1,3-Dipolar cycloadditions of D-erythrose- and D-threose-derived nitrones to maleimides

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To Fritz Sauter on the occasion of his 70th birthday
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Abstract
The nitrones derived from cyclic acetals of D-erythrose **1a,b** and D-threose **2a,b** react with *N*-phenylmaleimide (**3**) to afford the corresponding diastereomeric isoxazolidines. The stereoselectivity is dependent on the steric hindrance of the nitrone. In the case of D-*erythro*-derived nitrones **1a,b** the cycloaddition is *exo*-selective. The major products are in the C-3/C-4 *erythro*- and C-3/C-3a *trans*-configuration. This finding can be rationalized by a less hindered *exo*-attack of the (*Z*)-nitrone in an antiperiplanar manner with respect to the largest group of the cyclic acetal. The cycloaddition to the chiral maleimides **12** and **13** is less stereoselective.

Keywords: Cycloaddition, nitrones, microwave heating, isoxazolidines, maleimides

Introduction

The nitrone – olefin 1,3-dipolar cycloaddition is a powerful reaction in that it can create as many as three new contiguous stereogenic centers in a single step.[1] Based on an evaluation of the nitrone cycloaddition, it was felt that the configuration of these new centers could be influenced if the reaction system was properly designed.[2] Regio- and stereoselective nitrone cycloaddition, followed by reduction of the N-O bond to produce both an amino and a hydroxy functionality, allows the synthesis of many products of potential interest.[3]

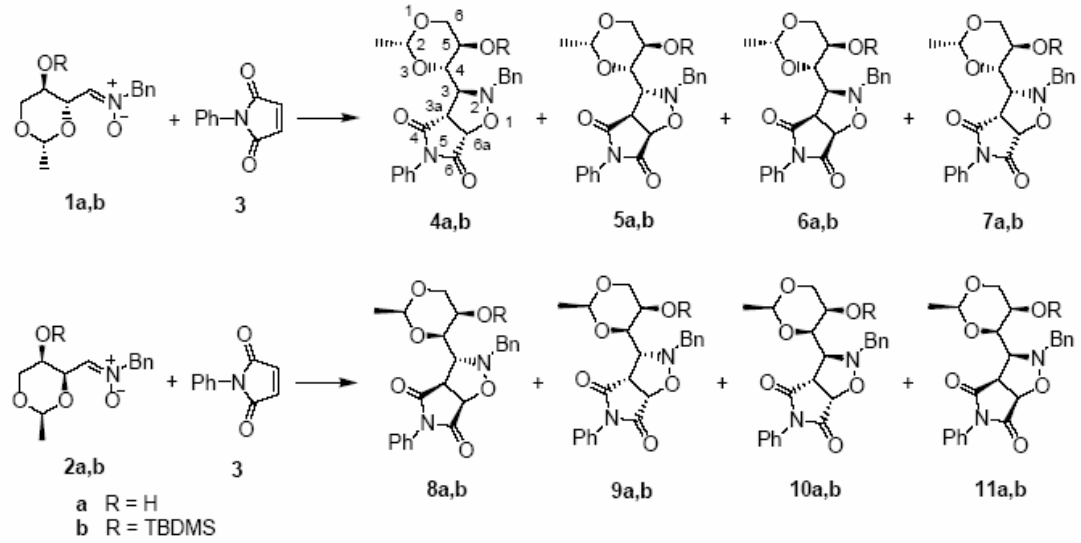
Over the years, nitrones have become important building blocks in organic synthesis [1,4] However, in spite of their well-documented utility there are only scattered reports

dealing with the preparation of nitrones with a chiral C-substituent.[5,6] With the goal of developing a simple route to polyhydroxylated derivatives of pyrrolizidines, [7] which have been shown to display antiviral activity, [8] via an asymmetric 1,3-dipolar cycloaddition we have recently published the preparation of new D-erythrose- and D-threose- derived nitrones and the stereoselectivity of their cycloadditions to styrene.[9,10]

In this paper we report the stereoselectivity of the cycloaddition of chiral sugar-derived nitrones **1a,b** and **2a,b** with *N*-phenylmaleimide (**3**) and the chiral maleimides **12** and **13**.

Results and Discussion

The diastereomerically pure (*Z*)-nitrones **1a,b** and **2a,b** were subjected to 1,3-dipolar cycloaddition reactions. Our task was to study the asymmetric induction from the nitrone part. There are four possible products; *cis*- and *trans*-isomers from *anti*- and *syn*-attack (Scheme 1). With each of the nitrones the reaction proceeded smoothly in high yields.



Scheme 1

The structure assignments of the products are based on straightforward analysis of NMR spectra. The stereochemistry of the cycloadducts was deduced by their NOE experiments. The most important and decisive information obtained from these experiments is the presence or absence of the NOE interaction between the protons 3-H/3a-H and 6a-H/3-H in the corresponding *exo*- and *endo*-cycloadducts, respectively. Finally, the relative 3-C/4-C *erythro*-configuration in the isolated adducts was assigned by comparison with the analogue prepared by the cycloaddition from nitrone **1a** with styrene, the structure of which was elucidated by X-ray analysis.[10] The ratio of diastereoisomers was determined from ^{13}C NMR spectra by integration of the peaks of the 3a-C signals of the isoxazolidine products.

The cycloadditions were first carried out in boiling toluene with *N*-phenylmaleimide (**3**). In the case of D-*erythro*-derived nitrones **1a,b** only two diastereoisomers, *erythro-trans* **4a,b** and *threo-trans* **5a,b** were formed (entries 1 and 2, Table 1). 3,3a-*cis*-Disubstituted *endo*-adducts **6** and **7** were not detected in the crude reaction mixture by NMR spectra (Scheme 1). The cycloadducts **4a,b** and **5a** were separated by column chromatography.

Table 1. 1,3-Dipolar cycloaddition of C-α-alkoxyalkyl-substituted nitrones to maleimides

Entry	Imide	Nitrone	Yield (%)	*erythro-trans*	*erythro-cis*	*threo-trans*	*threo-cis*	*erythro: threo*	*trans: cis*
1	**3**	1a	90	50	–	50	–	50:50	>95:5
2	**3**	1b	74	63	–	37	–	63:37	>95:5
3	**3**	1b[a]	66	39	6	55	–	45:55	94:6
4	**3**	2a	95	73	15	8	4	88:12	81:19
5	**3**	2b	89	46	28	26	–	74:26	72:28
6	**3**	2b[a]	90	46	32	17	5	78:22	63:37
7	**12**	1a	70	43	18	25	14	61:39	68:32
8	**13**	1a	69	51	7	42	–	58:42	93:7
9	**13**	1b	80	64	–	36	–	64:36	>95:5
10	**12**	2a	64	50	20	17	13	70:30	67:33

[a] Microwave.

The analysis of product configuration indicates that **4a,b** and **5a,b** arise from a cycloaddition which has occurred on the more sterically accessible face of the nitrone, via an *exo*-transition state with syn periplanar relationship of the *N*-phenyl and *N*-benzyl group. Dipolar cycloaddition of *C*-α-alkoxy-substituted nitrones have been shown to occur preferentially via transition states in which the developing carbon-carbon bond avoids steric interaction with the more bulky group.[2,10,11] We consider that both isoxazolidines **4** and **5** result from a 100% *exo*-attack of the dipolarophile maleimide (**3**) on the (*Z)*-nitrone **1a,b**, because the corresponding (*E*)-nitrones were not detected by ^{1}H NMR. There was no thermal interconversion between the prepared adducts in refluxing toluene, thus indicating that the cycloaddition proceeded irreversibly under the reaction conditions to give the kinetically controlled products **4** and **5**, respectively. Such total *exo* selectivity may be ascribed to the steric interaction in the transition state between the phenyl group of maleimide (**3**) and the heterocyclic moiety of the nitrone **1a,b** in corresponding *endo*-transition state that would lead to the cycloadducts **6a,b** and **7a,b**.

The reaction of D-*threo*-derived nitrone **2a** with **3** furnished the corresponding cycloadducts **8a**, **9a**, **10a** and **11a** in a ratio of 73:15:8:4 (Entry 4, Table 1). The minor product **10a** was isolated as a pure compound. On the other hand, from the reaction of protected D-*threo*-derived nitrone **2b** with **3** all three cycloadducts **8b**, **9b** and **10b** were isolated in a pure state 46:28:26 (Entry 5, Table 1).

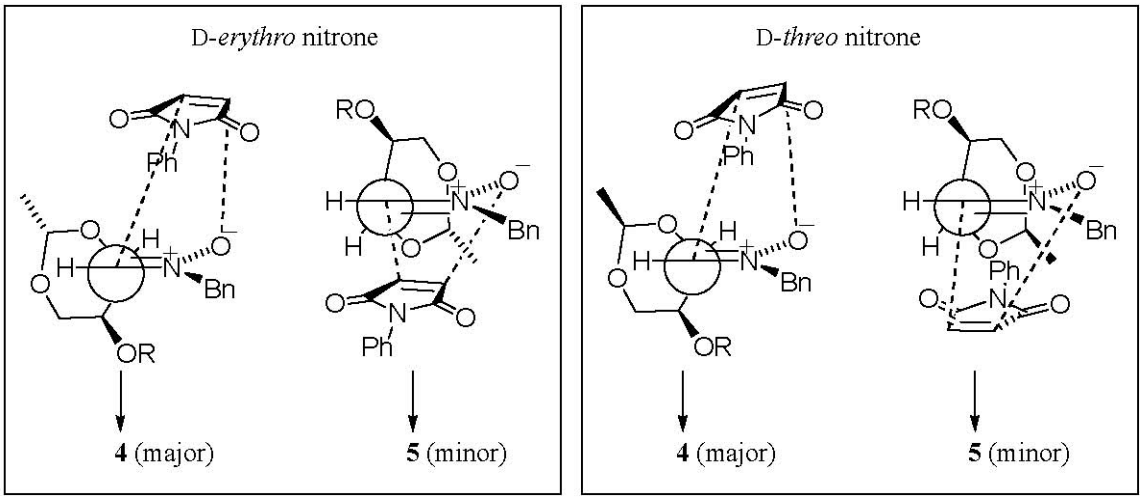
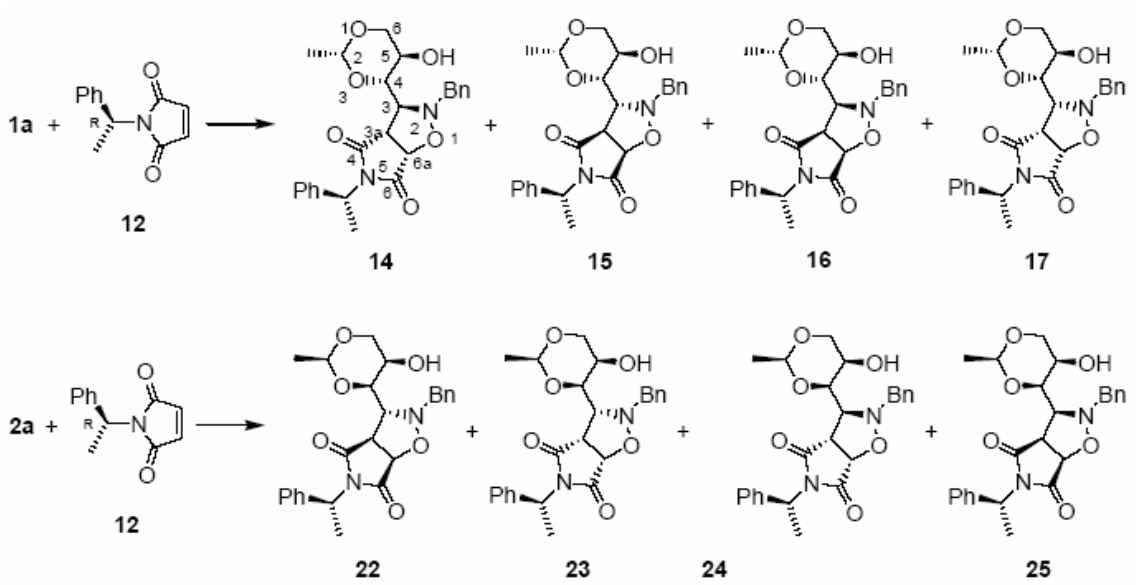


Figure 1

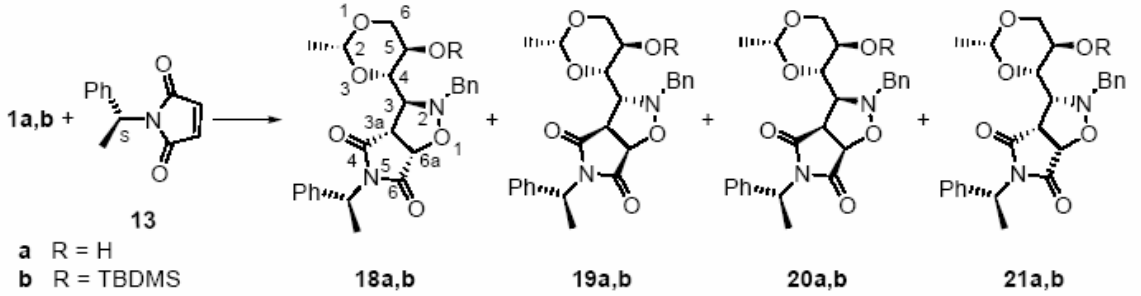
The diastereofacial selectivities of the above-mentioned cycloadditions are highly dependent on the structures of nitrone and maleimide. While the reactions employing D-*erythro*-derived nitrones **1a,b** (Entries 1–3, Table 1) gave poor *anti*-selectivities, the reactions using D-*threo*-derived nitrones **2a,b** gave good stereoselectivities (entries 4-6, Table 1). The lowest *erythro*:*threo* ratio of 50:50 has been observed in the case of D-*erythro*-derived nitrone **1a** (Entry 1, Table 1). These differences in *anti/syn*-selectivity can be rationalized by considering the transition states in the cycloaddition (Figure 1). Since the cycloadditions proceed from (*Z*)-nitrone preferentially via the less hindered *exo*-transition state and in an antiperiplanar manner with respect to the largest group of the heterocyclic acetal, the methyl substituent in the nitrone is oriented in the *syn/anti*-position relative to the maleimide **3**. Accordingly, the use of D-*threo*-derived nitrones **2a** and **2b** having the methyl group in the axial position gave better selectivities. The diastereofacial selectivities observed are comparable to the previously published results obtained by the cycloadditions of these nitrones with styrene[10] as well as to results reported for a cyclic nitrone with *N*-benzylmaleimide.[12]

Next, the nitrones **1a,b** and **2a** were treated with chiral maleimides **12** and **13** (Schemes 2 and 3). The *exo*-product, *erythro-trans* **14**, **18**, and **22** was isolated as the major isomer in each case. The diastereofacial selectivities of the cycloaddition to chiral maleimides **12** and **13** are only moderate (Entries 7-10, Table 1). Although the chiral maleimides **12** and **13** are enantiomers, the product ratios of formed isoxazolidines resulting from the cycloaddition of the D-*erythro*-derived nitrone **1a** are not similar. The stereogenic centre in chiral maleimides has an influence on the *trans*:*cis* ratio of the isomers formed (68:32 and 93:7, Entries 7 and 8, Table 1). On the other hand, in the reaction of the protected D-*erythro* derived nitrone **1b** with the chiral maleimide **13** only two *exo*-diastereoisomers, *erythro-trans* **18b** and *threo-trans* **19b** were formed (Entry 9, Table 1).



Scheme 2

It is noteworthy that our attempts to accelerate the cycloaddition by microwave irradiation were successful. Indeed, microwave irradiation dramatically decreased the reaction times of the cycloadditions. For example, in the case of the cycloaddition of nitrone **1b** with dipolarophile **3**, the reaction time decreased from 11 h to 8 min. Moreover, microwave irradiation could even reverse the ratio of *erythro-trans* / *erythro-cis* adducts from 63:37 to 39:55 for **1b** (Entries 2 and 3, Table 1). To the best of our knowledge this reversal of stereoselectivity of the nitrone cycloaddition using microwave irradiation is a very rare phenomenon. On the other hand, in the case of the cycloaddition of nitrone **2b** to imide **3** microwave irradiation only slightly changed the ratio of diastereomers (Entry 6, Table 1) while the reaction time decreased from 3 h to 10 min.



Scheme 3

Experimental Section

General Procedures. All starting materials and reagents are commercially available (Fluka, Merck or Avocado) and were used without further purification. Solvents were dried before use.

Thin-layer chromatography (TLC, on aluminium plates coated with silica $60F_{254}$, 0.25 mm thickness, Merck) was used for monitoring of reaction courses; 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. Elemental analyses were performed by the microanalysis service of the Department of Analytical Chemistry, Slovak University of Technology, Bratislava.

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 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 solvent.

The nitrones **1a,b** and **2a,b** were prepared from the corresponding aldehydes by the reaction with *N*-benzylhydroxylamine[13] in dichloromethane in the presence of anhydrous magnesium sulfate according to the procedure used in the literature for the preparation of chiral *N*-benzyl nitrones.[13] Previously described methods were used to prepare the corresponding aldehydes[15-18] and maleimides.[19]

(3*S*,3a*R*,6a*S*)-2-benzyl-3-[(2*S*,4*R*,5*R*)-5-hydroxy-2-methyl-1,3-dioxan-4-yl]-5-phenylperhydropyrrolo[3,4-*d*]isoxazole-4,6-dione (4a) and (3*R*,3aR,6a*R*)-2-benzyl-3-[(2*R*,4*S*,5*R*)-5-hydroxy-2-methyl-1,3-dioxan-4-yl)]-5-phenylperhydropyrrolo[3,4-*d*]-isoxazole-4,6-dione (5a). To a stirred solution of the nitrone **1a** (378 mg, 1.5 mmol) in toluene (10 mL) was added *N*-phenylmaleimide (**3**) (300 mg, 1.73 mmol), and the solution was heated at reflux for 10 h. The resulting mixture was evaporated under reduced pressure. The crude mixture of two diastereoisomers **4a** and **5a** (ratio 50:50 by ^{13}C NMR) was purified and separated by column chromatography on silica gel (2.5 x 32 cm) eluting with EtOAc/isohexane (33:67) to give **4a** as a first fraction (303.4 mg, 45%) and **5a** as the second fraction (303.6 mg, 45%); combined yield 607 mg (90%).

4a. Colourless crystals, R_f = 0.25 (EtOAc/isohexane 33:67); mp 185–186 °C; [α]= +50.7 (c 1.2, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$/TMS): δ 7.54–7.23 (m, 10H, H_{Ph}), 5.10 (d, 1H, *J* = 8.0 Hz, H-6a), 4.66 (q, 1H, *J* = 5.0 Hz, 2-H), 4.33 (d, 1H, *J* = 12.0 Hz, C*H*$_A$H$_B$Ph), 4.29 (br s, 1H, OH), 4.22 (dd, 1H, *J* = 1.5, 8.0 Hz, 3a-H), 4.08 (dd, 1H, *J* = 4.0, 10.1 Hz, 6$_A$-H), 4.01 (dd, 1H, *J* = 1.5, 8.3 Hz, 3-H), 3.81 (d, 1H, *J* = 12.0 Hz, CH$_A$*H*$_B$Ph), 3.39–3.25 (m, 3H, 4-H, 5-H, 6$_B$-H), 1.36 (d, 3H, *J* = 5.0 Hz, CH_3). ^{13}C NMR (100.6 MHz, $CDCl_3$/TMS): δ 175.3, 173.5 (2 C=O), 134.3, 131.7 (2C, 1-C$_{Ph}$), 129.9, 129.6, 129.5, 129.3, 129.2, 126.1, (10C, 2-6C$_{Ph}$), 99.7 (2-C), 78.6 (6a-C), 77.9 (4-C), 70.6 (3-C), 70.2 (6-C), 65.9 (4-C), 63.6 (CH_2Ph), 51.8 (3a-C), 20.9 (2-CH_3). Anal. calcd. for $C_{23}H_{24}N_2O_6$ (424.45): C, 65.08, H, 5.70, N, 6.60. Found: C, 64.81, H, 5.73, N, 6.52.

5a. Colourless crystals, R_f = 0.18 (EtOAc/isohexane 33:67); mp 193–194 °C; [α]= –33.6 (c 1.1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$/TMS): δ 7.55–7.26 (m, 10 H, H_{Ph}), 4.98 (d, 1H, *J* = 7.7 Hz, 6a-H), 4.65 (q, 1H, *J* = 5.0 Hz, 2-H), 4.28 (d, 1H, *J* = 12.6 Hz, C*H*$_A$H$_B$Ph), 4.14 (dd, 1H, *J* = 3.2, 7.7 Hz, 3a-H), 4.08 (dd, 1H, *J* = 5.4, 10.0 Hz, 6$_A$-H), 4.04 (d, 1H, *J* = 12.6 Hz, CH$_A$*H*$_B$Ph), 3.88

(dd, 1H, *J* = 3.2, 5.5 Hz, 3-H), 3.69 (m, 1H, 5-H), 3.60 (dd, 1H, *J* = 5.5, 9.0 Hz, 4-H), 2.77 (br, 1H, OH), 1.33 (d, 3H, *J* = 5.0 Hz, CH_3). ^{13}C NMR (100.6 MHz, $CDCl_3$/TMS): δ 176.5, 172.6 (2 C=O), 135.9, 130.1 (2C, 1-C_{Ph}), 130.1, 129.6, 129.3, 129.2, 128.7, 126.4, (10C, 2-6C_{Ph}), 99.4 (2-C), 82.0 (3-C), 78.5 (6a-C), 70.2 (6-C), 67.8 (3-C), 63.8 (*C*H_2Ph), 63.2 (4-C), 52.2 (3a-C), 20.8 (2-CH_3). Anal. calcd. for $C_{23}H_{24}N_2O_6$, (424.45): C, 65.08, H, 5.70, N, 6.60. Found: C, 64.90, H, 5.60, N, 6.69.

(3*S*,3a*R*,6a*S*)-2-Benzyl-3-[(2*S*,4*R*,5*R*)-5-[1-(*tert*-butyl)-1,1-dimethylsilyl]oxy-2-methyl-1,3-dioxan-4-yl]-5-phenylperhydropyrrolo[3,4-*d*]isoxazole-4,6-dione (4b). To a stirred solution of the nitrone **1b** (50 mg, 0.14 mmol) in toluene (2.5 mL) was added *N*-phenylmaleimide (**3**) (30 mg, 0.16 mmol), and the reaction was heated at reflux for 11 h. The resulting mixture was evaporated under reduced pressure. The crude mixture of two diastereoisomers **4b** and **5b** (73 mg, 99%; ratio 63:37; ^{13}C NMR) was purified by column chromatography on silica gel (1.0 x 23 cm) eluting with EtOAc/isohexane (40:60) to give pure **4b** and an unseparable mixture of diastereoisomers **4b** and **5b**.

4b. Colourless crystals, R_f = 0.64 (EtOAc/isohexane 50:50), R_f = 0,40 (EtOAc/isohexane 30:70); mp 119–120 °C. ^{1}H NMR (300MHz, $CDCl_3$/TMS): δ 7.56–7.26 (m, 10H, H_{Ph}), 4.99 (d, 1H, *J* = 7.6 Hz, 6a-H), 4.77 (q, 1H, *J* = 5.0 Hz, 2-H), 4.28 (d, 1H, *J* = 13.2 Hz, C*H*$_A$H$_B$Ph), 4.15 (dd, 1H, *J* = 7.6, 2.6 Hz, 3a-H), 4.07 (dd, 1H, *J* = 10.8, 9.6 Hz, 6$_A$-H), 3.99 (dd, 1H, *J* = 2.6, 2.6 Hz, 3-H), 3.98 (d, 1H, *J* = 13.2 Hz, CH$_A$*H*$_B$Ph), 3,69–3.65 (m, 2H, 4-H, 5-H), 3.38 (dd, 1H, *J* = 10.8 Hz, 6$_B$-H), 1.34 (d, 3H, *J* = 5.0 Hz, CH_3), 0.77 [s, 9H, C(CH_3)$_3$], 0.08, 0.07 [2s, 3H, 3H, Si(CH_3)$_2$]. ^{13}C NMR (75 MHz, $CDCl_3$/TMS): δ 175.6, 173.2 (2 C=O), 135.5. 131.5 (2C, 1-C_{Ph}), 129.4, 129.0, 128.9, 128.6, 127.9, 126.0 (10C, 2-6-C_{Ph}), 98.5 (2-C), 82.9 (4-C), 78.4 (6a-C), 71.9 (6-C), 66.5 (3-C), 63.5 (*C*H Ph), 62.9 (5-C), 50.3 (3a-C), 25.6 [C(*C*H_3)$_3$], 20.4 (2-CH_3), 17.7 [*C*(CH_3)$_3$], –4.3 and –4.9 [2C, Si(CH_3)$_2$].

Microwave irradiation. To a stirred solution of the nitrone **1b** (300 mg, 0.82 mmol) in toluene (15 mL) was added *N*-phenylmaleimide (**3**) (170 mg, 0.92 mmol) and the reaction was carried out under microwave irradiation (1000 W) in toluene for 7.5 min. The resulting mixture was evaporated under reduced pressure. The crude mixture of three diastereoisomers **4b**, **5b** and **6b** ratio (39:6:55; ^{13}C NMR) was purified by column chromatography on silica gel (2.0 x 28 cm) eluting with EtOAc/iso-hexane (40:60) to give a mixture of three diastereoisomers (290 mg, 66%).

(3*R*,3a*S*,6a*R*)-2-benzyl-3-[(2*R*,4*S*,5*R*)-5-hydroxy-2-methyl-1,3-dioxan-4-yl]-5-phenylperhydropyrrolo[3,4-*d*]isoxazole-4,6-dione (8a) and (3*S*,3a*R*,6a*S*)-2-benzyl-3-[(2*R*,4*S*,5*R*)-5-hydroxy-2-methyl-1,3-dioxan-4-yl]-5-phenylperhydropyrrolo[3,4-*d*]-isoxazole-4,6-dione (10a). To a stirred solution of the nitrone **2a** (500 mg, 2.0 mmol) in toluene (10 mL) was added *N*-phenylmaleimide (**3**) (517 mg, 3.0 mmol) and the reaction was heated at reflux for 4 h. The resulting mixture was evaporated under reduced pressure. The crude mixture of four diastereoisomers **8a**, **9a**, **10a** and **11a** (ratio 73:15:8:≤4; ^{13}C NMR) was purified and separated by column chromatography on silica gel (2.5 x 32 cm) eluting with EtOAc/isohexane (54:46) to give product **10a** as a first fraction (60 mg, 7%) and a mixture of diastereomers **8a**, **9a**

and **11a** (680 mg, 81%); combined yield 740 mg (89%).

10a. colourless solid, mp = 103–105 °C. ^{1}H NMR (400 MHz, $CDCl_3$/TMS): δ 7.57-7.19 (m, 10H, H_{Ph}), 5.06 (d, 1H, *J* = 8.0 Hz, 6a-H), 4.76 (m, 2H, 5-H, 2-H), 4.33 (d, 1H, *J* = 8.0 Hz, 3a-H), 4.29 (d, 1H, *J* = 12.0 Hz, C*H*$_A$H$_B$Ph), 4.22-4.19 (m, 2H, 3-H, 6$_A$-H), 3.79 (d, 1H, *J* = 12.9 Hz, H-6$_B$-H), 3.71 (d, 1H, *J* = 12.0 Hz, CH$_A$*H*$_B$Ph), 3.60 (d, 1H, *J* = 9.6 Hz, 4-H), 1.41 (d, 3H, *J* = 5.0 Hz, CH_3). ^{13}C NMR (100.6 MHz, $CDCl_3$/TMS): δ 175.4, 174.1 (2 C=O), 134.9, 131.8 (2C, 1-C$_{Ph}$), 129.9, 129.6, 129.5, 129.4, 128.7, 126.1, (10C, 2-6C$_{Ph}$), 100.1 (2-C), 78.8 (6a-C), 75.8 (4-C), 68.6 (6-C), 66.0 (3-C), 65.1 (5-C), 63.6 (*C*H_2Ph), 50.9 (3a-C), 21.1 (2-CH_3).

8a. ^{1}H NMR (400 MHz, $CDCl_3$/TMS): δ 7.57–7.28 (m, 10H, H_{Ph}), 5.01 (d, 1H, *J* = 7.6 Hz, 6a-H), 4.75 (q, 1H, *J* = 5.0 Hz, 2-H), 4.25 (m, 2H, 3-H, 3a-H), 4.29 (d, 1H, *J* = 12.6 Hz, C*H*$_A$H$_B$Ph), 4.07 (dd, 1H, *J* = 12.0, 2.0 Hz, 6$_A$-H), 3.90 (d, 1H, *J* = 12.5 Hz, CH$_A$*H*$_B$Ph), 3.79 (d, 1H, *J* = 12.0, 1.3 Hz, 6$_B$-H), 3.69 (br s, 1H, 5-H), 3.49 (dd, *J* = 1.1, 9.3 Hz, 4-H), 1.41 (d, 3H, *J* = 5.0 Hz, CH_3). ^{13}C NMR (100.6 MHz, $CDCl_3$/TMS): δ 175.5, 173.7 (2 C=O), 135.4, 131.8 (2C, 1-C$_{Ph}$), 129.5, 129.4, 129.0, 128.6, 128.1, 126.3, 125.7 (10C, 2-6C$_{Ph}$), 99.9 (2-C), 78.2 (6a-C), 77.3 (4-C), 71.7 (6-C), 67.2 (3-C), 63.3 (*C*H_2Ph), 62.8 (5-C), 50.3 (3a-C), 20.8 (2-CH_3).

(3*R*,3a*S*,6a*R*)-2-Benzyl-3-[(2*R*,4S,5*R*)-5-[1-(*tert*-butyl)-1,1-dimethylsilyl]oxy-2-methyl-1,3-dioxan-4-yl]-5-phenylperhydropyrrolo[3,4-*d*]isoxazole-4,6-dione (8b) and (3*R*,3a*R*,6a*S*)-2-Benzyl-3-[(2*R*,4S,5*R*)-5-[1-(*tert*-butyl)-1,1-dimethylsilyl]oxy-2-methyl-1,3-dioxan-4-yl]-5-phenylperhydropyrrolo[3,4-*d*]isoxazole-4,6-dione (9b) and (3*S*,3a*R*,6a*S*)-2-Benzyl-3-[(2*R*,4S,5*R*)-5-[1-(*tert*-butyl)-1,1-dimethylsilyl]oxy-2-methyl-1,3-dioxan-4-yl]-5-phenylperhydropyrrolo[3,4-*d*]isoxazole-4,6-dione (10b). To a stirred solution of the nitrone **2b** (539 mg, 1.5 mmol) in toluene (25 mL) was added *N*-phenylmaleimide (**3**) (255 mg, 1.5 mmol), and the reaction was heated at reflux for 3 h. The resulting mixture was evaporated under reduced pressure. The crude mixture of three diastereoisomers (ratio 46:28:26 by ^{13}C NMR) was purified by column chromatography on silica (3.0 x 24 cm) eluting with EtOAc/isohexane (90:10 → 50:50) to give as first fraction the minor diastereoisomer **9b** (109 mg, 14%), as second fraction the major product **8b** (279 mg, 35%), and as the third fraction the minor product **10b** (203 mg, 26%); combined yield 591 mg (75%).

Major product **8b**. Colourless oil, R_f = 0.42 (EtOAc/isohexane 60:40); [α]= +22.4 (c = 0.3, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$/TMS): δ 7.54–7.25 (m, 10H, H_{Ph}), 4.92 (d, 1H, *J* = 8.0 Hz, 6a-H), 4.74 (q, 1H, *J* = 5.0 Hz, 2-H), 4.38 (dd, 1H, *J* = 8.0, 0.8 Hz, 3a-H), 4.26 (dd, 1H, *J* = 8.3, 0.8 Hz, 3-H), 4.10–3.99 (m, 2H, *J* = 13.9, 12.5, 0.6 Hz, 6$_A$-H, C*H*$_A$H$_B$Ph), 3.88 (d, 1H, *J* = 13.9 Hz, CH$_A$*H*$_B$Ph), 3.85 (br, 1H, *J* = 1.5, 1.5, 0.6 Hz, 5-H), 3.73 (dd, 1H, *J* = 12.5, 1.5 Hz, 6$_B$H), 3.50 (dd, 1H, *J* = 8.3, 1.5 Hz, 4-H), 1.38 (d, 3H, *J* = 5.0 Hz, CH_3), 0.93 [s, 9H, C(CH$_3$)$_3$], 0.15, 0.09 [2s, 3H, 3H, Si(CH$_3$)$_2$]. ^{13}C NMR (75 MHz, $CDCl_3$/TMS): δ 175.7, 173.9 (2 C=O), 136.1, 131.5 (2C, 1-C$_{Ph}$), 129.4, 128.8, 128.5, 127.8, 125.9, 125.7 (10C, 2-6C$_{Ph}$), 99.2 (2-C), 78.0 (6a-C), 77.9 (4-C), 71.1 (6-C), 68.4 (3-C), 64.4 (5-C), 62.9 (*C*H_2Ph), 50.6 (3a-C), 25.9 [C(*C*H$_3$)$_3$], 20.9 (2-CH_3), 18.2 [*C*(CH$_3$)$_3$], -4.0, -4.2 [2C, Si(*C*H$_3$)$_2$].

9b. Colourless oil, R_f = 0.51 (EtOAc/isohexane 60:40); [α]= –45.4 (c = 0.3, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$/TMS): δ 7.53–7.24 (m, 10H, H_{Ph}), 4.85 (d, 1H, *J* = 7.5 Hz, 6a-H), 4.72 (d, 1H,

J = 15.4 Hz, C*H*$_A$H$_B$Ph), 4.71 (q, 1H, *J* = 5.1 Hz, 2-H), 4.45 (br, 1H, *J* = 1.6, 1.6 Hz, 5-H), 4.05 (d, 1H, *J* = 15.4 Hz, CH$_A$*H*$_B$Ph), 4.02, 3.82 (2 x dd, 1H, 1H, *J* = 12.6, 1.6 Hz, 6$_A$-H, 6$_B$-H), 3.94 (dd, 1H, *J* = 9.6, 1.6 Hz, H-4), 3.64 (dd, 1H, *J* = 7.2, 7.5 Hz, H-3a), 3.51 (dd, 1H, *J* = 7.2, 9.6 Hz, 3-H), 1.34 (d, 3H, *J* = 5.1 Hz, CH$_3$), 0.95 [s, 9H, C(C*H*$_3$)$_3$], 0.19, 0.12 [2s, 3H, 3H, Si(C*H*$_3$)$_2$]. ^{13}C NMR (75 MHz, CDCl$_3$/TMS): δ 173.5, 173.4 (2 C=O), 136.3, 131.3 (2C, 1-C$_{Ph}$), 129.2, 129.1, 129.0, 128.0, 126.9, 126.3 (10C, 2-6C$_{Ph}$), 98.6 (2-C), 78.1 (4-C), 74.7 (6a-C), 71.0 (6-C), 66.3 (3-C), 64.6 (5-C), 60.3 (*C*H$_2$Ph), 49.4 (3a-C), 25.9 [C(*C*H$_3$)$_3$], 20.9 (2-CH$_3$), 18.3 [Si*C*(CH$_3$)$_3$], –3.7 and –4.3 [2C, Si(*C*H$_3$)$_2$].

10b. Colourless oil, R$_f$ = 0.22 (EtOAc/isohexane 60:40); [α]= –21.2 (c = 0.3, CHCl$_3$). ^{1}H NMR (300 MHz, CDCl$_3$/TMS): δ 7.51–7.25 (m, 10H, H$_{Ph}$), 4.85 (d, 1H, *J* = 7.6 Hz, 6a-H), 4.80 (q, 1H, *J* = 5.0 Hz, 2-H), 4.24, 4.15 (2d, 1H, 1H, *J* = 14.1 Hz, C*H*$_A$H$_B$Ph), 4.12 (dd, 1H, *J* = 12.5, 1.7 Hz, 6$_A$-H), 3.94 (dd, 1H, *J* = 8.7, 3.0 Hz, 3-H), 3.82–3.75 (m, 2H, 4-H, 5-H), 3.77 (dd, 1H, *J* = 12.5, 1.4 Hz, 6$_B$-H), 3.67 (dd, 1H, *J* = 7.6, 3.0 Hz, 3a-H), 1.38 (d, 3H, *J* = 5.0 Hz, CH$_3$), 0.93 [s, 9H, C(CH$_3$)$_3$], 0.15, 0.13 [2s, 3H, 3H, Si(CH$_3$)$_2$]. ^{13}C NMR (75 MHz,): δ 173.89, 172.68 (2 C=O), 136.5, 131.4 (2C, 1-C$_{Ph}$), 129.3, 128.9, 128.3, 127.4, 126.2, (10C, 2-6C$_{Ph}$), 98.9 (2-C), 78.3 (4-C), 76.4 (6a-C), 71.2 (6-C), 67.2 (3-C), 64.8 (5-C), 60.4 (*C*H$_2$Ph), 51.1 (3a-C), 25.9 [C(*C*H$_3$)$_3$], 20.9 (2-CH$_3$), 18.4 [*C*(CH$_3$)$_3$], –3.8 and –4.1 [2C, Si(CH$_3$)$_2$].

Microwave irradiation. To a stirred solution of the nitrone **2b** (100 mg, 0.27 mmol) in toluene (5 mL) was added *N*-phenylmaleimide (**3**) (47 mg, 0.27 mmol) and the reaction was carried out under microwave irradiation (1000 W) in toluene for 10 min as before. The resulting mixture was evaporated under reduced pressure. The crude mixture of three diastereoisomers **8b**, **9b**, **10b** and **11b** (ratio 46:5:32:17 by ^{13}C NMR) was purified by column chromatography on silica gel (2.0 x 16 cm) eluting with EtOAc/isohexane (30:70) to give a mixture of three diastereoisomers (133 mg, 90%).

(3*R*,3a*S*,6a*R*)-2-benzyl-3-[(2*S*,4*R*,5*R*)-5-hydroxy-2-methyl-1,3-dioxan-4-yl]-5-[(*1R*)-*1*-phenylethyl)]perhydropyrrolo[3,4-*d*]isoxazole-4,6-dione (15) and (3*S*,3a*R*, 6a*S*)-2-benzyl-3-[(2*S*,4*R*,5*R*)-5-hydroxy-2-methyl-1,3-dioxan-4-yl]-5-[(*1R*)-*1*-phenyl-ethyl)]-perhydropyrrolo[3,4-*d*]isoxazole-4,6-dione (14). To a stirred solution of the nitrone **1a** (250 mg, 1.0 mmol) in toluene (10 mL) was added *N*-(1-phenylethyl)maleimide (**12**) (200 mg, 1.0 mmol), and the reaction was heated at reflux for 10 h. The resulting mixture was evaporated under reduced pressure. The crude mixture of four diastereoisomers (ratio 43:18:25:14 by ^{13}C NMR) was purified by column chromatography on silica gel (2.0 x 20 cm) eluting with EtOAc/petroleum ether (40:60) to give mixture of all diastereoisomers (315 mg, 70%). The mixture of diastereoisomers was separated by column chromatography on silica gel (2.0 x 35 cm, EtOAc/petroleum ether 25:75) affording only the major product **14** and one minor product **15**.

14. Colorless solid, R$_f$ = 0.53 (EtOAc/petroleum ether 50:50); mp = 57–59 °C. ^{1}H NMR (400 MHz, CDCl$_3$/TMS): δ 7.56-7.53 (m, 2H, H$_{Ph}$), 7.38–7.28 (m, 6H, H$_{Ph}$), 7.00-6.96 (m, 2H, H$_{Ph}$), 5.48 (q, 1H, *J* = 7.3 Hz, CH$_3$C*H*Ph), 4.82 (d, 1H, *J* = 7.8 Hz, 6a-H), 4.59 (q, 1H, *J* = 5.0 Hz, 2-H), 4.59 (dd, 1H, *J* = 5.4, 10.8 Hz, 6$_A$-H), 4.00 (d, 1H, *J* = 12.3 Hz, C*H*$_A$H$_B$Ph), 3.90 (dd, 1H, *J* = 2.7, 7.9 Hz, 3a-H), 3.64 (dd, 1H, *J* = 2.6, 5.0 Hz, 3-H), 3.58 (m, 1H, 5-H), 3.40 (dd, 1H, *J* = 5.3,

9.1 Hz, 4-H), 3.35 (d, 1H, *J* = 12.3 Hz, CH$_A$*H*$_B$Ph), 3.34 (dd, 1H, *J* = 10.8, 10.5 Hz, 6$_B$-H), 2.64 (br s, 1H, OH), 1.90 (d, 3H, *J* = 7.3 Hz, C*H*$_3$CHPh), 1.31 (d, 3H, *J* = 5.0 Hz, CH$_3$). ^{13}C NMR (100.6 MHz, $CDCl_3$/TMS): δ 176.9, 173.9 (2 C=O), 138.1, 135.7 (2C, 1-C$_{Ph}$), 129.9, 129.7, 129.3, 129.1, 129.0, 128.9, 128.8, 128.5, 128.5 (10C, 2-6C$_{Ph}$), 99.4 (2-C), 81.6 (4-C), 78.7 (6a-C), 70.1 (6-C), 67.2 (3-C), 63.2 (*C*H$_2$Ph), 62.9 (5-C), 51.5 (2C, 5-CH$_3$*C*HPh, 3a-C), 20,9 (2-CH$_3$), 16.3 (5-*C*H$_3$CHPh).

15. Colorless solid, R$_f$ = 0.53 (EtOAc/petroleum ether 50:50); mp = 75–78 °C. ^{1}H NMR (400 MHz, $CDCl_3$/TMS): δ 7.67–7.58 (m, 2H, H$_{Ph}$), 7.27–7.16 (m, 6H, H$_{Ph}$), 6.85–6.83 (m, 2H, H$_{Ph}$), 5.41 (q, 1H, *J* = 7.3 Hz, CH$_3$C*H*Ph), 4.79 (d, 1H, *J* = 7.9 Hz, 6a-H), 4.52 (q, 1H, *J* = 5.0 Hz, 2-H), 4.39 (br s, 1H, OH), 4.95 (dd, 1H, *J* = 4.7, 10.8 Hz, 6$_A$-H), 3.86 (dd, 1H, *J* = 1.2, 8.2 Hz, 3a-H), 3.68 (d, 1H, *J* = 11.9 Hz, C*H*$_A$H$_B$Ph), 3.68 (m, 1H, 3-H), 3.29 (dd, 1H, *J* = 10.8, 9.6 Hz, 6$_B$- H), 3.20-3.11 (m, 2H, 4-H, 5-H), 3.17 (d, 1H, *J* = 11.9 Hz, CH$_A$*H*$_B$Ph), 1.90 (d, 3H, *J* = 7.3 Hz, C*H*$_3$CHPh), 1.20 (d, 3H, *J* = 5.0 Hz, CH$_3$). ^{13}C NMR (100.6 MHz, $CDCl_3$/TMS), δ 175.7, 174.5 (2 C=O), 138.0, 134.3 (2C, 1-C$_{Ph}$), 129.8, 129.3, 129.1, 129.0, 128.8, 128.5, 127.9, 126.8, 126.3, 126.2 (10C, 2-6C$_{Ph}$), 99.6 (2-C), 78.4 (4-C), 78.0 (6a-C), 70.4 (3-C), 70.0 (6-C), 65.8 (5-C), 63.2 (*C*H$_2$Ph), 52.2 (5-CH$_3$*C*HPh), 51.6 (3a-C), 20.9 (2-CH$_3$), 16.3 (5-*C*H$_3$CHPh).

(3*R*,3a*S*,6a*R*)-2-benzyl-3-[(2*S*,4*R*,5*R*)-5-hydroxy-2-methyl-1,3-dioxan-4-yl]-5-[(1*S*)-*1*-phenylethyl)]perhydropyrrolo[3,4-*d*]isoxazole-4,6-dione (19a) and (3*S*,3a*R*, 6a*S*)-2-benzyl-3-[(2*S*,4*R*,5*R*)-5-hydroxy-2-methyl-1,3-dioxan-4-yl]-5-[(1*S*)-*1*-phenylethyl)]perhydropyrrolo[3,4-*d*]isoxazole-4,6-dione (18a). To a stirred solution of the nitrone **1a** (312, 1.24 mmol) in toluene (15 mL) was added *N*-(1-phenylethyl)maleimide (**13**) (250 mg, 1.24 mmol), and the reaction was heated at reflux for 10 h. The resulting mixture was evaporated under reduced pressure. The crude mixture of three diastereoisomers (ratio 51:7:42 by ^{13}C NMR) was purified and separated by column chromatography on silica gel (2.0 x 35 cm) eluting with EtOAc/petroleum ether (25:75) to give as first mixture of all diastereoisomers (111 mg, 20%) and cycloadducts **18a** and **19a** (279 mg, 49%) as second fraction.

19a. R$_f$ = 0.52 (EtOAc/petroleum ether 50:50). ^{1}H NMR (300 MHz, $CDCl_3$/TMS): δ 7.57–7.55 (m, 2H, H$_{Ph}$), 7.33–7.20 (m, 6H, H$_{Ph}$), 6.79–6.76 (m, 2H, H$_{Ph}$), 5.49 (q, 1H, *J* = 7.4 Hz, CH$_3$C*H*Ph), 4.90 (d, 1H, *J* = 8.1 Hz, 6a-H), 4.56 (q, 1H, *J* = 5.0 Hz, CH$_3$), 4.37 (br, 1H, OH), 3.97 (dd, 1H, *J* = 4.9, 10.9 Hz, 6$_A$-H), 3.89 (dd, 1H, *J* = 1.2, 8.1 Hz, 3a-H), 3.86 (d, 1H, *J* = 12.0 Hz, C*H*$_A$H$_B$Ph), 3.63 (dd, 1H, *J* = 1.2, 7.0 Hz, 3-H), 3.25 (dd, 1H, *J* = 9.6, 11.0 Hz, 6$_B$-H), 3.08 (m, 2H, 4-H, 5-H), 2.99 (d, 1H, *J* = 12.0 Hz, CH$_A$*H*$_B$Ph), 2.64 (br s, 1H, OH), 1.90 (d, 3H, *J* = 7.4 Hz, C*H*$_3$C*H*Ph), 1.26 (d, 3H, *J* = 5.0 Hz, CH$_3$). ^{13}C NMR (75 MHz, $CDCl_3$/TMS): δ 175.7, 174.5 (2 C=O), 137.6, 134.1 (2C, 1-C$_{Ph}$), 129.8, 129.2, 129.0, 128.9, 128.7, 127.8 (10C, 2-6C$_{Ph}$), 99.6 (2-C), 78.5 (6a-C), 78.0 (4-C), 70.0 (6-C, 3-C), 65.7(5-C), 63.3 (*C*H$_2$Ph), 51.8 (5-CH$_3$*C*HPh), 51.6 (3a-C), 20.9 (2-CH$_3$), 16.0 (5-*C*H$_3$CHPh).

18a. R$_f$ = 0.52 (EtOAc/petroleum ether 50:50). ^{1}H NMR (400 MHz, $CDCl_3$/TMS): δ 7.57–7.50 (m, 2H, H$_{Ph}$), 7.32–7.26 (m, 6H, H$_{Ph}$), 7.05–7.02 (m, 2H, H$_{Ph}$), 5.48 (q, 1H, *J* = 7.4 Hz, CH$_3$C*H*Ph), 4.79 (d, 1H, *J* = 7.9 Hz, 6a-H), 4.58 (q, 1H, *J* = 5.0 Hz, CH$_3$), 4.04 (dd, 1H, *J* = 5.4, 10.8 Hz, 6$_A$-H), 3.90 (d, 1H, *J* = 12.7 Hz, C*H*$_A$H$_B$Ph), 3.90 (dd, 1H, *J* = 2.8, 7.9 Hz, 3a-H), 3.70

(dd, 1H, *J* = 2.8, 5.3 Hz, 3-H), 3.58 (m, 1H, 5-H), 3.35 (d, 1H, *J* = 12.6 Hz, CH_AH_BPh), 3.42 (dd, 1H, *J* = 5.3, 9.1 Hz, 4-H), 3.30 (dd, 1H, *J* = 10.8, 10.1 Hz, 6_B-H), 2.77 (br s, 1H, OH), 1.87 (d, 3H, *J* = 7.4 Hz, CH_3CHPh), 1.28 (d, 3H, *J* = 5.0 Hz, CH_3). ^{13}C NMR (100.6 MHz, $CDCl_3$/TMS): δ 176.9, 174.0 (2 C=O), 138.5, 135.8 (2C, 1-C_{Ph}), 129.9, 129.8, 129.3, 129.1, 129.0, 128.8, 128.4, 128.3 (10C, 2-6C_{Ph}), 99.3 (2-C), 81.6 (4-C), 78.5 (6a-C), 70.1 (6-C), 67.7 (3-C), 63.4 (CH_2Ph), 62.9 (5-C), 51.9 (5-CH_3CHPh), 51.5 (3a-C), 20.8 (2-CH_3), 16.5 (5-CH_3CHPh).

(3*S*,3a*R*,6a*S*)-2-benzyl-3-[(2*S*,4*R*,5*R*)-5-[1-(*tert*-butyl)-1,1-dimethylsilyl]oxy-2-methyl-1,3-dioxan-4-yl]-5-[(1*S*)-*1*-phenylethyl)]perhydropyrrolo[3,4-*d*]isoxazole-4,6-dione (18b). To a stirred solution of the nitrone **1b** (260 mg, 0.71 mmol) in toluene (10 mL) was added (1*S*)-*N*-(1-phenylethyl)maleimide (**13**) (180 mg, 0.89 mmol) and the reaction mixture was heated at reflux for 10 h. The resulting mixture was evaporated under reduced pressure. The crude mixture of two diastereoisomers **18b** and **19b** (ratio 64:36 by ^{13}C NMR) was purified by column chromatography on silica gel (2.0 x 20 cm) eluting with EtOAc/isohexane (3:97 → 20:80) to give a mixture of diastereoisomers (321 mg, 80%).

18b. Colourless oil, R_f = 0.41 (EtOAc/isohexane 30:70). ^{1}H NMR (400 MHz, $CDCl_3$/TMS): δ 7.57–6.90 (m, 10H, H_{Ph}), 5.51 (q, 1H, *J* = 7.3 Hz, CH_3CHPh), 4.71 (d, 1H, *J* = 7.9 Hz, 6a-H), 4.64 (q, 1H, *J* = 5.0, 2-H), 4.14 - 4.04 (m, 3H, 3-H, 4-H, 6_A-H), 3.86 (dd, 1H, *J* = 7.9, 2.1 Hz, 3a-H), 3.60 (d, 1H, *J* = 13.7 Hz, CH_AH_BPh), 3.52 (dd, 1H, *J* = 8.5, 3.5 Hz, 4-H), 3.41 (d, 1H, *J* = 13.7 Hz, CH_AH_BPh), 3.36 (dd, 1H, *J* = 9.9, 9.9 Hz, 6_B-H), 1.90 (d, 3H, *J* = 7.6 Hz, CH_3CHPh), 1.30 (d, 3H, *J* = 5.0 Hz, CH_3), 0.88 [s, 9H, $C(CH_3)_3$], 0.10, 0.06 [2s, 3H, 3H, $Si(CH_3)_2$]. ^{13}C HMR (75 MHz, $CDCl_3$/TMS): δ 176.9, 174.8 (2 C=O), 138.4. 136.8 (2C, 1-C_{Ph}), 129.1, 129.0, 128.7, 128.5, 128.4, 127.7 (10C, 2-6C_{Ph}), 99.7 (2-C), 83.6 (4-C), 78.4 (6a-C), 71.6 (6-C), 68.1 (3-C), 63.7 (5-C, CH_2Ph), 52.7 (3a-C), 51.4 (5-CH_3CHPh), 26.2 [$C(CH_3)_3$], 20.9 (2-CH_3), 18.2 [$C(CH_3)_3$], 16.3 (5-CH_3CHPh), -3.2, -4.1 [2C, $Si(CH_3)_2$].

(3*R*,3a*S*,6a*R*)-2-Benzyl-3-[(2*R*,4S,5*R*)-5-hydroxy-2-methyl-1,3-dioxan-4-yl]-5-[(1*R*)-1-phenylethyl)]perhydropyrrolo[3,4-*d*]isoxazole-4,6-dione (22) and (3*R*,3a*R*, 6a*S*)-2-Benzyl-3-[(2*R*,4S,5*R*)-5-hydroxy-2-methyl-1,3-dioxan-4-yl]-5-[(1*R*)-1-phenyl-ethyl)] phenylperhydropyrrolo[3,4-*d*]isoxazole-4,6-dione (23). To a stirred solution of the nitrone **2a** (250 mg, 1.0 mmol) in toluene (10 mL) was added *N*-(1-phenylethyl)-maleimide (**12**) (200 mg, 1.0 mmol) and the reaction mixture was heated at reflux for 10 h. The resulting mixture was evaporated under reduced pressure. The crude mixture of four diastereoisomers (ratio 50:20:17:13 by ^{13}C NMR) was purified by column chromato-graphy on silica gel (2.0 x 20 cm) eluting with EtOAc/ petroleum ether (40:60) to give a mixture of all diastereoisomers **22**–**25** (288 mg, 64%). Separation of the mixture of diastereoisomers by column chromatography on silica gel (2.0 x 35 cm, EtOAc/petroleum ether, 25:75) afforded only the major product **22** and one minor product **23**.

22. Colourless crystals, R_f = 0.28 (EtOAc/ petroleum ether 50:50); mp 129–131 °C; [α]= + 7.9 (c = 1.5, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$/TMS): δ 7.57–7.54 (m, 2H, H_{Ph}), 7.34–7.20 (m, 6H, H_{Ph}), 6.92–6.87 (m, 2H, H_{Ph}), 5.46 (q, 1H, *J* = 7.5 Hz, CH_3CHPh), 4.76 (d, 1H, *J* = 8.1 Hz, 6a-H), 4.65 (q, 1H, *J* = 5.1 Hz, CH_3), 3.97 (dd, 1H, *J* = 1.2, 8.1 Hz, 3a-H), 3.94 (dd, 1H, *J* = 2.0,

12.0 Hz, 6A-H), 3.88 (m, 1 H, *J* = 1.3, 2.0, 1.4, 9.6 Hz, 5-H), 3.69 (dd, 1H, *J* = 12.0, 1.4 Hz, 6B-H), 3.67 (d, 1H, *J* = 12.6 Hz, C*H*AHBPh), 3.53 (m, 1H, 3-H), 3.33 (dd, 1H, *J* = 9.6, 1.3 Hz, 4-H), 3.22 (d, 1H, *J* = 12.6 Hz, CHA*H*BPh), 2.16 (br s, 1H, OH), 1.87 (d, 3H, *J* = 7.5 Hz, C*H*3CHPh), 1.33 (d, 3H, *J* = 5.1 Hz, CH3). ^{13}C NMR (100.6 MHz, $CDCl_3$/TMS): δ 176.6, 175.1 (2 C=O), 138.0, 135.9 (2C, 1-CPh), 129.7, 129.1, 129.0, 128.9, 128.8, 128.6, 128.3 (10C, 2-6CPh), 100.2 (2-C), 78.0 (6a-C), 77.9 (4-C), 72.1 (6-C), 67.0 (5-C), 63.3 (*C*H_2Ph), 63.2 (3-C), 51.8 (5-CH_3*C*HPh), 50.6 (3a-C), 21.3 (2-CH_3), 16.2 (5-*C*H_3CHPh).

23. Colourless oil ^{1}H NMR (400 MHz, $CDCl_3$/TMS): δ 7.47–7.44 (m, 2H, HPh), 7.36–7.23 (m, 8H, HPh), 5.48 (q, 1H, *J* = 7.3 Hz, CH_3C*H*Ph), 4.63 (d, 1H, *J* = 7.3 Hz, 6a-H), 4.58 (d, 1H, *J* = 15.4 Hz, C*H*AHBPh), 4.65 (q, 1H, *J* = 5.0 Hz, 2-H), 4.20 (m, 1H, 5-H), 3.95 (dd, 1H, *J* = 2.2, 12.0 Hz, 6A-H), 3.84 (d, 1H, *J* = 15.4 Hz, CHA*H*BPh), 3.70 (dd, 1H, *J* = 12.0, 1.4 Hz, 6B-H), 3.56 (dd, 1H, *J* = 7.3, 7.0 Hz, 3a-H), 3.54 (dd, 1H, *J* = 9.6, 0.6 Hz, 4-H), 3.30 (dd, 1H, *J* = 9.6, 7.0 Hz, 3-H), 2.76 (br s, 1H, OH), 1.82 (d, 3H, *J* = 7.3 Hz, C*H*3CHPh), 1.27 (d, 3H, *J* = 5.0 Hz, CH3). ^{13}C NMR (100.6 MHz, $CDCl_3$/TMS): δ 174.6, 174.5 (2 C=O), 139.4, 137.6 (2C, 1-CPh), 128.7, 128.6, 128.5, 128.2, 127.8, 127.3 (10C, 2-6CPh), 99.6 (2-C), 78.2 (4-C), 75.0 (6a-C), 72.1 (6-C), 67.3 (3-C), 64.3 (5-C), 60.8 (*C*H_2Ph), 50.7 (5-CH_3*C*HPh), 49.4 (3a-C), 21.2 (2-CH_3), 16.5 (5-CH_3*C*HPh).

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