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Diastereoselectivity of Chiral Nitrone 1,3-Dipolar Cycloaddition to *Baylis-Hillman* Adducts

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Summary. 1,3-Dipolar cycloadditions of chiral nitrones to *Baylis-Hillman* adducts (β-hydroxy-α-methylene esters) proceed with complete regioselectivity in good yields to afford the corresponding diastereomeric 3,5,5-trisubstituted isoxazolidines. Attack of the dipole from the less sterically hindered side of the dipolarophiles affords C-3/C-5 *cis* isoxazolidines as the predominant isomers. The strong preference for the C-3/C-5 *cis* isoxazolidines provided more sterically demanding *O-tert*-butyldimethylsilylsubstituted nitrone **2**. Addition of *Lewis* acids accelerates the reaction and increases the portion of C-3/C-5 *trans* isoxazolidines. Microwave irradiation accelerates the reaction, but it produces only a small effect on the diastereoisomeric product ratio.

Keywords. Dipolar cycloaddition; Stereoselectivity; Nitrones; Isoxazolidines; Microwave heating.

Introduction

Over the years, nitrones have become important building blocks in organic synthesis. The nitrone-olefin 1,3-dipolar cycloaddition is a powerful reaction in that it can create as many as three new contiguous stereogenic centres in a single step [1–3]. Regio- and stereoselective nitrone cycloaddition, followed by reduction of the N–O bond to produce both an amino and a hydroxy function, allows the synthesis of many products of potential interest. Based on an evaluation of the nitrone cycloaddition, it

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Dedicated to Prof. *Peter Stanetty* on his 60th birthday

was felt that the stereochemistry of these new centers could be controlled if the reaction system were properly designed [4]. Diastereoselectivity of the cycloadditions depends mainly upon the nature of dipole and dipolarophile.

Lewis acids are often used as catalysts in 1,3-dipolar cycloadditions of nitrones [5–8]. Recently we have described (i) the effect of the addition of Mg(II) additive upon the stereoselectivity of reactions of *C*-phenyl-*N*-methylnitrone with *Baylis-Hillman* adducts **3** and **6** as well as (ii) the acceleration of this cycloaddition by microwave irradiation [9]. With our continuing efforts to utilize chiral 1,3-dipolar cycloadditions we have found, that the stereoselectivity of the cycloaddition is influenced by the steric hindrance of both the *N*- and *C*-substituent of the nitrone, *i.e.* the selectivity increases as the nitrogen/carbon substituent of the nitrone becomes bulkier [10–12]. The best diastereoselectivity was achieved with the *N*-benzyl chiral sugar-derived nitrones **1** and **2** [13–15]. Therefore, we report in the present communication the investigation of the effect of the addition of *Lewis* acid upon the stereoselectivity of reactions of chiral nitrones **1** and **2** with *Baylis-Hillman* adducts **3** and **6**.

Results and Discussions

The results are presented in the Tables 1–3. In all cases the reactions proceeded with complete regioselectivity, leading to the formation of diastereomeric isoxazolidines **4a**–**4f** (Scheme 1), **5a** and **5b** (Scheme 2), and **7a**–**7e** (Scheme 3) as a mixture of diastereoisomers in a good overall yield. Only the 5-substituted

Table 1. 1,3-Dipolar cycloaddition of nitrone **1** to *Baylis-Hillman* adduct **3**

Entry	Reaction conditions	Yield	*cis*:*trans*	Cycloadduct ratio				
		%		**4a**	**4b**	**4c**	**4d**	**4e**
1	CH_2Cl_2, rt, 14 d	88	85:15	48	28	9	8	7
2	CH_2Cl_2, rt, 14 d[a]	92	82:18	61	15	6	9	9
3	CH_2Cl_2, reflux, 7 d	80	94:6	57	29	8	–	6
4	CH_2Cl_2, rt, 7 d, 4 Å MS, $MgBr_2 \cdot OEt_2$	20	90:10	52	33	5	5	5
5	CH_2Cl_2, rt, 7 d, MgI_2–I_2	37	68:32	54	14	–	–	32
6	CH_2Cl_2, rt, 7 d, 4 Å MS, MgI_2–I_2	–[b]	–	–	–	–	–	–
7	CH_2Cl_2, reflux, 12 d, MeMgBr	35	51:49	14	21	16	4	45
8	CH_2Cl_2, rt, 14 d, $ZnCl_2$	23	66:34	19	17	30	–	34
9	CH_2Cl_2, rt, 14 d, ZnI_2	15	97:3	44	15	38	–	3
10	CH_2Cl_2, rt, 17 h, $TiCl_4$	–[b]	–	–	–	–	–	–
11	CH_2Cl_2, −30 to 8°C, 20 h, $TiCl_4$	–[b]	–	–	–	–	–	–
12	toluene, reflux, 24 h	46	63:37	36	20	7	–	37
13	toluene, reflux, 8.5 h, MeMgBr	53	58:42	31	14	13	15	27
14	toluene, reflux, 16.5 h, PhMgBr	30[c]	58:42	28	15	15	17	25
15	CCl_4, mw, 1000 W, 1 h	39	77:23	49	23	5	12	11
16	neat, 50°C, 2 h	92	96:4	76	20	–	4	–

[a] 3 equiv. of alkene were used; [b] no detectable amount of cycloadduct in crude reaction mixture; [c] the nitrone **1** was slowly dropwise added

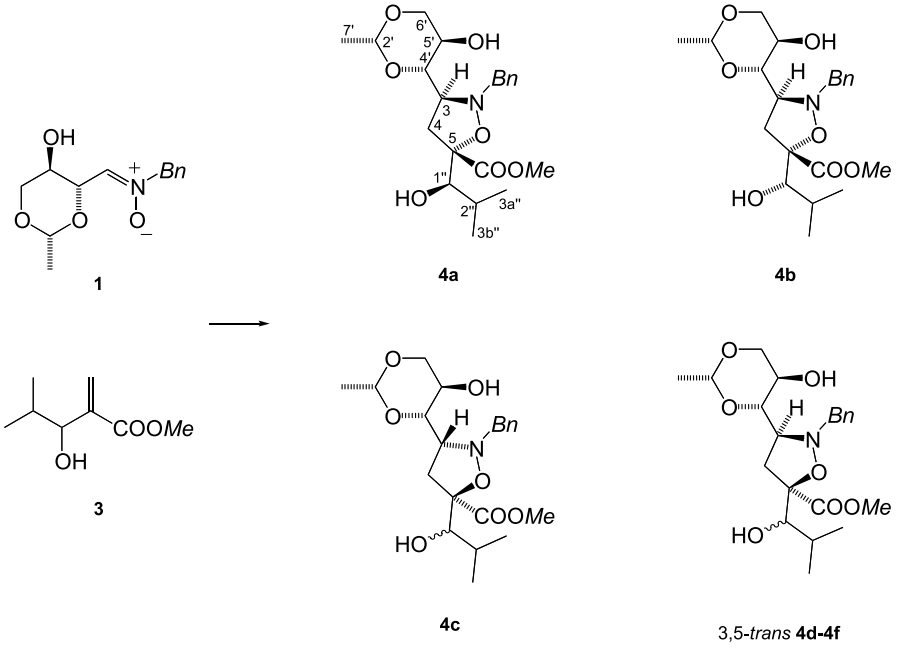
Table 2. 1,3-Dipolar cycloaddition of nitrone **2** to *Baylis-Hillman* adduct **3**

Entry	Reaction conditions	Yield	Cycloadduct ratio	
		%	**5a**	**5b**
1	CH_2Cl_2, rt, 180 d	47	64	36
2	CH_2Cl_2, rt, 7 d, $MgBr_2 \cdot OEt_2$	–[a]	–	–
3	CCl_4, reflux, 48 h	72	56	44
4	toluene, reflux, 39 h	80	53	47
5	*THF*, reflux, 3 d	52	61	39
6	*THF*, reflux, 16 h, 4 Å MS, MgI_2–I_2	–[a]	–	–
7	*THF*, reflux, 16 h, MgI_2–I_2	–[a,b]	–	–
8	*THF*, reflux, 16 h, 4 Å MS, MgI_2–I_2	6[b]	–	>95

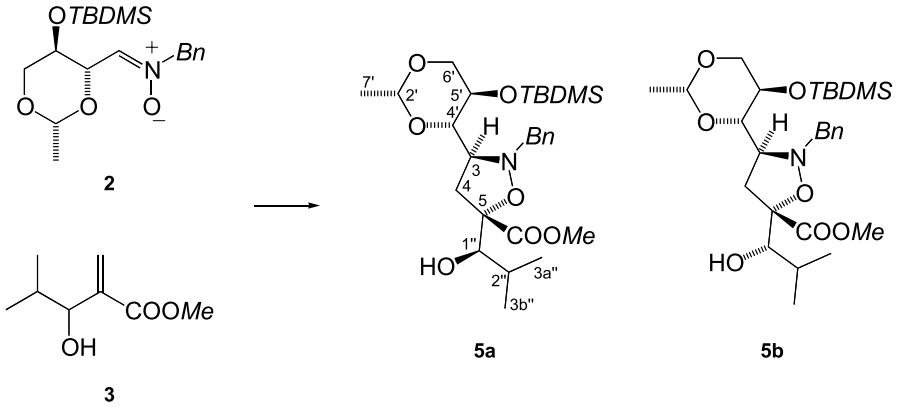
[a] no detectable amount of cycloadduct in crude reaction mixture; [b] 5 equiv. of alkene were used

Table 3. 1,3-Dipolar cycloaddition of nitrone **1** to *Baylis-Hillman* adduct **6**

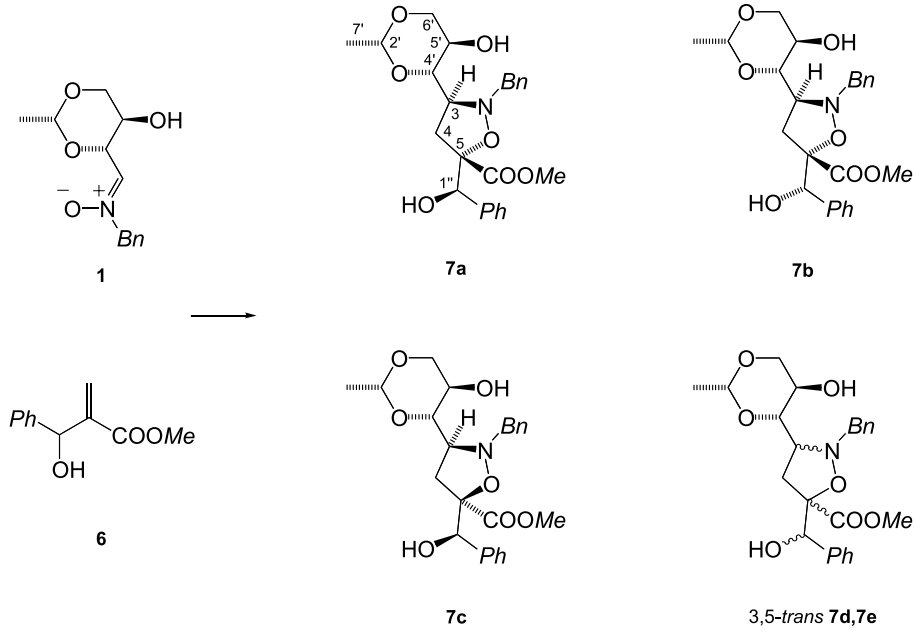
Entry	Reaction conditions	Yield	*cis*:*trans*	Cycloadduct ratio				
		%		**7a**	**7b**	**7c**	**7d**	**7e**
1	CCl_4, reflux, 24 h	80	54:46	37	17	13	21	12
2	CCl_4, reflux, 7 d, MeMgBr	23	78:22	48	30	6	–	16
3	CCl_4, mw, 1000 W, 1 h	65	58:42	38	20	10	21	11
4	toluene, reflux, 8.5 h	94	53:47	38	15	11	23	13
5	toluene, reflux, 8.5 h, MeMgBr	39	42:58	26	16	18	20	20



Scheme 1



Scheme 2



Scheme 3

isoxazolidines **4a**–**4f**, **5a**, **5b**, and **7a**–**7e** were formed irrespective of the presence or absence of *Lewis* acid. Change of solvent, alteration of reaction temperature, or microwave irradiation has no influence on the regioselectivity of the reaction. Purification by flash chromatography allowed the isolation of the pure diastereoisomers **4a**, **4c**, **4d**, **5a**, **5b**, **7a**, **7c**, and **7d**, while the characterization of minor isomers **4f**, **7b**, and **7e** was possible only from some relevant signals corresponding to aforementioned minor isomers clearly observed in the other enriched fractions. The pure diastereoisomer **4b** was obtained by deprotection of **5b** using *TBAF* in *THF*. The regiochemistry of the cycloadducts **4**, **5**, and **7** was readily deduced from resonance positions of C-3, C-4, and C-5 and spin multiplicity of protons H-3 and H-4 and the stereochemistry of these adducts was identified by spectroscopic

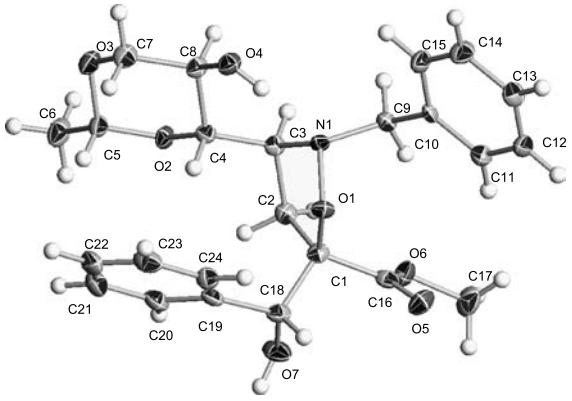


Fig. 1. X-ray analysis of **7c**

analysis, particularly N*O*E difference experiments, and subsequently confirmed by X-ray-crystallographic analysis in the case of **7c**. The most important and decisive information obtained from N*O*E experiments is the presence or absence of the interaction between the protons H-4/H-3, H-4/H-1′, and H-3/H-1′ in the corresponding cycloadducts [9]. For instance, the *cis* relationship of the dioxane ring at C-3 and methoxycarbonyl substituent at C-5 in **4a** has been assigned on the basis of N*O*EDS. The enhancement on signal H-4_A and the enhancement on signal H-3 and H-1′ following saturation of signal H-4_B show a *cis* relationship between the aforementioned substituents at C-3 and C-5; irradiation of H-4_A causes only enhancement on H-4_B. Moreover, the missing interactions between H-4_A and H-3 and between H-4_A and H-1′ confirm this *cis* relationship. X-Ray analysis of **7c** reveals a C-4′/C-3 *erythro*- and C-3/C-5 *trans*-stereochemistry (Fig. 1). The ratio of diastereoisomers was determined from quantitative ^{13}C NMR spectra, by integration of the peaks from C-4 and C-5 of the isoxazolidines, respectively.

The stereoselectivity of the cycloaddition is dependent on the substituent being attached in the starting nitrones **1** and **2** as well as upon reaction conditions (Tables 1–3). Attack of the dipole **1** from the less sterically hindered side of the dipolarophiles **3** affords C-3/C-5 *cis* isoxazolidines **4a**–**4c** as the predominant isomers (Scheme 1, Table 1). On the other hand the cycloaddition of more sterically demanding *O-tert*-butyldimethylsilylsubstituted nitrone **2** proceeded more selective. The corresponding C-3/C-5 *cis*- C-4′/C-3 *erythro*-isoxazolidines **5a** and **5b** were formed exclusively (Scheme 2, Table 2). Addition of *Lewis* acids accelerates the reaction and in the case of nitrone **1** increases the portion of C-3/C-5 *trans*-isoxazolidines **4d**–**4f** (Table 1). Reaction of nitrone **1** and phenyl *Baylis-Hillman* adduct **6** proceeded in analogous fashion (Scheme 3, Table 3).

It is noteworthy to mention that our attempts to accelerate the cycloaddition of nitrone **1** by microwave irradiation were successful. Indeed, microwave irradiation decreased the reaction times of the cycloadditions (Table 1, entry 15, Table 3, entry 3). On the other hand, microwave irradiation produces only a small effect on the diastereoisomeric product ratio.

In conclusion, 1,3-dipolar cycloadditions of chiral sugar derived nitrones **1**, **2** and *C*-phenyl-*N*-methylnitrone [9] with *Baylis-Hillman* adducts **3** and **6** proceeded fully

analogously. The addition of a *Lewis* acid in contrast to mesitonitrile oxide cycloaddition [16, 17] exerts only a slight influence on the stereoselectivity of the reaction. Cycloadditions of chiral nitrones **1** and **2** to β-hydroxy-α-methylene esters **3** and **6** proceed with complete regioselectivity in good yields to afford the corresponding diastereomeric 3,5,5-trisubstituted isoxazolidines. Attack of the dipole from the less sterically hindered side of the dipolarophiles affords C-3/C-5 *cis*-isoxazolidines as the predominant isomers. The strong preference for the C-3/C-5 *cis*-isoxazolidines provided more sterically demanding *O-tert*-butyldimethylsilylsubstituted nitrone **2**. Addition of *Lewis* acids accelerates the reaction and increases the portion of C-3/C-5 *trans* isoxazolidines. Microwave irradiation accelerates the reaction, but it has only a small effect on the diastereoisomeric product ratio.

Experimental

All starting materials and reagents are commercially available (Fluka, Merck, Avocado, or Aldrich) and were used without further purification. Solvents were dried before use. Thin-layer chromatography (TLC, on glass plates coated with silica $60F_{254}$ Merck) was used for monitoring of reactions, eluents are given in the text. For column chromatography the flash chromatography technique was employed using silica 60 (0.040–0.063 mm, Merck). Melting points (mp) were determined on a *Kofler* hot plate apparatus and are uncorrected.

IR Spectra were recorded on FTIR NICOLET MAGNA 750 instrument. The ^{1}H and ^{13}C NMR spectra of deuterochloroform solutions were obtained using Varian VXR-300 (300 MHz) and Bruker DRX-400 (400 MHz) instruments, tetramethylsilane (TMS) being the internal reference. Optical rotations [α] were measured on an IBZ Messtechnik Polar-LμP polarimeter at the sodium D line (589 nm) using a 1 dm cell with chloroform as a solvent. HRMS were performed on a Finnigan MAT 8230 spectrometer (70 eV). Elemental analyses were conducted using the Carlo Erba 1106, their results were found to be in good agreement with the calculated values.

Nitrones **1** and **2** were prepared from the corresponding aldehyde by the reaction with *N*-benzylhydroxylamine according to the procedure already described [13, 14]. The *Baylis-Hillman* alkenes **3** and **6** were prepared by the reaction of isobutyraldehyde and benzaldehyde with methyl acrylate in the presence of a catalytic amount of *DABCO* respectively [18, 19].

The *Lewis* acids ($ZnCl_2$, ZnI_2, $TiCl_4$, and *Me*MgBr as 1.4 *M* solution in *THF*) used for cycloadditions are commercially available reagents. The $MgBr_2 \cdot OEt_2$ and MgI_2–I_2 were freshly prepared prior to use.

General Procedures

Method A: Cycloadditions in the Absence of Lewis Acids

To a round-bottom flask equipped with magnetic stirring bar nitrone (1 equiv.), alkene (1 equiv.), and solvent (10 cm^3) were added. The appropriate solvent, reaction time, and temperature for each reaction are listed in Tables 1–3. The reaction mixture was stirred until complete conversion of nitrone (monitored by TLC). Alternatively, when the conversion was not complete, the reaction was stopped after 14 days. The solvent was evaporated and quantitative ^{13}C NMR of crude reaction mixture was recorded. The reaction mixture was then subjected to column chromatography. The yields of the isolated mixtures of cycloadducts for each experiment are given in Tables 1–3.

Method B: Cycloadditions in the Presence of Lewis Acids

The reactions were carried out under argon atmosphere. To the dry round-bottom flask equipped with magnetic stirring bar and rubber septum alkene was added. The solution of *Lewis* acid (1 equiv.) was

dropwise added at room temperature and the mixture was treated for 15–30 min at the same temperature. Then the solution of nitrone (1 equiv.) was dropwise added with a syringe. The appropriate solvent, reaction time, and temperature are listed in Tables 1–3. The mixture was stirred until complete conversion of nitrone (monitored by TLC). The reaction was quenched with saturated NH_4Cl solution, extracted with CH_2Cl_2 (in the case of MgI_2–I_2 mediated cycloadditions the collected organic layers were washed with 10% $Na_2S_2O_7$ solution to remove I_2), dried over Na_2SO_4, and the solvent was evaporated.

Method C: Microwave Mediated Cycloadditions

The reactions were carried out in a conventional kitchen microwave oven at the rate of 1000 W. The equimolar solution of nitrone and alkene in CCl_4 was put into the 100 cm^3 *Erlenmayer* flask, cooled to 0°C, the flask was inserted into the microwave oven, and the mixture was irradiated for 5 min. The flask was than taken out and the reaction was monitored by TLC. The mixture was again cooled down to 0°C and the whole sequence was repeated until complete conversion of nitrone (12 times) was observed. The solution was then transferred to the round-bottom flask and the solvent was removed by rotary evaporation.

*1,3-Dipolar Cycloaddition Reactions of Nitrone **1** with Alkene **3***

The cycloaddition of nitrone **1** (0.960 g, 3.8 mmol) with alkene **3** (0.610 g, 3.8 mmol) in CCl_4 (50 cm^3) was carried out according to method C. The mixture of 5 diastereoisomers (5:11:49:12:23) was purified and separated by flash column chromatography on silica gel (200 g, 48×3 cm) eluting with *EtOAc*:hexane = 40:60 to give 530 mg (34%) of mixture **4a**–**4e**, 59 mg (4%) of **4c**, 14 mg (1%) of **4f**, and 5 mg (0.3%) of **4d**. Combined yield 608 mg (39%). Pure major cycloadduct **4a** (155 mg, 10%) was obtained by crystallisation from *EtOAc*:hexane (20:80).

2-Benzyl-3-(5-hydroxy-2-methyl[1,3]dioxan-4-yl)-5-(1-hydroxy-2-methylpropyl)isoxazolidine-5-carboxylic acid methyl ester (**4a**, $C_{21}H_{31}NO_7$)

Colourless solid; R_f = 0.47 (*EtOAc*:hexane = 50:50); mp 150–151°C (from *EtOAc*/hexane); ^{1}H NMR (400 MHz): δ = 7.34–7.30 (m, 5H_{Ph}), 4.78 (br, OH), 4.55 (q, J = 5.0 Hz, H-2′), 4.13, 4.09 (2d, J = 13.3, 13.1 Hz, $\underline{CH_2}$Ph), 4.03 (dd, J = 8.8, 3.2 Hz, H-6′e), 3.80 (s, $CO_2\underline{CH_3}$), 3.70 (dd, J = 6.7, 4.7 Hz, H-1″), 3.35 (ddd, J = 8.6, 7.3, 2.8 Hz, H-3), 3.33–3.27 (m, H-5′, 6′a), 3.22 (dd, J = 9.1, 7.5 Hz, H-4′), 3.00 (dd, J = 13.6, 2.8 Hz, H-4a), 2.78 (dd, J = 13.6, 8.5 Hz, H-4b), 2.38 (d, J = 6.4 Hz, OH), 1.67–1.59 (m, H-2″), 1.28 (d, 3H, J = 5.0 Hz, H-7′), 0.95, 0.92 (2d, 2×3H, J = 6.9, 6.6 Hz, H-3a″, 3b″) ppm; ^{13}C NMR (100 MHz): δ = 173.8 (C=O), 135.4, 129.3, 128.7, 128.0 (6C_{Ph}), 99.1 (C-2′), 90.2 (C-5), 78.4 (C-4′), 78.0 (C-1″), 70.0 (C-6′), 67.8 (C-3), 64.8 (C-5′), 62.7 ($\underline{CH_2}$Ph), 52.8 ($CO_2\underline{CH_3}$), 34.2 (C-4), 30.6 (C-2″), 20.6 (C-3b″), 20.5 (C-7′), 16.9 (C-3a″) ppm; IR (KBr): $\bar{\nu}$ = 3547, 3209, 2985, 2974, 2856, 1739, 1443, 1408, 1267, 1208, 1156, 1123, 1037, 1015 cm^{-1}; $[\alpha]_D^{25} = -52.7°\ cm^2\ g^{-1}$ (c = 0.2, $CHCl_3$).

2-Benzyl-3-(5-hydroxy-2-methyl[1,3]dioxan-4-yl)-5-(1-hydroxy-2-methylpropyl)isoxazolidine-5-carboxylic acid methyl ester (**4c**, $C_{21}H_{31}NO_7$)

Colourless solid; R_f = 0.47 (*EtOAc*:hexane = 50:50); mp 105–110°C (from *EtOAc*/hexane); ^{1}H NMR (400 MHz): δ = 7.29–7.19 (m, 5H_{Ph}), 4.57 (br, OH), 4.45 (q, J = 5.0 Hz, H-2′), 4.14 (d, J = 12.6 Hz, $\underline{CH_2}$Ph), 3.96 (d, J = 12.6 Hz, $\underline{CH_2}$Ph), 3.96 (dd, J = 10.2, 4.4 Hz, H-6′e), 3.72 (s, $CO_2\underline{CH_3}$), 3.63 (d, J = 3.5 Hz, H-1″), 3.31 (ddd, J = 8.8, 7.9, 2.0 Hz, H-3), 3.21 (dd, J = 10.2, 9.9 Hz, H-6′a), 3.15 (ddd, J = 9.9, 8.2, 4.4 Hz, H-5′), 2.99 (dd, J = 8.8, 8.5 Hz, H-4′), 2.89 (dd, J = 13.4, 2.0 Hz, H-4a), 2.75 (dd, J = 13.4, 7.9 Hz, H-4b), 1.92 (br, OH), 1.60–1.52 (m, H-2″), 1.20 (d, 3H, J = 5.0 Hz, H-7′), 0.92, 0.80 (2d, 2×3H, J = 7.0, 6.7 Hz, H-3a″, 3b″) ppm; ^{13}C NMR (100 MHz): δ = 173.3 (C=O), 135.1,

129.5, 128.8, 128.2 ($6C_{Ph}$), 99.0 (C-2′), 90.8 (C-5), 78.2 (C-4′), 77.7 (C-1″), 70.0 (C-6′), 67.1 (C-3), 65.5 (C-5′), 63.2 ($\underline{CH_2}Ph$), 52.6 ($CO_2\underline{CH_3}$), 37.6 (C-4), 30.9 (C-2″), 21.0 (C-3a″), 20.4 (C-7′), 16.3 (C-3b″) ppm; IR (KBr): $\bar{\nu} = 3533, 3507, 3323, 3246, 2961, 2935, 2872, 1735, 1732, 1456, 1401, 1279, 1264, 1209, 1118, 1083, 1058, 1036\,cm^{-1}$.

2-Benzyl-3-(5-hydroxy-2-methyl[1,3]dioxan-4-yl)-5-(1-hydroxy-2-methylpropyl)isoxazolidine-5-carboxylic acid methyl ester (**4d**, $C_{21}H_{31}NO_7$)

Colourless viscous oil; $R_f = 0.50$ (*Et*O*Ac*:hexane = 50:50); ^{1}H NMR (400 MHz): $\delta = 7.38–7.30$ (m, $5H_{Ph}$), 4.95 (br, OH), 4.62 (q, $J = 5.0$ Hz, H-2′), 4.12 (d, $J = 12.0$ Hz, $\underline{CH_2}Ph$), 3.99 (dd, $J = 10.8$, 5.6 Hz, H-6′e), 3.81 (s, $CO_2\underline{CH_3}$), 3.80 (d, $J = 4.7$ Hz, H-1″), 3.66 (d, $J = 12.0$ Hz, $\underline{CH_2}Ph$), 3.46 (ddd, $J = 9.1$, 8.8, 2.4 Hz, H-3), 3.35 (dd, $J = 9.1$ Hz, H-4′), 3.28 (dd, $J = 10.8$, 10.2 Hz, H-6′a), 3.21 (dd, $J = 13.7$, 8.5 Hz, H-4a), 3.08 (ddd, $J = 9.9$, 9.1, 5.6 Hz, H-5′), 2.75 (br, OH), 2.72 (dd, $J = 13.7$, 2.3 Hz, H-4b), 1.63–1.56 (m, H-2″), 1.26 (d, 3H, $J = 5.0$ Hz, H-7′), 0.97, 0.94 (2d, 2×3H, $J = 6.7$, 6.7 Hz, H-3a″, 3b″) ppm; ^{13}C NMR (100 MHz): $\delta = 174.3$ (C=O), 134.9, 129.5, 128.8, 128.4 ($6C_{Ph}$), 99.1 (C-2′), 91.6 (C-5), 79.1 (C-4′), 76.1 (C-1″), 69.7 (C-6′), 69.2 (C-3), 65.5 (C-5′), 62.5 ($\underline{CH_2}Ph$), 52.9 ($CO_2\underline{CH_3}$), 32.5 (C-4), 30.1 (C-2″), 20.6 (C-3a″), 20.5 (C-7′), 16.4 (C-3b″) ppm; IR (KBr): $\bar{\nu} = 3456, 3203, 2925, 2854, 1735, 1462, 1269, 1151, 1113, 1086, 1018\,cm^{-1}$; $[\alpha]_D^{25} = +73.8^\circ\,cm^2\,g^{-1}$ ($c = 0.01$, $CHCl_3$).

Some relevant signals corresponding to minor isomers **4e** and **4f** were also clearly observed in the other enriched fraction.

2-Benzyl-3-(5-hydroxy-2-methyl[1,3]dioxan-4-yl)-5-(1-hydroxy-2-methylpropyl)isoxazolidine-5-carboxylic acid methyl ester (**4e**, $C_{21}H_{31}NO_7$)

$R_f = 0.47$ (*Et*O*Ac*:hexane = 50:50); ^{1}H NMR (300 MHz): $\delta = 7.36–7.34$ (m, $5H_{Ph}$), 5.04 (br, OH), 4.60 (q, $J = 5.1$ Hz, H-2′), 4.30 (d, $J = 12.4$ Hz, $\underline{CH_2}Ph$), 4.00 (dd, $J = 10.6$, 5.4 Hz, H-6′e), 3.81 (s, $CO_2\underline{CH_3}$), 3.70 (d, $J = 13.4$ Hz, H-1″), 3.65 (d, $J = 12.1$ Hz, $\underline{CH_2}Ph$), 3.50 (dd, $J = 9.0$, 8.5 Hz, H-4′), 3.34–3.27 (m, 2H, $J = 10.6$, 10.4, 8.5, 3.0 Hz, H-6′a, 3), 3.13–3.00 (m, 2H, $J = 13.7$, 10.2, 8.8, 8.5, 5.6 Hz, H-5′, 4a), 2.83 (dd, $J = 14.1$, 3.0 Hz, H-4b), 2.62 (br, OH), 1.67–1.57 (m, H-2″), 1.25 (d, 3H, $J = 5.1$ Hz, H-7′), 0.99, 0.89 (2d, 2×3H, $J = 6.7$, 6.8 Hz, H-3a″, 3b″) ppm; ^{13}C NMR (75 MHz): $\delta = 173.8$ (C=O), 135.3, 129.57, 128.8, 128.2 ($6C_{Ph}$), 99.1 (C-2′), 90.3 (C-5), 78.9 (C-4′), 78.7 (C-1″), 69.7 (C-6′), 67.4 (C-3), 65.2 (C-5′), 62.9 ($\underline{CH_2}Ph$), 52.5 ($CO_2\underline{CH_3}$), 39.8 (C-4), 31.1 (C-2″), 21.2 (C-3a″), 20.4 (C-7′), 15.8 (C-3b″) ppm.

2-Benzyl-3-(5-hydroxy-2-methyl[1,3]dioxan-4-yl)-5-(1-hydroxy-2-methylpropyl)isoxazolidine-5-carboxylic acid methyl ester (**4f**, $C_{21}H_{31}NO_7$)

Brown viscous oil; $R_f = 0.50$ (*Et*O*Ac*:hexanes = 50:50); ^{1}H NMR (400 MHz): $\delta = 7.44–7.27$ (m, $5H_{Ph}$), 4.62 (q, $J = 5.0$ Hz, H-2′), 4.12 (d, $J = 11.4$ Hz, $\underline{CH_2}Ph$), 3.96 (dd, $J = 10.8$, 5.5 Hz, H-6′e), 3.87 (d, $J = 3.2$ Hz, H-1″), 3.82 (s, $CO_2\underline{CH_3}$), 3.64 (d, $J = 11.4$ Hz, $\underline{CH_2}Ph$), 3.50–3.38 (m, H-3, 4′), 3.26 (dd, $J = 10.5$, 10.2 Hz, H-6′a), 3.21 (dd, $J = 13.4$, 8.2 Hz, H-4a), 2.97 (ddd, $J = 9.9$, 8.5, 5.5 Hz, H-5′), 2.72 (dd, $J = 13.4$, 2.0 Hz, H-4b), 1.62–1.54 (m, H-2″), 1.26 (d, 3H, $J = 5.0$ Hz, H-7′), 1.01, 0.94 (2d, 2×3H, $J = 7.0$, 6.7 Hz, H-3a″, 3b″) ppm; ^{13}C NMR (100 MHz): $\delta = 174.6$ (C=O), 134.7, 129.8, 128.6, 128.3 ($6C_{Ph}$), 99.0 (C-2′), 92.4 (C-5), 78.3 (C-4′), 75.0 (C-1″), 69.6 (C-6′), 68.9 (C-3), 65.6 (C-5′), 62.4 ($\underline{CH_2}Ph$), 52.7 ($CO_2\underline{CH_3}$), 31.4 (C-4), 29.8 (C-2″), 20.9 (C-3a″), 20.3 (C-7′), 15.8 (C-3b″) ppm; IR (KBr): $\bar{\nu} = 3455, 3211, 2995, 2971, 2874, 1736, 1453, 1416, 1269, 1216, 1152, 1112, 1086, 1025\,cm^{-1}$.

*1,3-Dipolar Cycloaddition Reactions of Nitrone **2** with Alkene **3***

The cycloaddition of nitrone **2** (1.000 g, 2.7 mmol) with alkene **3** (0.432 g, 2.7 mmol) in CCl_4 (30 ml) was carried out according to method A. The mixture of 2 diastereoisomers (56:44) was purified

and separated by flash column chromatography on silica gel (130 g, 13×4.5 cm) eluting with *Et*OAc:hexane = 20:80 to give 260 mg (18%) of a mixture **5a**, **5b** 358 mg (25%) of **5b**, and 419 mg (29%) of **5a**. Combined yield 1.037 g (72%).

2-Benzyl-3-[5-(tert-butyldimethylsilanyloxy)-2-methyl[1,3]dioxan-4-yl]-5-(1-hydroxy-2-methylpropyl)isoxazolidine-5-carboxylic acid methyl ester (**5a**, $C_{27}H_{45}NO_7Si$)

Colourless oil; $R_f = 0.40$ (*Et*OAc:hexane = 30:70); ^{1}H NMR (400 MHz): $\delta = 7.43$–7.31 (m, $5H_{Ph}$), 4.62 (q, $J = 5.0$ Hz, H-2′), 4.26, 4.03 (2d, $J = 14.6$, $\underline{CH_2}Ph$), 4.00 (dd, $J = 10.5$, 4.7 Hz, H-6′e), 3.79 (s, $CO_2\underline{CH_3}$), 3.55 (dd, $J = 4.7$, 4.4 Hz, H-1″), 3.45 (ddd, $J = 9.4$, 9.1, 4.7 Hz, H-5′), 3.40 (dd, $J = 9.4$ Hz, H-4′), 3.33–3.25 (m, $J = 10.5$, 9.6 Hz, H-6′a, 3), 3.04 (dd, $J = 12.6$, 7.0 Hz, H-4a), 2.52 (dd, $J = 12.6$, 9.4 Hz, H-4b), 2.26 (br, OH), 1.69–1.61 (m, H-2″), 1.33 (d, 3H, $J = 5.0$ Hz, H-7′), 0.98, 0.91 (2d, 2×3H, $J = 6.7$, 6.7 Hz, H-3a″, 3b″), 0.86 (s, $C(\underline{CH_3})_3$), 0.05, 0.02 (2s, $Si(\underline{CH_3})_2$) ppm; ^{13}C NMR (100 MHz): $\delta = 173.6$ (C=O), 135.8, 129.5, 128.2, 127.3 ($6C_{Ph}$), 98.6 (C-2′), 87.6 (C-5), 79.0 (C-4′), 78.5 (C-1″), 71.2 (C-6′), 64.3 (C-3), 63.4 (C-5′), 59.8 ($\underline{CH_2}Ph$), 52.3 ($CO_2\underline{CH_3}$), 33.7 (C-4), 30.3 (C-2″), 25.6 ($C(\underline{CH_3})_3$), 20.9 (C-3a″), 20.4 (C-7′), 17.8 ($\underline{C}(CH_3)_3$), 16.7 (C-3b″), −4.4, −4.9 ($Si(\underline{CH_3})_2$) ppm; IR (KBr): $\bar{\nu} = 3521$, 2957, 2858, 1741, 1463, 1411, 1260, 1115, 1049, 1017 cm^{-1}; HRMS (70 eV): calcd. for (M^+) 523.2965, found 523.2978; $[\alpha]_D^{25} = -81.0^\circ$ cm^2 g^{-1} ($c = 0.1$, $CHCl_3$).

2-Benzyl-3-[5-(tert-butyldimethylsilanyloxy)-2-methyl[1,3]dioxan-4-yl]-5-(1-hydroxy-2-methylpropyl)isoxazolidine-5-carboxylic acid methyl ester (**5b**, $C_{27}H_{45}NO_7Si$)

Colourless oil; $R_f = 0.55$ (*Et*OAc:hexane = 30:70); ^{1}H NMR (400 MHz): $\delta = 7.43$–7.25 (m, $5H_{Ph}$), 4.67 (q, $J = 5.0$ Hz, H-2′), 4.57 (d, 1H, $J = 14.9$ Hz, $\underline{CH_2}Ph$), 4.07–4.00 (m, 2H, $J = 14.9$, 11.1, 4.4 Hz, H-6′e, $\underline{CH_2}Ph$), 3.78 (s, $CO_2\underline{CH_3}$), 3.66–3.62 (m, H-1″, 3, 4′), 3.41 (dd, $J = 11.1$, 9.9 Hz, H-6′a), 2.98 (br, H-5′), 2.89 (dd, $J = 13.2$, 7.3 Hz, H-4a), 2.56 (dd, $J = 13.2$, 9.4 Hz, H-4b), 2.15 (br, OH), 1.60–1.52 (m, H-2″), 1.32 (d, 3H, $J = 5.0$ Hz, H-7′), 0.90 (m, 12H, H-3a″, $C(\underline{CH_3})_3$), 0.89 (d, 3H, $J = 2.6$ Hz, H-3b″), 0.10, 0.09 (2s, $Si(\underline{CH_3})_2$) ppm; ^{13}C NMR (100 MHz): $\delta = 173.8$ (C=O), 136.9, 129.4, 127.9, 127.0 ($6C_{Ph}$), 98.4 (C-2′), 87.0 (C-5), 83.9 (C-4′), 76.4 (C-1″), 71.1 (C-6′), 66.2 (C-3), 65.4 (C-5′), 61.1 ($\underline{CH_2}Ph$), 52.4 ($CO_2\underline{CH_3}$), 36.0 (C-4), 30.1 (C-2″), 25.8 ($C(\underline{CH_3})_3$), 20.3 (C-3a″), 20.3 (C-7′), 17.8 ($\underline{C}(CH_3)_3$), 17.0 (C-3b″), −4.0, −4.5 ($Si(\underline{CH_3})_2$) ppm; IR (KBr): $\bar{\nu} = 3523$, 2956, 2929, 2857, 1739, 1463, 1410, 1363, 1260, 1212, 1104, 1009 cm^{-1}; HRMS (70 eV): calcd. for (M^+) 523.2965, found 523.2974; $[\alpha]_D^{25} = -52.2^\circ$ cm^2 g^{-1} ($c = 0.1$, $CHCl_3$).

*Preparation of **4b** by Deprotection of **5b***

The solution of **5b** (0.197 g, 0.4 mmol) and *TBAF* · xH$_2$O (0.154 g, 0.5 mmol) in *THF* (10 ml) was stirred for 5 h at room temperature. Saturated $NaHCO_3$ solution (4 ml) was added, the mixture was extracted with CH_2Cl_2, dried over Na_2SO_4, and the solvent was evaporated. The product was obtained by flash column chromatography on silica gel (20 g, 17×1.5 cm) eluting with *Et*OAc:hexane = 30:70 to give 140 mg (91%) of **4b**.

2-Benzyl-3-(5-hydroxy-2-methyl[1,3]dioxan-4-yl)-5-(1-hydroxy-2-methylpropyl)isoxazolidine-5-carboxylic acid methyl ester (**4b**, $C_{21}H_{31}NO_7$)

Colourless viscous oil; $R_f = 0.47$ (*Et*OAc:hexane = 50:50); ^{1}H NMR (400 MHz): $\delta = 7.27$–7.19 ($5H_{Ph}$), 4.95 (br, OH), 4.56 (q, $J = 5.0$ Hz, H-2′), 4.22 (d, 1H, $J = 14.3$ Hz, $\underline{CH_2}Ph$), 4.07 (dd, $J = 10.8$, 5.3 Hz, H-6′e), 3.89 (d, 1H, $J = 14.6$ Hz, $\underline{CH_2}Ph$), 3.81 (ddd, $J = 9.6$, 9.4, 5.3 Hz, H-5′, OH), 3.70 (s, $CO_2\underline{CH_3}$), 3.59 (d, $J = 4.4$ Hz, H-1″), 3.40 (dd, $J = 9.1$, 4.4 Hz, H-4′), 3.30–3.24 (m, $J = 10.8$, 10.2 Hz, H-6′a, 3), 2.86 (dd, $J = 13.7$, 6.7 Hz, H-4a), 2.60 (dd, $J = 13.7$, 10.2 Hz, H-4b), 2.18 (br, OH), 1.60–1.52 (m, H-2″), 1.24

(d, 3H, $J = 5.3$ Hz, H-7′), 0.86, 0.84 (2d, $J = 7.0$, 6.7 Hz, H-3a″, 3b″) ppm; ^{13}C NMR (100 MHz): $\delta = 173.4$ (C=O), 135.3, 128.8, 128.4, 127.6 ($6C_{Ph}$), 99.3 (C-2′), 87.9 (C-5), 78.5 (C-4′), 76.9 (C-1″), 69.9 (C-6′), 67.5 (C-3), 61.8 (C-5′), 60.3 ($\underline{CH_2}$Ph), 52.5 ($CO_2\underline{CH_3}$), 34.4 (C-4), 30.2 (C-2″), 20.5 (C-3a″), 20.4 (C-7′), 16.8 (C-3b″) ppm; IR (KBr): $\bar{\nu} = 3452$, 2963, 2873, 1736, 1498, 1455, 1409, 1368, 1276, 1207, 1146, 1114, 1087, 1052 cm^{-1}; HRMS (70 eV): calcd. for (M^+) 409.2100, found 409.2098; $[\alpha]_D^{25} = +97.8^\circ$ cm^2 g^{-1} ($c = 0.1$, $CHCl_3$).

*1,3-Dipolar Cycloaddition Reactions of Nitrone **1** with Alkene **6***

The cycloaddition of nitrone **1** (1.000 g, 4.0 mmol) with alkene **6** (0.770 g, 4.0 mmol) in CCl_4 (50 ml) was carried out according to method C. The mixture of 6 diastereoisomers (10:20:11:37:19:3) was purified and separated by flash column chromatography on silica gel (250 g, 25×4.5 cm) eluting with *Et*OAc:hexane = 30:70 to give 1022 mg of **7a**–**e**, 40 mg (2%) of **7c** and 59 mg (3%) of **7d**. Combined yield 1.121 g (63%). The major cycloadduct **7a** (184 mg, 10%) was obtained by crystallisation of mixture of cycloadducts **7a**–**e** from *Et*OAc:hexanes (9:91).

2-Benzyl-3-(5-hydroxy-2-methyl[1,3]dioxan-4-yl)-5-(hydroxyphenylmethyl)isoxazolidine-5-carboxylic acid methyl ester (**7a**, $C_{24}H_{29}NO_7$)

Colourless solid; $R_f = 0.43$ (*Et*OAc:hexane = 50:50); mp 171–175°C (from *Et*OAc/hexane); ^{1}H NMR (400 MHz): $\delta = 7.38$–7.29 (m, $10H_{Ph}$), 5.09 (d, $J = 4.4$ Hz, H-1″), 4.71 (br, OH), 4.48 (q, $J = 5.0$ Hz, H-2′), 4.15 (d, 1H, $J = 12.6$ Hz, $\underline{CH_2}$Ph), 3.97 (dd, $J = 10.8$, 5.0 Hz, H-6′e), 3.77 (d, 1H, $J = 12.6$ Hz, $\underline{CH_2}$Ph), 3.77 (s, $CO_2\underline{CH_3}$), 3.33 (ddd, $J = 8.2$, 7.9, 2.3 Hz, H-3), 3.24 (dd, $J = 10.8$, 9.6 Hz, H-6′a), 3.15 (ddd, $J = 9.4$, 8.8, 5.0 Hz, H-5′), 3.09 (dd, $J = 8.5$, 8.2 Hz, H-4′), 2.90 (dd, $J = 13.4$, 2.3 Hz, H-4a), 2.87 (d, $J = 5.0$ Hz, OH), 2.82 (dd, $J = 13.4$, 7.9 Hz, H-4b), 1.23 (d, 3H, $J = 5.0$ Hz, H-7′) ppm; ^{13}C NMR (100 MHz): $\delta = 172.9$ (C=O), 137.9, 135.3, 129.3, 128.8, 128.7, 128.3, 128.1, 127.0 ($12C_{Ph}$), 99.0 (C-2′), 91.4 (C-5), 78.1 (C-4′), 75.5 (C-1″), 69.9 (C-6′), 67.5 (C-3), 64.9 (C-5′), 63.1 ($\underline{CH_2}$Ph), 52.7 ($CO_2\underline{CH_3}$), 33.2 (C-4), 20.4 (C-7′) ppm; IR (KBr): $\bar{\nu} = 3502$, 3477, 3115, 2854, 1745, 1433, 1414, 1272, 1206, 1138, 1126, 1086, 1051, 1033, 1009 cm^{-1}; $[\alpha]_D^{25} = -38.7$ ($c = 0.1$, $CHCl_3$).

(3S, 5R, 2′R, 4′S, 5′R, 1″R)-2-Benzyl-3-(5-hydroxy-2-methyl[1,3]dioxan-4-yl)-5-(hydroxyphenylmethyl)isoxazolidine-5-carboxylic acid methyl ester (**7c**, $C_{24}H_{29}NO_7$)

Colourless solid; $R_f = 0.55$ (*Et*OAc:hexanes = 50:50); mp 187–188°C (from *Et*OAc/hexane); ^{1}H NMR (400 MHz): $\delta = 7.35$–7.17 (m, $10H_{Ph}$), 5.07 (s, H-1″), 4.70 (br, OH), 4.08 (d, 1H, $J = 12.0$ Hz, $\underline{CH_2}$Ph), 3.97 (q, $J = 5.0$ Hz, H-2′), 3.74 (dd, $J = 10.9$, 3.2 Hz, H-6′e), 3.71 (s, $CO_2\underline{CH_3}$), 3.21 (ddd, $J = 9.1$, 8.8, 1.2 Hz, H-3), 3.14 (dd, $J = 13.7$, 8.5 Hz, H-4a), 2.87–2.79 (m, H-6′a, 5′, OH), 2.57 (dd, $J = 13.7$, 1.2 Hz, H-4b), 1.86–1.82 (m, H-4′), 1.09 (d, 3H, $J = 5.0$ Hz, H-7′) ppm; ^{13}C NMR (100 MHz): $\delta = 173.9$ (C=O), 138.7, 134.8, 129.5, 128.8, 128.6, 128.3, 128.2, 128.0 ($12C_{Ph}$), 98.5 (C-2′), 90.3 (C-5), 77.0 (C-4′), 75.3 (C-1″), 69.6 (C-6′), 68.0 (C-3), 65.4 (C-5′), 62.3 ($\underline{CH_2}$Ph), 52.9 ($CO_2\underline{CH_3}$), 33.0 (C-4), 20.2 (C-7′) ppm; IR (KBr): $\bar{\nu} = 3331$, 3197, 2972, 2893, 1734, 1466, 1433, 1412, 1356, 1260, 1211, 1153, 1111, 1056, 1016 cm^{-1}; $[\alpha]_D^{25} = +38.5^\circ$ cm^2 g^{-1} ($c = 0.04$, $CHCl_3$).

2-Benzyl-3-(5-hydroxy-2-methyl[1,3]dioxan-4-yl)-5-(hydroxyphenylmethyl)isoxazolidine-5-carboxylic acid methyl ester (**7d**, $C_{24}H_{29}NO_7$)

Yellowish solid; $R_f = 0.54$ (*Et*OAc:hexane = 50:50); mp 139–142°C (from *Et*OAc/hexane); ^{1}H NMR (400 MHz): $\delta = 7.47$–7.34 (m, $10H_{Ph}$), 5.24 (br, OH), 5.14 (s, H-1″), 4.48 (q, $J = 5.0$ Hz, H-2′), 4.34 (br, OH), 4.28 (d, 1H, $J = 11.4$ Hz, $\underline{CH_2}$Ph), 3.95 (dd, $J = 10.8$, 5.3 Hz, H-6′e), 3.77 (s, $CO_2\underline{CH_3}$), 3.66 (d, 1H, $J = 11.7$ Hz, $\underline{CH_2}$Ph), 3.43 (ddd, $J = 9.6$, 8.5, 2.0 Hz, H-3), 3.18 (dd, $J = 10.8$, 9.9 Hz, H-6′a),

3.06 (dd, $J = 14.0$, 8.5 Hz, H-4a), 3.03 (dd, $J = 9.6$, 9.1 Hz, H-4′), 2.94 (ddd, $J = 10.2$, 9.6, 5.3 Hz, H-5′), 2.83 (dd, $J = 14.0$, 2.0 Hz, H-4b), 1.28 (d, 3H, $J = 5.0$ Hz, H-7′) ppm; ^{13}C NMR (100 MHz): $\delta = 173.7$ (C=O), 137.6, 134.7, 130.0, 128.8, 128.6, 128.4, 128.4, 127.2 ($12C_{Ph}$), 99.0 (C-2′), 92.8 (C-5), 77.8 (C-4′), 74.6 (C-1″), 69.6 (C-6′), 68.2 (C-3), 65.6 (C-5′), 62.7 ($\underline{CH_2}$Ph), 52.7 ($CO_2\underline{CH_3}$), 31.7 (C-4), 20.4 (C-7′) ppm; IR (KBr): $\bar{\nu} = 3369$, 2927, 2858, 1732, 1455, 1408, 1263, 1244, 1153, 1118, 1079, 1067, 1047 cm^{-1}; $[\alpha]_D^{25} = +50.4^\circ$ cm^2 g^{-1} ($c = 0.2$, $CHCl_3$).

Some relevant signals corresponding to a minor isomers **7b** and **7e** were also clearly observed in the other enriched fraction.

2-Benzyl-3-(5-hydroxy-2-methyl[1,3]dioxan-4-yl)-5-(hydroxyphenylmethyl)isoxazolidine-5-carboxylic acid methyl ester (**7b**, $C_{24}H_{29}NO_7$)

Colourless oil; $R_f = 0.28$ (*EtOAc*:hexane = 50:50); ^{1}H NMR (400 MHz): $\delta = 7.39$–7.31 (m, $10H_{Ph}$), 5.05 (s, H-1″), 4.59 (q, $J = 5.3$ Hz, H-2′), 4.27 (d, 1H, $J = 14.6$ Hz, $\underline{CH_2}$Ph), 4.10 (dd, $J = 10.8$, 5.2 Hz, H-6′e), 4.04 (d, 1H, $J = 14.6$ Hz, $\underline{CH_2}$Ph), 3.84 (s, OH) 3.79 (ddd, $J = 9.6$, 9.4, 5.3 Hz, H-5′), 3.72 (s, $CO_2\underline{CH_3}$), 3.41 (dd, $J = 9.1$, 4.4 Hz, H-4′), 3.31 (dd, $J = 10.8$, 9.9 Hz, H-6′a), 3.26 (ddd, $J = 9.9$, 6.1, 3.8 Hz, H-3), 2.81 (dd, $J = 14.0$, 6.7 Hz, H-4a, OH), 2.67 (dd, $J = 14.0$, 9.9 Hz, H-4b), 1.29 (d, 3H, $J = 5.3$ Hz, H-7′) ppm; ^{13}C NMR (100 MHz): $\delta = 172.7$ (C=O), 137.4, 135.3, 128.9, 128.5, 128.5, 128.2, 127.7, 127.2 ($12C_{Ph}$), 99.3 (C-2′), 88.3 (C-5), 78.5 (C-4′), 74.9 (C-1″), 69.8 (C-6′), 67.3 (C-3), 61.7 (C-5′), 60.6 ($\underline{CH_2}$Ph), 52.5 ($CO_2\underline{CH_3}$), 33.6 (C-4), 20.4 (C-7′) ppm; IR (film): $\bar{\nu} = 3448$, 2992, 2953, 2869, 1739, 1496, 1454, 1409, 1370, 1247, 1204, 1138, 1112, 1086, 1048 cm^{-1}; HRMS (70 eV): calcd. for (M^+) 443.1944, found 443.1935.

2-Benzyl-3-(5-hydroxy-2-methyl[1,3]dioxan-4-yl)-5-(hydroxyphenylmethyl)isoxazolidine-5-carboxylic acid methyl ester (**7e**, $C_{24}H_{29}NO_7$)

Colourless oil; $R_f = 0.43$ (*EtOAc*:hexane = 50:50); ^{1}H NMR (400 MHz): $\delta = 7.41$–7.32 (m, $10H_{Ph}$), 5.06 (s, H-1″), 4.78 (br, OH), 4.49 (q, $J = 5.0$ Hz, H-2′), 4.24 (d, 1H, $J = 12.6$ Hz, $\underline{CH_2}$Ph), 4.00 (dd, $J = 10.8$, 5.0 Hz, H-6′e), 3.87 (d, 1H, $J = 12.6$ Hz, $\underline{CH_2}$Ph), 3.62 (s, $CO_2\underline{CH_3}$), 3.35 (ddd, $J = 9.1$, 7.2, 2.3 Hz, H-3), 3.25 (dd, $J = 10.5$, 10.2 Hz, H-6′a), 3.16 (ddd, $J = 9.9$, 8.5, 5.0 Hz, H-5′), 3.06 (dd, $J = 8.8$, 8.6 Hz, H-4′), 3.02 (dd, $J = 13.6$, 2.3 Hz, H-4a), 2.96 (dd, $J = 13.4$, 7.3 Hz, H-4b), 1.71 (br, OH), 1.26 (d, 3H, $J = 5.0$ Hz, H-7′) ppm; ^{13}C NMR (100 MHz): $\delta = 172.9$ (C=O), 138.5, 135.4, 129.5, 128.8, 128.6, 128.3, 128.1, 127.4 ($12C_{Ph}$), 99.0 (C-2′), 90.9 (C-5), 78.0 (C-4′), 75.1 (C-1″), 69.9 (C-6′), 67.4 (C-3), 65.4 (C-5′), 63.1 ($\underline{CH_2}$Ph), 52.6 ($CO_2\underline{CH_3}$), 35.3 (C-4), 20.4 (C-7′) ppm; IR (KBr): $\bar{\nu} = 3435$, 3031, 2952, 2871, 1732, 1496, 1454, 1409, 1367, 1251, 1213, 1161, 1122, 1082, 1043 cm^{-1}; HRMS (70 eV): calcd. for (M^+) 443.1944, found 443.1937.

Crystallographic data for the structure **7c** has been deposited with the Cambridge Crystallographic Data Centre; reference number CCDC 222335 (**7c**). Copies of the data can be obtained on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Email: deposit@ccdc.cam.ac.uk).

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