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Nucleophilic additions of Grignard reagents to N-benzyl-2,3-O-isopropylidene-D-glyceraldehyde nitrone (BIGN). Synthesis of (2S,3R) and (2S,3S)-3-phenylisoserine. [1]

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Abstract

A remarkable Lewis acid tuning has been observed in the nucleophilic addition of Grignard reagent to BIGN, the N-benzyl nitrone derived from 1,2-O-isopropylidene-D-glyceraldehyde. The obtained α,β-dialkoxy hydroxylamines can serve as starting points for the synthesis of both aminodiols and α-hydroxy-β-amino acids. This synthetic approach is illustrated by the synthesis of the antipode of the C-13 side chain of Taxotere as well as its C-3 epimer.

Keywords: Nitrones; hydroxylamines, hydroxy acids and derivatives; amino alcohols

Introduction

Recently there has been an increase in interest in α-hydroxy-β-amino acids because of their presence in a number of biologically active compounds [1-6]. The most interesting members of this class of compounds are (2R,3S)-N-benzoyl-3-phenylisoserine **1a** and (2R,3S)-N-(tert-butoxycarbonyl)-3-phenylisoserine **1b**, the C-13 side chains of the important antitumor drugs Taxol and Taxotere™, respectively [7]. Other important α-hydroxy-β-amino acids are cyclohexylnorstatine **2**, the C-terminal residue of KRI 1314, an inhibitor of renin [8-10] and (2S,3R)-3-amino-2-hydroxydecanoic acid **3**, the N-terminal component of microginin, an

[1] This work, taken in part from the Ph.D. Thesis of E.C., was presented at the First Spanish Japanese Organic Chemistry Symposium, Alicante (Spain), September 1997.

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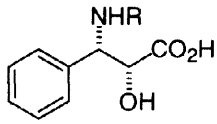
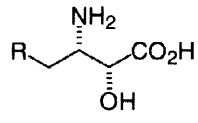
inhibitor of the angiotensin-converting enzyme [11,12].

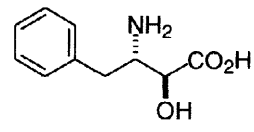
All these compounds have as a common property the *syn* configuration of their hydroxy and amino groups. Nevertheless, the relative stereochemistry of the functional groups in α-hydroxy-β-amino acids may have a large impact on their activity profiles. Thus, whereas (2R,3S)-3-benzylisoserine **4** is the non-leucine part of the immunosupressor bestatin [13,14], its C-2 epimer, allophenylnorstatine **5**, is an important constituent of kynostatins, a class of HIV-1 protease inhibitors [15].



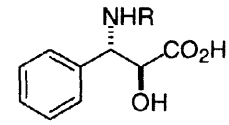
1a R = PhCO-
1b R = ^{t}BuOCO-



2 R = cyclohexyl
3 R = hexyl
4 R = phenyl



5

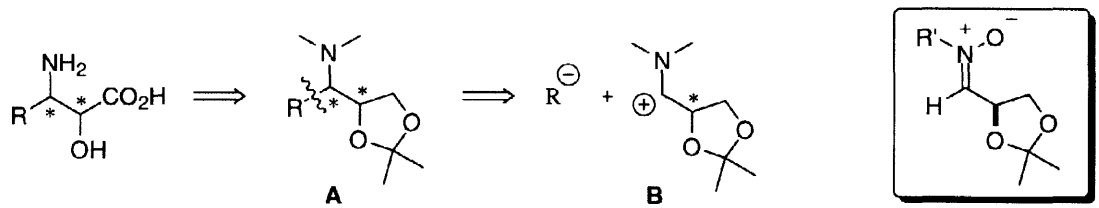


6a R = PhCO-
6b R = ^{t}BuOCO-

In this context, a recent report of Greene and co-workers has also pointed out the importance of having access to the corresponding *anti* derivatives (2S,3S)-N-benzoyl and N-(tert-butoxycarbonyl)-phenylisoserine **6** [16]. Therefore, and as a consequence of the biological importance of α-hydroxy-β-amino acids, many synthetic efforts have been devoted to this class of molecules [1-29]. Nevertheless, the significant roles exerted by both *syn* and *anti* isomers mean that synthetic routes of general applicability towards *syn* and *anti* α-hydroxy-β-amino acids remain still desirable.

We have recently reported that the readily available [30] N-benzyl nitrone **7** derived from 1,2-O-isopropylidene-D-glyceraldehyde undergoes nucleophilic additions with a total stereocontrol depending on the Lewis acid used as a pre-complexing agent [30-33]. Based on this reactivity and taking advantage of the synthetic equivalence of the dioxolane ring with the α-hydroxy carboxyl unit, it occurred to us that BIGN **7**, provided the correct sequence of reactions were followed, could be considered as a suitable starting material.[2]

Scheme 1



A **B**

BIGN, **7**

Conceptually the simplest strategy for the synthesis of the targeted α-hydroxy-β-amino acids involves the addition of the corresponding nucleophile to the nitrone **7**. This strategy is illustrated in the retrosynthetic analysis depicted in Scheme 1.

[2] Similar strategies could be based on the use of different C=N functionalities such as imines, oximes or hydrazones. However, the main advantage of the nitrone group is the total stereocontrol of the addition that can be exerted by means of pre-complexation with Lewis acids.

We report herein the results of the addition of several Grignard reagents to nitrone **7** and further conversion of the resulting α,β-dialkoxy hydroxylamines into 3-amino-1,2-diols, which in turn can be transformed into α-hydroxy-β-amino acids. The synthetic approach is illustrated with the synthesis of (2S,3R)-N-(tert-butoxycarbonyl)-3-phenylisoserine, the antipode of the C-13 side chain of the antitumor agent Taxotere™ as well as its (2S,3S) isomer.

Results and Discussion

The addition of Grignard reagents to nitrone **7** (Scheme 2) was initially explored using a variety of conditions [34]. The best results obtained for accessing both *syn* and *anti* α,β-dialkoxy hydroxylamines are summarized in Table 1.

Scheme 2

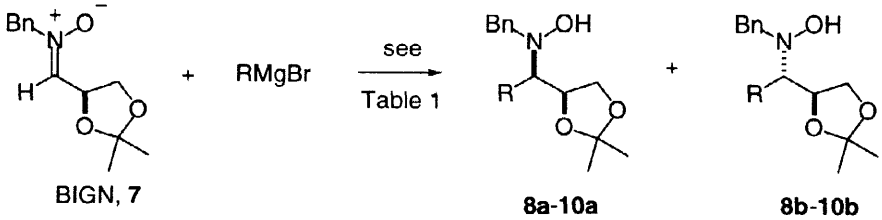


Table 1.
Stereoselective Additions of Grignard Reagents to Nitrone 7.[a]

entry	RMgBr[b]	solvent	Lewis acid[c]	hydroxylamine	*syn* : anti[d]	yield[e] (%)	isolated yield[f] (%)
1	PhMgBr	THF	none	**8**	80 : 20	84	67 (*syn*)
2	PhMgBr	Et_2O	$ZnBr_2$	**8**	90 : 10	86	77 (*syn*)
3	PhMgBr	Et_2O	Et_2AlCl	**8**	5 : 95	72	68 (*anti*)
4	MeMgBr	THF	none	**9**	76 : 24	81	62 (*syn*)
5	MeMgBr	Et_2O	$ZnBr_2$	**9**	91 : 9	82	75 (*syn*)
6	MeMgBr	Et_2O	Et_2AlCl	**9**	18 : 82	77	63 (*anti*)
7	EtMgBr	THF	none	**10**	75 : 25	74	56 (*syn*)
8	EtMgBr	Et_2O	$ZnBr_2$	**10**	78 : 22	72	56 (*syn*)
9	EtMgBr	Et_2O	Et_2AlCl	**10**	30 : 70	81	57 (*anti*)

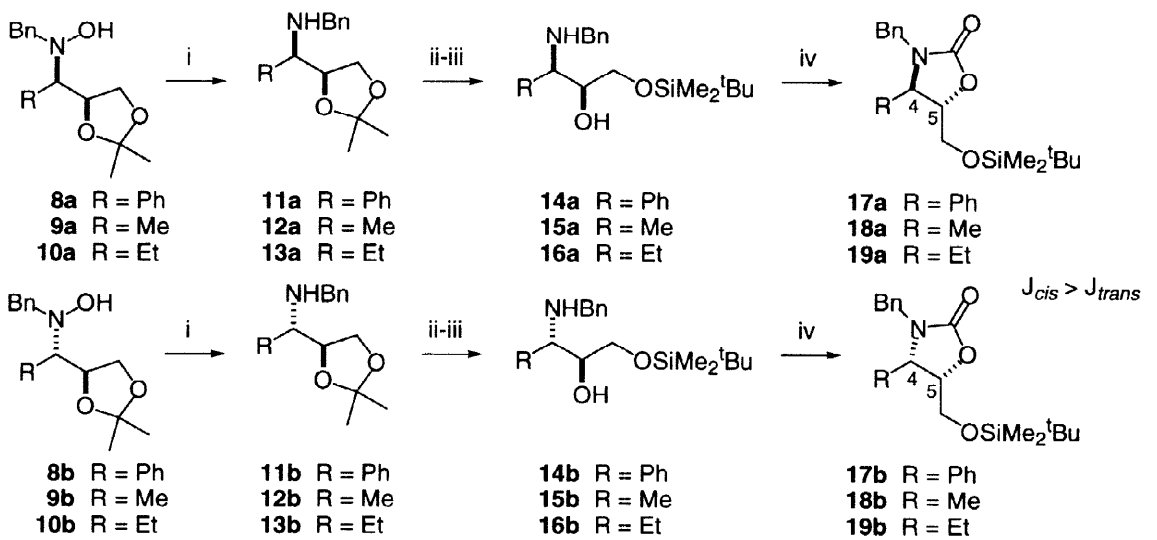
[a] All reactions were carried out at -60 °C for 6 h.
[b] 1.5 equiv. were used.
[c] 1.0 equiv. were used.
[d] Measured from the intensities of ^1H NMR signals.
[e] Determined on isolated mixture of diastereomers
[f] After purification by column chromatography.

It is worth mentioning that by carrying out the addition reaction at -60°C instead of -40°C, the temperature given in our previous communication [34], better results regarding both selectivity and chemical yield were obtained, no longer time of reaction being needed in any case. Table 1 shows wide applicability of the reaction. The high levels of diastereofacial

selectivity were not nucleophile dependent and when the reaction was conducted either in the absence of any Lewis acid or using $ZnBr_2$ as a precomplexing agent the corresponding *syn* isomer was obtained as the major product of the reaction. Interestingly, the reaction of **7** with Grignard reagents in the presence of Et_2AlCl gave the *anti* isomers predominantly. In all cases the mixtures of *syn* and *anti* adducts could be separated by column chromatography (see experimental). Thus each diastereomer could be prepared selectively only by changing the choice of Lewis acid.

The relative stereochemistries of the α-alkoxyhydroxylamines were assigned by transforming compounds **8-10** into the corresponding 1,3-oxazolidin-2-ones **17-19**. This conversion was achieved by deoxygenation of the hydroxylamine moiety according to Trombini [35], acid-catalyzed acetonide hydrolysis, selective protection of the resulting primary hydroxyl group and cyclization with carbonyl diimidazole as shown in Scheme 3.

Scheme 3



Reagents and conditions: i, Zn-Cu(OAc)$_2$, AcOH, 70°C. ii, p-TosOH (cat.), MeOH, reflux. iii, ^{t}BuMe$_2$SiCl, DMF, imidazole, r.t. iv, Im$_2$CO, THF, r.t.

When H-4 was irradiated, NOE was observed for H-5 in all 4,5-*cis*-disubstituted oxazolidinones **17b-19b** but not for the 4,5-*trans* disubstituted derivatives **17a-19a** (Figure 1). In such a case, however, a NOE was observed between H-4 and the methylene protons (-CH_2-) of the tert-butyldimethylsiloxymethyl group.

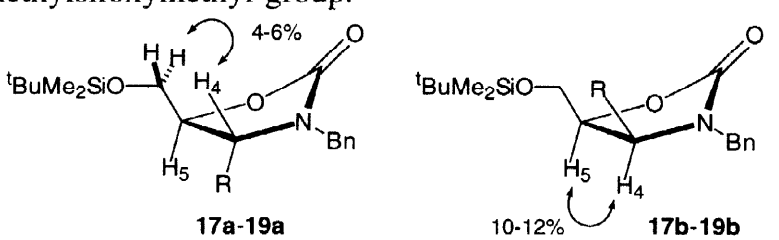


Figure 1

Determination of the stereochemistry in oxazolidinones **17-19**.

Also, 1,3-oxazolidin-2-ones **17-19** allowed the stereochemical assignment of the precursor hydroxylamines on the basis of a well-known empirical rule, i.e. coupling constants of 4,5-*trans* isomers are smaller than those of 4,5-*cis* isomers (Table 2) [36,37].

Table 2.

Selected ^{1}H NMR data for oxazolidinones **17-19**.[a]

trans	R	$J_{4,5}$ (Hz)	δ H-4[c]	δ H-5[c]	*cis*	R	$J_{4,5}$ (Hz)	δ H-4[c]	δ H-5[c]
17a	Ph	6.4	4.47	4.27	**17b**	Ph	8.3	4.55	4.65
18a	Me	6.3	3.56	4.00	**18b**	Me	8.2	3.74	4.40
19a	Et	4.6	3.45	4.14	**19b**	Et	7.6	3.57	4.43

[a] Chemical shifts (δ) in ppm; coupling constants (J) in hertzs.

[b] **a** and **b** series refer to *syn* and *anti* compounds, respectively.

[c] Assignments were based on signal multiplicities (see experimental)

Mechanistic Considerations

The present nucleophilic addition of Grignard reagents to nitrone **7** is characterized by the different effect exerted by $ZnBr_2$ and Et_2AlCl. The high *syn* selectivity observed when $ZnBr_2$ was used as a precomplexing agent requires that an α-chelate model should be invoked (Figure 2, **A**). On the other hand, the *anti* selectivity observed in the presence of Et_2AlCl is in agreement with a β-chelate model (Figure 2, **B**).

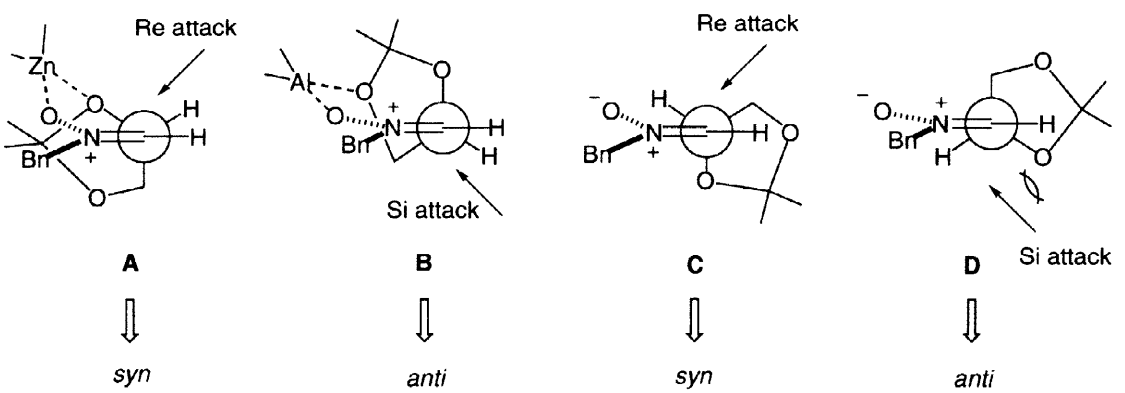


Figure 2

Models for addition to BIGN **7**.

Without taking into account the metal atoms, both models **A** and **B** correspond to classic Felkin-Anh models. Whereas model **B** refers to the Felkin-Anh proposal [38-40] (further confirmed by Houk [41,42]) for nucleophilic additions to carbonyl compounds, model **A** is similar to the *alkoxy inside* model proposed by Houk for several 1,3-dipolar cycloadditions [43]. In any case those models should not be considered in the absence of Lewis acids due to unfavourable electronic interactions between the nitrone oxygen and the oxygen atoms of the

dioxolane ring. A similar fact has been pointed out by Fisera and co-workers for dialdose-derived nitrones [44,45]. The presence of the metal atom contributes to stabilize such electronic interactions.

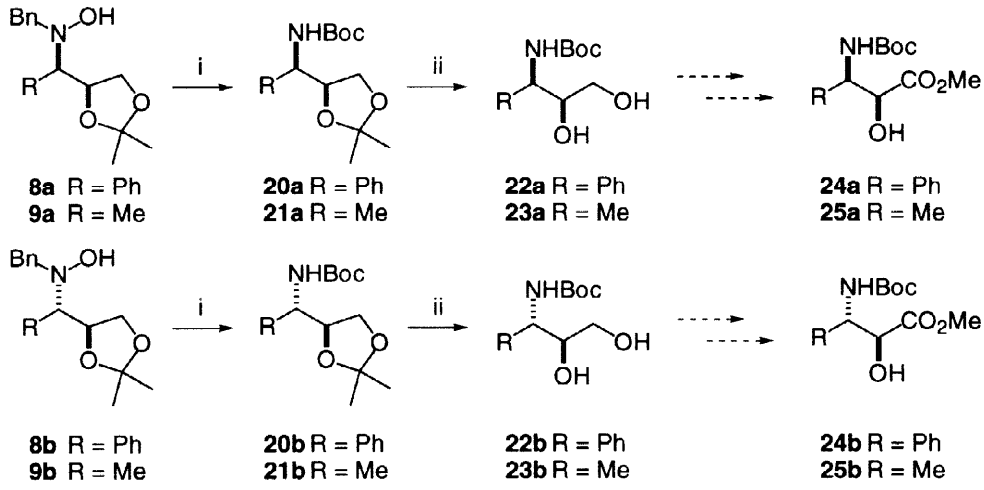
On the other hand, the *syn* selectivity observed in the addition of Grignard reagents in the absence of any chelating agent can be explained by a model similar to that proposed by Houk for asymmetric additions to double bonds [46] (Figure 2, **C**). The other possible Houk model in which the -CH_2-O- group is considered as the larger one (Figure 2, **D**) should be discarded on the basis that it could lead to unfavourable electronic interactions between the incoming nucleophile and the lone pairs of the oxygen. Moreover, model **C** has been previously invoked to explain the stereochemical outcome of several 1,3-dipolar cycloadditions of nitrones [47].

The formation of complexes between the nitrone **7** and several Lewis acids has been well-demonstrated by us through ^1H and ^{13}C NMR spectroscopy [48].

Synthesis of α-Hydroxy-β-Amino Acids

Hydroxylamines **8** and **9** were easily transformed into the protected 3-amino-1,2-diols **20** and **21**, respectively, through catalytic hydrogenation using $Pd(OH)_2$-C as a catalyst and subsequent treatment with di-tert-butyl dicarbonate as shown in Scheme 4. The acid-catalyzed hydrolysis of the acetonide moiety afforded aminodiols **22** and **23** in almost quantitative yields.

Scheme 4

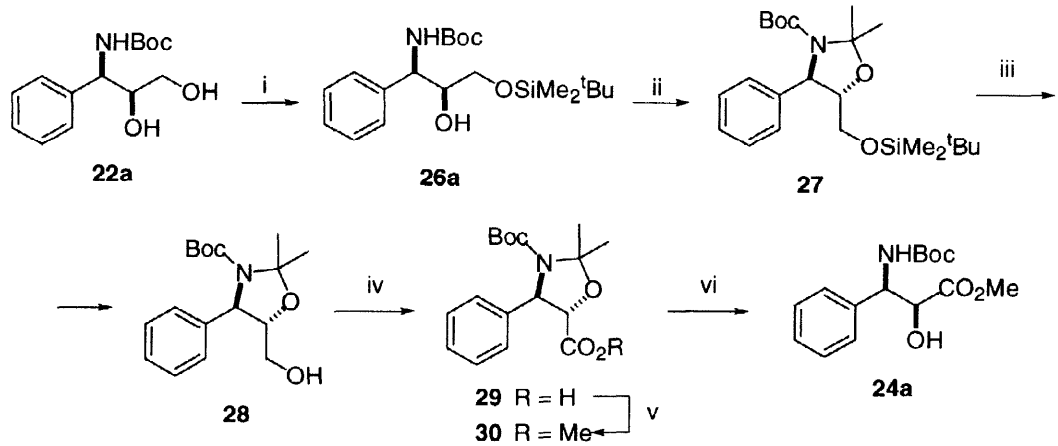


Reagents and conditions: i, H_2, $Pd(OH)_2$-C, 70 psi, r.t., then Boc_2O, dioxane. ii, p-TosOH (cat.), MeOH, reflux.

Further conversion of these compounds into the corresponding α-hydroxy-β-amino acids has previously been described for their enantiomers by Pericas and co-workers [2]. In order to illustrate the accessibility to α-hydroxy-β-amino acids following our synthetic

approach, we chose 3-phenyl-D-isoserine **24a**, the antipode of the C-13 side chain of Taxotere™, and its C-3 epimer **24b** as target compounds. The interest in this sort of compounds has been well demonstrated in the recent literature [49-55]. Thus compound **22a** (prepared from hydroxylamine **8a**) was selectively protected at the primary hydroxyl group as the tert-butyldimethylsilyl ether **26a** [56]. This compound was transformed into the immediate precursor of the 3-phenylisoserine by acid-catalyzed formation of the 1,3-oxazolidine **27** (80%) and subsequent fluoride-mediated removal of the silyl group. The resulting primary alcohol **28** was obtained in 86% yield and then oxidized by using the system $RuCl_3$-$NaIO_4$ to afford crude carboxylic acid **29** which was isolated and characterized as the methyl ester **30** (60% overall yield). Finally, deprotection of **30** afforded 3-phenyl-D-isoserine **24a** in 93% yield (Scheme 5). The optical and spectroscopic properties of **24a** were in good agreement with those reported for its enantiomer [2], except for the sign of the optical rotation.

Scheme 5



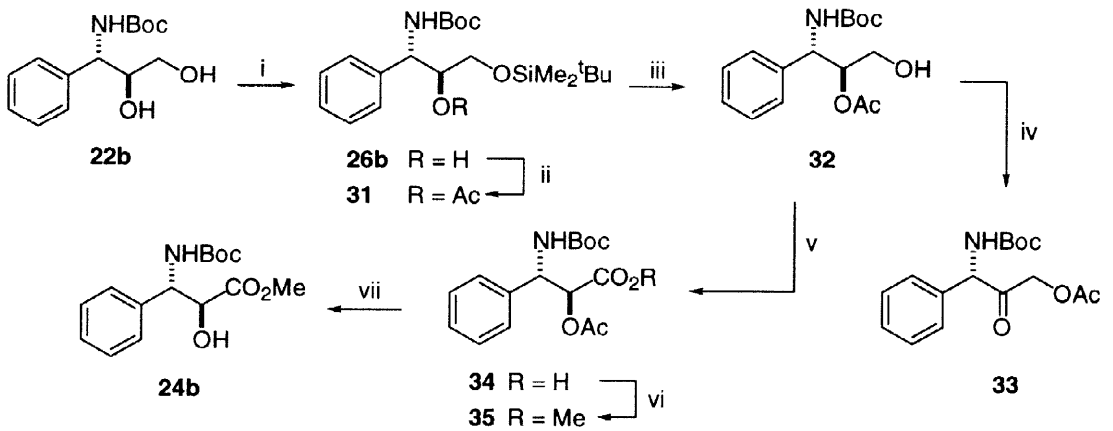
Reagents and conditions: i, $^tBuMe_2SiCl$, DMF, imidazole, r.t. ii, 2,2-dimethoxypropane, C_6H_6, CSA, r.t. iii, Bu_4NF, THF, r.t. iv, RuO_2, $NaIO_4$, CH_3CN-H_2O-CCl_4, r.t. v, CH_2N_2, Et_2O, 0°C. vi, p-TosOH (cat.), MeOH, reflux.

The *anti* aminoalcohol **22b** was used as starting material for the preparation of the (2S,3S)-phenylisoserine derivative **24b**. Protection of the primary hydroxyl group with tert-butyldimethyl silyl chloride [56] gave **26b** in 86% yield (Scheme 6). Difficulties were then encountered in protecting the 1,2-aminoalcohol functionality as the corresponding 1,3-oxazolidine. In the best case (10 eq. of 2,2-DMP, C_6H_6, reflux, 4 h) the reaction proceeded in only 10-15% yield with additional formation of large quantities of the deprotected diol **22b**. This behaviour might be attributed to the *anti* disposition of the substituents in **26b** which would led to a rather unstable cis-1,2-oxazolidine.[3] In order to circumvent the problems associated with the protection of the secondary hydroxyl group, other protective groups

[3] In fact, it has been described that *cis*-1,3-derived oxazolidines can be easily epimerized. See ref. 52

(including MOM, MEM and acetyl) were briefly examined. The best result was obtained with the acetyl group and thus compound **31** was obtained. Subsequent fluoride-promoted elimination of the tert-butyldimethylsilyl group afforded compound **32** in 80% overall yield from **26b**. Efforts to oxidize **32** to the corresponding acid (**34**) employing a number of standard reagents (ruthenium dioxide, ruthenium trichloride or chromium trioxide) [57] were complicated by the formation of **33** as a consequence of the acetyl group migration. This behaviour had also been observed previously by Pericas and co-workers [2].

Scheme 6



Reagents and conditions: i, $^tBuMe_2SiCl$, DMF, imidazole, r.t. ii, Ac_2O, Py, DMAP, r.t.. iii, Bu_4NF, THF, r.t. iv, RuO_2, $NaIO_4$, CH_3CN-H_2O-CCl_4, r.t. v, DMSO, $(COCl)_2$, CH_2Cl_2, -80°C, then $KMnO_4$, Na_2HPO_4, ^tBuOH, r.t. vi, CH_2N_2, Et_2O, 0°C. vii, MeONa, MeOH, r.t.

At this point we did not attempt to prepare differentially protected derivatives at the secondary hydroxyl group, as we turned instead to previous procedures for oxidizing primary alcohols to carboxylic acids in which a two-step protocol is used.[4] Oxidation of **32** under Swern conditions gave the corresponding aldehyde which was oxidized *in situ* with potassium permanganate in a mixture of tert-butanol and aqueous NaH_2PO_4 as a reaction medium [58] to afford the crude carboxylic acid **34** in 50% overall yield. This compound was characterized as the corresponding methyl ester **35**. Finally, deacetylation with sodium methoxide in methanol gave the α-hydroxy-β-aminoacid derivative **24b** in almost quantitative yield. The physical and spectroscopic properties of **24b** were identical with those reported in the literature [16].

Conclusions

In conclusion, we have introduced a new approach to α-hydroxy-β-amino acids based on nitrone chemistry which offers the possibility of a general applicability. The effectiveness of

[4] Such a two-step protocol involves oxidation of the primary alcohol to an aldehyde and *in situ* oxidation to carboxylic acid under neutral conditions

this approach has been demonstrated with the syntheses of the enantiomer of the C-13 side chain of the anticancer agent Taxotere™ and its C-3 epimer.

Experimental Part

General Methods. The reaction flasks and other equipment were stored in an oven at 130 °C overnight and assembled in a stream of argon. Syringes were assembled and fitted with needles while hot and cooled in a stream of argon. Special techniques were used in handling moisture- and air-sensitive materials [59] and solvents were purified and dried by standard methods [60]. Preparative chromatography was performed on columns of silica gel (60-240 mesh) and solvents were distilled prior to use. Reactions were monitored by TLC on silica gel 60 F254; the positions of the spots were detected with 254 nm UV light or iodine. Melting points were determined on a Büchi 510 melting point apparatus and are uncorrected. Optical rotations were measured on a Perkin Elmer 241 polarimeter at 20 °C in the stated solvent. Elemental analyses were performed on a Perkin Elmer 240B microanalyzer. ^{1}H and ^{13}C NMR spectra were recorded either on a Varian 300 Unity or a Bruker 300 spectrometers operating at 300 MHz for ^{1}H and 75.5 MHz for ^{13}C at 20 °C in $CDCl_3$ unless otherwise specified. Chemical shifts are given in parts per million down field from tetramethylsilane.

Starting Materials. Grignard reagents (phenylmagnesium bromide, methylmagnesium bromide and ethylmagnesium bromide) were used in THF or Et_2O from 1.0 M commercial solutions. Diethylaluminum chloride was used in hexane from a 1.0 M commercial solution. Zinc dibromide was purchased from Aldrich and used without further purification. Nitrone **5** was prepared as described [30].

Addition of Grignard Reagents to Nitrone 7. *Method A (without Lewis acids).* To a cooled solution (-60 °C) of nitrone (0.47 g, 2 mmol) in THF (20 mL) was added dropwise a solution of the Grignard reagent (3 mmol, 3.0 mL of a 1.0 M solution in THF). During the addition the temperature of the reaction mixture was not allowed to rise above -60 °C. The mixture was stirred for 6 h at -60 °C, quenched with saturated aqueous NH_4Cl (15 mL), stirred again at ambient temperature for 10 min and diluted with diethyl ether (10 mL). The organic layer was separated and the aqueous layer extracted with diethyl ether (3 x 20 mL). The combined organic extracts were washed with brine, dried ($MgSO_4$) and the solvent evaporated in vacuo. The crude product was purified by column chromatography on silica gel. The overall yield from the corresponding nitrone and the mixture of solvents employed for chromatography are reported below for each compound.

Method B (with Lewis acids). To a well-stirred solution of nitrone (0.47 g, 2 mmol) in

diethyl ether (40 mL) was added the Lewis acid (2 mmol) in one portion at room temperature and stirring was continued for 15 min. The mixture was then cooled to -60°C and treated with a solution of the Grignard reagent (3 mmol, 3.0 mL of a 1.0 M solution in Et_2O). The mixture was stirred for 6 h at -60 °C and then treated with 1 N aqueous NaOH (25 mL). After additional stirring for 15 min at ambient temperature the mixture was extracted with diethyl ether (3 x 20 mL). The combined organic extracts were washed with brine, dried ($MgSO_4$) and the solvent evaporated in vacuo. The crude product was purified by column chromatography on silica gel. The overall yield from the corresponding nitrone and the mixture of solvents employed for chromatography are reported below for each compound.

(2S,3R)-N-Benzyl-3-(hydroxyamino)-1,2-O-isopropylidene-3-phenyl-1,2-propanediol (8a). Method B ($ZnBr_2$). (hexane/ diethyl ether, 80:20) (0.483 g, 77%); oil; $[\alpha]_D$ -6.5 (c 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.40 (s, 3H), 1.43 (s, 3H), 3.43 (dd, 1H, J = 6.6, 8.5 Hz), 3.66 (dd, 1H, J = 6.6, 8.5 Hz), 3.67 (d, 1H, J = 13.2 Hz), 3.73 (d, 1H, J = 8.8 Hz), 3.82 (d, 1H, J = 13.2 Hz), 4.79 (td, 1H, J = 6.6, 8.8 Hz), 6.64 (bs, 1H, ex. D_2O), 7.21-7.44 (m, 10H). ^{13}C NMR ($CDCl_3$) δ 25.8, 26.7, 61.5, 67.3, 72.4, 76.2, 109.8, 127.2, 127.7, 128.1, 128.7, 129.4, 129.8, 135.9, 137.5. Anal. Calcd. for $C_{19}H_{23}NO_3$: C, 72.82; H, 7.40; N, 4.47. Found: C, 73.02; H, 7.57; N, 4.40.

(2S,3S)-N-Benzyl-3-(hydroxyamino)-1,2-O-isopropylidene-3-phenyl-1,2-propanediol (8b). Method B (Et_2AlCl). (hexane/diethyl ether, 80:20) (0.427 g, 68%); mp 141-143 °C; $[\alpha]_D$ -17.5 (c 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.24 (s, 3H), 1.29 (s, 3H), 3.52 (d, 1H, J = 13.4 Hz), 3.67 (d, 1H, J = 13.4 Hz), 3.70 (d, 1H, J = 6.7 Hz), 3.94 (dd, 1H, J = 6.7, 8.4 Hz), 4.15 (dd, 1H, J = 6.3, 8.4 Hz), 4.75 (dt, 1H, J = 6.3, 6.7 Hz), 4.86 (bs, 1H, ex. D_2O), 7.23-7.43 (m, 10H). ^{13}C NMR ($CDCl_3$) δ 24.5, 26.5, 62.2, 68.3, 73.6, 76.4, 109.1, 127.3, 128.0, 128.2, 128.3, 129.3, 130.1, 136.3, 137.7. Anal. Calcd. for $C_{19}H_{23}NO_3$: C, 72.82; H, 7.40; N, 4.47. Found: C, 72.77; H, 7.60; N, 4.55.

(2S,3R)-N-Benzyl-3-(hydroxyamino)-1,2-O-isopropylidene-1,2-butanediol (9a). Method B ($ZnBr_2$). (hexane/diethyl ether, 70:30) (0.377 g, 75%); oil; $[\alpha]_D$ -19.8 (c 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.02 (d, 3H, J = 6.6 Hz), 1.33 (s, 3H), 1.34 (s, 3H), 2.91 (quin, 1H, J = 6.6 Hz), 3.72 (dd, 1H, J = 8.5, 7.8 Hz), 3.80 (d, 1H, J = 13.2 Hz), 3.88 (dd, 1H, J = 8.8, 5.8 Hz), 3.92 (d, 1H, J = 13.2 Hz), 4.23 (m, 1H), 6.40 (bs, 1H, ex. D_2O), 7.28-7.40 (m, 5H). ^{13}C NMR ($CDCl_3$) δ 9.1, 25.6, 26.5, 60.9, 63.7, 66.7, 76.7, 108.8, 127.3, 128.3, 129.2, 137.70. Anal. Calcd. for $C_{14}H_{21}NO_3$: C, 66.91; H, 8.42; N, 5.57. Found: C, 67.04; H, 8.38; N, 5.61.

(2S,3S)-N-Benzyl-3-(hydroxyamino)-1,2-O-isopropylidene-1,2-butanediol (9b). Method B (Et_2AlCl). (hexane/diethyl ether, 70:30) (0.317 g, 63%); mp 84-86 °C; $[\alpha]_D$ -8.3 (c 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.24 (d, 3H, J = 6.6 Hz), 1.34 (s, 3H), 1.39 (s, 3H), 2.84

(dq, 1H, J = 7.3, 6.6 Hz), 3.71 (d, 1H, J = 13.2 Hz), 3.86 (dd, 1H, J = 8.4, 6.3 Hz), 3.96 (d, 1H, J = 13.2 Hz), 4.08 (dd, 1H, J = 8.4, 6.3 Hz), 4.20 (dt, 1H, J = 7.3, 6.3 Hz), 5.60 (bs, 1H. D_2O), 7.24-7.32 (m, 5H). ^{13}C NMR ($CDCl_3$) δ 9.0, 25.4, 26.7, 61.0, 63.9, 68.3, 76.6, 109.1, 127.4, 128.4, 129.2, 138.0. Anal. Calcd. for $C_{14}H_{21}NO_3$: C, 66.91; H, 8.42; N, 5.57. Found: C, 66.85; H, 8.40; N, 5.77.

(2S,3R)-N-Benzyl-3-(hydroxyamino)-1,2-O-isopropylidene-1,2-pentanediol (10a). Method B ($ZnBr_2$). (hexane/diethyl ether, 70:30) (0.297 g, 56%); oil; $[\alpha]_D$ +24.9 (c 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.99 (t, 3H, J = 6.8 Hz), 1.34 (s, 3H), 1.38 (s, 3H), 1.59 (m, 1H), 1.78 (m, 1H), 2.78 (ddd, 1H. J = 8.8, 6.4, 5.2 Hz), 3.75 (pseudo t, 1H, J = 7.6 Hz), 3.93 (d, 1H, J = 13.1 Hz), 4.00 (dd, 1H, J = 7.6, 6.2 Hz), 4.08 (d, 1H, J = 13.1 Hz), 4.43 (pseudo dt, 1H, J = 6.3. 4.7 Hz), 5.50 (bs, 1H, ex. D_2O), 7.28-7.42 (m, 5H). ^{13}C NMR ($CDCl_3$) δ 11.8, 19.8, 25.5, 26.6, 61.1, 67.0, 68.0, 75.4, 108.5, 127.1, 128.2, 129.1, 138.5. Anal. Calcd. for $C_{15}H_{23}NO_3$: C, 67.90; H, 8.74; N, 5.28. Found: C, 67.54; H, 8.63; N, 5.22.

(2S,3S)-N-Benzyl-3-(hydroxyamino)-1,2-O-isopropylidene-1,2-pentanediol (10b). Method B (Et_2AlCl). (hexane/diethyl ether, 70:30) (0.303 g, 57%); oil; $[\alpha]_D$ -13.0 (c 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.06 (t, 3H, J = 7.0 Hz), 1.36 (s, 3H), 1.40 (s, 3H), 1.63 (m, 1H), 1.80 (m, 1H), 2.61 (pseudo dt, 1H, J = 7.1, 5.7 Hz), 3.69 (dd, 1H, J = 8.5, 6.8 Hz), 3.75 (d, 1H, J = 13.2 Hz), 3.83 (d, 1H, J = 13.2 Hz), 4.11 (dd, 1H, J = 8.5, 5.7 Hz), 4.19 (pseudo q, 1H, J = 7.1 Hz), 5.71 (bs, 1H, ex. D_2O), 7.25-7.39 (m, 5H). ^{13}C NMR ($CDCl_3$) δ 12.04, 19.71, 25.45, 26.56, 60.20, 68.65, 69.73, 76.00, 108.71, 127.22, 128.24, 129.34, 138.32. Anal. Calcd. for $C_{15}H_{23}NO_3$: C, 67.90; H, 8.74; N, 5.28. Found: C, 68.02; H, 8.89; N, 5.23.

Deoxygenation of hydroxylamines. Synthesis of benzyl amines 11-13. To a solution of copper (II) acetate (22.5 mg, 0.15 mmol) in acetic acid (2 mL), Zn dust (0.5 g, 7.65 mmol) was added and the mixture was stirred at ambient temperature for 15 min under Ar. A solution of the hydroxylamine (1.5 mmol) in acetic acid (2 mL) and water (0.7 mL) was added and the mixture was heated at 70°C for 1 h. After cooling to 20°C the disodium salt of EDTA (1.5 g) was added and the solution was made alkaline (pH=10) by the addition of 3 M NaOH. The solution was extracted with ethyl acetate (3 x 15 mL); the combined organic extracts were washed with saturated aqueous EDTA (20 mL) and with brine (20mL). The organic layer was dried ($MgSO_4$) and the solvent evaporated under reduced pressure to give the crude benzylmines **11-13** which were purified by column chromatography on silica gel. The chemical yield from the corresponding secondary amine and the mixture of solvents employed for chromatography are reported below for each compound.

(2S,3R)-3-(Benzylamino)-1,2-O-isopropylidene-3-phenyl-1,2-propanediol (11a). (hexane/ethyl acetate, 30:70) (0.294 g. 66%); oil; $[\alpha]_D$ -65.6 (c 0.68, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.35 (s, 3H), 1.39 (s, 3H), 3.47 (d, 1H, J = 13.5 Hz), 3.60 (dd, 1H, J = 6.1, 8.5

Hz), 3.65 (d, 1H, J = 9.0 Hz), 3.66 (dd, 1H, J = 6.1, 8.5 Hz), 3.72 (d, 1H, J = 13.5 Hz), 3.90 (bs, 1H, ex. D_2O), 4.27 (dt, 1H, J = 6.1, 9.0 Hz), 7.23-7.37 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 25.5, 27.0, 50.6, 65.3, 66.7, 79.8, 109.9, 127.0, 127.5, 127.9, 128.1, 128.2, 128.7, 138.9, 139.7. Anal. Calcd for $C_{19}H_{23}NO_2$: C, 76.73; H, 7.80; N, 4.71. Found: C, 76.85; H, 8.01; N, 4.60.

(2S,3S)-3-(Benzylamino)-1,2-O-isopropylidene-3-phenyl-1,2-propanediol (11b). (hexane/ethyl acetate, 30:70) (0.303 g. 68%); oil; $[\alpha]_D$ +42.3 (c 0.73, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.34 (s, 3H), 1.38 (s, 3H), 2.16 (bs, 1H, ex. D_2O), 3.56 (d, 1H, J = 13.4 Hz), 3.74 (d, 1H, J = 13.4 Hz), 3.78 (dd, 1H, J = 6.1, 8.3 Hz), 4.02 (d, 1H, J = 4.3 Hz), 4.10 (t, 1H, J = 8.3 Hz), 4.32 (ddd, 1H, J = 4.3, 6.1, 8.3 Hz), 7.29-7.38 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 25.6, 26.9, 51.0, 63.3, 65.4, 79.7, 109.2, 127.0, 127.67, 127.8, 128.0, 128.3, 128.6, 139.5, 141.2. Anal. Calcd for $C_{19}H_{23}NO_2$: C, 76.73; H, 7.80; N, 4.71. Found: C, 76.63; H, 7.98; N, 4.66.

(2S,3R)-3-(Benzylamino)-1,2-O-isopropylidene-1,2-butanediol (12a). (hexane/ethyl acetate, 50:50) (0.212 g. 60%); oil; $[\alpha]_D$ +11.2 (c 1.15, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.08 (d, 3H, J = 6.3 Hz), 1.33 (s, 3H), 1.39 (s, 3H), 2.82 (bs, 1H, ex. D_2O), 3.71-3.74 (m, 1H), 3.84-3.90 (m, 2H), 3.97-4.01 (m, 3H), 7.30-7.38 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 16.2, 25.2, 26.4, 51.2, 53.7, 66.2, 79.3, 108.9, 126.9, 18.0, 128.4, 140.5. Anal. Calcd for $C_{14}H_{21}NO_2$: C, 71.46; H, 8.99; N, 5.95. Found: C, 71.32; H, 8.77; N, 6.08.

(2S,3S)-3-(Benzylamino)-1,2-O-isopropylidene-1,2-butanediol (12b). (hexane/ethyl acetate, 50:50) (0.247 g. 70%); oil; $[\alpha]_D$ +24.3 (c 0.50, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.11 (d, 3H, J = 6.3 Hz), 1.35 (s, 3H), 1.42 (s, 3H), 2.84 (quin, 1H, J = 6.3 Hz), 3.50 (bs, 1H, ex. D_2O), 3.77 (d, 1H, J = 13.1 Hz), 3.87 (dd, 1H, J = 6.8, 8.1 Hz), 3.94 (d, 1H, J = 13.1 Hz), 4.02 (dd, 1H, J = 6.5, 8.1 Hz), 4.06-4.09 (m, 1H), 7.25-7.37 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 16.2, 25.2, 26.4, 51.3, 53.7, 66.2, 79.4, 108.9, 126.9, 128.0, 128.4, 140.5. Anal. Calcd for $C_{14}H_{21}NO_2$: C, 71.46; H, 8.99; N, 5.95. Found: C, 71.53; H, 8.79; N, 5.84.

(2S,3R)-3-(Benzylamino)-1,2-O-isopropylidene-1,2-pentanediol (13a). (hexane/ethyl acetate, 50:50) (0.238 g. 64%); oil; $[\alpha]_D$ -2.1 (c 0.50, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.93 (t, 3H, J = 7.6 Hz), 1.33 (s, 3H), 1.37 (s, 3H), 1.46 (ddq, 1H, J = 5.7, 7.6, 13.0 Hz), 1.55 (ddq, 1H, J = 5.7, 7.6, 13.0 Hz), 2.27 (bs, 1H, ex. D_2O), 2.57 (dt, 1H, J = 5.7, 6.8 Hz), 3.69 (dd, 1H, J = 7.4, 8.0 Hz), 3.77 (d, 1H, J = 13.1 Hz), 3.91 (d, 1H, J = 13.1 Hz), 3.99 (dd, 1H, J = 6.1, 8.0 Hz), 4.12 (ddd, 1H, J = 6.1, 6.8, 7.4 Hz), 7.26-7.35 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 9.9, 22.7, 25.5, 26.7, 51.2, 60.1, 67.0, 77.9, 108.9, 127.0, 128.3, 128.4, 140.4. Anal. Calcd for $C_{15}H_{23}NO_2$: C, 72.25; H, 9.30; N, 5.62. Found: C, 72.38; H, 9.46; N, 5.51.

(2S,3S)-3-(Benzylamino)-1,2-O-isopropylidene-1,2-pentanediol (13b). (hexane/ethyl acetate, 50:50) (0.239 g. 64%); oil; $[\alpha]_D$ +11.1 (c 0.27, $CHCl_3$); ^1H NMR

($CDCl_3$) δ 0.92 (t, 3H, J = 7.5 Hz), 1.33 (s, 3H), 1.39 (s, 3H), 1.49-1.52 (m, 2H), 1.90 (bs, 1H, ex. D_2O), 2.54-2.60 (m, 1H), 3.75 (d, 1H, J = 13.0 Hz), 3.83 (d, 1H, J = 13.0 Hz), 3.89 (dd, 1H, J = 7.2, 7.8 Hz), 4.00 (dd, 1H, J = 7.5, 7.8 Hz), 4.04-4.12 (m, 1H), 7.27-7.39 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 9.7, 23.1, 25.2, 26.5, 51.7, 59.6, 66.4, 77.5, 108.7, 127.0, 128.1, 128.3, 140.4. Anal. Calcd for $C_{15}H_{23}NO_2$: C, 72.25; H, 9.30; N, 5.62. Found: C, 72.10; H, 9.50; N, 5.75.

Synthesis of 1,3-Oxazolidin-2-ones 17-19. The corresponding benzyl amine (1 mmol) obtained as indicated above was dissolved in methanol (10 mL) and treated with p-toluensulfonic acid monohydrate (38 mg, 0.2 mmol). The resulting mixture was refluxing for 4 h at which time saturated aqueous $NaHCO_3$ (15 mL) was added. The reaction mixture was extracted with ethyl acetate (3 x 10 mL); the combined organic layers were dried ($MgSO_4$) and the solvent distilled under reduced pressure. The crude 3-amino-1,2-diol was then dissolved in anhydrous DMF (2 mL) and treated with imidazole (1.14 g, 2.1 mmol), tert-butyldimethylsilyl chloride (0.273 g, 1.2 mmol) and N,N-dimethylaminopyridine (4.88 mg, 0.04 mmol). The solution was stirred at ambient temperature for 14 h. The crude mixture was poured into water (20 mL) and extracted with dichloromethane (2 x 15 mL). The combined organic layers were washed with brine (10 mL), dried ($MgSO_4$) and distilled in vacuo to give a crude product which was dissolved in THF (15 mL) and treated with carbonyldiimidazole (0.16 g, 1 mmol). The solution was stirred at ambient temperature for 12 h and then treated with brine (10 mL). The resulting mixture was extracted with dichloromethane (3 x 10 mL); the combined organic extracts were dried ($MgSO_4$) and distilled in vacuo. The crude product was purified by column chromatography on silica gel. The overall yield from the corresponding hydroxylamine and the mixture of solvents employed for chromatography are reported below for each compound.

(4R,5S)-3-Benzyl-5-(tert-butyldimethylsiloxymethyl)-4-phenyl-1,3-oxazolidin-2-one (17a). (hexane/diethyl ether, 70:30) (0.231 g, 58%); sticky oil; $[\alpha]_D$ -5.7 (c 1.26, $CHCl_3$); ^1H NMR ($CDCl_3$) δ -0.22 (s, 3H), -0.14 (s, 3H), 0.78 (s, 9H), 3.64 (d, 1H, J = 14.5 Hz), 3.64 (dd, 1H, J = 11.5, 3.3 Hz), 3.76 (dd, 1H, J = 11.5, 4.2 Hz), 4.27 (ddd, 1H, J = 6.4, 4.2, 3.3 Hz), 4.47 (d, 1H, J = 6.4 Hz), 4.87 (d, 1H, J = 14.5 Hz), 7.12-7.36 (m, 10H). ^{13}C NMR ($CDCl_3$) δ -5.3, -5.0, 18.1, 25.7, 29.6, 45.8, 60.0, 62.0, 127.3, 127.9, 128.5, 128.6, 128.7, 129.2, 135.3, 137.8, 157.8. Anal. Calcd. for $C_{23}H_{31}NO_3Si$: C, 69.48; H, 7.86; N, 3.52. Found: C, 69.51; H, 7.90; N, 3.60.

(4S,5S)-3-Benzyl-5-(tert-butyldimethylsiloxymethyl)-4-phenyl-1,3-oxazolidin-2-one (17b). (hexane/diethyl ether, 70:30) (0.227 g, 57%); sticky oil; $[\alpha]_D$ +48.0 (c 0.61, $CHCl_3$); ^1H NMR ($CDCl_3$) δ -0.23 (s, 3H), -0.16 (s, 3H), 0.74 (s, 9H), 3.21 (dd, 1H, J = 10.7, 6.6 Hz), 3.50 (dd, 1H, J = 10.7, 5.7 Hz), 3.60 (d, 1H, J = 14.5 Hz), 4.55 (d, 1H, J = 8.3 Hz),

4.65 (ddd, 1H, J = 8.3, 6.6, 5.7 Hz), 4.90 (d, 1H, J = 14.5 Hz), 7.10-7.37 (m, 10H). ^{13}C NMR ($CDCl_3$) δ -5.3, -5.2, 18.1, 25.7, 29.7, 46.0, 60.9, 61.4, 127.9, 128.2, 128.5, 128.7, 128.8, 129.0, 134.7, 136.7, 158.0. Anal. Calcd. for $C_{23}H_{31}NO_3Si$: C, 69.48; H, 7.86; N, 3.52. Found: C, 69.62; H, 7.63; N, 3.49.

(4R,5S)-3-Benzyl-5-(tert-butyldimethylsiloxymethyl)-4-methyl-1,3-oxazolidin-2-one (18a). (hexane/diethyl ether, 60:40) (0.208 g, 62%); sticky oil; $[\alpha]_D$ +3.1 (c 0.32, $CHCl_3$); ^1H NMR ($CDCl_3$) δ -0.01 (s, 3H), 0.01 (s, 3H), 0.81 (s, 9H), 1.23 (d, 3H, J = 6.3 Hz), 3.56 (dq, 1H, J = 6.3, 6.3 Hz), 3.68 (m, 2H), 4.00 (dt, 1H, J = 6.3, 4.3), 4.08 (d, 1H, J = 15.3 Hz), 4.75 (d, 1H, J = 15.3 Hz), 7.22-7.35 (m, 5H). ^{13}C NMR ($CDCl_3$) δ -5.3, -5.1, 12.3, 18.3, 25.7, 29.5, 45.7, 52.0, 62.6, 128.0, 128.1, 128.7, 136.0, 157.2. Anal. Calcd. for $C_{18}H_{29}NO_3Si$: C, 64.44; H, 8.71; N, 4.17. Found: C, 64.21; H, 8.80; N, 4.31.

(4S,5S)-3-Benzyl-5-(tert-butyldimethylsiloxymethyl)-4-methyl-1,3-oxazolidin-2-one (18b). (hexane/diethyl ether, 60:40) (0.205 g, 61%); sticky oil; $[\alpha]_D$ +4.2 (c 0.50, $CHCl_3$); ^1H NMR ($CDCl_3$) δ -0.01 (s, 3H), 0.00 (s, 3H), 0.81 (s, 9H), 1.22 (d, 3H, J = 6.4 Hz), 3.74 (dq, 1H, J = 8.2, 6.4 Hz), 3.80 (m, 2H), 4.07 (d, 1H, J = 15.1 Hz), 4.40 (pseudo dt, 1H, J = 8.2, 5.5 Hz), 4.78 (d, 1H, J = 15.1 Hz), 7.24-7.33 (m, 5H). ^{13}C NMR ($CDCl_3$) δ -5.5, -5.2, 12.3, 18.1, 25.8, 29.6, 45.5, 52.1, 60.8, 127.9, 128.1, 128.7, 136.2, 157.7. Anal. Calcd. for $C_{18}H_{29}NO_3Si$: C, 64.44; H, 8.71; N, 4.17. Found: C, 64.32; H, 8.59; N, 4.01.

(4R,5S)-3-Benzyl-5-(tert-butyldimethylsiloxymethyl)-4-ethyl-1,3-oxazolidin-2-one (19a). (hexane/diethyl ether, 60:40) (0.210 g, 60%); sticky oil; $[\alpha]_D$ -23.4 (c 0.45, $CHCl_3$); ^1H NMR ($CDCl_3$) δ -0.03 (s, 3H), -0.01 (s, 3H), 0.81 (s, 9H), 0.90 (t, 3H, J = 7.3 Hz), 1.50 (m, 2H), 3.45 (ddd, 1H, J = 7.6, 4.6, 3.2 Hz), 3.62 (m, 2H), 4.03 (d, 1H, J = 15.0 Hz), 4.14 (quin, 1H, J = 4.6 Hz), 4.79 (d, 1H, J = 15.0 Hz), 7.24-7.35 (m, 5H). ^{13}C NMR ($CDCl_3$) δ -5.5 (2C), 7.8, 10.3, 18.2, 25.8, 29.7, 45.8, 56.5, 63.5, 127.8, 128.0, 128.7, 136.0, 157.9. Anal. Calcd. for $C_{19}H_{31}NO_3Si$: C, 65.29; H, 8.94; N, 4.01. Found: C, 65.51; H, 9.03; N, 4.00.

(4S,5S)-3-Benzyl-5-(tert-butyldimethylsiloxymethyl)-4-ethyl-1,3-oxazolidin-2-one (19b). (hexane/diethyl ether, 60:40) (0.199 g, 57%); sticky foam; $[\alpha]_D$ +109.8 (c 0.26, $CHCl_3$); ^1H NMR ($CDCl_3$) δ -0.03 (s, 3H), -0.01 (s, 3H), 0.81 (s, 9H), 0.83 (t, 3H, J = 7.3 Hz), 1.60 (m, 2H), 3.57 (ddd, 1H, J = 7.6, 4.1, 2.6 Hz), 3.84 (m, 2H), 4.05 (d, 1H, J = 15.0 Hz), 4.43 (dt, 1H, J = 5.2, 7.6 Hz), 4.78 (d, 1H, J = 15.0 Hz), 7.24-7.35 (m, 5H). ^{13}C NMR ($CDCl_3$) δ -5.5, -5.2, 7.3, 10.3, 18.3, 25.6, 29.4, 46.1, 57.8, 63.5, 127.9, 128.5, 128.7, 136.2, 158.4. Anal. Calcd. for $C_{19}H_{31}NO_3Si$: C, 65.29; H, 8.94; N, 4.01. Found: C, 65.43; H, 8.72; N, 4.06.

Synthesis of N-Boc deriatives 20-21. A solution of the corresponding hydroxylamine (1 mmol) in MeOH (15 mL) was treated with $Pd(OH)_2$-C (13 mg) and the resulting suspension

was stirred under hydrogen at 70 psi for 3 days (Parr hydrogenation apparatus). The mixture was filtered through a pad of Celite and the filtrate was concentrated. The residue was dissolved in 1,4-dioxane (10 mL) and treated with ditert-butyl dicarbonate (0.28 g, 1.3 mmol). The solution was stirred at ambient temperature for 16 h. The mixture was partitioned between saturated aqueous $NaHCO_3$ (15 mL) and dichloromethane (15 mL), and the organic layer separated. The aqueous layer was extracted with dichloromethane (2 x 10 mL). The combined organic extracts were dried ($MgSO_4$) and evaporated under reduced pressure to give the crude product which was purified by column chromatography on silica gel. The overall yield from the corresponding hydroxylamine and the mixture of solvents employed for chromatography are reported below for each compound.

(2S,3R)-3-(tert-Butoxycarbonylamino)-1,2-O-isopropylidene-3-phenyl-1,2-propanediol (20a). (hexane/ethyl acetate, 50:50) (0.258 g, 84%); sticky oil; $[\alpha]_D$ -27.5 (c 0.67, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.35 (s, 3H), 1.42 (s, 9H), 1.49 (s, 3H), 3.76 (dd, 1H, J = 6.8, 8.3 Hz), 3.95 (dd, 1H, J = 6.5, 8.3 Hz), 4.33 (ddd, 1H, J = 4.0, 6.5, 6.8 Hz), 4.66 (dd, 1H, J = 4.0, 7.5 Hz), 5.30 (d, 1H, J = 7.5 Hz), 7.23-7.38 (m, 5H). ^{13}C NMR ($CDCl_3$) δ 25.0, 26.2, 28.2, 55.4, 66.7, 78.1, 79.5, 109.7, 126.8, 127.4, 128.4, 140.4, 155.5. Anal. Calcd. for $C_{17}H_{25}NO_4$: C, 66.43; H, 8.20; N, 4.56. Found: C, 66.21; H, 8.16; N, 4.49.

(2S,3S)-3-(tert-Butoxycarbonylamino)-1,2-O-isopropylidene-3-phenyl-1,2-propanediol (20b). (hexane/ethyl acetate, 50:50) (0.249 g, 81%); white solid; mp 117-119 °C; $[\alpha]_D$ 27.2 (c 0.44, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.29 (s, 3H), 1.32 (s, 3H), 1.40 (s, 9H), 3.70 (dd, 1H, J = 6.0, 8.8 Hz), 3.91 (dd, 1H, J = 6.7, 8.8 Hz), 4.37 (ddd, 1H, J = 5.4, 6.0, 6.7 Hz), 4.72 (dd, 1H, J = 5.4, 8.3 Hz), 5.18 (d, 1H, J = 8.3 Hz), 7.30-7.40 (m, 5H). ^{13}C NMR ($CDCl_3$) δ 25.4, 26.2, 28.8, 57.3, 66.5, 79.2, 80.5, 109.8, 127.7 (2C), 128.3, 140.0, 156.2. Anal. Calcd. for $C_{17}H_{25}NO_4$: C, 66.43; H, 8.20; N, 4.56. Found: C, 66.20; H, 8.19; N, 4.67.

(2S,3R)-3-(tert-Butoxycarbonylamino)-1,2-O-isopropylidene-1,2-butanediol (21a). (hexane/ethyl acetate, 40:60) (0.218 g, 89%); white solid; mp 92-94 °C; $[\alpha]_D$ -28.7 (c 0.25, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.11 (d, 3H, J = 7.0 Hz), 1.32 (s, 3H), 1.40 (s, 3H), 1.42 (s, 9H), 3.71-3.77 (m, 2H), 3.96-4.04 (m, 2H), 4.47 (bs, 1H). ^{13}C NMR ($CDCl_3$) δ 16.1, 20.0, 26.2, 28.3, 48.5, 66.6, 78.8, 79.3, 109.4, 155.2. Anal. Calcd. for $C_{12}H_{23}NO_4$: C, 58.75; H, 9.45; N, 5.71. Found: C, 58.90; H, 9.36; N, 5.59.

(2S,3S)-3-(tert-Butoxycarbonylamino)-1,2-O-isopropylidene-1,2-butanediol (21b). (hexane/ethyl acetate, 40:60) (0.211 g, 86%); sticky oil; $[\alpha]_D$ -10.9 (c 0.34, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.21 (d, 3H, J = 6.8 Hz), 1.34 (s, 3H), 1.42 (s, 3H), 1.44 (s, 9H), 3.67-3.70 (m, 2H), 4.00-4.11 (m, 2H), 4.60 (bs, 1H). ^{13}C NMR ($CDCl_3$) δ 16.1, 18.7, 26.3, 27.4, 49.2, 66.4, 78.4, 79.3, 109.1, 155.7. Anal. Calcd. for $C_{12}H_{23}NO_4$: C, 58.75; H, 9.45; N, 5.71. Found: C, 58.63; H, 9.22; N, 5.82.

Synthesis of 3-amino-1,2-diols 22-23. A solution of the N-Boc derivative (1 mmol) in methanol (25 mL) was treated with p-toluensulfonic acid monohydrate (38 mg, 0.2 mmol). The solution was refluxed for 4 h, then saturated aqueous $NaHCO_3$ (15 mL) was added. The reaction mixture was extracted with ethyl acetate (3 x 10 mL); the combined organic extracts were dried ($MgSO_4$) and the solvent distilled under reduced pressure. The residue was purified by column chromatography on silica gel. The chemical yield from the corresponding N-Boc derivative and the mixture of solvents employed for chromatography are reported below for each compound.

(2S,3R)-3-(tert-Butoxycarbonylamino)-3-phenyl-1,2-propanediol (22a). (hexane/ethyl acetate, 50:50) (0.257 g, 96%); white solid; mp 102-103 °C; $[\alpha]_D$ -23.4 (c 0.82, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.41 (s, 9H), 2.60 (bs, 2H, ex. D_2O), 3.45-3.60 (m, 2H), 3.90 (dd, 1H, J = 5.0, 10.4 Hz), 4.72 (dd, 1H, J = 4.2, 8.1 Hz), 5.50 (d, 1H, J = 8.1 Hz), 7.28-7.38 (m, 5H). ^{13}C NMR ($CDCl_3$) δ 28.2, 56.7, 63.7, 75.0, 80.4, 126.8, 127.4, 129.0, 139.7, 155.9. Anal. Calcd. for $C_{14}H_{21}NO_4$: C, 62.90; H, 7.92; N, 5.24. Found: C, 63.03; H, 7.81; N, 5.36.

(2S,3S)-3-(tert-Butoxycarbonylamino)-3-phenyl-1,2-propanediol (22b). (hexane/ethyl acetate, 50:50) (0.267 g, 100%); white solid; mp 116-118 °C; $[\alpha]_D$ 51.0 (c 0.65, $CHCl_3$) [Lit. [2]: mp 109-116 °C; $[\alpha]_D$ 52.7 (c 1.00, $CHCl_3$)]; ^1H NMR ($CDCl_3$) δ 1.40 (s, 9H), 2.40 (bs, 2H, ex. D_2O), 3.52-3.60 (m, 2H), 3.75-3.79 (m, 1H), 4.54 (t, 1H, J = 7.7 Hz), 5.14 (bs, 1H), 7.29-7.47 (m, 5H). ^{13}C NMR ($CDCl_3$) δ 28.1, 57.4, 62.6, 74.3, 80.6, 127.6, 128.1, 128.2, 129.0, 156.3. Anal. Calcd. for $C_{14}H_{21}NO_4$: C, 62.90; H, 7.92; N, 5.24. Found: C, 63.70; H, 7.81; N, 5.43.

(2S,3R)-3-(tert-Butoxycarbonylamino)-1,2-butanediol (23a). (hexane/ethyl acetate, 30:70) (0.199 g, 97%); sticky foam; $[\alpha]_D$ -17.1 (c 0.60, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.23 (d, 3H, J = 6.7 Hz), 1.45 (s, 9H), 2.80 (bs, 2H, ex. D_2O), 3.32-3.38 (m, 1H), 3.57-3.70 (m, 3H), 4.58 (bs, 1H). ^{13}C NMR ($CDCl_3$) δ 17.0, 28.2, 47.8, 63.0, 75.5, 80.2, 156.5. Anal. Calcd. for $C_9H_{19}NO_4$: C, 52.65; H, 9.33; N, 6.82. Found: C, 52.71; H, 9.00; N, 6.69.

(2S,3S)-3-(tert-Butoxycarbonylamino)-1,2-butanediol (23b). (hexane/ethyl acetate, 30:70) (0.197 g, 96%); white solid; mp 73-74 °C; $[\alpha]_D$ -6.2 (c 0.87, $CHCl_3$) [Lit. [2]: mp 74-75 °C; $[\alpha]_D$ -5.8 (c 1.00, $CHCl_3$)]; ^1H NMR ($CDCl_3$) δ 1.23 (d, 3H, J = 6.6 Hz), 1.46 (s, 9H), 2.96 (bs, 2H), 3.30-3.38 (m, 1H), 3.59-3.63 (m, 2H), 3.69-3.71 (m, 1H), 5.00 (bd, 1H, 7.8 Hz). ^{13}C NMR ($CDCl_3$) δ 16.5, 28.0, 48.2, 63.9, 74.9, 80.6, 155.4. Anal. Calcd. for $C_9H_{19}NO_4$: C, 52.65; H, 9.33; N, 6.82. Found: C, 52.83; H, 9.41; N, 6.62.

(2S,3R)-3-(tert-Butoxycarbonylamino)-1-(tert-butyldimethylsiloxy)-3-phenyl-2-propanol (26a). A solution of aminodiol **22a** (0.27 g, 1 mmol) in anhydrous DMF (2 mL) was treated sequentially with imidazole (1.09 g, 2 mmol), tert-butyldimethylsilyl chloride

(0.27 g, 1.2 mmol) and 4-(dimethylamino)pyridine (4.9 mg, 0.04 mmol). The solution was stirred at ambient temperature for 14 h. The crude mixture was poured into water (20 mL) and extracted with dichloromethane (2 x 15 mL). The combined organic layers were washed with brine, dried ($MgSO_4$) and distilled in vacuo. The crude product was purified by column chromatography on silica gel (hexane/diethyl ether, 60:40) to afford 0.347 g (91%) of pure **26a** as a sticky foam; $[\alpha]_D$ -3.4 (c 0.78, $CHCl_3$) [Lit. for enantiomer [2]: $[\alpha]_D$ +2.65 (c 1.10, $CHCl_3$)]; ^1H NMR ($CDCl_3$) δ 0.06 (s, 3H), 0.08 (s, 3H), 0.92 (s, 9H), 1.40 (s, 9H), 2.57 (d, 1H, J = 3.8 Hz, ex. D_2O), 3.54 (dd, 1H, J = 6.8, 10.1 Hz), 3.65 (dd, 1H, J = 4.9, 10.1 Hz), 3.78 (ddt, 1H, J = 3.8, 4.9, 6.8 Hz), 4.69 (dd, 1H, J = 3.8, 7.9 Hz), 5.82 (d, 1H, 7.9 Hz), 7.30-7.41 (m, 5H). ^{13}C NMR ($CDCl_3$) δ -5.7, -5.6, 18.1, 25.7, 28.2, 55.9, 64.3, 74.5, 79.3, 126.7, 127.2, 128.3, 141.0, 155.6. Anal. Calcd. for $C_{20}H_{35}NO_4Si$: C, 62.95; H, 9.25; N, 3.67. Found: C, 63.04; H, 9.10; N, 3.80.

(4R,5S)-3-(tert-Butoxycarbonyl)-5-[(tert-butyldimethylsiloxy)methyl]-4-phenyl-1,3-oxazolidin-2-one (27). A solution of compound **26a** (0.3 g, 0.79 mmol), 2,2-dimethoxypropane (1 mL, 8.23 mmol) and (1R)-(-)-10-camphorsulfonic acid (116 mg, 0.5 mmol) in acetone (15 mL) was stirred at ambient temperature for 30 min at which time the solvent was removed under reduced pressure. The residue was partitioned between saturated aqueous $NaHCO_3$ (10 mL) and diethyl ether (15 mL). The organic layer was separated, washed with brine, dried ($MgSO_4$) and concentrated in vacuo to give the crude product. Purification by column chromatography on silica gel (hexane/diethyl ether, 70:30) gave **27** (0.266 g, 80%) as an oil; $[\alpha]_D$ -16.8 (c 1.34, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.04 (s, 3H), 0.06 (s, 3H), 0.89 (s, 9H), 1.17 (s, 9H), 1.66 (s, 3H), 1.71 (s, 3H), 3.70 (dd, 1H, J = 4.4, 11.2 Hz), 3.79 (dd, 1H, J = 4.0, 11.2 Hz), 3.92 (ddd, 1H, J = 4.0, 4.4, 7.4 Hz), 4.66 (d, 1H, J = 7.4 Hz), 7.18-7.32 (m, 5H). ^{13}C NMR ($CDCl_3$) δ -5.5, -5.6, 18.3, 25.7, 25.9, 28.0, 28.1, 60.0, 62.8, 63.4, 79.5, 94.8, 126.7, 127.9, 128.5, 141.5, 152.0. Anal. Calcd. for $C_{23}H_{39}NO_4Si$: C, 65.52; H, 9.32; N, 3.32. Found: C, 65.14; H, 9.01; N, 3.73.

(4R,5S)-3-(tert-Butoxycarbonyl)-5-(hydroxymethyl)-4-phenyl-1,3-oxazolidin-2-one (28). A solution of compound **27** (0.25 g, 0.60 mmol) in THF (25 mL) was treated with Bu_4NF (0.7 mmol, 0.7 mL of a 1.0 M solution in THF) at ambient temperature. After 1h saturated aqueous $NaHCO_3$ (10 mL) was added and the mixture extracted with diethyl ether (3 x 10 mL). The combined organic extracts were washed with brine, dried ($MgSO_4$) and distilled under reduced pressure. Purification of the crude product by column chromatography on silica gel (hexane/diethyl ether, 60:40) gave pure **28** (0.159 g, 86%) as an oil; $[\alpha]_D$ -8.4 (c 0.18, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.15 (s, 9H), 1.68 (s, 3H), 1.73 (s, 3H), 1.85 (bs, 1H, ex. D_2O), 3.63 (dd, 1H, J = 3.9, 12.2 Hz), 3.81 (dd, 1H, J = 2.8, 12.2 Hz), 3.95 (ddd, 1H, J = 2.8, 3.9, 8.4 Hz), 4.64 (d, 1H, J = 8.4 Hz), 7.20-7.40 (m, 5H). ^{13}C NMR

($CDCl_3$) δ 25.5, 26.1, 28.1, 59.3, 64.4, 66.3, 79.7, 96.3, 126.8, 127.7, 128.8, 140.5, 152.9. Anal. Calcd. for $C_{17}H_{25}NO_4$: C, 66.43; H, 8.20; N, 4.56. Found: C, 66.27; H, 7.99; N, 4.61.

(4R,5S)-3-(tert-Butoxycarbonyl)-5-(methoxycarbonyl)-4-phenyl-1,3-oxazolidin-2-one (30). To a well-stirred solution of $NaIO_4$ (0.6 g, 2.93 mmol) in the mixture H_2O (10 mL), CCl_4 (10 mL) and CH_3CN (15 mL) was added RuO_2 monohydrate (83 mg, 0.6 mmol). After 30 min solid $NaHCO_3$ (4.00 g, 44.8 mmol) was added followed by 5 mL of water. After 5 min the resulting mixture was treated with a solution of **28** (0.15 g, 0.49 mmol) in CH_3CN (5 mL). The solution turned black and after 5 min, enough $NaIO_4$ (about 0.2 g) was added to turn the colour dark green. The mixture was diluted with water (6 ml) and extracted with ethyl acetate (2 x 5 mL). The aqueous layer was acidified with 1N HCl (pH=2) and reextracted with ethyl acetate (3 x 10 mL). The combined organic extracts were washed with 40% aqueous sodium bisulfite and brine, dried ($MgSO_4$) and evaporated. The residue containing the crude acid was taken up in diethyl ether (20 mL) and treated with diazomethane. The solvent was evaporated and the residue was purified by column chromatography on silica gel (hexane/diethyl ether, 80:20) to afford the pure methyl ester **30** (99 mg, 60%) as an oil; $[\alpha]_D$ -8.9 (c 0.12, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.25 (s, 9H), 1.67 (s, 3h), 1.78 (s, 3H), 4.10 (s, 3H), 4.52 (d, 1H, J = 5.6 Hz), 5.23 (d, 1H, J = 5.6 Hz), 7.28-7.42 (m, 5H). ^{13}C NMR ($CDCl_3$) δ 25.7, 26.6, 28.3, 50.9, 60.6, 70.0, 79.6, 95.6, 126.7, 127.9, 128.5, 141.3, 152.0, 173.1. Anal. Calcd. for $C_{18}H_{25}NO_5$: C, 64.46; H, 7.51; N, 4.18. Found: C, 64.32; H, 7.78; N, 7.63.

Methyl (2S,3R)-3-(tert-butoxycarbonylamino)-2-hydroxy-3-phenyl propanoate (24a). To a solution of **30** (90 mg, 0.27 mmol) in methanol (15 mL), p-toluensulfonic acid monohydrate (1.8 mg, 9.6 μmmol) was added and the mixture was heated under reflux for 2 h. The reaction mixture was treated with saturated aqueous $NaHCO_3$ (10 mL) and extracted with diethyl ether (3 x 11 mL). The combined organic layers were dried ($MgSO_4$) and the solvent distilled under reduced pressure. The crude product was chromatographed on silica gel (hexane/diethyl ether, 50:50) to give 74 mg (93%) of pure **24a** as a white solid; mp 130-132 °C; $[\alpha]_D$ +7.2 (c 0.22, $CHCl_3$) [Lit. for enantiomer [2]: mp 128 °C; $[\alpha]_D$ -7.6 (c 1.20, $CHCl_3$)]; ^1H NMR ($CDCl_3$) δ 1.40 (s, 9H), 3.10 (bs, 1H), 3.88 (s, 3H), 4.42-4.53 (m, 1H), 5.17-5.19 (m, 1H), 5.60 (d, 1H, J = 8.0 Hz), 7.30-7.40 (m, 5H). ^{13}C NMR ($CDCl_3$) δ 28.0, 53.8, 55.8, 73.4, 80.5, 126.9, 127.5, 128.8, 139.3, 156.0, 172.3. Anal. Calcd. for $C_{15}H_{21}NO_5$: C, 61.00; H, 7.17; N, 4.74. Found: C, 61.18; H, 6.93; N, 4.78.

(2S,3S)-3-(tert-Butoxycarbonylamino)-1-(tert-butyldimethylsiloxy)-3-phenyl-2-propanol (26b). Treatment of **22b** (0.27 g, 1 mmol) under the conditions described above for the preparation of **26a** gave, after column chromatography (hexane/diethyl ether, 60:40), pure **26b** (0.351 g, 92%) as a white solid; mp 44-46 °C; $[\alpha]_D$ +26.8 (c 0.46, $CHCl_3$) [Lit. [2]:

mp 43.5-45.5 °C; $[\alpha]_D$ +25.9 (c 0.21, $CHCl_3$)]; ^1H NMR ($CDCl_3$) δ 0.04 (s, 3H), 0.06 (s, 3H), 0.88 (s, 9H), 1.40 (s, 9H), 1.82 (bs, 1H), 3.40 (dd, 1H, J = 3.7, 10.2 Hz), 3.53 (dd, 1H, J = 4.3, 10.2 Hz), 3.81 (ddd, 1H, J = 3.7, 4.3, 5.6 Hz), 4.84 (dd, 1H, J = 5.6, 8.6 Hz), 6.00 (d, 1H, J = 8.6 Hz), 7.24-7.46 (m, 5H). ^{13}C NMR ($CDCl_3$) δ -5.0, -4.8, 17.5, 25.6, 27.6, 58.0, 62.5, 73.2, 79.0, 126.8, 127.5, 127.9, 138.9, 154.6. Anal. Calcd. for $C_{20}H_{35}NO_4Si$: C, 62.95; H, 9.25; N, 3.67. Found: C, 62.79; H, 9.38; N, 3.53.

(2S,3S)-2-(Acetoxy)-3-(tert-butoxycarbonylamino)-1-(tert-butyldimethyl-siloxy)-3-phenyl-propane (31). A solution of compound **26b** (0.3 g, 0.786 mmol) in CH_2Cl_2 (5 mL) at room temperature was treated sequentially with pyridine (5 mL) and acetic anhydride (5 mL). The resulting mixture was allowed to stir for 1 h, at which time it was diluted with CH_2Cl_2 (10 mL) and then poured into saturated aqueous $CuSO_4$ (15 mL). After stirring vigorously for 5 min, the layers were separated and the organic layer was sequentially washed with saturated aqueous $CuSO_4$, water and brine. The solution was dried ($MgSO_4$) and concentrated under reduced pressure to give a colorless oil which was subjected to purification by column chromatography on silica gel (hexane/diethyl ether, 60:40), to afford the acetylated product **31** (0.333 g, 100%) as a colorless oil; $[\alpha]_D$ +2.8 (c 0.73, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.02 (s, 3H), 0.04 (s, 3H), 0.93 (s, 9H), 1.40 (s, 9H), 2.06 (s, 3H), 3.59-3.62 (m, 2H), 4.90 (pseudo q, 1H, J = 4.6), 5.06 (m, 1H), 6.37 (d, 1H, J = 8.3 Hz), 7.26-7.30 (m, 5H). ^{13}C NMR ($CDCl_3$) δ -5.7 (2C), 18.1, 21.0, 25.7, 28.3, 56.4, 61.9, 74.3, 79.1, 126.8, 127.5, 128.5, 138.9, 155.7, 170.3. Anal. Calcd. for $C_{22}H_{37}NO_5Si$: C, 62.38; H, 8.80; N, 3.31. Found: C, 62.44; H, 8.98; N, 3.29.

(2S,3S)-2-(Acetoxy)-3-(tert-butoxycarbonylamino)-3-phenyl-1-propanol (32). Compound **31** (0.297 g, 0.7 mmol) was dissolved in THF (15 mL) and treated with Bu_4NF (0.8 mmol, 0.8 mL of a 1.0 M solution in THF) at ambient temperature. After 1h saturated aqueous $NaHCO_3$ (10 mL) was added and the mixture extracted with diethyl ether (3 x 25 mL). The combined organic extracts were washed with brine, dried ($MgSO_4$) and distilled under reduced pressure. Purification of the crude product by column chromatography on silica gel (hexane/diethyl ether, 40:60) gave pure **32** (0.180 g, 83%) as a white solid; mp 128-130 °C; $[\alpha]_D$ +15.6 (c 1.11, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.39 (s, 9H), 2.04 (s, 3H), 2.66 (bs, 1H, ex. D_2O), 3.89 (dd, 1H, J = 6.8, 11.6 Hz), 4.03 (dd, 1H, J = 4.0, 11.6 Hz), 4.14 (dd, 1H, J = 4.8, 6.2 Hz), 4.78 (ddd, 1H, J = 4.0, 4.8, 6.8 Hz), 5.47 (d, 1H, J = 6.2 Hz), 7.24-7.35 (m, 5H). ^{13}C NMR ($CDCl_3$) δ 20.8, 28.3, 56.7, 65.7, 72.0, 80.0, 127.5, 128.0, 149.8, 155.4, 171.1. Anal. Calcd. for $C_{16}H_{23}NO_5$: C, 62.12; H, 7.49; N, 4.53. Found: C, 62.26; H, 7.62; N, 4.44.

(1S)-3-(acetoxy)-1-(tert-butoxycarbonylamino)-1-phenylpropanone (33). Treatment of **32** (0.2 g, 0.65 mmol) under the conditions described above for the preparation

of **30**, by oxidizing **28**, gave, after column chromatography (hexane/diethyl ether, 60:40), pure **33** (0.14 g, 70%) as an oil; $[\alpha]_D$ +9.9 (c 0.41, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.41 (s, 9H), 2.09 (s, 3H), 4.56 (d, 1H, J = 17.0 Hz), 4.75 (d, 1H, J = 17.0 Hz), 5.41 (bs, 1H), 5.64 (bs, 1H), 7.29-7.41 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 20.2, 28.3, 61.9, 66.1, 80.3, 128.0, 128.9, 129.4, 136.1, 150.3, 169.7, 170.5. Anal. Calcd for $C_{16}H_{21}NO_5$: C, 62.53; H, 6.89; N, 4.56. Found: C, 62.70; H, 6.78; N, 4.68.

Methyl (2S,3S)-2-(Acetoxy)-3-(tert-butoxycarbonylamino)-3-phenyl propanoate (35). To a solution of 9.8 mg (0.77 mmol) of oxalyl chloride in 5 mL of dichloromethane at -60°C under argon were added 109 μL (120 mg, 1.53 mmol) of DMSO. After stirring for 10 min, 0.2 g (0.65 mmol) of **32** were added at -60°C. After stirring for 15 min, 0.47 mL (34 mg, 3.36 mmol) of triethylamine were added and the resulting solution was stirred for additional 10 min. The reaction mixture was allowed to warm to room temperature over a 1-h period, 5 mL of water were added, and the mixture was stirred overnight. The organic layer was washed with 1 N hydrochloric acid and water and dried over magnesium sulfate. After the volatile materials were removed with a rotatory evaporator, the residue was taken up in tert-butanol (4 mL) and diluted with an aqueous 1.25 M sodium phosphate buffer solution (2.5 mL). To the resulting mixture an aqueous 1M potassium permanganate solution (4.0 ml) was added with vigorous stirring. After 15 min at ambient temperature, a saturated solution of sodium bisulfite (3 mL) was added and the pH of the mixture was adjusted to 3 with cold (0°C) hydrochloric acid. The resaction mixture was diluted with ethyl acetate (10 mL) and the organic layer was separated. The aqueous layer was extracted with ethyl acetate (2 x 10 mL). The combined organic extracts were dried ($MgSO_4$) and evaporated under reduced pressure. The residue containing the crude acid was taken up in diethyl ether (10 mL) and treated with an ethereal solution of diazomethane. The solvent was evaporated and the residue was purified by column chromatography on silica gel (hexane/diethyl ether, 60:40) to afford the pure methyl ester **35** (71 mg, 50%) as an oil; $[\alpha]_D$ 25.3 (c 0.18, $CHCl_3$) [Lit.[61]: $[\alpha]_D$ +24.8 (c 0.50, $CHCl_3$)]; ^1H NMR (DMSO-d_6, 140 °C) δ 1.40 (s, 9H), 2.01 (s, 3H), 3.68 (s, 3H), 5.12 (dd, 1H, J = 8.2, 6.1 Hz), 5.34 (d, 1H, J = 6.1 Hz), 6.30 (bd, 1H, J = 8.2 Hz), 7.29-7.37 (m, 5H). Anal. Calcd. for $C_{17}H_{23}NO_6$: C, 60.52; H, 6.87; N, 4.15. Found: C, 60.73; H, 6.66; N, 4.21.

Methyl (2S,3S)-3-(tert-Butoxycarbonylamino)-2-hydroxy-3-phenyl propanoate (24b). To a solution of **35** (60 mg, 0.18 mmol) in methanol (5 mL) was added sodium metoxide (27 mg, 0.5 mmol) at room temperature. After stirring for 1 h the reaction mixture was diluted with aqueous NH_4Cl (10 mL) and ethyl acetate (10 mL). The organic layer was separated, washed with brine, dried ($MgSO_4$) and evaporated under reduced pressure to give a residue which after purification by preparative TLC (hexane/diethyl ether, 50:50) afforded

52 mg (98%) of pure **24b** as a white solid. mp 134-136 °C; $[\alpha]_D$ +29.8 (c 0.31, $CHCl_3$) [Lit.[16]: mp 136-137 °C; $[\alpha]_D$ +30.1 (c 0.50, $CHCl_3$)]; ^1H NMR ($CDCl_3$) δ 1.40 (s, 9H), 2.80 (bs, 1H), 3.72 (s, 3H), 4.60 (d, 1H, J = 4.2 Hz), 5.12 (dd, 1H, J = 4.2, 8.2 Hz), 5.72 (bd, 1H, J = 8.2 Hz), 7.26-7.37 (m, 5H). ^{13}C NMR ($CDCl_3$) δ 28.0, 52.5, 56.1, 73.9, 80.6, 127.4, 128.2, 128.6, 137.0, 156.4, 171.9. Anal. Calcd. for $C_{15}H_{21}NO_5$: C, 61.00; H, 7.17; N, 4.74. Found: C, 60.85; H, 7.03; N,4.70 .

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