Thermal Rearrangement of Alkyl *O*-Vinylcarbohydroximates to 2-Alkyloxazoles

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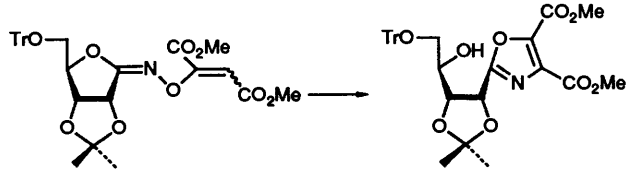
Alkyl *O*-vinylcarbohydroximates, lactoxime *O*-vinyl ethers, and sugar lactoxime *O*-vinyl ethers undergo a novel thermal rearrangement to afford the corresponding 2-alkyloxazoles, 2-(ω-hydroxyalkyl)oxazoles, and oxazoles bearing a sugar moiety, respectively. This rearrangement can also occur under photochemical conditions.

As part of the application of sugar lactoximes to organic synthesis,[1] we wished to examine the thermal reaction of the D-ribose lactoxime *O*-vinyl ether **1**, which was easily available from reaction of the corresponding lactoxime[1c] with dimethyl acetylenedicarboxylate (DMAD).

In this study we found an unprecedented thermal rearrangement.[2] This report deals with the scope and limitations of the rearrangement.

Results and Discussion

The starting compound **1** was prepared by the reaction of *N*-hydroxy-2,3-*O*-isopropylidene-5-trityl-D-ribonimido-1,4-lactone with DMAD in the presence of triethylamine (*Z*-vinyl ether **1a**: 62%; *E*-vinyl ether **1b**: 23%) (Scheme 1).



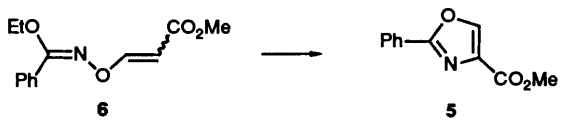
1a; *Z*-isomer
1b; *E*-isomer

2

Scheme 1 *Conditions:* heat

When compound **1a** was heated at 200 °C for 2 min under nitrogen, a rearranged product **2** was obtained as an oil in 88% yield. In addition, compound **2** could be prepared both from the isomer **1a** in refluxing toluene in 46% yield and from isomer **1b** at 200 °C in 70% yield.

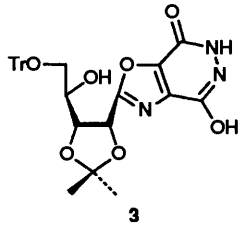
The structure of compound **2** was established by spectral evidence (see Experimental section) and the following results. (a) Reaction of compound **2** with hydrazine gave the corresponding 4,7-dihydroxyoxazolo[4,5-*d*]pyridazine derivative **3**. (b) The ^{1}H NMR data of compound **2** were different from those of the isoxazole **4** which was prepared by the reaction of 2,3-*O*-isopropylidene-5-*O*-trityl-D-ribononitrile oxide with DMAD.[1c] (c) Pyrolysis of compound **4** gave a small amount of compound **2** together with decomposed material.† The ^{13}C NMR data of compound **2** showed signals at δ 157.0, 136.0 and 142.8 ppm, respectively, values very close to those of 4-ethoxycarbonyl-2-phenyloxazole **5** [162.36 (C-2), 134.58 (C-4), and 143.6 ppm (C-5)].[4]



6 **5**

Scheme 2 *Conditions:* heat

If the present reaction were to take place in common oxime *O*-vinyl ethers, ethyl *N*-[(2′-ethoxycarbonylvinyl)oxy]benzimidate **6** would afford **5**. Thus, compound **6** was heated at 170 °C for 1 min to give the expected product **5** in 22% yield (Scheme 2).



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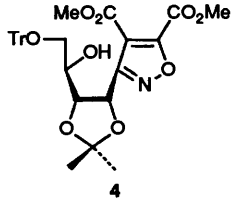
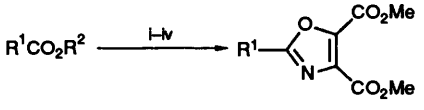


4

As alkyl *O*-vinylcarbohydroximates,‡ ethyl *N*-{[1′,2′-bis(methoxycarbonyl)vinyl]oxy}benzimidate and methyl *N*-{[1′,2′-bis(methoxycarbonyl)vinyl]oxy}dodecanimidate, which were prepared from the corresponding esters, underwent the thermal rearrangement to give the corresponding 2-substituted oxazole derivatives **8a** and **8b** in 50 and 36%, respectively (Scheme 3).



7a; R^1 = Ph, R^2 = Et
7b; R^1 = Me[CH_2]$_{10}$, R^2 = Me

8a; R^1 = Ph (50%)
8b; R^1 = Me[CH_2]$_{10}$ (36%)

Scheme 3 *Reagents and conditions:* i, O/S exchange reagent; ii, NH_2OH; iii, DMAD; iv, heat

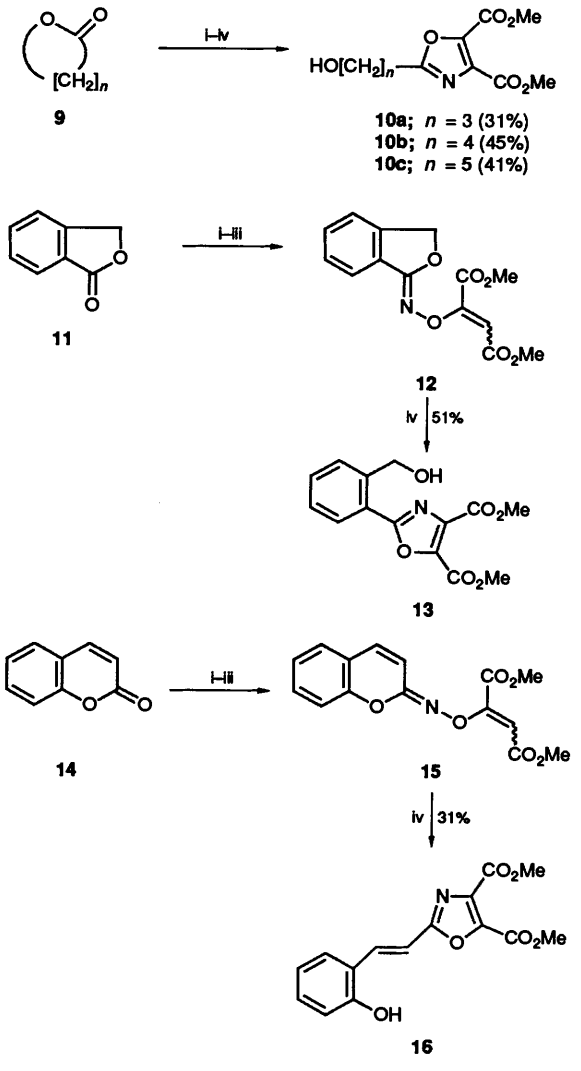
The reaction was applied to several lactones **9**, **11** and **14** to give the corresponding 2-substituted oxazoles **10**, **13** and **16** in moderate yield (Scheme 4).

Further, the reaction was applied to several sugar lactoxime *O*-vinyl ethers to afford the expected oxazoles bearing a sugar moiety at the 2-position, **17**–**20**, in poor to moderate yield (Table 1).

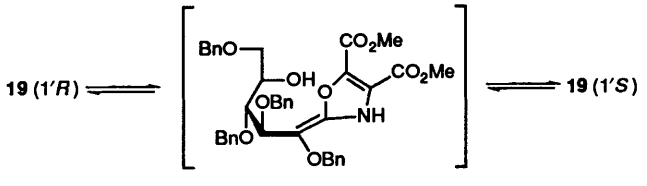
In the case of glucose, mannose and maltose derivatives, some epimerization took place at C-2 position of the sugars. The epimerization is considered to occur *via* an intermediate such as

† Pyrolysis of isoxazoles is known to give the corresponding oxazoles.[3]

‡ These compounds were previously called *O*-(1′,2′-dimethoxycarbonylvinyl)-*N*-hydroxyiminobenzoates.[5] Systematic nomenclature is used in this paper.



Scheme 4 *Reagents and conditions:* i, O/S exchange reagent; ii, NH_2OH; iii, DMAD; iv, heat



Scheme 5

21 (Scheme 5). That is, compound **19** (1'*R*/1'*S* = 7/2) was further heated at 200 °C for 6 min to change the ratio (1'*R*/1'*S* = 2/5) of the diastereo-mixture. In a similar way, a diastereo-mixture of **19** (1'*S*/1'*R* = 3/2) obtained from mannose derivatives was heated at 200 °C for 6 min to afford the same ratio (1'*R*/1'*S* = 2/5) of the diastereo-mixture.

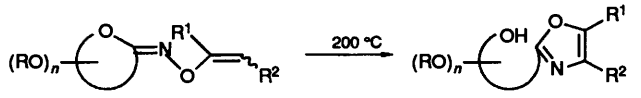
Next, the obtained oxazoles bearing a sugar moiety were deprotected in the usual way (Scheme 6). Compound **2** was converted into its bisamide derivative **22** and this was then deprotected. The deprotected compounds were identified as their acetyl derivatives.

The mechanism of this novel rearrangement can be tentatively considered in the case of the benzimidate **6** as follows (Scheme 7): Initially the cleavage of the N–O bond in substrate **6** gives radical fragments **26**, which then form an intermediate **27** having the more stable C–N bond (bond strength: N–O 53.0 kcal/mol; C–N 69.7 kcal/mol).[6,*] The species **27** is converted into **5** the oxazole *via* the dihydro compound **28** by intramolecular cyclization followed by elimination of ethanol.

Compound **2** was also prepared by irradiation of its isomer **1** in 35% yield. This result strongly supports the initial N–O bond cleavage shown in Scheme 7, because the transformation of **1** to **2** can be regarded just the same as that of **6** to **5**. Furthermore, compound **14** was detected as a by-product in the thermal reaction of diester **15**. This fact also supports the presence of an intermediate such as **26** because coumarin **14** can be derived by N–O bond cleavage of intermediate **15**. However, the detailed mechanism† is not clear and further investigations are underway to elucidate its mechanism.

As a similar reaction, the thermal reaction of ketone oxime *O*-vinyl ethers has been reported:[8] The pyrrole derivatives were isolated after concerted cleavage of an N–O bond and formation of a new C–C bond. However, the present rearrangement has not hitherto been reported. As a useful aspect of this reaction, these oxazole derivatives are expected to have interesting biological activities because some macrocyclic antibiotics,[9] alkaloids,[10] and hypolimidaemic drugs[11] contain a substituted oxazole ring. Further extension of this reaction is underway in our laboratory.

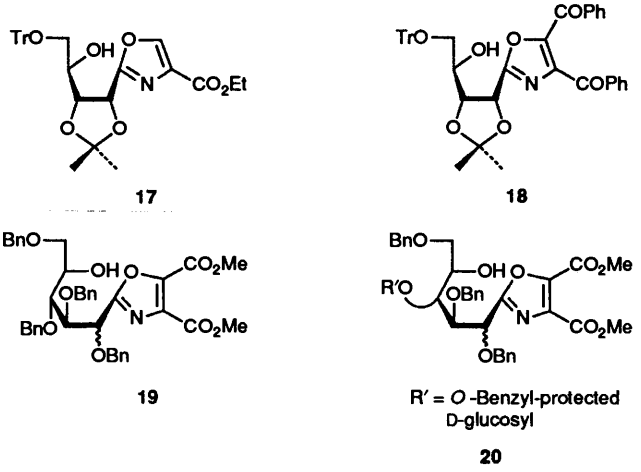
Table 1



Starting compounds

Protected sugar moiety	R^1/R^2	*t*/min	Product	Yield (%)
Ribose	H/CO_2Et	30	**17**	19
Ribose	COPh/COPh	2	**18**	19
Glucose	CO_2Me/CO_2Me	6	**19**	64[a]
Mannose	CO_2Me/CO_2Me	6	**19**	74[b]
Maltose	CO_2Me/CO_2Me	2	**20**	88[c]

[a] A diastereo-mixture of isomers **19** (1'*R*/1'*S* 7:2). [b] A diastereo-mixture of isomers **19** (1'*S*/1'*R* 3:2). [c] A diastereo-mixture of isomers **20** (1'*R*/1'*S* 3:1).

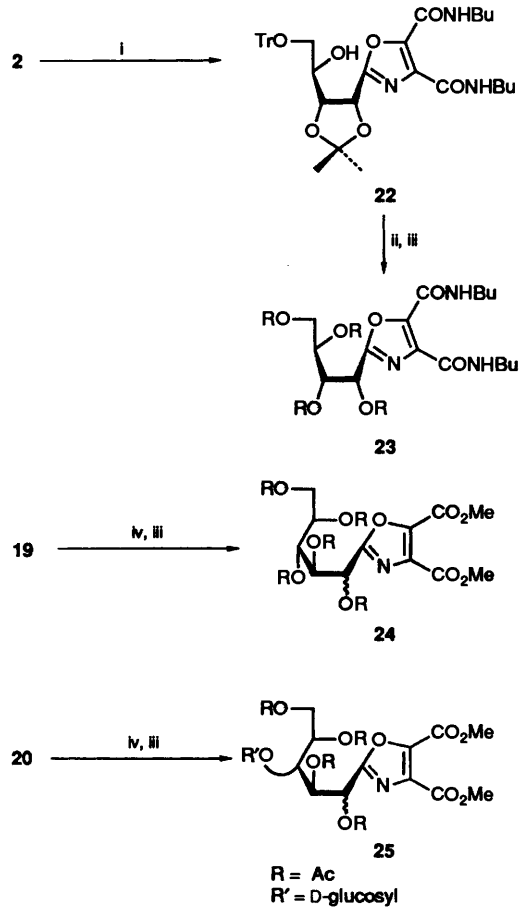


* 1 cal = 4.184 J.

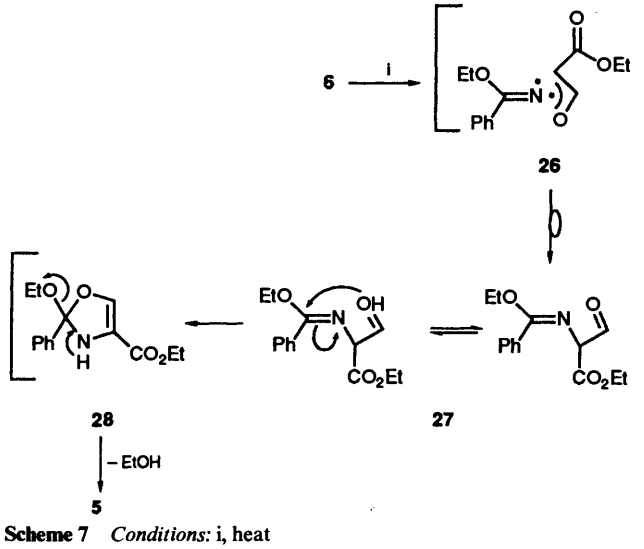
† A detailed mechanism for this kind of rearrangement has been described in the literature.[7]

Experimental

Microanalyses were performed with a Perkin-Elmer 240 elemental analyser at the Chemical Analysis Center of Chiba



Scheme 6 *Reagents:* i, $BuNH_2$; ii, HCl–MeOH; iii, 10% Pd/C; iv, Ac_2O, pyridine



Scheme 7 *Conditions:* i, heat

University. IR spectra, for neat specimens unless otherwise stated, were recorded on a Hitachi 215 spectrometer. Mass spectra were obtained on a JEOL JMS-HX 110A for FAB and on a Hitachi M-60 for EI. ^1H and ^{13}C NMR spectra, for $CDCl_3$ solution, 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 preparative TLC (PLC). Optical rotations $[\alpha]_D$ were measured on a JASCO-DIP-370 polarimeter, values for $[\alpha]_D$ are given in units of 10^{-1} deg cm^2 g^{-1}.

(Z)- *and* (E)-N-[1′,2′-*Bis*(*methoxycarbonyl*)*vinyloxy*]-2,3-O-*isopropylidene*-5-O-*trityl*-D-*ribonimido*-1,4-*lactone* **1a** *and* **1b**.—A mixture of *N*-hydroxy-2,3-*O*-isopropylidene-5-*O*-trityl-D-ribonimido-1,4-lactone (223 mg, 0.5 mmol), DMAD (0.1 cm^3, 0.8 mmol), Et_3N (0.07 cm^3, 0.5 mmol) and dry CH_2Cl_2 (1 cm^3) was stirred for 2 h at room temperature. Purification by PLC on silica gel [AcOEt–hexane (2:3)] gave products **1a** (62%, needles, m.p. 149–150 °C); and **1b** (23%, powder, m.p. 71–72 °C).

Compound **1a** (Found: C, 67.5; H, 5.7; N, 2.4. $C_{33}H_{33}NO_9$ requires C, 67.5; H, 5.7; N, 2.4%); *m/z* (EI) 587 (M^+); ν_{max}/cm^{-1} 3019 (Ar, CH), 2970, 2920 (CH), 1720 (CO) and 1680 (C=N); δ_H 1.34 and 1.51 (3 H × 2, s, CMe_2), 2.98 (1 H, dd, J_{gem} 10.8, $J_{4,5}$ 1.8, 5-H), 3.69 and 3.71 (3 H × 2, s, CO_2Me × 2), 3.73 (1 H, dd, J_{gem} 10.8, $J_{4,5'}$ 2.8, 5-H′), 4.56 (1 H, br d, $J_{2,3}$ 5.9, 3-H), 4.78 (1 H, m, 4-H), 5.36 (1 H, d, $J_{2,3}$ 5.9, 2-H), 6.15 (1 H, s, 2′-H) and 7.22–7.41 (15 H, m, Ph × 3); δ_C 25.8 and 26.9 (CMe_2), 51.8 (2′-CO_2Me), 52.7 (1′-CO_2Me), 63.5 (C-5), 78.3, 80.1 and 87.3 (C-2, -3, -4), 87.7 (CPh_3), 107.5 (C-2′), 113.7 (CMe_2), 127.3–128.8 (Ph), 143.0 (Ph-*ipso*), 153.2 (C-1′ and 161.2, 162.9 and 164.8 (C-1, CO × 2).

Compound **1b** (Found: C, 67.1; H, 5.5; N, 2.2%); *m/z* (EI) 587 (M^+); ν_{max}/cm^{-1} 3019 (Ar, CH), 2970 and 2920 (CH), 1720 (CO) and 1680 (C=N); δ_H 1.36 and 1.49 (3 H × 2, s, CMe_2), 3.02 (1 H, dd, J_{gem} 10.7, $J_{4,5}$ 1.7, 5-H), 3.67 (1 H, dd, J_{gem} 10.7, $J_{4,5'}$ 2.8, 5-H′), 3.69 and 3.95 (3 H × 2, s, CO_2Me × 2), 4.61 (1 H, br d, $J_{2,3}$ 5.8, 3-H), 4.78 (1 H, m, 4-H), 5.41 (1 H, d, $J_{2,3}$ 5.8, 2-H), 6.01 (1 H, s, 2′-H) and 7.22–7.38 (15 H, m, Ph × 3); δ_C 25.5 and 26.8 (CMe_2), 51.6 (2′-CO_2Me), 53.1 (1′-CO_2Me), 63.5 (C-5), 78.5, 79.9 and 87.8 (C-2, -3, -4), 87.9 (CPh_3), 95.7 (C-2′), 114.0 (CMe_2), 127.3–128.5 (Ph), 142.9 (Ph-*ipso*) and 160.5, 162.9 and 163.5 (C-1′, CO × 2).

Dimethyl 2-[(1′R,2′R,3′R)-3′-*Hydroxy*-1′,2′-*isopropylidenedioxy*-4′-*trityloxybutyl*]*oxazole*-4,5-*dicarboxylate* **2**.—When compound **1a** (80 mg, 0.136 mmol) was heated in glass tube oven (Shibata GTO-250RS) at 200 °C for 2 min, the colourless foam changed into a brown syrup. The crude syrup was purified by PLC on silica gel [Et_2O–hexane (2:1)] to give *compound* **2** as a foam in 88% yield (Found: C, 67.4; H, 5.8; N, 2.2. $C_{33}H_{33}NO_9$ requires C, 67.5; H, 5.7; N, 2.4%); *m/z* (EI) 587 (M^+); ν_{max}/cm^{-1} 3400 (OH), 3040 (Ar, CH), 2900 (CH) and 1725 (CO); δ_H 1.43 and 1.57 (3 H × 2, s, CMe_2), 2.42 (1 H, d, $J_{3',O}$ 6.1, OH), 3.31 (1 H, dd, J_{gem} 9.7, $J_{3',4'}$ 3.1, 4′-H), 3.37 (1 H, dd, J_{gem} 9.7, $J_{3',4''}$ 5.1, 4′-H′), 3.58 (1 H, m, 3′-H), 3.94 (3 H, s, OMe), 4.51 (1 H, dd, $J_{2',3'}$ 9.2, $J_{1',2'}$ 6.2, 2′-H), 5.41 (1 H, d, $J_{1',2'}$ 6.2, 1′-H) and 7.21–7.44 (15 H, m, Ph × 3); δ_C 25.4 and 26.8 (CMe_2), 52.8 and 52.9 (OMe × 2), 64.3 (C-4′), 69.2, 73.1 and 78.1 (C-1′, -2′, -3′), 86.8 (CPh_3), 111.6 (CMe_2), 127.1–128.6 (Ph), 136.0 (C-4), 142.8 (C-5), 143.6 (Ph-*ipso*), 157.0 (C-2) and 160.6 and 162.4 (CO × 2).

Photolysis of Compound **1**.—Compound **1** (50 mg, 0.085 mmol) in a quartz tube was irradiated by low-pressure mercury lamp (15 W) under argon for 17 h. The reaction mixture was worked up in the usual way by PLC on silica gel [Et_2O–hexane (2:1)] to give compound **2** in 35% yield. The rest was almost all starting material.

2-[(1′R,2′R,3′R)-3′-*Hydroxy*-1′,2′-*isopropylidenedioxy*-4′-*trityloxybutyl*]*oxazolo*[4,5-d]*pyridazine*-4,7-*diol* **3**.—To a mixture of compound **2** (91 mg, 0.155 mmol) and MeOH (1 cm^3) was added a methanolic solution (1 cm^3) of NH_2NH_2·H_2O

(8×10^{-3} cm^3). The resulting mixture was stirred for 20 min at room temperature to give *compound* **3** in 16% yield as plates, m.p. 178 °C (decomp.) (from MeOH) (Found: C, 66.9; H, 5.5; N, 7.5. $C_{31}H_{29}N_3O_7$ requires C, 67.0; H, 5.3; N, 7.6%); *m/z* (FAB) 556 $(M + 1)^+$; ν_{max}/cm^{-1} 3340, 3270 and 3150 (NH, OH), 3040 (Ar, CH), 2950 (CH) and 1670 (CO); δ_H 1.43 and 1.60 (3 H × 2, s, CMe_2), 3.30–3.38 (2 H, m, 4'-H), 3.64 (1 H, br, OH), 4.50 (1 H, m, 3'-H), 4.51 (1 H, dd, $J_{1',2'}$ 6.3, $J_{2',3'}$ 8.7, 2'-H), 5.43 (1 H, d, $J_{1',2'}$ 6.3, 1'-H), 7.21–7.43 (15 H, m, Ph), 9.94 (1 H, br, NH) and 12.9 (1 H, br, OH).

Ethyl N-[(2'-*Ethoxycarbonylvinyl*)*oxy*]*benzimidate* **6**.—A mixture of ethyl benzoate (2.10 g, 14 mmol), Lawesson's reagent (2.83 g, 7 mmol), and *o*-xylene (10 cm^3) was refluxed for 5 h under nitrogen. The resulting mixture was evaporated under reduced pressure to give a yellow oil, which was purified by column chromatography on silica gel with hexane as eluent. The *O*-ethyl thiobenzoate thus obtained (1.78 g, 76% yield) was dissolved in ethanol (40 cm^3). The resultant solution was stirred at room temperature for 4 h with hydroxylamine hydrochloride (2.08 g, 30 mmol) and sodium acetate (2.46 g, 30 mmol). The mixture was then filtered and the filtrate was evaporated under reduced pressure to give a yellow oil. Purification by column chromatography on silica gel [AcOEt–hexane (1:2)] gave ethyl *N*-hydroxybenzimidate as an oil in 69% yield.

A mixture of ethyl *N*-hydroxybenzimidate (0.18 g, 1.1 mmol), ethyl propiolate (0.13 g, 1.3 mmol), and triethylamine (0.04 g) was stirred at room temperature for 10 min. The resulting mixture was evaporated under reduced pressure to give a brown oil, which was purified by column chromatography on silica gel [AcOEt–hexane (1:2)] to afford *compound* **6** (100%) (Found: C, 63.9; H, 6.3; N, 5.5. $C_{14}H_{17}NO_4$ requires C, 63.9; H, 6.5; N, 5.3%); *m/z* (FAB) 264 $(M + 1)^+$; ν_{max}/cm^{-1} 3040 (Ar, CH), 2960 (CH), 1700 (CO) and 1630 (C=C); δ_H(*E,Z*-mixture), 1.26 and 1.40 (3 H × 2, t, *J* 7.3, OCH_2Me × 2), 4.19 and 4.29 (2 H × 2, q, *J* 7.3, CH_2 × 2), 5.68 and 5.71 (1 H, d, *J* 11.3 for *Z*, *J* 13.0 for *E*, 2'-H), 8.35–8.74 (4 H, m, Ph) and 8.79 and 8.91 (1 H, d, *J* 11.3 for *Z*, *J* 13.0 for *E*, 1'-H).

Ethyl *N*-hydroxybenzimidate and methyl *N*-hydroxydodecanimidate were prepared by the same procedure as described in the preparation of compound **6**, starting from ethyl benzoate **7a** and methyl dodecanoate **7b**, respectively.

Ethyl N-{[1',2'-*Bis*(*methoxycarbonyl*)*vinyl*]*oxy*}*benzimidate*.—A mixture of ethyl *N*-hydroxybenzimidate (0.18 g, 1.1 mmol), DMAD (0.16 cm^3, 1.3 mmol), and triethylamine (0.04 g) was treated by the same way as described in the preparation of compound **6**: oil (Found: C, 58.8; H, 5.6; N, 4.7. $C_{15}H_{17}NO_6$ requires C, 58.6; H, 5.6; N, 4.6%); *m/z* (FAB) 308 $(M + 1)^+$; ν_{max}/cm^{-1} 3040 (Ar, CH), 2930 (CH) and 1715 (CO); δ_H(*E,Z*-mixture) 1.38 and 1.44 (3 H, t, *J* 7.7, CH_2Me), 3.67, 3.71, 3.83 and 3.88 (3 H × 2, s, CO_2Me), 4.17 and 4.62 (2 H, g, *J* 7.7, CH_2), 5.91 and 6.04 (1 H, s, 2'-H), 7.41 (3 H, m, Ph) and 7.69 and 7.89 (2 H, m, Ph).

Methyl N-{[1',2'-*Bis*(*methoxycarbonyl*)*vinyl*]*oxy*}*dodecanimidate*.—This compound was prepared from the reaction of methyl *N*-hydroxydodecanimidate with DMAD by the same way as mentioned above: oil (Found: C, 61.1; H, 9.1; N, 3.6. $C_{19}H_{33}NO_6$ requires C, 61.4; H, 9.0; N, 3.8%); *m/z* (FAB) 372 $(M + 1)^+$; ν_{max}/cm^{-1} 2840 and 2900 (CH) and 1720 (CO); δ_H(*E,Z*-mixture) 0.89 (3 H, t, *J* 7.3, 12-H_3), 1.26 and 1.30 (16 H, m, 4-, 5-, 6-, 7-, 8-, 9-, 10-, 11-H_2), 1.60 and 1.74 (2 H, m, 3-H_2), 2.41 and 2.51 (2 H, t, *J* 7.6, 2-H_2), 3.62 (3 H, s, OMe), 3.84 (3 H × 2, s, CO_2Me) and 5.78 and 5.86 (1 H, s, 2'-H).

Conversion of **6** *into Compound* **5**.—Compound **6** (204 mg, 0.77 mmol) was heated in glass tube oven at 170 °C for 1 min to give a black oil, which was then purified by PLC on silica gel [AcOEt–hexane (1:2)] to afford compound **5**[4] (37.5 mg, 22%).

Dimethyl 2-*Phenyloxazole*-4,5-*dicarboxylate* **8a**.—A mixture of ethyl *N*-{[1',2'-bis(methoxycarbonyl)vinyl]oxy-*N*-hydroxybenzimidate (0.22 g, 0.72 mmol) and *o*-dichlorobenzene (0.5 cm^3) was refluxed for 1 h. The resulting black solution was purified by PLC on silica gel [AcOEt–hexane (1:3)] to give *compound* **8a** as crystals, m.p. 85–86 °C, 50% yield (Found: C, 59.5; H, 4.2; N, 5.2. $C_{13}H_{11}NO_5$ requires C, 59.8; H, 4.2; N, 5.4%); *m/z* (FAB) 262 $(M + 1)^+$; ν_{max}/cm^{-1} 3000 (Ar, CH) and 1730 (CO); δ_H 3.94 (3 H × 2, s, Me × 2), 7.36 (3 H, m, Ph) and 8.02 (2 H, m, Ph); δ_C 52.9 and 53.0 (Me × 2), 125.4 (C-1'), 127.5, 129.0 and 132.2 (Ph), 137.3 (C-4), 142.0 (C-5), 157.3 (C-2) and 161.0 and 162.5 (CO).

Dimethyl 2-*Undecyloxazole*-4,5-*dicarboxylate* **8b**.—This compound was prepared in 36% yield from methyl *N*-{[1',2'-bis(methoxycarbonyl)vinyl]oxy}dodecanimidate in the same way as mentioned for compound **8a**. *Compound* **8b**: crystals, m.p. 37–38 °C (Found: C, 63.6; H, 8.5; N, 4.0. $C_{18}H_{29}NO_5$ requires C, 63.7; H, 8.6; N, 4.1%); *m/z* (FAB) 340 $(M + 1)^+$; ν_{max}/cm^{-1} 2890 and 2830 (CH) and 1730 (CO); δ_H 0.88 (3 H, t, *J* 6.9, 11'-H_3), 1.26–1.38 (16 H, m, 3'–10'-H_2), 1.81 (2 H, m, 2'-H_2), 2.84 (2 H, t, *J* 7.7, 1'-H_2) and 3.96 (6 H, s, Me × 2); δ_C 14.1 (C-11'), 22.7, 26.8, 28.2, 29.1, 29.3, 29.4, 29.6 and 31.9 (C-2'–11'), 52.8 (Me × 2), 136.0 (C-4), 142.3 (C-5), 157.3 (C-2) and 160.9 and 166.8 (CO × 2).

Dimethyl 2-(3'-*Hydroxypropyl*)*oxazole*-4,5-*dicarboxylate* **10a**.—γ-Thiobutyrolactone was prepared according to the literature[12] and was then converted into γ-butyrolactone oxime by reaction with hydroxylamine.[13] The oxime thus obtained was allowed to react with DMAD to give *O*-[1',2'-bis(methoxycarbonyl)vinyl]-γ-butyrolactone oxime in quantitative yield.

The *O*-vinyl derivative was treated by the same way as mentioned for compound **8a** to give *compound* **10a** as crystals in 31% yield; m.p. 45–47 °C (Found: C, 49.5; H, 5.4; N, 6.0. $C_{10}H_{13}NO_6$ requires C, 49.4; H, 5.4; N, 5.8%); *m/z* (FAB) 244 $(M + 1)^+$; ν_{max}/cm^{-1} 3330 (OH), 2910 and 2850 (CH) and 1720 (CO); δ_H 2.07 (2 H, m, 2'-H_2), 3.02 (2 H, t, *J* 7.6, 1'-H_2), 3.71 (2 H, t, *J* 5.9, 3'-H_2), 2.64 (1 H, s, OH) and 3.94 (6 H, s, Me × 2); δ_C 24.9 (C-2'), 29.3 (C-1'), 52.9 (Me × 2), 61.3 (C-3'), 135.9 (C-4), 142.4 (C-5), 157.2 (C-2) and 160.8 and 166.4 (CO).

Dimethyl 2-(4'-hydroxybutyl)oxazole-4,5-dicarboxylate **10b** and dimethyl 2-(5'-hydroxypentyl)oxazole-4,5-dicarboxylate **10c** were prepared by the same method as mentioned for compound **10a**, starting from the corresponding *O*-vinyl derivatives.

Compound **10b**: oil, 45% yield (Found: C, 51.5; H, 5.8; N, 5.4. $C_{11}H_{15}NO_6$ requires C, 51.3; H, 5.9; N, 5.4%); *m/z* (FAB) 258 $(M + 1)^+$; ν_{max}/cm^{-1} 3330 (OH), 2915 and 2850 (CH) and 1720 (CO); δ_H 1.66 (2 H, m, 3'-H_2), 1.94 (2 H, m, 2'-H_2), 2.50 (1 H, s, OH), 2.91 (2 H, t, *J* 7.8, 1'-H_2), 3.69 (2 H, t, *J* 7.0, 4'-H_2), and 3.98 (6 H, s, Me × 2); δ_C 23.0, 27.9 and 31.8 (C-1'–3'), 52.9 (Me × 2), 61.9 (C-4'), 135.9 (C-4), 142.4 (C-5), 157.3 (C-2) and 160.8 and 166.5 (CO × 2).

Compound **10c**: crystals, m.p. 48–49 °C; 41% yield (Found: C, 53.1; H, 6.3; N, 5.0. $C_{12}H_{17}NO_6$ requires C, 53.1; H, 6.3; N, 5.2%); *m/z* (FAB) 272 $(M + 1)^+$; ν_{max}/cm^{-1} 3360 (OH), 2910 and 2850 (CH) and 1725 (CO); δ_H 1.43–1.65 (5 H, m, 2'-,3'-H_2, OH), 1.86 (2 H, m, 4'-H_2), 2.87 (2 H, t, *J* 7.7, 1'-H_2), 3.65 (2 H, t, *J* 6.4, 5'-H_2) and 3.96 (3 H × 2, s, Me × 2); δ_C 25.24, 26.40 and 28.11 (C-2'–4'), 32.08 (C-1'), 52.89 (Me × 2), 62.32 (C-5'), 135.90 (C-4), 142.31 (C-5), 157.26 (C-2) and 160.84 and 166.54 (CO × 2).

Dimethyl (1,3-*Dihydroisobenzofuran*-1-*ylidenaminoxy*)*butenedioate* **12**.—The preparation was carried out starting from phthalide **11** by the same method as mentioned for compound **6**.

Title compound **12** was an oil; 40% (O/S-exchange), >80% (oxime), 100% (*O*-vinyl ether) (Found: C, 57.7; H, 4.5; N, 4.8. $C_{14}H_{13}NO_6$ requires C, 57.5; H, 4.6; N, 4.7%); *m/z* (FAB) 292 $(M + 1)^+$; ν_{max}/cm^{-1} 3025 (Ar, CH), 2990 and 2940 (CH), 1720 (CO) and 1630 (C=C); δ_H 3.73 and 3.88 (3 H × 2, s, Me × 2), 5.55 (2 H, s, CH_2), 6.11 (1 H, s, 2'-H) and 7.40–7.66 (4 H, m, Ph); δ_C 51.8 and 52.9 (Me × 2), 75.7 (C-3), 105.6 (C-2'), 121.5 and 122.4 (C-5, -6), 127.3 (C-9), 128.9 and 131.9 (C-4, -7), 141.9 (C-8), 152.5 (C-1') and 160.9, 162.8 and 165.5 (C-1, CO × 2).

Dimethyl 2-(O-*Hydroxymethylphenyl*)*oxazole*-4,5-*dicarboxylate* **13**.—Compound **12** was treated by the same way as mentioned in the preparation of compound **8a**. *Compound* **13** was obtained as crystals, m.p. 117–118 °C; 51% yield (Found: C, 57.7; H, 4.5; N, 4.8. $C_{14}H_{13}NO_6$ requires C, 57.4; H, 4.5; N, 4.7%); *m/z* (EI) 291 (M^+); ν_{max}/cm^{-1} 3180 (OH), 2940 (CH) and 1730 (CO); δ_H 4.00 and 4.02 (3 H × 2, s, Me × 2), 4.84 (2 H, s, CH_2), 5.06 (1 H, s, OH), 7.26–7.56 (3 H, m, Ph) and 8.14 (1 H, q, $J_{5',6'}$ 7.8, $J_{4',6'}$ 1.0, 6'-H); δ_C 53.1 and 53.0 (Me × 2), 64.3 (CH_2OH), 124.0 (C-1'), 132.5, 131.0, 129.5 and 128.4 (C-3'–6'), 136.7 (C-4), 141.5 (C-2'), 141.9 (C-5), 157.1 (C-2) and 160.5 and 161.8 (CO × 2).

Dimethyl (2H-[1]*Benzopyran*-2-*ylidenaminoxy*)*butenedioate* **15**.—The preparation was carried out starting from coumarin in the same way as mentioned for compound **6**. The *title compound* **15** was an oil; 93% (O/S-exchange), 95% (oxime), 100% (*O*-vinyl ether) (Found: C, 59.1; H, 4.2; N, 4.5. $C_{15}H_{13}NO_6$ requires C, 59.4; H, 4.3; N, 4.6%); *m/z* (FAB) 304 $(M + 1)^+$; ν_{max}/cm^{-1} 2980 and 2930 (CH), 1710 (CO) and 1620 (C=C); δ_H(*E*,*Z*-mixture) 3.71, 3.74, 3.87 and 3.95 (3 H × 2, s, Me × 2), 5.94 and 6.12 (1 H, s, 2'-H), 6.28 and 6.36 (1 H, d, *J* 9.5, 4-H), 7.06 and 7.18 (1 H, d, *J* 9.5, 3-H) and 7.23–7.40 (4 H, m, 5–8-H).

Dimethyl 2-[(E)-2'-O-*Hydroxyphenylvinyl*]*oxazole*-4,5-*dicarboxylate* **16**.—Compound **15** was treated by the same way as mentioned in the preparation of compound **8a**. In this thermal reaction a small amount of coumarin was isolated as a by-product. *Compound* **16** was isolated as yellow crystals, m.p. 179–180 °C; 31% yield (Found: C, 59.4; H, 4.2; N, 4.5. $C_{15}H_{13}NO_6$ requires C, 59.4; H, 4.3; N 4.6%); *m/z* (FAB) 304 $(M + 1)^+$; ν_{max}/cm^{-1} 3150 (OH), 1715 (CO) and 1620 (C=C); δ_H 3.98 (6 H, s, Me × 2), 6.89 (2 H, m, 6'-, 7'-H), 7.16 (1 H, m, 8'-H), 7.20 (1 H, d, *J* 16.7, 2'-H), 7.42 (1 H, m, 5'-H), 8.01 (1 H, d, *J* 16.7, 1'-H) and 9.59 (1 H, s, OH); δ_C 52.8 (Me × 2), 112.2, 116.6, 119.7, 129.3, 131.2 and 137.8 (C-1', -2', and 5'–8'), 121.8 (C-3'), 137.3 (C-4), 141.1 (C-5), 157.0 (C-4'), 157.4 (C-2) and 161.0 and 163.5 (CO × 2).

N-{[2'-(*Ethoxycarbonyl*)*vinyl*]*oxy*}-2,3-O-*isopropylidene*-5-O-*trityl*-D-*ribonimido*-1,4-*lactone*.—The preparation was carried out in a similar way to that for compounds **1a** and **1b** by using ethyl propiolate (392 mg, 4.0 mmol): *Title compound* was a foam, 64% (Found: C, 70.8; H, 6.2; N, 2.8. $C_{32}H_{33}NO_7$ requires C, 70.7; H, 6.1; N, 2.6%); *m/z* (EI) 543 (M^+); ν_{max}/cm^{-1} 3350 (OH), 3050 (Ar, CH) and 1700 (CO); δ_H 1.30 (3 H, t, *J* 6, CH_2Me), 1.40 and 1.52 (3 H, × 2, s, CMe_2), 1.70 (1 H, br, OH), 3.10 and 3.76 (1 H × 2, dd, J_{gem} 11, $J_{4,5} = J_{4,5'} = 4$, 5-H_2), 4.20 (2 H, q, *J* 6, CH_2Me), 4.68 (1 H, m, 3-H), 4.80 (1 H, br, 4-H), 5.42 (1 H, d, *J* 7, 2-H), 5.80 (1 H, d, $J_{1',2'}$ 12, 2'-H), 7.25–7.60 (15 H, br s, Ph) and 8.05 (1 H, d, $J_{1',2'}$ 12, 1'-H).

N-[(1',2'-*Dibenzoylvinyl*)*oxy*]-2,3-O-*isopropylidene*-5-O-*trityl*-D-*ribonimido*-1,4-*lactone*.This *compound* was prepared in a similar way to that above by using dibenzoylacetylene (608 mg, 2.6 mmol); *Z*-vinyl ether, pale yellow foam (50%) and *E*-vinyl ether, yellow foam (10%) (Found: C, 75.8; H, 5.4; N, 2.1. $C_{43}H_{37}NO_7$ requires C, 75.9; H, 5.4; N, 2.1%); *m/z* (EI) 679 (M^+); ν_{max}/cm^{-1} 3050 (Ar, CH) and 1660 and 1680 (CO); δ_H 1.39 and 1.52 (3 H × 2, s, CMe_2), 3.00 (1 H, dd, J_{gem} 10.8, $J_{4,5}$ 1.7, 5-H), 3.67 (1 H, dd, J_{gem} 10.8, $J_{4,5'}$ 2.6, 5-H), 4.63 (1 H, m, 3-H), 4.77 (1 H, m, 4-H), 5.50 (1 H, d, $J_{2,3}$ 6.0, 2-H), 7.10–8.10 (15 H, m, Ph).

Ethyl (1'R,2'R,3'R)-2-(3'-*Hydroxy*-1',2'-*isopropylidenedioxy*-4'-*trityloxybutyl*)*oxazole*-4-*carboxylate* **17** *and* 4,5-*Dibenzoyl*-(1'R,2'R,3'R)-2-(3'-*Hydroxy*-1',2'-*isopropylidenedioxy*-4'-*trityloxybutyl*)*oxazole* **18**.—The reaction was performed by the same way as in the preparation of compound **2** but using *N*-{[2'-(ethoxycarbonyl)vinyl]oxy}-2,3-*O*-isopropylidene-5-O-trityl-D-ribonimido-1,4-lactone and *N*-(1',2'-dibenzoylvinyl)-oxy]-2,3-*O*-isopropylidene-5-O-trityl-D-ribonimido-1,4-lactone as starting compounds.

Compound **17**: foam, 19% (Found: C, 70.8; H, 6.2; N, 2.6. $C_{32}H_{33}NO_7$ requires C, 70.7; H, 6.1; N, 2.5%); *m/z* (EI) 543 (M^+); δ_H 1.37 (3 H, t, *J* 7.2, CH_2Me), 1.43 and 1.58 (3 H × 2, s, CMe_2), 2.67 (1 H, d, $J_{3',O}$ 5.9, OH), 3.30 (1 H, dd, J_{gem} 9.7, $J_{3',4'}$ 3.1, 4'-H), 3.36 (1 H dd, J_{gem} 9.7, $J_{3',4''}$ 5.3, 4'-H), 3.58 (1 H, m, 3'-H), 4.37 (2 H, q, *J* 7.2, CH_2Me), 4.51 (1 H, dd, $J_{1',2'}$ 6.2, $J_{2',3'}$ 9.2, 2'-H), 5.40 (1 H, d, $J_{1',2'}$ 6.2, 1'-H), 7.20–7.43 (15 H, m, Ph × 3) and 7.70 (1 H, s, 5-H); δ_C 14.2 (CH_2Me), 25.5 and 26.9 (CMe_2), 61.5 and 64.4 (CH_2Me, C-4'), 69.3, 73.4 and 78.2 (C-1', -2', -3'), 86.8 (CPh_3), 111.4 (CMe_2), 127.1, 127.9 and 128.6 (Ph), 133.9 (C-4), 142.9 (C-5), 143.7 (Ph-*ipso*), 157.6 (C-2) and 164.2 (CO).

Compound **18**: pale yellow foam, 19% (Found: C, 75.8; H, 5.5; N, 2.1. $C_{43}H_{37}NO_7$ requires C, 75.9; H, 5.4; N, 2.1%); *m/z* (EI) 679 (M^+); δ_H 1.40 and 1.51 (3 H × 2, s, CMe_2), 2.50 (1 H, br, OH), 3.25 (1 H, dd, J_{gem} 9.7, $J_{3',4'}$ 3.5, 4'-H), 3.32 (1 H, dd, J_{gem} 9.7, $J_{3',4''}$ 4.9, 4'-H'), 3.50 (1 H, m, 3'-H), 5.29 (1 H, d, $J_{1',2'}$ 6.2, 1'-H), 5.48 (1 H, dd, $J_{1',2'}$ 6.2, $J_{2',3'}$ 8.9, 2'-H), 7.19–7.59 (21 H, m, Ph), 7.90–7.96 and 8.29–8.31 (2 H × 2, m, Ph); δ_C 25.5 and 26.8 (CMe_2), 64.4 (C-4'), 69.2 (C-3'), 72.9 (C-2'), 78.0 (C-1'), 86.7 (CPh_3), 111.3 (CMe_2), 126.2–132.0 (Ph), 143.5 (C-4), 143.6 (Ph-*ipso*), 156.6 (C-5), 159.6 (C-2), 189.3 (CO) and 193.6 (CO).

(E)-2,3,4,6-*Tetra*-O-*benzyl*-N-{[(Z *and* E)-1',2'-*bis*(*methoxycarbonyl*)*vinyl*]*oxy*}-D-*gluconimido*-1,5-*lactone*.—A stirred solution of (*E*)-2,3,4,6-tetra-*O*-benzyl-*N*-hydroxy-D-gluconimido-1,5-lactone[14] (89 mg, 0.16 mmol) and DMAD (40 × 10^{-3} cm^3, 0.33 mmol) in dry CH_2Cl_2 (1 cm^3) was treated with triethylamine (18 × 10^{-3} cm^3) at room temperature. After being stirred for 1 h, the reaction mixture was purified by PLC on silica gel [Et_2O–hexane (1:1)] to give a diastereoisomeric mixture of *Z*-vinyl ether and *E*-vinyl ether in 99% yield (*Z*-vinyl ether: *E*-vinyl ether 4:1). The mixture was separated by further PLC on silica gel [$CHCl_3$–MeOH (90:1)].

Z-Vinyl ether: syrup (Found: C, 69.2; H, 6.0; N, 1.9. $C_{40}H_{41}NO_{10}$ requires C, 69.0; H, 5.9; N, 2.1%); *m/z* (EI) 695 (M^+); ν_{max}/cm^{-1} 3010 (Ar, CH), 2910 and 2845 (CH) and 1725, 1715 and 1635 (CO); δ_H 3.61 and 3.80 (3 H × 2, s, CO_2Me × 2), 3.83 (1 H, dd, J_{gem} 11.9, $J_{5,6}$ 3.9, 6-H), 3.88 (1 H, dd, $J_{3,4}$ 5.2, $J_{4,5}$ 8.2, 4-H), 3.90 (1 H, dd, J_{gem} 11.9, $J_{5,6'}$ 1.9, 6-H'), 3.92 (1 H, dd, $J_{3,4}$ 5.2, $J_{2,3}$ 1.9, 3-H), 4.02 (1 H, d, $J_{2,3}$ 1.9, 2-H), 4.31–4.76 (2 H × 4, m, CH_2Ph × 4), 4.62 (1 H, ddd, $J_{5,6}$ 3.9, $J_{5,6'}$ 1.9, 5-H), 6.06 (1 H, s, 2'-H) and 7.16–7.40 (20 H, m, Ph × 4); δ_C 51.6 and 52.6 (Me × 2), 67.7, 70.6, 71.6, 73.2 and 73.7 (OCH_2Ph × 4, C-6), 72.8, 77.2, 77.3 and 81.5 (C-2, -3, -4, -5), 97.0 (C-2'), 106.2 (C-6), 127.5–128.4 (Ph), 136.9, 137.1, 137.7 and 138.4 (Ph-*ipso*) and 153.1, 154.1, 163.0 and 165.0 (C-1, -1', CO × 2).

E-*Vinyl ether*: syrup (Found: C, 69.1; H, 5.9; N, 2.0%); *m/z* (EI) 695 (M^+); ν_{max}/cm^{-1} 3010 (Ar, CH), 2890 and 2850 (CH), 1740 and 1710 (CO) and 1615 (C=N); δ_H 3.72 and 3.88

(3 H × 2, s, CO_2Me × 2), 3.74 (1 H, dd, $J_{5,6}$ 2.7, J_{gem} 12.0, 6-H), 3.80 (1 H, dd, $J_{3,4}$ 4.2, $J_{4,5}$ 6.1, 4-H), 3.82 (1 H, dd, J_{gem} 12.0, $J_{5,6'}$ 2.0, 6-H'), 3.91 (1 H, dd, $J_{3,4}$ 4.1, $J_{2,3}$ 2.2, 3-H), 4.08 (1 H, d, $J_{2,3}$ 2.2, 2-H), 4.32–4.74 (2 H × 4, m, OCH_2Ph × 4), 4.61 (1 H, ddd, $J_{5,6}$ 2.7, $J_{5,6'}$ 2.0, $J_{4,5}$ 6.1, 5-H), 5.88 (1 H, s, 2'-H) and 7.16–7.38 (20 H, m, Ph × 4); δ_C 51.6 and 52.9 (Me × 2), 67.5, 70.8, 71.6, 72.9 and 73.4 (OCH_2Ph × 4, C-6), 72.3, 77.2, 77.3 and 80.7 (C-2, -3, -4, -5), 95.6 (C-2'), 127.6–128.6 (Ph), 136.5, 136.9, 137.5 and 137.9 (Ph-*ipso*) and 155.8, 160.6, 162.9 and 166.6 (C-1, -1', CO × 2).

Dimethyl (1'R,2'S,3'R,4'R)- *and* (1'S,2'S,3'R,4'R)-2-(1',2',3',5'-*Tetrabenzyloxy-4'-hydroxypentyl*)*oxazole-4,5-dicarboxylate* (1'R)-**19** *and* (1'S)-**19**.—(*E*)-Tetra-*O*-benzyl-*N*-{[1',2'-Bis(methoxycarbonyl)vinyl]oxy}-D-gluconomido-1,5-lactone (*Z*-vinyl ether) (86.9 mg, 0.125 mmol) was treated by the same way as in the preparation of compound **2** (150 °C; 65 min) to give an oil, which was purified by PLC on silica gel [AcOEt–hexane (1:2)] to afford (1'*R*)-**19** and (1'*S*)-**19** in 64% yield [(1'*R*):(1'*S*) 7:2]. Compound **19** was similarly prepared (200 °C; 60 min) from the isomeric D-mannonimido-1,5-lactone in 74% yield [(1'*R*):(1'*S*) 2:3].

Compound (1'R)-**19** (Found: C, 68.9; H, 5.7; N, 2.1. $C_{40}H_{41}NO_{10}$ requires C, 69.0; H, 5.9; N, 2.1%); *m/z* (FAB) 696 $(M + 1)^+$; ν_{max}/cm^{-1} 3450 (OH), 3020 (Ar, CH), 2900 and 2850 (CH) and 1740 (CO); δ_H 2.85 (1 H, d, *J* 4.9, OH), 3.52 (1 H, dd, J_{gem} 9.8, $J_{4',5'}$ 5.0, 5'-H), 3.59 (1 H, dd, J_{gem} 9.8, $J_{4',5'}$ 3.4, 5'-H'), 3.65 (1 H, dd, $J_{2',3'}$ 4.1, $J_{3',4'}$ 7.3, 3'-H), 3.89 and 3.94 (3 H × 2, s, Me × 2), 3.99 (1 H, m, 4'-H), 4.25 (1 H, dd, $J_{2',3'}$ 4.1, $J_{1',2'}$ 6.9, 2'-H), 4.92–4.31 (8 H, m, $PhCH_2$ × 4), 5.08 (1 H, d, $J_{1',2'}$ 6.9, 1'-H) and 7.04–7.35 (20 H, m, Ph × 4).

Compound (1'S)-**19** (Found: C, 69.1; H, 6.0; N, 1.9%); *m/z* (FAB) 696 $(M + 1)^+$; ν_{max}/cm^{-1} 3450 (OH), 3020 (Ar, CH), 2900 and 2850 (CH) and 1740 (CO); δ_H 2.55 (1 H, d, *J* 6.4, OH), 3.64 (1 H, dd, J_{gem} 9.5, $J_{4',5'}$ 4.8, 5'-H), 3.70 (1 H, dd, J_{gem} 9.5, $J_{4',5''}$ 3.0, 5'-H), 3.92 and 3.95 (3 H × 2, s, Me × 2), 4.05 (1 H, m, 4'-H), 4.30–4.70 (10 H, m, $PhCH_2$ × 4, 2'-, 3'-H), 4.92 (1 H, d, $J_{1',2'}$ 8.8, 1'-H) and 7.04–7.37 (20 H, m, Ph × 4).

(E)-2,3,4,6-*Tetra*-O-*benzyl*-N-{[(Z *and* E)-1',2'-*bis*(*methylcarbonyl*)*vinyl*]*oxy*}-D-*mannonimido*-1,5-*lactone*.—The same procedure as described in the preparation of compound **1** was performed using 2,3,4,6-tetra-*O*-benzyl-*N*-hydroxy-D-mannonimido-1,5-lactone[14] as starting compound. Purification by PLC on silica gel [AcOEt–hexane (1:1)] gave a diastereoisomeric mixture of *Z*-vinyl ether and *E*-vinyl ether in 80% yield (*Z*-vinyl ether:*E*-vinyl ether 4:1). The mixture was separated by further PLC on silica gel [CH_2Cl_2–hexane (6:1)].

Z-Vinyl ether (Found: C, 69.2; H, 5.7; N, 2.0%); *m/z* (FAB) 696 $(M + 1)^+$; ν_{max}/cm^{-1} 3050 and 3020 (Ar, CH), 2900 and 2860 (CH), 1730 and 1715 (CO) and 1640 (C=N); δ_H 3.61 and 3.81 (2 H × 2, s, CO_2Me × 2), 3.70 (1 H, dd, $J_{5,6}$ 8.8, J_{gem} 3.0, 6-H), 3.81 (1 H, dd, $J_{2,3}$ 3.0, $J_{3',4}$ 8.4, 3-H), 3.84 (1 H, dd, J_{gem} 8.8, $J_{5,6}$ 3.7, 6-H'), 4.16 (1 H, d, $J_{2,3}$ 3.0, 2-H), 4.22 (1 H, ddd, $J_{5,6}$ 3.0, $J_{5,6'}$ 3.7, $J_{4,5}$ 7.7, 5-H), 4.34 (1 H, dd, $J_{3,4}$ 8.4, $J_{4,5}$ 7.7, 4-H), 4.45–4.85 (8 H, m, $PhCH_2$ × 4), 6.08 (1 H, s, 2'-H) and 7.20–7.39 (20 H, m, Ph × 4); δ_C 50.6 and 51.7 (Me × 2), 67.7, 69.6, 70.8, 72.4 and 73.6 (C-6, $PhCH_2$ × 4), 69.6, 72.6, 78.0 and 80.7 (C-2, -3, -4, -5), 94.6 (C-2'), 126.6–127.5 (Ph), 136.1, 136.6, 136.9 and 137.1 (Ph-*ipso*) and 152.3, 153.8, 161.9 and 163.7 (C-1, -1', CO × 2).

E-*Vinyl ether* (Found: C, 69.1; H, 5.9; N, 1.9%); *m/z* (FAB) 696 $(M + 1)^+$; ν_{max}/cm^{-1} 3050 and 3020 (Ar, CH), 2900 and 2840 (CH), 1740 and 1710 (CO) and 1610 (C=N); δ_H 3.72 and 3.89 (3 H × 2, s, Me × 2), 3.73–3.84 (3 H, m, 4-H and 6-H), 4.15 (1 H, m, 5-H), 4.21 (1 H, d, $J_{2,3}$ 3.0, 2-H), 4.27 (1 H, m, 3-H), 4.45–4.81 (8 H, m, $PhCH_2$ × 4), 5.84 (1 H, s, 2'-H) and 7.18–7.34 (20 H, m, Ph × 4); δ_C 51.6 and 53.0 (Me × 2), 68.5, 70.9, 72.0, 72.1 and 73.4 (C-6, $PhCH_2$ × 4), 70.5, 73.4, 78.6 and 81.8 (C-2, -3, -4, -5), 95.8 (C-2'), 127.6–128.4 (Ph), 136.8, 137.5, 137.7 and 137.8 (Ph-*ipso*) and 156.0, 160.8, 162.9 and 166.5 (C-1, -1', CO × 2).

2,2',3,3',4',6,6'-*Hepta*-O-*benzyl*-N-{[1'',2''-*bis*(*methoxycarbonyl*)*vinyl*]*oxy*}-D-*maltonimido*-1,4-*lactone*.—A mixture of Ac_2O (100 cm^3), AcONa (10 g, 120 mmol), and maltose (20 g, 58 mmol) was refluxed for 10 min. The reaction mixture was poured into ice–water (300 cm^3). To the resulting solution was added $NaHCO_3$ (3 g) and the mixture was kept overnight. The precipitate was collected, and recrystallized from ethanol to give 1,2,2',3,3',4',6,6'-octa-*O*-acetylmaltose in quantitative yield.

Next, a mixture of octa-*O*-acetylmaltose obtained above (6 g, 8.8 mmol), 25% HBr (15.9 cm^3), and acetic acid (60.4 cm^3) was stirred at room temperature for 1 h. The reaction mixture was quenched with ice–water and then extracted with chloroform. The extract was neutralized with aq. $NaHCO_3$ and then dried over $CaCl_2$. Evaporation of the extract gave 2,2',3,3',4',6,6'-hepta-*O*-acetyl-1-bromomaltose as an oil.

The hepta-*O*-acetyl-1-bromomaltose (20.3 g, 29 mmol) was dissolved in chloroform (60 cm^3) and then treated with a mixture of KOH (1.63 g, 29 mmol), dry MeOH (60 cm^3), and *p*-chloro(thiophenol) (4.7 g, 33 mmol). The resulting mixture was refluxed for 1 h and then quenched with cold water, followed by extraction with chloroform. The extract was washed successively with aq. Na_2CO_3 and aq. NaCl, and dried over Na_2SO_4. Evaporation of the extract gave 2,2',3,3',4',6,6'-hepta-*O*-acetyl-1β-(*p*-chlorophenylthio)maltose[15] as crystals (recrystallized from EtOH) in 70% yield.

Thus obtained 2,2',3,3',4',6,6'-hepta-*O*-acetyl-1β-(*p*-chlorophenylthio)maltose was deacetylated (MeONa–MeOH) and then benzylated (NaH, dimethylformamide, BnBr) in the usual way to give 2,2',3,3',4',6,6'-*hepta*-O-*benzyl*-1β-(p-*chlorophenylthio*)*maltose* as a syrup in 75% yield (Found: C, 73.5; H, 6.2; S, 3.1. $C_{67}H_{67}ClO_{10}S$ requires C, 73.2; H, 6.1; S, 2.9%); *m/z* (FAB) 1100 $(M + 1)^+$; ν_{max}/cm^{-1} 3020 and 3040 (Ar, CH) and 2850 and 2900 (CH); δ_H 3.40–4.20 (13 H, m, sugar protons, 4.40–4.90 (14 H, m, CH_2Ph × 7), 5.60 [1 H, d, *J* 3, 1-H(α)] and 7.05–7.52 (39 H, m, Ph × 7, SC_6H_4Cl).

Method A. Syrupy 2,2',3,3',4',6,6'-hepta-*O*-benzyl-1β-(*p*-chlorophenylthio)maltose (5.0 g, 4.6 mmol) was dissolved in acetone (160 cm^3) and aq. silver nitrate[16] [1.8 g in distilled water (11 cm^3)] was then added to the above solution. The resultant mixture was kept in the dark at room temperature and stirred for 6 days. A deposit was filtered off with the aid of a filter-cell and the filtrate was concentrated under reduced pressure to give a syrupy residue, which was then treated with $CHCl_3$ and aq. $NaHCO_3$. The organic layer was washed with water, dried over $MgSO_4$, and evaporated to give a crude syrup (4.7 g), which was then column chromatographed. From benzene fractions, the starting material (5.9 g) was recovered and benzene–AcOEt (5:1) fractions then gave pure 2,2',3,3',4',6,6'-hepta-*O*-benzylmaltose in 65% yield.

Method B. To a solution of 2,2',3,3',4',6,6'-hepta-*O*-benzyl-1β-(*p*-chlorophenylthio)maltose (0.8 g, 0.74 mmol) and CH_2Cl_2 (5 cm^3) was added a mixture of *N*-bromosuccinimide (0.26 g, 1.5 mmol) and CH_2Cl_2 (15 cm^3). The resulting mixture was stirred for 1 h and was then washed successively with aq. $NaHCO_3$ and aq. $NaHSO_3$. The colour of the solution changed from yellow to colourless. After being dried over Na_2SO_4, the solution was evaporated under reduced pressure to give an oil, which was then purified by column chromatography on silica gel [AcOEt–hexane (1:2)] to afford 2,2',3,3',4',6,6'-*hepta*-O-*benzylmaltose* as a syrup in 40% yield; $[\alpha]_D$ +16.3 (*c* 1.36, $CHCl_3$) (Found: C, 75.0; H, 6.7. $C_{61}H_{64}O_{11}$ requires C, 75.3; H, 6.6%); *m/z* (FAB) 974 $(M + 1)^+$; ν_{max}/cm^{-1} 3300–3400 (OH),

3020 and 3040 (Ar, CH) and 2850–2900 (CH); δ_H 3.00–3.90 (14 H, m, sugar protons), 4.00–4.98 (14 H, m, CH_2Ph × 7), 5.22 and 5.62 [1 H, d, $J_{1,2}$ 4; 3, 1-H(β,α)] and 7.09–7.33 (35 H, br s, Ph × 7).

A mixture of hepta-*O*-benzylmaltose (0.69 g, 0.71 mmol), NH_2OH·HCl (0.25 g, 3.5 mmol), AcONa (0.29 g, 3.5 mmol), and EtOH (10 cm^3) was refluxed for 3 h. The reaction mixture was evaporated under reduced pressure and the residue was treated with water. The solution was extracted with chloroform. Usual work-up gave the corresponding oxime in quantitative yield by column chromatography on silica gel [AcOEt–hexane (1:2)].

This oxime (0.42 g, 0.43 mmol) was dissolved in CH_2Cl_2 (4 cm^3) and then treated dropwise with water (10 cm^3) containing 5% NaOCl (6 cm^3) while being stirred at 0 °C. After being stirred for an additional 1 h, the reaction mixture was extracted with dichloromethane and then evaporated under reduced pressure. Purification by PLC [$CHCl_3$–MeOH (30:1)] gave 2,2′,3,3′,4′,6,6′-*hepta*-O-*benzyl*-N-*hydroxy*-D-*maltonimido*-1,4-*lactone* as a syrup in 75% yield (Found: C, 74.1; H, 6.4; N, 1.3. $C_{61}H_{63}NO_{11}$ requires C, 74.3; H, 6.4; N, 1.4%); *m/z* (FAB) 987 $(M + 1)^+$; ν_{max}/cm^{-1} 3320 (OH), 3035 (Ar, CH) and 2930 and 2850 (CH); δ_H 3.32 and 3.49 (1 H × 2, dd, J_{gem} 10.7, $J_{5',6'}$ 1.6, 2.6, 6′-H), 3.52 (1 H, dd, $J_{2,3}$ 3.7, $J_{3,4}$ 9.7, 3-H), 3.66 (1 H, dd, $J_{3',4'} = J_{4',5'}$ 9.4, 4′-H), 3.72 (1 H, ddd, $J_{4',5'}$ 9.4, $J_{5',6'}$ 1.6, 2.6, 5′-H), 3.85 (3 H, m, 4-, 6-, 3′-H), 3.97 (1 H, dd, $J_{1',2'}$ 1.9, $J_{2',3'}$ 3.7, 2′-H), 4.09 (1 H, d, $J_{1',2'}$ 1.9, 1′-H), 4.18 (1 H, dd, J_{gem} 10.1, $J_{5,6}$ 3.7, 6-H), 4.72 (1 H, ddd, $J_{4,5}$ 10.1, $J_{5,6}$ 3.7, 5-H), 4.26–4.89 (14 H, m, CH_2Ph × 7), 5.13 (1 H, d, $J_{2,3}$ 3.7, 2-H) and 7.11–7.34 (36 H, m, Ph × 7, OH).

Finally, the hepta-*O*-benzyl-D-maltonimido-1,4-lactone was converted into 2,2′,3,3′,4′,6,6′-*hepta*-O-*benzyl*-N-{[1″,2″-*bis*(*methoxycarbonyl*)*vinyl*]*oxy*}-D-*maltonimido*-1,4-*lactone* [purification by PLC: AcOEt–hexane (1:2)] in 87% yield by the same method as described in the preparation of compounds **1a** and **1b** (Found: C, 71.2; H, 6.0; N, 1.0. $C_{67}H_{69}NO_{15}$ requires C, 71.3; H, 6.1; N, 1.2%); *m/z* (FAB) 1129 $(M + 1)^+$; ν_{max}/cm^{-1} 3030 (Ar, CH), 2900 and 2850 (CH) and 1720 (CO); δ_H 3.40–5.10 (27 H, m), 3.58 and 3.76 (3 H × 2, s, Me × 2), 6.02 (1 H, s, 2′-H) and 7.00–7.70 (35 H, m, Ph × 7).

Compound **20**.—2,2′,3,3′,4′,6,6′-Hepta-*O*-benzyl-*N*-{[1″,2″-bis(methoxycarbonyl)vinyl]oxy}-D-maltonimido-1,4-lactone (125 mg, 0.11 mmol) was heated by the usual way (200 °C; 2 min). Purification was performed by PLC on silica gel [PhH/AcOEt (10:1)] to give *compound* **20** as a syrup in 88% yield (1′*R*-form:1′*S*-form 3:1) (Found: C, 71.4; H, 6.2; N, 1.3. $C_{67}H_{69}NO_{15}$ requires C, 71.3; H, 6.1; N, 1.2%); *m/z* (FAB) 1129 $(M + 1)^+$; δ_H 3.50–3.66 (7 H, m), 3.80–4.00 (8 H, m), 4.10–5.00 (18 H, m) and 7.15–7.32 (35 H, m, Ph × 7); difference in isomers' spectra: δ 5.23 (1/2 H, d, $J_{1',2'}$ 8.4, 1′-H of 1′*S*-form) and 5.28 (1/2 H, d, $J_{1',2'}$ 6.2, 1′-H of 1′-*R*-form).

(1′R,2′R,3′R)-N,N′-*Dibutyl*-2-(3′-*hydroxy*-1′,2′-*isopropylidenedioxy*-4′-*trityloxybutyl*)*oxazole*-4,5-*dicarboxamide* **22**.—A mixture of compound **2** (270 mg, 0.46 mmol) and butylamine (1.3 cm^3) was stirred under nitrogen for 1 h at room temperature. The reaction mixture was evaporated under reduced pressure to give an oil, which was purified by PLC on silica gel [AcOEt–hexane (2:3)] to afford the *diamide* **22**; 95%, as a powder, m.p. 71–72 °C (Found: C, 69.8; H, 6.8; N, 6.0. $C_{39}H_{47}N_3O_7$ requires C, 69.9; H, 7.0; N, 6.2%); *m/z* (FAB) 670 $(M + 1)^+$; ν_{max}/cm^{-1} 3300 (OH), ~3200 (NH), 3040 (Ar, CH) and 2900 (CH); δ_H 0.94 and 0.95 (3 H × 2, s, CMe_2), 1.38–1.46 (4 H × 2, m, CH_2CH_2 × 2), 1.61 (3 H × 2, t, *J* 6, Me × 2), 1.58 and 3.41 (2 H × 2, m, $NHCH_2$ × 2), 2.44 (1 H, br, OH), 3.38 and 3.42 (2 H, m, 4′-H_2), 3.60 (1 H, m, 3′-H), 4.53 (1 H, dd, $J_{1',2'}$ 9, 2′-H), 5.37 (1 H, d, $J_{1',2'}$ 6, 1′-H), 7.23–7.31 (9 H, br s, Ph × 3), 7.40–7.42 (6 H, br s, Ph × 3) and 7.47 and 10.7 (1 H × 2, br, NH × 2).

Deprotection of Compound **22**.—A mixture of compound **22** (164 mg, 0.25 mmol) and 6% HCl–MeOH (1 cm^3) was stirred for 2 h at room temperature. The successive procedures of ion-exchange chromatography of the reaction mixture (200 cm^3 of Amberlite IRA-410, washed with MeOH), condensation, and washing with dichloromethane three times gave a deprotected product, **23** (R = H).

Compound **23** (R = H) was stirred with dry pyridine (1 cm^3) and acetic anhydride (1 cm^3) for 3.5 h at room temperature. The resulting mixture was evaporated under reduced pressure to give an oil, which was purified by PLC on silica gel [AcOEt–hexane (3:5)] to give the *tetraacetate* **23** (R = Ac): 78%, as a syrup [Found: *m/z* (FAB), 556.2507. $C_{25}H_{38}N_3O_{11}$ $(M + 1)^+$, requires *m/z* 556.2504]; ν_{max}/cm^{-1} 3100–3300 (NH), 2900 (CH) and 1720 (CO); δ_H 1.24–1.46 (4 H × 2, m, CH_2CH_2 × 2), 1.61–1.62 (3 H × 2, m, Me × 2), 2.00–2.20 (3 H × 4, m, Ac × 4), 3.41 and 3.45 (2 H × 2, t, *J* 7, $NHCH_2$ × 2), 4.13 and 4.37 (2 H, m, 4′-H_2), 5.38 (1 H, m, 3′-H), 5.67 (1 H, dd, $J_{1',2'}$ 4.5, $J_{2',3'}$ 7.5, 2′-H), 6.10 (1 H, d, $J_{1',2'}$ 4.5, 1′-H) and 7.46 and 10.65 (1 H × 2, br, NH × 2).

Deprotection of Compound **19** (*a Diastereo-mixture of* 1′R *and* 1′S *Forms*).—A mixture of compound **19** (200 mg, 0.29 mmol), dry cyclohexene (2 cm^3), 10% Pd/C (200 mg), and dry ethanol (4 cm^3) was stirred under hydrogen for 3 h at 40 °C. The reaction mixture was filtered through Celite and the filter pad was washed with ethanol. The combined filtrate and washings were evaporated under reduced pressure to give syrupy penta-hydroxy diester **24** (R = H). Product **24** (R = H) was treated in the same way as described in the preparation of compound **23** (R = Ac). Purification by PLC on silica gel [AcOEt–hexane (2:1)] gave *pentaacetate* **24** (R = Ac) 88%, as a syrup [Found: *m/z* (FAB), 546.1461. $C_{22}H_{28}NO_{15}$ $(M + 1)^+$ requires *m/z* 546.1457]; ν_{max}/cm^{-1} 2900 (CH) and ~1720 (CO); δ_H 2.00–2.17 (3 H × 5, s, Ac × 5), 3.94 and 3.96 (3 H × 2, s, Me × 2), 4.10–4.14 (2 H, m, 5′-H_2), 4.23–4.24 (1 H, m, 3′-H), 5.14–5.15 (1 H, m, 4′-H), 5.59–5.63 (1 H, m, 2′-H) and 5.74–5.75 (1 H, m, 1′-H).

Deprotection of Compound **20**.—The reaction was carried out by the same procedure as mentioned in the deprotection of compound **19**. Tetraacetoxy diester **25** (R = Ac) was produced in 70% yield, as a syrup [Found: *m/z* (FAB), 834.2307. $C_{34}H_{44}NO_{23}$ $(M + 1)^+$ requires *m/z* 834.2301]; ν_{max}/cm^{-1} 2920 (CH) and ~1730 (CO); δ_H 2.00–2.21 (3 H × 8, s, Ac × 8), 3.95 and 3.96 (3 H × 2, s, Me × 2), 4.01–4.62 (7 H, m) and 4.99–5.63 (5 H, m); difference in isomers' spectra: δ 5.91 (1/2 H, d, $J_{1',2'}$ 8.4, 1′-H of 1′*S*-form) and 6.20 (1/2 H, d, $J_{1',2'}$ 4.8, 1′-H of 1′*R*-form).

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