.48 (15 H, br s, Ph × 3); NOE C(1′,2′,3′)–H ⟷ CMe_2.

Minor β riboside of **7**: Foam; ν/cm^{-1} 3060 (Ar, CH), 2930 and 2850 (CH) and 1710–1740 (CO); δ_H 1.30, 1.52 (3 H × 2, s, CMe_2), 3.17 and 3.20 (2 H, d, J_{gem} 15.7, CH_2), 3.10 (1 H, dd, J_{gem} 10.2, $J_{4',5'}$ 4.3, 5′-H), 3.30 (1 H, dd, J_{gem} 10.2, $J_{4',5'}$ 4.9, 5′-H), 3.43, 3.58, 3.67 and 3.76 (3 H × 4, s, CO_2Me × 4), 4.14 (1 H, m, 4′-H), 4.52 (1 H, m, 3′-H), 4.82 (1 H, m, 2′-H), 5.18 (1 H, d, $J_{1',2'}$ 3.0, 1′-H), 7.21–7.50 (15 H, br s, Ph × 3); NOE C(1′,2′,3′)–H ⟷ CMe_2.

2-(2,3-O-*Isopropylidene*-β-D-*ribosyl*)-3,4,5-*tris*(*methoxycarbonyl*)-3-*methoxycarbonylmethyl*-2,3-*dihydroisoxazole* **8**.—A mixture of the α riboside of compound **7** (293 mg, 0.4 mmol), a small amount of $FeCl_3$, and CH_2Cl_2 (30 cm^3) was stirred for 1 h at 0 °C. The reaction mixture was worked up by the usual PLC on silica gel to give *compound* **8** in 63% yield: oil (Found: C, 49.0; H, 5.6; N, 3.0. $C_{20}H_{27}NO_{13}$ requires C, 49.1; H, 5.6; N, 2.9%); *m/z* (FAB) 490 $(M + 1)^+$; $[\alpha]_D$ −31° (*c* 0.54, $CHCl_3$); ν/cm^{-1} 3600–3200 (OH), 3050 (Ar, CH), 2970 and 2940 (CH) and 1720, 1730 and 1735 (CO); δ_H 1.33 and 1.50 (3 H × 2, s, CMe_2), 3.16 and 3.23 (2 H, d, J_{gem} 15.8, CH_2), 3.40 (1 H, m, 5′-H), 3.64 (1 H, m, 5′-H), 3.67, 3.73, 3.81 and 3.90 (3 H × 4, s, CO_2Me × 4), 4.34 (1 H, m, 4′-H), 4.76 (1 H, m, 3′-H), 4.91 (1 H, m, 2′-H) and 5.05 (1 H, d, $J_{1',2'}$ 1.6, 1′-H); NOE C(1′,2′,3′)–H ⟷ CMe_2.

Compound **8** was also obtained, in 79% yield, starting from the β riboside of compound **7**. The conversion of the carbohydrate **8** into compound **4** was carried out by the same method as previously described for the preparation of compound.[4]

(1'S,2'R,3'R)-3-(3'-*Hydroxy*-1',2'-*isopropylidenedioxy*-4'-*trityloxybutyl*)-4,5-*bis*(*methoxycarbonyl*)*isoxazole* **10a**.—To a stirred mixture of compound **5a** (223 mg, 0.5 mmol), DMAD (0.5 cm^3, 4 mmol), and CH_2Cl_2 (2 cm^3) was added a solution of 5% aq. NaOCl and triethylamine (0.02 cm^3) at 0 °C. The mixture was stirred at the same temperature for 6 h. The colour of the solution changed to blue. The resulting solution was extracted with CH_2Cl_2 and the extract was dried over $MgSO_4$ and then evaporated. The residue was purified by PLC on silica gel (CH_2Cl_2) to give *compound* **10a** as a foam in 86% yield (Found: C, 67.6; H, 5.9; N, 2.3. $C_{33}H_{33}NO_9$ requires C, 67.5; H, 5.7; N, 2.4%); *m/z* (EI) 586 $(M - 1)^+$; ν/cm^{-1} (KBr) 3515 (OH), 3040 (Ar, CH), 2970 and 2940 (CH) and 1740 (CO); δ_H 1.42 (3 H, s, Me), 1.49 (3 H, s, Me), 2.21 (1 H, d, OH), 3.25–3.35 (2 H, m, CH_2), 3.49 (1 H, m, 3'-H), 3.88 (3 H, s, CO_2Me), 3.99 (3 H, s, CO_2Me), 4.46 (1 H, dd, $J_{1',2'}$ 6.1, $J_{2',3'}$ 9.5, 2'-H), 5.77 (1 H, d, $J_{1',2'}$ 6.1) and 7.21–7.48 (15 H, m, Ph); δ_C 25.3 (Me), 26.9 (Me), 52.7 (CO_2Me), 53.4 (CO_2Me), 64.6 (CH_2), 69.2, 72.6 and 79.9 (C-1', -2' and -3'), 86.9 (Ph_3CO), 110.4 (C-4), 115.0 (CMe_2), 127.0–128.7 (Ar), 143.7 (Ar-*ipso*), 156.9 (C-5) and 160.1, 160.8 and 161.0 (C-3, CO × 2).

(1'S,2'R,3'R)-3-(3'-*Hydroxy*-1',2'-*isopropylidenedioxy*-4'-*trityloxybutyl*)-4-*methoxycarbonylisoxazole* **10b**.—The reaction was carried out by the same method as mentioned above but using ethyl propiolate in place of DMAD: *Foam*, 70% (Found: C, 70.8; H, 6.1; N, 2.4. $C_{32}H_{33}NO_7$ requires C, 70.7; H, 6.1; N, 2.6%); *m/z* (EI) 542 $(M - 1)^+$; δ_H 1.41 and 1.50 (3 H, s, Me), 1.41 (3 H, d, *J* 7.1, CH_2Me), 2.51 (1 H, br s, OH), 3.32–3.37 (3 H, m, $J_{1',2'}$ 6.4, $J_{2',3'}$ 8.8, CH_2), 5.44 (1 H, d, $J_{1',2'}$ 6.4, 1'-H) and 7.21–7.43 (15 H, m, Ph); δ_C 14.1 (CH_2Me), 25.1 and 27.0 (Me), 62.3 (CH_2Me), 64.9 (CH_2OTr), 69.0 (C-3'), 72.6 (C-2'), 77.8 (C-1'), 86.9 (CMe_2), 109.2 (C-4), 110.3 (CPh_3), 127.1, 127.8 and 128.6 (Ph), 143.7 (Ph-*ipso*), 156.7 (CO), 160.2 (C-5) and 163.2 (C-3).

2,3-O-*Isopropylidene*-5-O-*trityl*-D-*ribonohydroximo*-1,4-*lactone* **11**.—Aq. NaOCl (2.4 cm^3) was added dropwise to a solution of compound **5a** (447 mg, 1 mmol) in CH_2Cl_2 (5 cm^3) at 0 °C. The reaction mixture was stirred for 20 min at the same temperature and then for 30 min at room temperature. The resultant mixture was extracted with CH_2Cl_2 and the extract was dried over $MgSO_4$. Purification by TLC on silica gel [CH_2Cl_2–AcOEt (20:1)] gave compound **11** as a foam in 99% yield (lit.,[8] 88.3%); ν/cm^{-1} (KBr) 3350 (OH), 3020 (Ar, CH), 2990–2850 (CH) and 1690 (C=N); δ_H 1.32 (3 H, s, Me), 1.46 (3 H, s, Me), 2.96 (1 H, dd, $J_{4,5}$ 3, J_{gem} 9.2, 5-H), 3.60 (1 H, dd, $J_{4,5'}$ 3.2, J_{gem} 9.2, 5'-H), 4.53 (2 H, m, 3- and 4-H), 5.12 (1 H, d, $J_{2,3}$ 6, 2-H), 7.19–7.38 (15 H, m, Ph × 3) and 7.54 (1 H, s, OH).

(1'S,2'R,3'R)-3-(3'-*Hydroxy*-1',2'-*isopropylidenedioxy*-3'-*trityloxybutyl*)-5-*phenyl*-2,5-*dihydroisoxazole* **12**.—The reaction was performed using styrene in place of DMAD in the same way as described in the preparation of compound **10a**. For *compound* **12** (Found: C, 76.5; H, 6.6; N, 2.6. $C_{35}H_{35}NO_5$ requires C, 76.5; H, 6.4; N, 2.6%); *m/z* (EI) 549 (M^+); ν/cm^{-1} (KBr) 3350 (NH), 3050 (Ar, CH) and 2920 and 2970 (CH); δ_H 1.22 (3 H, s, Me), 1.38 (3 H, s, Me), 2.30 (1 H, br, OH), 2.80 (1 H × 2, br, J_{gem} 11, 4'-Hz), 3.60 (1 H, m, 3'-H), 4.00 (1 H, d, *J* 8, 5-H), 4.40 (1 H, d, *J* 8, CH), 4.44 (1 H, m, 2'-H), 5.08 (1 H, d, $J_{1',2'}$ 6, 1'-H), 6.80–7.24 (20 H, m, Ph × 4) and 8.10 (1 H, br s, NH).

(1'S,2'R,3'R)-3-(3'-*Hydroxy*-1',2'-*isopropylidene*-3'-*trityloxybutyl*)*isoxazole* **14**.—To a mixture of compound **5a** (223 mg, 0.5 mmol), divinyl sulphone (470 mg, 4.0 mmol), and CH_2Cl_2 (2.0 cm^3) was added 5% aq. NaOCl (2.0 cm^3). The resulting mixture was stirred at 0 °C for 1 h and was then added with water. Extraction of CH_2Cl_2 was performed and the extract was evaporated to give compound **13** as an oil.

A mixture of intermediate **13**, dry MeOH (10 cm^3), Na_2HPO_4 (284 mg, 2 mmol), and 5% Na/Hg (2 g) was stirred at room temperature for 1 h. The reaction mixture was filtered through Celite and washed with diethyl ether. The filtrate was purified by PLC [AcOEt–hexane (1:1)] to give *compound* **14** as a foam in 37% yield (Found: C, 69.2; H, 5.9; N, 2.8. $C_{29}H_{29}NO_7$ requires C, 69.2; H, 5.8; N, 2.8%); *m/z* (EI) 503 (M^+); ν/cm^{-1} (KBr) 3350 (OH), 3040 (Ar, CH) and 2900 (CH); δ_H 1.42 (3 H, s, Me), 1.49 (3 H, s, Me), 2.75 (1 H, d, *J* 5.3, OH), 3.29 (1 H, dd, J_{gem} 9.7, $J_{3',4'}$ 3.11, 4'-H), 3.34 (1 H, dd, J_{gem} 9.7, $J_{3',4'}$ 5.3, 4'-H), 3.44–3.50 (1 H, m, 3'-H), 4.51 (1 H, dd, $J_{1',2'}$ 6.4, $J_{2',3'}$ 9.3, 2'-H), 5.46 (1 H, d, $J_{1',2'}$ 6.4, 1'-H), 6.36 (1 H, d, $J_{4,5}$ 1.7, 5-H), 7.20–7.44 (15 H, m, Ph × 3) and 8.40 (1 H, dd, $J_{4,5}$ 1.7, $J_{1',4}$ 0.4, 4-H); δ_C 25.1 (Me), 27.1 (Me), 64.8 (C-4'), 69.2 (C-3'), 72.8 (C-2'), 77.9 (C-1'), 86.7 (CMe_2), 104.3 (C-4), 110.1 (CPh_3), 127.0, 127.8 and 128.6 (Ph), 143.8 (Ar-*ipso*), 158.2 (C-5) and 161.8 (C-3).

Deprotection of Compound **14**.—A mixture of compound **14** (503 mg, 1 mmol), MeOH (1 cm^3), and aq. 5% HCl (5 cm^3) was stirred for 3 h at 0 °C. Ion-exchange chromatography [Amberlite-IRA-410 (30 cm^3)] with MeOH was performed. The resulting filtrate was condensed to give an oil, which was then washed with hexane to remove triphenylmethanol. The *deprotected compound* **14** was obtained in 95% yield. Purity was determined by HPLC [Nucleosil $5NH_2$, eluent: MeCN–water (3:2)] (Found: C, 44.6; H, 5.9; N, 7.7. $C_7H_{11}NO_5$ requires C, 44.4; H, 5.9; N, 7.4%); *m/z* (FAB) 190 $(M + 1)^+$.

(3S,5S,7R,8R,9R)-8,9-*Isopropylidenedioxy*-3-*methoxycarbonyl*-1-[2'-(*methoxycarbonyl*)*ethyl*]-7-*trityloxymethyl*-2,6-*dioxa*-1-*azaspiro*[4.4]*nonane* **16**.—A mixture of compound **11** (111 mg, 0.25 mmol), methyl acrylate (0.5 cm^3, 5.5 mmol), and dry toluene (1.5 cm^3) was heated at 120 °C in a sealed tube (volume 5 cm^3) for 10 h. The solution was evaporated and the residue was dried *in vacuo* for 15 min to yield crude products, which were purified by PLC on silica gel [AcOEt–hexane (2:3)] to give an isomeric mixture in 97% yield. Additional purification with THF–cyclohexane (2:3) as developer gave *compound* **16** as a foam in 85% yield; m.p. 56–57 °C (Found: C, 68.0; H, 6.3; N, 2.3. $C_{35}H_{39}NO_9$ requires C, 68.1; H, 6.4; N, 2.3%); *m/z* (EI) 617 (M^+); ν/cm^{-1} (KBr) 3040 (Ar, CH), 2960 and 2930 (CH) and 1725 (CO); δ_H 1.32 (3 H, s, Me), 1.52 (3 H, s, Me), 2.32 (1 H, ddd, J_{gem} 15.8, $J_{1',2'} = J_{1'',2''}$ = 7.9, 1'-H), 2.53 (1 H, dd, J_{gem} 12.4, $J_{3,4}$ 8.9, 4-H), 2.62 (1 H, ddd, J_{gem} 15.8, $J_{1',2'}$ 5.3, $J_{1'',2''}$ 8.4, 1'-H), 2.94 (1 H, ddd, J_{gem} 13.2, $J_{1',2'}$ 7.9, $J_{1'',2'}$ 5.3, 2'-H), 2.99 (1 H, dd, J_{gem} 12.4, $J_{3,4'}$ 7.4, 4'-H), 3.06 (1 H, ddd, J_{gem} 13.2, $J_{1',2'}$ 7.9, $J_{1'',2'}$ 8.4, 2'-H), 3.15 (2 H, m, 10-H_2), 3.59 (3 H, s, COMe), 3.72 (3 H, s, COMe), 4.72 (1 H, ddd, $J_{7,10} = J_{7,10'}$ = 6.4, $J_{7,8}$ 2.4, 7-H), 4.49 (1 H, d, $J_{8,9}$ 6.8, 9-H), 4.53 (1 H, dd, $J_{3,4}$ 8.9, $J_{3,4'}$ 7.4, 3-H), 4.57 (1 H, dd, $J_{8,7}$ 2.4, $J_{8,9}$ 6.8, 8-H) and 7.22–7.43 (15 H, m, Ph × 3); δ_C 25.2 (Me), 26.5 (Me), 32.4 and 35.9 (C-4, -21), 45.9 (C-1'), 51.4 and 52.4 (CO*Me* × 2), 63.7 (C-10), 75.3, 81.4, 83.7 and 84.1 (C-3, -7, -8 and -9), 86.9 (Ph_3CO), 104.5 (C-5), 113.7 (Me_2C), 127.1, 127.9 and 128.6 (Ph), 143.7 (Ph-*ipso*) and 172.2 and 172.6 (CO).

(3S,5R,7R,8R,9R)-3-*Acetyl*-8,9-*isopropylidenedioxy*-1-(3'-*oxobutyl*)-7-*trityloxymethyl*-2,6-*dioxa*-1-*azaspiro*[4.4]*nonane* **17**.—A mixture of methyl vinyl ketone (0.5 cm^3, 6 mmol), compound **11** (225 mg, 0.5 mmol), and toluene (1.5 cm^3) was heated at 120 °C for 10 h in a sealed tube under nitrogen. The reaction mixture was evaporated to give an oil. Purification by TLC on silica gel [AcOEt–hexane (1:1)] gave compound **17** as a powder in 48% yield, together with the 3*R*-isomer of compound **17** (37%); m.p. 177–178 °C (Found: C, 71.8; H, 6.7; N, 2.4. $C_{35}H_{39}NO_7$ requires C, 71.6; H, 6.7; N, 2.3%); *m/z* (EI) 585

(M^+); ν/cm^{-1} (KBr) 3010 (Ar, CH), 2950 and 2900 (CH) and 1710 (CO); δ_H 1.32 (3 H, s, Me), 1.51 (3 H, s, Me), 2.15 (3 H, s, COMe), 2.29 (3 H, s, COMe), 2.44 (1 H, dd, J_{gem} 13.4, $J_{3,4}$ 4.7, 4-H), 2.68 (1 H, ddd, J_{gem} 0, $J_{1',2'} = J_{1'',2'}$ = 6.2, 2'-H), 2.94 (1 H, dd, J_{gem} 13.4, $J_{3,4'}$ 10.0, 4'-H), 3.01 (1 H, ddd, J_{gem} 12.4, $J_{1',2'} = J_{1',2''}$ = 6.2, 1'-H), 3.04 (1 H, ddd, J_{gem} 12.4, $J_{1',2} = J_{1'',2''}$ = 6.2, 1'-H), 3.21 (2 H, d, $J_{7,10}$ 5.3, CH_2OTr), 4.06 (1 H, ddd, $J_{7,8}$ 3.4, 7-H), 4.39 (1 H, dd, $J_{3,4}$ 4.7, $J_{3,4'}$ 10.0, 3-H), 4.56–4.61 (2 H, m, 4-H) and 7.22–7.44 (15 H, m, Tr).

(5R,7R,8R,9R)-3-*Cyano*-1-(2'-*cyanoethyl*)-8,9-*isopropylidenedioxy*-7-*trityloxymethyl*-2,6-*dioxa*-1-*azaspiro*[4.4]*nonane* **18**.—The reaction was carried out in the same way as described in the preparation of compound **16** [**11** (90 mg, 0.2 mmol), acrylonitrile (239 mg, 4.5 mmol), toluene (1.5 cm^3); 120 °C; 14 h; 48% yield]. *Powder* (Found: C, 71.7; H, 6.1; N, 7.5. $C_{33}H_{33}N_3O_5$ requires C, 71.9; H, 6.0; N, 7.6%); m/z (EI) 551 (M^+); ν/cm^{-1} (KBr) 3050 (Ar, CH), 2920 and 2960 (CH) and 2240 (CN); δ_H 1.30–1.33 (3 H, m, Me), 1.50–1.52 (3 H, m, Me), 2.23 and 2.40 (1 H × 2, m, 2'-H_2), 2.60 and 2.80 (1 H × 2, m, 4-H_2), 3.05 and 3.12 (1 H × 2, m, CH_2OTr), 3.18 and 3.25 (1 H × 2, m, 1'-H_2), 4.10–4.70 (3 H, m, 7-, 8- and 9-H), 4.85 (1 H, m, 3-H) and 7.20–7.50 (15 H, m, Ph × 3).

(2R,3R,4R,5R,8S)-8-*Hydroxy*-3,4-*isopropylidenedioxy*-6-[2'-(*methoxycarbonyl*)*ethyl*]-7-*oxo*-2-*trityloxymethyl*-1-*oxa*-6-*azaspiro*[4.4]*nonane* **19**.—A mixture of Raney nickel (*ca.* 1 g), compound **16** (77 mg, 0.125 mmol), and methanol (2 cm^3) was refluxed for 2 h. The reaction mixture was filtered through Celite and the filtrate was evaporated to give an oil. Purification by PLC on silica gel [AcOEt–hexane (1:1)] gave *compound* **19** in 70% yield: crystals; m.p. 75–77 °C (Found: C, 69.5; H, 6.4; N, 2.4. $C_{34}H_{37}NO_8$ requires C, 69.2; H, 6.4; N, 2.3%); m/z (EI) 587 (M^+); ν/cm^{-1} (KBr) 3380 (OH), 2960 (Ar, CH), 2920 and 2850 (CH) and 1720 and 1690 (CO); δ_H 1.35 (3 H, s, Me), 1.53 (3 H, s, Me), 2.37 (2 H, d, 2'-H), 2.67 (2 H, dd, 1'-H), 3.27 (2 H, dd, $J_{8,9}$ 3.4, $J_{8,9'}$ 8.0, 9-H_2), 3.50 (2 H, m, 10-H_2), 3.53 (3 H, s, CO_2Me), 3.93 (1 H, dd, $J_{8,9}$ 3.4, $J_{8,9'}$ 8.0, 8-H), 4.42 (1 H, m, 2-H), 4.70 (1 H, m, 3-H), 4.70 (1 H, d, $J_{3,4}$ 7.8, 4-H) and 7.20–7.52 (15 H, m, Ph × 3).

(2R,3R,4R,5R,8S)-8-*Hydroxy*-6-(3'-*hydroxypropyl*)-3,4-*isopropylidenedioxy*-2-*trityloxymethyl*-1-*oxa*-6-*azaspiro*[4.4]-*nonane* **20**.—To a dry THF solution of compound **19** (56 mg, 0.095 mmol) was added $LiAlH_4$ (11.4 mg, 0.3 mmol). The colour of solution changed to red gradually. The reaction mixture was refluxed for 3.5 h and then ice-cooled and quenched with water and 0.1 mol dm^{-3} NaOH. The resulting solution was filtered through Celite and washed with diethyl ether. Purification by PLC on silica gel [AcOEt–MeOH (9:1)] gave *compound* **20** as an oil in 40% yield (Found: C, 70.8; H, 6.7; N, 2.5. $C_{33}H_{37}NO_7$ requires C, 70.8; H, 6.7; N, 2.5%); m/z (FAB) 560 ($M + 1$)$^+$; δ_H 1.26 and 1.31 (3 H × 2, s, CMe_2), 1.60 and 1.74 (1 H × 2, m, 2'-H_2), 1.87 (1 H, ddd, J_{gem} 13.2, $J_{1',2'}$ 7.1, $J_{1',2''}$ 3.3, 2'-H), 2.13 (1 H, ddd, J_{gem} 13.2, $J_{1',2''}$ 3.3, $J_{1'',2''}$ 6.6, 2'-H), 2.36 (1 H, dd, J_{gem} 16.0, $J_{8,9}$ 5.2, 9-H), 2.62 (1 H, ddd, J_{gem} 16.0, $J_{8,9}$ 3.3, 9-H), 3.10 (1 H, br, 8-OH), 3.22 (1 H, dd, $J_{8,9}$ 5.2, $J_{8,9}$ 3.3, 8-H), 3.24 and 3.29 (1 H × 2, m, 3'-H_2), 3.41 and 3.44 (1 H × 2, m, 7-H_2), 3.73 (2 H, m, 3'-OH and 3-H), 3.83 (1 H, m, 2-H), 3.99 (1 H, dd, J_{gem} 9.3, $J_{2,10}$ 5.5, 10-H_2), 4.10 (1 H, dd, J_{gem} 9.3, $J_{2,10}$ 5.2, 10-H), 4.35 (1 H, d, $J_{3,4}$ 5.0, 4-H) and 7.21–7.48 (15 H, m, Ph × 3); δ_C 25.2, 27.6, 30.2, 38.1, 54.9, 61.5, 61.8, 62.6, 65.5, 68.6, 70.4, 77.2, 81.5, 86.2, 108.2, 127.0, 128.7, 143.9 and 144.0.

(3S,5R,7R,8R,9R)-3-*Hydroxymethyl*-8,9-*isopropylidenedioxy*-1-[2'-(*methoxycarbonyl*)*ethyl*]-7-*trityloxymethyl*-2,6-*dioxa*-1-*azaspiro*[4.4]*nonane* **21**.—To a stirred solution of compound **16** (55 mg, 0.089 mmol) in dry ethanol was added $NaBH_4$ (55 mg, 1.43 mmol), divided in 5 portions, during 20 min. When the reaction was almost complete, water (0.5 cm^3) was added. The reaction mixture was evaporated under reduced pressure and the residue was extracted with diethyl ether. Purification by PLC on silica gel [AcOEt–hexane (1:1)] gave *compound* **21** as a foam in 58% yield (Found: C, 69.3; H, 6.8; N, 2.4. $C_{34}H_{39}NO_8$ requires C, 69.3; H, 6.7; N, 2.4%); m/z (EI) 589 (M^+); ν/cm^{-1} (KBr) 3450 (OH), 3050 (Ar, CH), 2975 and 2920 (CH) and 1735 (CO); δ_H 1.32 and 1.52 (3 H × 2, s, CMe_2), 2.26 (1 H, ddd, $J_{1',2'}$ 5.3, $J_{1'',2'}$ 7.7, J_{gem} 15.9, 2'-H), 2.34 (1 H, ddd, $J_{1',2''}$ 4.9, $J_{1'',2''}$ 6.8, J_{gem} 15.9, 2'-H), 2.38 (1 H, dd, J_{gem} 12.6, $J_{3,4}$ 8.2, 4-H), 2.62 (1 H, dd, J_{gem} 12.6, $J_{3,4'}$ 8.2, 4'-H), 3.00 (2 H, m, 1'-H_2), 3.10 (1 H, br s, OH), 3.16 (1 H, dd, $J_{7,10}$ 6.7, J_{gem} 9.8, 10-H), 3.21 (1 H, dd, $J_{7,10'}$ 5.5, J_{gem} 9.8, 10-H), 3.54 and 3.73 (1 H × 2, br d, CH_2OH), 364 (3 H, s, CO_2Me), 4.21 (1 H, ddd, $J_{3,4} = J_{3,4'}$ = 8.2, $J_{3,3\alpha}$ 2.4, $J_{3,3\alpha'}$ 5.1, 3-H), 4.30 (1 H, ddd, $J_{7,8}$ 2.6, $J_{7,10}$ 6.7, $J_{7,10'}$ 5.5, 7-H), 4.53 (1 H, d, $J_{8,9}$ 6.6, 9-H), 4.57 (1 H, dd, $J_{7,8}$ 2.6, $J_{8,9}$ 6.6, 8-H), 7.22–7.45 (15 H, m, Ph × 3); δ_C 25.1 and 26.5 (CMe_2), 33.1 and 33.3 (C-2', -4), 46.1 (CH_2OH), 51.9 (OMe), 62.3 and 63.7 (C-1', -10), 78.8, 81.2, 83.1 and 83.9 (C-3, -7, -8, -9), 86.8 (CPh_3), 104.8 (C-5), 113.6 (CMe_2), 127.1, 127.9 and 128.6 (Ph), 143.6 (Ph-*ipso*) and 74.5 (CO).

(3S,5R,7R,8R,9R)-3-*Hydroxymethyl*-1-(3'-*hydroxypropyl*)-8,9-*isopropylidenedioxy*-7-*trityloxymethyl*-2,6-*dioxa*-1-*aza-spiro*[4.4]*nonane* **22**.—To a stirred solution of compound **16** (66.8 mg, 0.11 mmol) in dry THF (3 cm^3) at 0 °C was added $LiAlH_4$ (12.3 mg, 0.32 mmol). This reaction was complete immediately. Water (1 cm^3) was added to the reaction mixture, which was then filtered through Celite. After evaporation under reduced pressure, the residue was extracted with diethyl ether. Purification by PLC on silica gel [AcOEt–hexane (1:1)] gave *diol* **22** as a foam in 94% yield (Found: C, 70.6; H, 6.9; N, 2.6. $C_{33}H_{39}NO_7$ requires C, 70.6; H, 7.0; N, 2.5%); m/z (EI) 562 (M^+); ν/cm^{-1} (KBr) 3350 (OH), 3050 (Ar, CH) and 2910 (CH); δ_H 1.33 and 1.52 (3 H × 2, s, CMe_2), 1.60 (1 H, m, 2'-H), 1.72 (1 H, s, 3'-OH), 1.76 (1 H, m, 2-H), 2.31 (1 H, dd, J_{gem} 12.6, $J_{3,4}$ 6.7, 4-H), 2.46 (1 H, br, 3-CH_2OH), 2.74 (1 H, dd, J_{gem} 12.6, $J_{3,4}$ 8.9, 4-H), 2.78 (1 H, ddd, J_{gem} 13.5, $J_{2',3'}$ 5.8, $J_{2',3'}$ 7.7, 3'-H), 2.96 (1 H, ddd, J_{gem} 13.5, $J_{2',3''}$ 5.5, $J_{2'',3''}$ 6.1, 3'-H), 3.25 (2 H, d, J_{gem} 0, $J_{7,10}$ 5.5, 10-H_2), 3.59 (1 H, dd, J_{gem} 12.1, $J_{3,3\alpha}$ 3.6, 3-CHOH), 3.67 (2 H, m, 1'-H_2), 3.80 (1 H, dd, J_{gem} 12.1, $J_{3,3\alpha'}$ 2.5, 3-CHOH), 4.20 (1 H, ddd, $J_{7,10} = J_{7,10'}$ = 5.5, $J_{7,8}$ 3.6, 7-H), 4.29 (1 H, m, 3-H), 4.51 (1 H, d, $J_{8,9}$ 6.9, 9-H), 4.58 (1 H, dd, $J_{8,9}$ 6.9, $J_{7,8}$ 3.6, 8-H) and 7.22–7.46 (15 H, m, Ph × 3); δ_C 25.2 and 26.6 (CMe_2), 30.2 and 35.4 (C-2', -4), 47.4 (C-1'), 61.7, 63.0 and 63.6 (C-3', -10, 3-CH_2OH), 77.4, 80.9, 82.3 and 82.7 (C-3, -7, -8, -9), 86.9 (CPh_3), 104.3 (C-5), 114.2 (CMe_2), 127.1, 127.9 and 128.7 (Ph) and 143.7 (Ph-*ipso*).

(3R,5R)-3-[(1'R,2'R,3'R)-3'-*Hydroxy*-1',2'-*isopropylidenedioxy*-3'-*trityloxybutyl*]-5-*methoxycarbonyl*-2-[β-(*methoxycarbonyl*)*ethyl*]*isoxazolidine* **23** *and* **23'** (3S *Form of* **23**).—To a stirred solution of compound **16** (80 mg, 0.13 mmol) in EtOH (1.5 cm^3) containing AcOH (50 mm^3) was added $NaBH_3CN$ (128 mg, 2 mmol). After being stirred overnight the reaction mixture was evaporated and the residue was extracted with diethyl ether. Purification by PLC on silica gel [1, AcOEt–hexane (1:1); 2, benzene–AcOEt (10:1)] gave compound **23** (44%, foam) and compound **23'** (31%, foam).

Compound **23** (Found: C, 67.8; H, 6.7; N, 2.2. $C_{35}H_{41}NO_9$ requires C, 67.8; H, 6.7; N, 2.3%); m/z (EI) 620 (M^+); ν/cm^{-1} (KBr) 3275 (OH), 3025 and 3000 (Ar, CH), 2950 and 2910 (CH) and 1715 (CO); δ_H 1.31 and 1.32 (3 H × 2, s, CMe_2), 2.55 (1 H, ddd, J_{gem} 13.1, $J_{4,5}$ 8.7, $J_{3,4}$ 7.4, 4-H), 2.76 (2 H, 2β-H_2), 2.90 (2 H, 4-H and 2α-H), 3.17 (1 H, ddd, J_{gem} 12.5, $J_{2\beta,2\alpha'} = J_{2\alpha',2\beta'}$ = 6.3,

2α-H'), 3.32 (1 H, dd, J_{gem} 9.8, $J_{3',4''}$ 4.8, 4'-H), 3.39 (1 H, dd, J_{gem} 9.8, $J_{3',4'}$ 2.8, 4'-H), 3.48 (1 H, ddd, $J_{3,4}$ 7.2, $J_{3,4}$ 0, $J_{1',3}$ 9.9, 3-H), 3.62 (1 H, 3'-H), 3.67 and 3.76 (3 H × 2, s, CO_2Me), 3.97 (1 H, dd, $J_{1',3}$ 10.0, $J_{1',2'}$ 5.1, 1'-H), 4.38 (1 H, dd, $J_{2'',3''}$ 9.8, $J_{1',2'}$ 5.1, 2'-H), 4.58 (1 H, dd, $J_{4,5} = J_{4',5}$ = 8.9, 5-H), 4.65 (1 H, br, OH) and 7.22–7.52 (15 H, m, Ph × 3); δ_C 25.6 and 28.2 (CMe_2), 32.2 and 33.3 (C-2β, -4), 51.8 and 52.5 (OMe × 2), 53.2 (C-2α), 65.2 (C-4'), 65.9, 68.0, 75.3, 76.8 and 77.6 (C-3, -5, -1', -2', -3'), 86.4 (CPh_3), 108.8 (CMe_2), 126.8, 127.7 and 128.8 (Ph), 144.2 (Ph-*ipso*) and 172.4 and 172.9 (CO × 2).

Compound **23** (Found: C, 67.6; H, 6.7; N, 2.2. $C_{35}H_{41}NO_9$ requires C, 67.8; H, 6.7; N, 2.3%); *m/z* (EI) 620 (M^+); ν/cm^{-1} 3450 (OH), 3015 (Ar, CH), 2970, 2925 and 2875 (CH) and 1730 and 1720 (CO); δ_H 1.23 and 1.28 (3 H × 2, s, CMe_2), 2.32 (1 H, ddd, J_{gem} 13.3, $J_{3,4}$ 11.4, $J_{4,5}$ 5.6, 4-H), 2.70 (2 H, 2β-H and OH), 2.78 (1 H, ddd, J_{gem} 16.2, $J_{2\beta',2\alpha}$ 8.3, $J_{2\beta',2\alpha'}$ 5.9, 2β-H'), 2.94 (1 H, ddd, J_{gem} 13.3, $J_{3,4''}$ 13.5, $J_{4',5}$ 9.0, 4'-H), 3.08 (1 H, ddd, $J_{2\alpha,2\beta}$ 5.6, $J_{2\alpha,2\beta'}$ 7.8, J_{gem} 13.5, 2α-H), 3.24 (1 H, dd, J_{gem} 9.6, $J_{3',4'}$ 7.2, 4'-H), 3.25 (1 H, 3-H), 3.36 (1 H, ddd, J_{gem} 13.9, $J_{2\alpha',2\beta}$ 6.5, $J_{2\alpha',2\beta'}$ 8.3, 2α-H'), 3.43 (1 H, dd, J_{gem} 9.5, $J_{3',4}$ 2.9, 4'-H), 3.67 and 3.74 (3 H × 2, s, OMe × 2), 3.80 (1 H, 3'-H), 3.96 (1 H, dd, $J_{1',2'}$ 9.5, $J_{2',3'}$ 4.8, 2'-H), 4.12 (1 H, dd, $J_{1',2'}$ 9.5, $J_{1',3}$ 4.8, 1'-H), 4.45 (1 H, dd, $J_{4'',5}$ 9.4, $J_{4,5}$ 5.5, 5-H) and 7.22–7.47 (15 H, m, Ph); δ_C 25.8 and 28.0 (CMe_2), 32.9 and 36.8 (C-2β, -4), 51.6 and 52.3 (OMe × 2), 52.9 (C-2α), 64.8, 68.4, 74.1, 77.6 and 79.0 (C-3, -5, -1', -2', -3'), 65.0 (C(4'), 87.0 (CPh_3), 108.8 (CMe_2), 127.1, 127.9 and 128.6 (Ph), 143.7 (Ph-*ipso*) and 172.0 and 173.0 (CO).

(4R,5S,7R,8R,9S,10R)-8,9,10-*Tribenzyloxy*-7-*benzyloxymethyl*-4-*methoxycarbonyl*-1-[2'-(*methoxycarbonyl*)*ethyl*]-2,6-*dioxa*-1-*azaspiro*[4.5]*decane* **25** *and* (3S,5R,7R,8R,9S,10R)-8,9,10-*Tribenzyloxy*-7-*benzyloxymethyl*-3-*methoxycarbonyl*-1-[2'-(*methoxycarbonyl*)*ethyl*]-2,6-*dioxa*-1-*azaspiro*[4.5]*decane* **26**.—A mixture of compound **24**[9] (110 mg, 0.2 mmol), methyl acrylate (0.3 cm^3, 4.0 mmol), and dry toluene (0.3 cm^3) was heated at 120 °C in a sealed tube (volume 5 cm^3) for 14 h. The reaction mixture was evaporated, and the residue was purified by PLC on silica gel [1, AcOEt–hexane (2:3); 2, MeOH–THF (1:1); 3, benzene–AcOEt (10:1); 4, $CHCl_3$–MeOH (60:1)]; *compound* **25**, syrup, 44% (Found: C, 69.2; H, 6.5; N, 1.9. $C_{42}H_{47}NO_{10}$ requires C, 69.5; H, 6.5; N, 1.9%); *m/z* (EI) 726 (M^+); ν/cm^{-1} 3010 (Ar, CH), 2980 and 2940 (CH) and 1730 (CO); δ_H 2.56 (1 H, ddd, J_{gem} 15.9, $J_{1',2'} = J_{1',2''}$ = 5.8, 1'-H), 2.63 (1 H, ddd, J_{gem} 15.9, $J_{1'',2'}$ 5.3, $J_{1'',2''}$ 8.2, 1''-H), 2.94 (1 H, ddd, J_{gem} 13.6, $J_{1',2'}$ 5.8, $J_{1'',2'}$ 5.3, 2'-H), 3.58 (1 H, ddd, $J_{1',2'}$ 5.8, $J_{1'',2''}$ 8.2, 2'-H'), 3.63 and 3.68 (3 H × 2, s, CO_2Me × 2), 3.64 (1 H, ddd, J_{gem} 11.9, $J_{7,11} = J_{7,11'}$ = 1.7, 11-H), 3.72 (1 H, dd, J_{gem} 9.9, $J_{3,4}$ 6.7, 3-H), 3.79 (1 H, dd, J_{gem} 11.9, $J_{7,11} = J_{7,11'}$ = 1.7, 11-H'), 3.81 (1 H, dd, $J_{7,8} = J_{8,9}$ = 9.3, 8-H), 3.96 (1 H, dd, $J_{8,9}$ 9.3, $J_{9,10}$ 10.2, 9-H), 4.10 (1 H, ddd, $J_{7,8}$ 9.3, $J_{7,11}$ = $J_{7,11'}$ = 1.7, 7-H), 4.15 (1 H, dd, J_{gem} 9.9, $J_{3',4}$ 7.9, 3'-H), 4.20 (1 H, d, $J_{9,10}$ 10.2, 10-H), 4.42 (1 H, dd, $J_{3,4}$ 6.7, $J_{3',4}$ 7.9, 4-H), 4.44–5.05 (8 H, OCH_2Ph × 4) and 7.22–7.36 (20 H, m, Ph × 4); NOE 4-CO_2Me ⟷ 7-H; 1-CO_2Me ⟷ 9-H; δ_C 33.3 (C-1'), 46.9 (C-2'), 51.0 (C-4), 51.7 and 52.2 (CO_2Me × 2), 64.7 and 68.3 (C-3, -11), 72.6, 78.7, 79.0 and 83.0 (C-7, -8, -9, -10), 73.2, 74.9, 75.5 and 76.0 (OCH_2Ph × 4), 127.0–128.4 (Ph), 138.2, 138.3, 138.5 and 138.8 (Ph-*ipso*) and 168.6 and 173.0 (CO × 2).

Compound **26**: Syrup, 21% (Found: C, 69.3; H, 6.5; N, 1.9%); *m/z* (EI) 726 (M^+); ν/cm^{-1} 3040 (Ph, CH), 2900 and 2850 (CH) and 1735 and 1720 (CO); δ_H 2.55 (1 H, dd, J_{gem} 12.7, $J_{3,4}$ 5.8, 4-H), 2.64 (1 H, ddd, J_{gem} 15.9, $J_{1',2'} - J_{1',2''}$ = 5.8, 1'-H), 2.78 (1 H, ddd, J_{gem} 15.9, $J_{1'',2'}$ 6.8, $J_{1'',2''}$ 8.2, 1'-H'), 2.80 (1 H, dd, J_{gem} 12.7, $J_{3,4'}$ 8.3, 4-H'), 3.34–3.38 (2 H, m, 2'-H_2), 3.42 (1 H, ddd, $J_{7,8}$ 1.4, $J_{7,11}$ 10.4, $J_{7,11'}$ 2.8, 7-H), 3.50 (1 H, dd, J_{gem} 24.9, $J_{7,11}$ 10.4, 11-H), 3.57 (1 H, dd, $J_{8,9}$ 9.4, $J_{9,10}$ 9.5, 9-H), 3.58 and 3.67 (3 H × 2, s, CO_2Me × 2), 3.65 (1 H, dd, J_{gem} 24.9, $J_{7,11'}$ 2.8, 11-H'), 3.65 (1 H, d, $J_{9,10}$ 9.5, 10-H), 3.76 (1 H, dd, $J_{8,9}$ 9.4, $J_{7,8}$ 1.4, 8-H), 4.51 (1 H, dd, $J_{3,4}$ 5.9, $J_{3,4'}$ 7.9, 3-H), 4.55–4.91 (8 H, OCH_2Ph × 4) and 7.18–7.35 (20 H, m, Ph × 4); NOE 3-H ⟷ 4-H; 1-CO_2Me ⟷ 7-, 8-, 11-H; δ_C 33.2 and 37.0 (C-2', -4), 44.9 (C-1'), 51.6 and 52.2 (CO_2Me × 2), 68.6 (C-11), 73.4, 75.1, 75.6 and 75.8 (OCH_2Ph × 4), 73.9, 74.3, 77.4, 79.0 and 84.8 (C-3, -7, -8, -9, -10), 96.0 (C-5), 127.3–128.4 (Ph), 138.1, 138.4, 138.5 and 138.5 (Ph-*ipso*) and 171.0 and 173.0 (CO × 2).

(5S,7R,8R,9R)-8,9-*Isopropylidenedioxy*-3,4-*bis*(*methoxycarbonyl*)-1-*methyl*-7-*trityloxymethyl*-2,6-*dioxa*-1-*azaspiro*[4.4]*non*-3-*ene* **28**.—To a stirred mixture of compound **16** (91 mg, 0.2 mmol) and dry CH_2Cl_2 (0.7 cm^3) was added methyl trifluoromethanesulphonate (25 mm^3, 0.22 mmol). The mixture was stirred for an additional 2 h at room temperature and was then treated with DMAD (0.18 cm^3, 2.0 mmol). After being cooled at −78 °C, the mixture was treated with triethylamine (31 mm^3, 0.22 mmol) and was then stirred for 4 h. The resulting mixture was warmed to room temperature and then rotary evaporated. Purification by PLC on silica gel [AcOEt–hexane (1:3)] gave *compound* **28** as a foam in 99% yield (Found: C, 67.9; H, 6.0; N, 2.3. $C_{34}H_{35}NO_9$ requires C, 67.9; H, 5.9; N, 2.3%); *m/z* (EI) 601 (M^+); ν/cm^{-1} (KBr) 3050 (Ar, CH), 2960, 2925, 2900 and 2850 (CH) and 1755 and 1700 (CO); δ_H 1.33 and 1.56 (3 H × 2, s, CMe_2), 3.07 (1 H, dd, J_{gem} 9.9, $J_{7,10}$ 3.9, 10-H), 3.18 (3 H, s, NMe), 3.38 (1 H, dd, J_{gem} 9.9, $J_{7,10'}$ 8.0, 10-H'), 3.53 and 3.92 (3 H × 2, s, CO_2Me), 4.15 (1 H, ddd, $J_{7,10}$ 3.9, $J_{7,10'}$ 8.0, $J_{7,8}$ 5.6, 7-H), 4.71 (1 H, dd, $J_{7,8}$ 5.6, $J_{8,9}$ 6.0, 8-H), 5.06 (1 H, d, $J_{8,9}$ 6.0, 9-H) and 7.20–7.48 (15 H, m, Ph × 3); δ_C 24.9 and 27.0 (CMe_2), 37.7 (NMe), 51.6 and 53.3 (OMe × 2), 65.0 (C-10), 81.6, 84.2 and 84.6 (C-7, -8, -9), 86.6 (CMe_2), 104.3, 107.9 and 114.0 (C-4, CPh_3), 126.9–128.7 (Ph), 143.8 (Ph-*ipso*) and 153.8, 158.0 and 162.1 (C-3, CO × 2).

(3R,5S,7R,8R,9R)-8,9-*Isopropylidenedioxy*-3-*methoxycarbonyl*-1-*methyl*-7-*trityloxymethyl*-2,6-*dioxa*-1-*azaspiro*[4.4]*nonane* **29**.—The reaction was performed at room temperature in the same way as that above, by using methyl acrylate as a 1,3-dipolarophile. Purification by PLC on silica gel [AcOEt–hexane (1:2)] gave compound **29** as the main product in 49% yield. Two other isomers and a small amount of triphenylmethanol were also isolated.

Compound **29**: Foam (Found: C, 70.1; H, 6.6; N, 2.5. $C_{32}H_{35}NO_7$ requires C, 70.4; H, 6.5; N, 2.6%); *m/z* (EI) 545 (M^+); ν/cm^{-1} (KBr) 3030 (Ar, CH), 2970 and 2930 (CH) and 1750 and 1730 (CO); δ_H 1.32 and 1.53 (3 H × 2, s, CMe_2), 2.46 (NMe), 2.58 (1 H, dd, J_{gem} 12.8, $J_{3,4}$ 7.3, 4-H), 2.97 (1 H, dd, J_{gem} 12.8, $J_{3,4'}$ 9.2, 4-H'), 3.14 (1 H, dd, J_{gem} 9.8, $J_{7,10}$ 7.1, 10-H), 3.21 (1 H, dd, J_{gem} 9.8, $J_{7,10'}$ 5.3, 10-H'), 4.29 (1 H, ddd, $J_{7,8}$ 2.6, $J_{7,10}$ 7.1, $J_{7,10'}$ 5.3, 7-H), 3.74 (3 H, s, OMe), 4.43 (1 H, d, $J_{8,9}$ 6.6, 9-H), 4.50–4.55 (2 H, m, 3- and 8-H) and 7.21–7.45 (15 H, m, Ph × 3); NOE OMe ⟷ CMe_2; δ_C 25.1 and 26.5 (CMe_2), 35.1 (C-4), 38.2 (NMe), 52.4 (OMe), 63.7 (C-10), 72.5, 81.5, 83.6 and 84.2 (C-3, -7, -8, -9), 86.8 (CMe_2), 104.7 (C-5), 113.6 (CPh_3), 127.1–128.7 (Ph), 143.6 (Ph-*ipso*) and 172.3 (CO).

X-Ray Crystal Structure Determination of Compound **17**.—Crystals were prepared by slow evaporation of an ethanolic solution.

Crystal data. $C_{35}H_{39}NO_7$, M = 585.67, monoclinic, a = 11.722(1), b = 15.789(6), c = 8.593(7) Å, α = 90.000(0), β = 96.385(8), γ = 90.000(0)°, V = 1580.7 Å^3, space group $P2_1/n$, Z = 2, D_x = 1.231 g cm^{-3}.

Data collection and processing. An AFC 5 diffractometer was used, in the $\omega/2q$ mode with scan speed 4.0° min^{-1}; graphite-monochromated Cu-$K\alpha$ radiation was used; 2643 reflections were measured (2θ range 3° ≤ 2θ ≤ 120°, ±h, +k, +l); 2560

Table 2 Fractional atomic co-ordinates for compound

Atom	*x*	*y*	*z*
N(1)	0.3556	0.4930	0.9048
O(2)	0.3779	0.5298	1.0621
O(6)	0.5155	0.3990	0.9372
O(13)	0.5300	0.6784	0.6682
O(16)	0.3964	0.4306	1.4277
O(19)	0.7387	0.3331	0.9735
O(39)	0.2530	0.3014	0.8049
O(40)	0.3984	0.2085	0.8084
C(3)	0.3445	0.4672	1.1651
C(4)	0.3464	0.3820	1.0795
C(5)	0.3917	0.4047	0.9252
C(7)	0.5408	0.3131	0.8978
C(8)	0.4464	0.2867	0.7685
C(9)	0.3502	0.3510	0.7818
C(10)	0.4235	0.5452	0.8058
C(11)	0.3611	0.6279	0.7694
C(12)	0.4287	0.6898	0.6827
C(14)	0.3704	0.7711	0.6309
C(15)	0.4241	0.4676	1.3190
C(17)	0.5467	0.5053	1.3149
C(18)	0.6585	0.3095	0.8450
C(20)	0.8585	0.3378	0.9449
C(21)	0.8817	0.4196	0.8585
C(22)	0.9931	0.4351	0.8152
C(23)	1.0175	0.5117	0.7466
C(24)	0.9328	0.5725	0.7160
C(25)	0.8236	0.5582	0.7588
C(26)	0.7982	0.4829	0.8289
C(27)	0.9251	0.3453	1.1093
C(28)	1.0358	0.3148	1.1417
C(29)	1.0963	0.3275	1.2872
C(30)	1.0467	0.3717	1.4011
C(31)	0.9395	0.4029	1.3697
C(32)	0.8762	0.3920	1.2249
C(33)	0.8875	0.2572	0.8574
C(34)	0.8914	0.1807	0.9331
C(35)	0.9131	0.1071	0.6961
C(36)	0.9069	0.1060	0.8532
C(37)	0.9083	0.1831	0.6166
C(38)	0.8949	0.2576	0.6977
C(41)	0.2785	0.2145	0.7741
C(42)	0.2412	0.1926	0.6073
C(43)	0.2224	0.1590	0.8870

were given a unique absorption correction (average transmission factor 0.14) giving 2392 reflections with $I > 2\sigma(I)$.

Structure analysis and refinement. The structure was solved by the UNICS-III system (Library of Computer Center of Tokyo University) based on direct methods, and refined to a final *R*-value of 0.0559 (R_ω 0.064 blocked full-matrix least-squares refinement). Hydrogen atoms were located by the difference Fourier method using practical reflection data. Non-H atom co-ordinates are given in Table 2.*

* *Supplementary data* (see section 5.6.3 of Instructions for Authors, issue 1). Tables of bond lengths, bond angles and thermal parameters have been deposited at the Cambridge Crystallographic Data centre.

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