Chiral Auxiliaries as Docking/Protecting Groups in Biohydroxylation: The Hydroxylation of Enantiopure Spirooxazolidines Derived from Cyclopentanone Using *Beauveria bassiana* ATCC 7159

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The aim of this work was to explore the scope and limitations of chiral docking/protecting groups as chiral auxiliaries in the biohydroxylation of unactivated methylene groups. As a model compound, cyclopentanone **1** was reacted with a range of enantiomerically pure amino alcohols **2a**–**n** as well as **7a** and **b**, varying substituents R^1 and R^2. The resulting chiral spirooxazolidines **3a**–**n** as well as **8a** and **b** were exposed to the fungus *Beauveria bassiana* ATCC 7159 and the resultant hydroxylated products were characterised. Introducing chirality into the substrate before the fermentation was found to have a major effect on the course of the biohydroxylation relative to the achiral analogue **3a** (Table 1, entry 1). The nature of R^1/R^2 influenced both the product yield and the optical purity of the products (e.g. Table 1, entry 2). In addition, the absolute configuration of the final product **6** could be dictated solely by the nature of the docking/protecting group used (compare entry 8 with entry 9). Concerning the chain length of R^1/R^2, it was found that hydroxylation only took place in the cyclopentane ring when the heterocyclic ring was substituted with a methyl, ethyl or isopropyl (entries 2–5, 8, 9, 15, and 16). With increasing chain length, where R^1/R^2 are propyl, isobutyl or *sec*-butyl groups, a mixture of products was obtained in which the hydroxyl group was either on the cyclopentane ring or on the side-chain (entries 10–14).

Introduction

The chemical hydroxylation[1,2] of unactivated C−H bonds in organic compounds, in particular secondary and primary carbon atoms, remains an obstacle in classical synthetic chemistry. Bioconversion processes[3] for such difficult transformations represent a valuable alternative to "mainstream" preparative chemistry. Although biohydroxylations[4] performed by whole cells are well established in the production of medicinally valuable steroids and industrially important terpenes, applications in general synthetic chemistry are in relative infancy because of a number of drawbacks. Despite proposed models,[5−7] problems are experienced with the predictability of the hydroxylation position and not all functional groups remain intact upon exposure to fermentation conditions because they are susceptible to undesired reactions such as reduction or oxidation.[8,9]

To develop a general approach which could be used by organic chemists for the preparation of intermediates useful in synthesis, the concept of docking/protecting groups was devised.[9−12] The aim of this concept was not only to protect vulnerable functional groups in the substrate, but also to promote and direct the course of the hydroxylation.[9−12] Ease of substrate handling (UV activity for TLC detection, modification of polarity and volatility) was also envisaged as a further advantage of this approach. This concept has been successfully applied to carboxylic acids,[9,12] alcohols,[9] aldehydes,[13] and ketones[9] which were hydroxylated by whole cell systems as the corresponding benzoxazoles, isosaccharine derivatives, *N*-benzoylated oxazolidines and *N*-benzoylated spirooxazolidines, respectively.

In particular, for the hydroxylation of ketone substrates, it was found that the well-known fungus *Beauveria bassiana* ATCC 7159[4a,14] was particularly suited to hydroxylate *N*-benzoylspirooxazolidine derivatives.[9] These substrates were easily formed by a simple two-step, one-pot reaction. For example, cyclopentanone **1** was treated with amino eth-

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anol **2a** to give a spirooxazolidine which was subsequently benzoylated in situ with benzoyl chloride to afford **3a**. However, although **3a** led to hydroxylated compound **4a** in reasonable isolated yield, optical purity was far from being useful for synthetic purposes (Table 1, entry 1).[9] This result is in agreement with the literature because many other examples of moderate stereoselectivity have been reported[4,15] for the hydroxylating microorganism *Beauveria bassiana*. However, despite this general trend, a few highly selective biohydroxylations (80−90% optical purities) have also been observed[7,16,17] for this fungus. This encouraged us to attempt to improve the selectivity of the hydroxylation under consideration.

All attempts to find an alternative docking/protecting group for ketones were unsuccessful because selectivity was not improved.[11,18] Consequently, employing spirooxazolidine derivatives to apply the docking/protecting group principle to ketones was considered to be the best strategy. In addition, the use of other microorganisms, for example *Cunninghamella blakesleeana* DSM 1906 and *Bacillus megaterium* DSM 32, was not found to improve the overall yield and the optical purity of product **4a**.[19]

Methods to optimise the given substrate structure, sometimes coined "substrate engineering",[20−22] were considered as a way of achieving high yields and selectivities. One form of substrate engineering which has enjoyed good success[23] in the field of organic synthesis is the use of chiral auxiliaries.[23] It is well-known that the introduction of a stereogenic centre into the starting material can improve the stereoselectivity of a chemical transformation. However, this approach to increase selectivity has been reported only occasionally in the biotransformation field, for example to improve the enantioselectivity of lipase-catalysed hydrolysis and transesterification.[24,25] Bearing this in mind, it was envisaged that the use of a chiral amino alcohol instead of simple amino ethanol for preparing spiroxazolidine derivatives would have a favourable effect on the course of the biohydroxylation with respect to the optical purities of the products. In addition, it was hoped that it might be possible to obtain either configuration of the alcohols, depending on the configuration of the chiral auxiliary. We wish to report our investigations concerning the use of chiral amino alcohols as docking/protecting groups for the biohydroxylation of cyclic ketones.

Results and Discussion

To examine the scope and limitations of chiral docking/protecting groups in biohydroxylation, the model ketone cyclopentanone **1** was systematically reacted with a range of chiral amino alcohols, namely **2b**−**2n** as well as **7a** and **7b**. In this manner, the effect of subtle substrate structural changes − that is changes of R^1 and R^2 with respect to chain length and structure − on the course of the biohydroxylation could be examined.

Simple and Unbranched Side-Chain Substrates

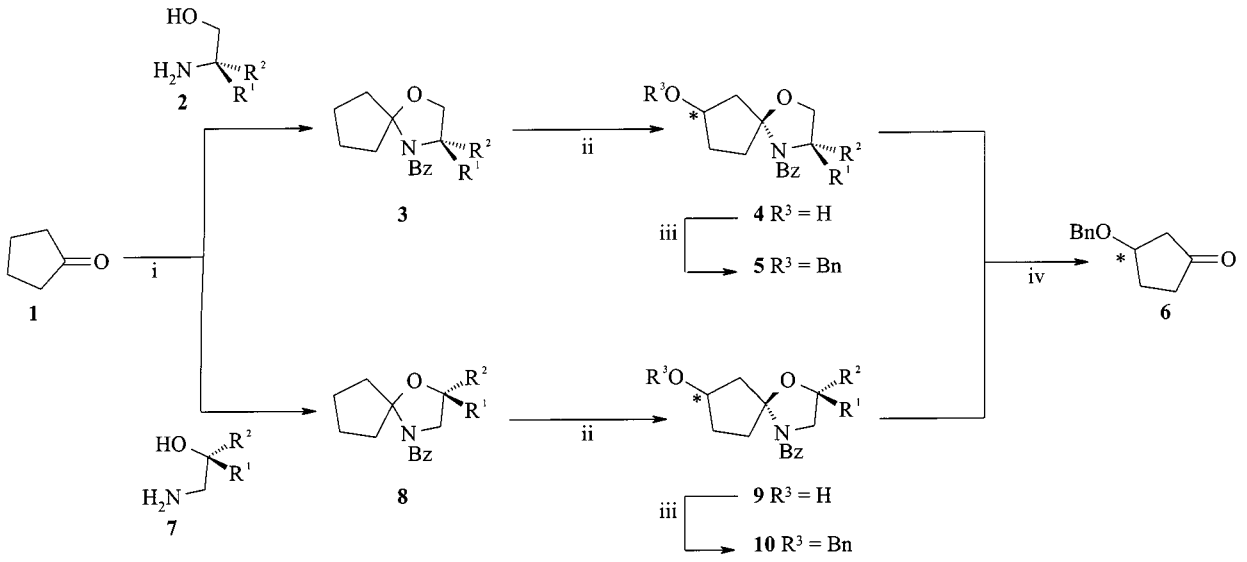
Commercially available (2*R*)-2-amino-1-propanol **2b** (98% *ee*) was treated with cyclopentanone **1** to give crystalline spirooxazolidine **3b** in good isolated yield (75%).[9] Substrate **3b** (Table 1, entry 2) was then incubated with *Beauveria bassiana* ATCC 7159. Satisfyingly, crystalline product **4b** was obtained in 84% isolated yield as a mixture of two

Table 1. Influence of the docking/protecting group on the outcome of the biohydroxylation

Entry	Substance	**3** yield (%)[b]	**4** yield (%)[b]	*de* (%)[c]	**5** yield (%)[b]	*de* (%)[c]	config.	**6**[a] yield (%)[b]	*ee* (%)[d]
1	**a**	63	60	40	73	n.d.	*R*	43	40
2	**b**	75	84[e]	90	85[e]	89	*R*	61	84
3	**c**	89	23	50	74	33	*R*	74	29
4	**d**	76	82	81	75	75	*R*	77	76
5	**e**	71	53[e]	47	71	45	*R*	71	53
6	**f**	76	0[f]	–	–	–	–	–	–
7	**g**	94	0[f]	–	–	–	–	–	–
8	**h**	81	42[e]	71	77	80	*R*	68	78
9	**i**	75	38[e]	20	80	33	*S*	49	20
10	**j**	83	54[e][g]	17	65	13	*R*	65	13
11	**k**	84	[g]	–	–	–	–	–	–
12	**l**	63	0[h]	–	–	–	–	–	–
13	**m**	52	[i]	–	–	–	–	–	–
14	**n**	84	[j]	–	–	–	–	–	–

Entry	Substance	**8** yield (%)[b]	**9** yield (%)[b]	*de* (%)[c]	**10** yield (%)[b]	*de* (%)[c]	config.	**6**[a] yield (%)[b]	*ee* (%)[d]
15	**a**	50	71	83	41	89	*R*	82	91
16	**b**	39	20	53	53	73	*R*	73	71

[a] The configuration, yield, and *ee* of benzyloxy ketone **6** is given as it was observed when performing the biohydroxylation on compounds **3a**−**3n** as well as **8a** and **8b**. − [b] Isolated yields only. If unchanged substrate was also recovered, the amount was taken into consideration when calculating yield. − [c] *de* was calculated with respect to the major stereoisomer and determined by NMR and HPLC. − [d] *ee* was calculated with respect tot he major enantiomer and determined by chiral GC. − [e] Major isomer was crystalline. − [f] Only unchanged starting was recovered. − [g] For **3j**: besides products **4j**, additional products were obtained as shown in Scheme 6. For **3k**: similar to **3j** a complex mixture was observed and this was not further investigated. − [h] Although the substrate was consumed, product formation was not observed. − [i] Here, hydroxylation occurred solely on R^2, see Scheme 6. − [j] A complex mixture was afforded which was not further investigated.

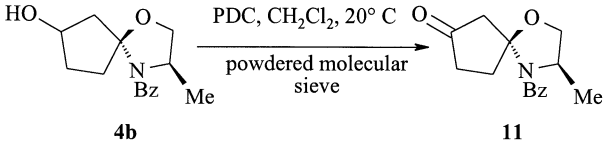


2 - 5	a	b	c	d	e	f	g	h	i	j	k	l	m	n	7 - 10	a	b
R^1	H	Me	H	Et	H	Ph	H	*i*Pr	H	Pr	H	*i*Bu	H	H	R^1	Me	H
R^2	H	H	Me	H	Et	H	Ph	H	*i*Pr	H	Pr	H	*i*Bu	*sec*Bu	R^2	H	Me

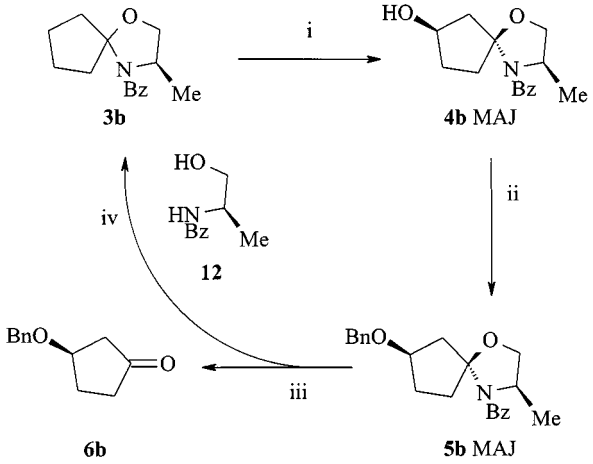
Scheme 1. Variation of the docking/protecting group for the biohydroxylation of cyclopentanone **1** with *Beauveria bassiana* ATCC 7159. The configuration of the stereogenic centre marked with the asterisk (*) is given in Table 1. Reagents and conditions: (i) amino alcohol **2** or **7**, K_2CO_3, CH_2Cl_2, 20 °C, 24 h then BzCl, 20 °C, 24 h; (ii) *Beauveria bassiana* ATCC 7159; (iii) BnBr, NaH, THF/DMF, 20 °C; (iv) IR 120 (H^+, cat), CH_3CN, 20 °C

chromatographically very similar isomers (*de* 90%, as determined by NMR and HPLC). The diastereomeric excess of this mixture could be further improved by recrystallisation.

As previously observed with achiral compound **3a**, hydroxylation occurred on the cyclopentane ring (Scheme 1) of **3b**. This conclusion was based on NMR experiments conducted with alcohol **4b** and ketone **11**, the latter having been synthesised from the former (Scheme 2).[26] Spectroscopic data from ketone **11** indicated that functionalisation had taken place on carbon atom 7[27] as the pair of protons attached to carbon atom 6 clearly gave rise to two doublets (δ = 3.50 and 2.40; J = 18.2 Hz). Before docking/protecting group removal, which was carried out under mild acidic conditions, compound **4b** was derivatised in order to prevent possible elimination of the alcohol as well as to ease detection (TLC) of the released ketone. For this purpose, the benzyl group was chosen because of its UV activity, acid stability as well as the fact that the resulting ketone (**6**) could also be prepared chemically as either enantiomer,[9] this attribute being very valuable for the assignment of the configuration. Benzylation of **4b** under standard conditions[28] afforded crystalline **5b** in good yield (85% yield, 89% *de* as determined by NMR). Removal of the docking/protecting group was effected smoothly with [H^+] exchange resin (IR 120) in acetonitrile at room temperature to give ketone **6** (61% yield). It should be noted at this point that the cleaved docking/protecting group **12** can be recycled to obtain additional amounts of starting material **3b** as shown in Scheme 3 (depicted for **4b** MAJ). This is an important criterion for the efficiency of a chiral auxiliary.[23]



Scheme 2. Conversion of alcohol **4b** to ketone **11**



Scheme 3. Recycling of the chiral docking/protecting group. Reagents and conditions: (i) *Beauveria bassiana* ATCC 7159; (ii) BnBr, NaH, THF/DMF, 20 °C; (iii) IR 120 (H^+, cat), CH_3CN, 20 °C; (iv) cyclopentanone **1**, benzene, reflux, pyridinium tosylate, molecular sieves

Once ketone **6** had been obtained, it was possible to establish the configuration of the newly formed stereogenic centre. Isolated ketone **6** was compared (GC) with chemic-

ally synthesised[29] (*S*)-3-benzyloxycyclopentanone (**6**) and found to have the (*R*)-configuration with an *ee* of 84%.

An additional advantage of the chiral docking/protecting group was evident upon X-ray analysis of the hydroxylation products afforded from **3b**. After chromatography and crystallisation, suitable crystals for both the minor (as the alcohol, **4b** MIN) and major (as the benzylated derivative, **5b** MAJ) isomers could be obtained (Figure 1). Because the configuration of the stereogenic centre in the docking/protecting group was already known, the configuration at carbon atom 7 could be confirmed and, more importantly, the absolute configuration of spiro-carbon atom 5 could also be evaluated. Determining the configuration of carbon atom 5 was deemed to be especially important because this knowledge could give insight into the stereochemical course of the biohydroxylation. It should also be mentioned at this point that upon removal of the docking/protecting group, this stereogenic centre is destroyed and so this information is lost. As can be seen more clearly from Scheme 4, hydroxylation *anti* or *syn* to the nitrogen moiety can give ketone **6** with the same configuration, thereby making the *anti* or *syn* "mode" of hydroxylation indistinguishable. NOE measurements failed to reveal the absolute configuration of this compound because of the large distance between the docking/protecting group of known chirality and the newly introduced stereogenic centre. Consequently, from XRD crystal-structure data, it could be concluded that hydroxylation had proceeded *anti* to the nitrogen moiety in both isomers. Indeed, as many examples of such hydroxylations *anti* to the nitrogen moiety can be found in the literature when employing *Beauveria bassiana* as the hydroxylating microorganism, this observation was in full agreement with previous findings.[4a]

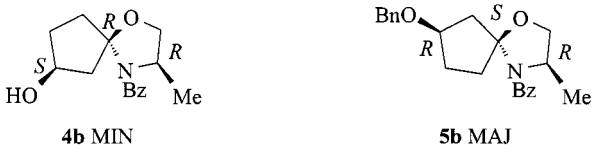
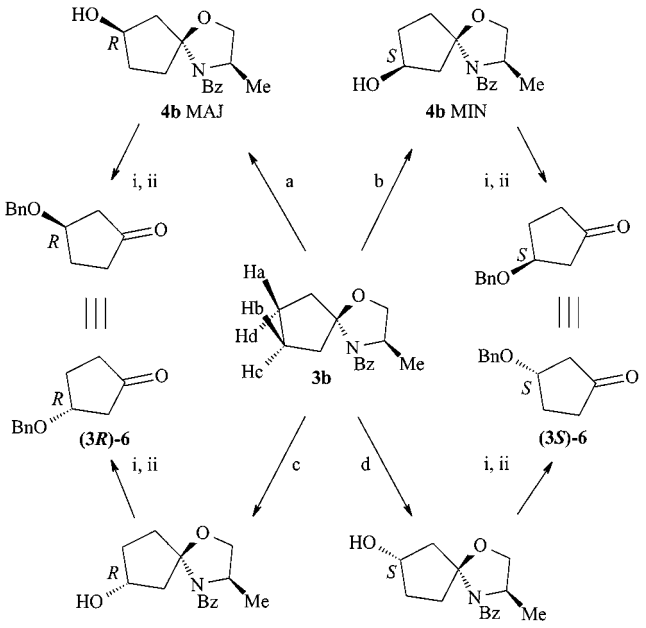


Figure 1. Configuration of compounds **4b** MIN and **5b** MAJ as determined by X-ray crystal-structure analysis

In summary, compared with the achiral analogue **3a** as starting material, the isolated product yield (**4a** 60% c.f. **4b** 84%) and diastereomeric purity (**4a** 40% c.f. **4b** 90% *de*) were markedly improved by the use of chiral auxiliary **2b**.

In order to examine the scope and limitations of these chiral docking/protecting groups, substrates **3c**−**3n** as well as **8a** and **8b** were also prepared. As can be seen from Table 1, all compounds could be synthesised in good yields as previously described for **3a** and **3b**.[9] The fermentations were then carried out under the same conditions as for **3b** and the hydroxylated products were isolated and characterised (NMR, HPLC, GC) as previously described.

As can be concluded from Table 1, hydroxylation occurred solely on the cyclopentane ring when the heterocyclic ring was substituted with either a methyl (entries 2, 3, 15, and 16), ethyl (entries 4 and 5) or isopropyl (entries 8 and 9) group. Nonetheless, employing substrate **3b** was still



Scheme 4. Hydroxylation of substrate **3b** *syn* or *anti* to the nitrogen atom. Reagents and conditions: Hydroxylation step; (a) overall substitution of Ha; (b) overall substitution of Hb; (c) overall substitution of Hc; (d) overall substitution of Hd; (i) BnBr, NaH, THF/DMF, 20 °C; (ii) IR 120 (H^+, cat), CH_3CN, 20 °C

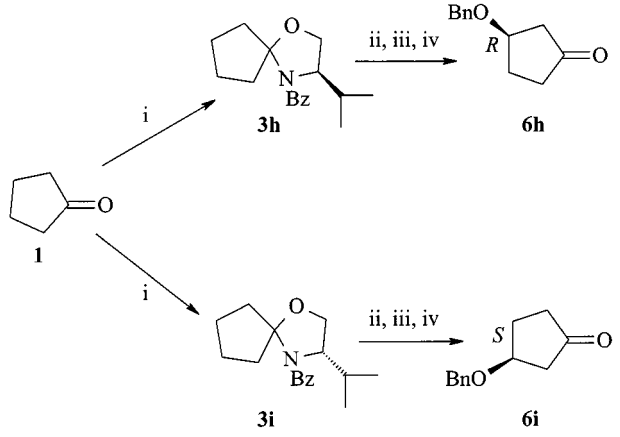
found to be superior with respect to the isolated product yield and to the diastereomeric excess. Interestingly, for substrates **3f** and **3g**, where phenyl groups were attached to the heterocyclic ring, hydroxylation was not observed for either enantiomer and only unchanged starting material was recovered. These observations could be accounted for by the low solubility of these substrates in the fermentation medium or by the unsuitability of this bulky docking/protecting group for this transformation.

Regarding general trends, it is interesting to note that differences in product yield and diastereomeric excess can be seen when comparing the enantiomeric substrate pairs. As depicted in Scheme 1, substrates where carbon atom 2 has the (*S*)-configuration or carbon atom 3 the (*R*)-configuration, for example R^1 = methyl or ethyl, afforded hydroxylated products in higher isolated yield and superior diastereomeric excess (**4b**, 84% yield, 90% *de*; **4d**, 82% yield, 81% *de*; **9a**, 71% yield, 83% *de*) than the respective enantiomer, i.e. R^2 = methyl or ethyl (**4c**, 23% yield, 50% *de*; **4e**, 53% yield, 47% *de*; **9b**, 20% yield, 40% *de*). Evidently, the existing stereogenic centre in the respective substrate had a notable influence on the outcome of the biohydroxylation. The absolute stereochemistry of a substrate affecting the selectivity of the biohydroxylation has been previously observed with *Beauveria bassiana* by Furstoss and coworkers.[16] Employing an enantiomeric pair of α-pinene derivatives, it was found that the site of hydroxylation was entirely controlled by the absolute stereochemistry of the substrate, in other words, each enantiomer gave rise to a different product. In addition, unlike the spirooxazolidine derivatives, the hydroxylation proceeded with high selectivity for both enantiomers and the two respective products were obtained with high optical purity (85−90%).

The major influence of one stereogenic centre on the product yield and the diastereomeric excess would suggest these substrates to be interesting for molecular modelling studies and such investigations could lead to the refinement of existing hydroxylation models.[5−7] The accuracy of an active-site model is strongly dependent on the knowledge that the reaction is catalysed by either one enzyme or by a number of closely related isozymes.[14] However, recent studies conducted by Holland and co-workers[14] suggest that *Beauveria bassiana* exhibits up to at least four distinct hydroxylase enzyme activities. A consequence of this observation is that in order to obtain a reliable "active-site model" for these spirooxazolidine substrates, further investigations into the nature of the hydroxylating enzyme/s would be important. Efforts in this context are currently in progress.

Branched Side-Chain Substrates

Upon examination of entries 8 and 9, it is clear that the isopropyl substrates **3h** and **3i** provided very interesting results. Depending on the configuration of the docking/protecting group used, either the (*S*)- or (*R*)-ketone **6** was obtained (Scheme 5). While (*R*)-**3h** afforded (*R*)-ketone **6** (78% *ee*), the (*S*)-enantiomer **3i** furnished (*S*)-ketone **6** (20% *ee*). Being able to choose, at will, the configuration of the introduced hydroxyl moiety by selecting the appropriate docking/protecting group has significant preparative potential and will be investigated further by this group.



Scheme 5. Synthesis of (3*R*)- or (3*S*)-benzyloxycyclopentanone **6** from cyclopentanone **1**. Reagents and conditions: (i) amino alcohol **2h** or **2i**, K_2CO_3, CH_2Cl_2, 20 °C, 24 h then BzCl, 20 °C, 24 h; (ii) *Beauveria bassiana* ATCC 7159; (iii) BnBr, NaH, THF/DMF, 20 °C; (iv) IR 120 (H^+, cat), CH_3CN, 20 °C

An insight into the possible course of the hydroxylation was also provided by alcohols **4h** and **4i**. Similar to the hydroxylated products obtained from **3b**, column chromatography and recrystallisation furnished crystals for both isomers (**4h** MAJ and **4h** MIN) and these were suitable for X-ray crystal-structure analysis. In addition, an X-ray crystal structure for the major isomer of product **4i** (**4i** MAJ) could also be obtained. Unfortunately, crystals of the minor isomer of **4i** suitable for X-ray crystal structure analysis could not be grown. In Figure 2, the X-ray crystal structures of all isomers are depicted.

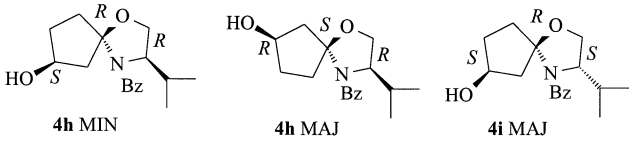


Figure 2. Configuration of compounds **4h** MIN, **4h** MAJ, and **4i** MAJ as determined by X-ray crystal-structure analysis

An interesting point is the fact that **4i** MAJ is the enantiomer of **4h** MAJ. This observation is reflected by the similar melting points (**4h** MAJ; M.p. 127.5−128.5 °C and **4i** MAJ; M.p. 127.0−128.0 °C), optical rotations (**4i** MAJ; $[\alpha]_D^{20}$ = −98.6 and **4h** MAJ; $[\alpha]_D^{20}$ = +93.5) and NMR spectroscopic data (Experimental Section) acquired for these compounds. Upon comparison of the experimental data obtained for **4h** MIN with **4i** MIN, for which an X-ray crystal structure could not be obtained, it is not unreasonable to assume that these compounds are also an enantiomeric pair (**4h** MIN; m.p. 169.5−170.5 °C, $[\alpha]_D^{20}$ = −82.6 and **4i** MIN; m.p. 174.0−174.5 °C, $[\alpha]_D^{20}$ = +79.6). The discrepancies evident between the melting points and optical rotations of these enantiomeric pairs could be explained by differences in their respective enantiomeric purities. However, because this parameter could not be evaluated (HPLC), full evidence for this proposal cannot be provided.

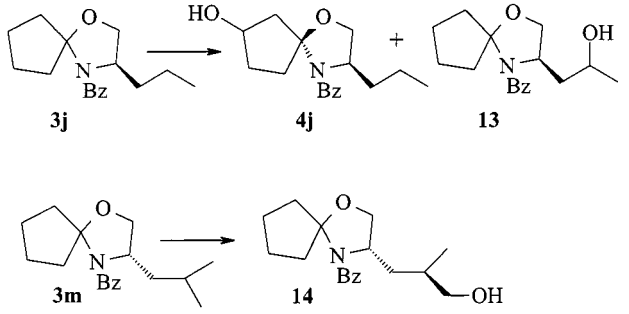
At first glance, it is clear from Figure 1 and 2 that regardless of the configuration of the hydroxyl group and the docking/protecting group, hydroxylation always occurred *anti* to the nitrogen moiety. This observation was also made for **4b** MAJ and **4b** MIN. Owing to the fact that experimental results support the view that **4i** MIN is the enantiomer of **4h** MIN, it is reasonable to assume that hydroxylation also proceeded *anti* to the nitrogen atom in this compound. As mentioned previously, this finding is in full accordance with the literature.[4a]

Concerning the general stereochemical course of the hydroxylation, for this set of compounds it seems that hydroxylation always occurred from the same side of the molecule. A similar observation was reported by Palmer et al.[30] employing the same microorganism to hydroxylate a lactam derivative. In addition, we found the same outcome for the benzoxazole substrates,[12] although another microorganism was employed in this case (*Cunninghamella blakesleeana* DSM 1906). However, as mentioned previously, until it is established that only one enzyme or closely related isozymes are responsible for the production of these hydroxylated products, any conclusions concerning the course of the hydroxylation, although tempting, are uncertain.

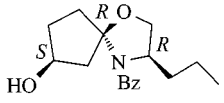
Long Side-Chain Substrates

Increasing the chain length of R^1/R^2 had a pronounced adverse effect on the regioselectivity of the hydroxylation, as can be seen from Table 1 (entries 10−14) and Scheme 6. Regardless of the enantiomer employed, propyl-substituted substrates **3j** and **3k** (Table 1, entries 10 and 11, respect-

ively) furnished complex mixtures after exposure to *Beauveria bassiana*. Taking this result into account, only one derivative was investigated in detail, namely **3j**. After exposure to *Beauveria bassiana*, a number of products were isolated from the fermentation broth by column chromatography. As the main product, the expected derivative **4j** was afforded in moderate isolated yield (54%) and very poor *de* (17%). The major (**4j** MAJ) and the minor isomer (**4j** MIN, a white crystalline solid) could be separated by a combination of chromatography and crystallisation. For **4j** MIN, the absolute configuration was elucidated by X-ray crystal-structure analysis (Figure 3). As expected, hydroxylation had again taken place *anti* to the nitrogen moiety. A minor product (**13**, isolated yield 1.5%) was also obtained which was tentatively assigned as having the structure depicted in Scheme 6, in which the penultimate carbon atom of the docking/protecting group had been hydroxylated [(ω − 1)-hydroxylation]. Investigations concerning the configuration of this newly introduced stereogenic centre are currently in progress. The other products which were also isolated have not been identified to date owing to the small amounts involved and to the presence of impurities. However, it can be said that evidence for hydroxylation on the terminal carbon atom (ω-hydroxylation) could not be found (NMR).



Scheme 6. Loss of hydroxylation regioselectivity upon extension of side-chain length



4j MIN

Figure 3. Configuration of compound **4j** MIN as determined by X-ray crystal-structure analysis

Homologation of the side-chain by an additional carbon atom to give the *iso*-butyl derivative **3m** (Table 1, entry 13) further enhanced this effect to such an extent that the sole product observed was syrupy ω-hydroxylated **14** (13% yield). As the hydroxylation had generated a new stereogenic centre, it was necessary to establish the absolute configuration of this compound by X-ray crystal-structure analysis. Esterification of **14** with (1*S*)-camphanic acid produced a crystalline compound[31] suitable for this method. As indicated in Scheme 6, the newly formed centre was found to have the (*R*)-configuration. Because unchanged starting material **3m** was not recovered from this transformation, it can be concluded that substrate **3m** was predominantly metabolised through general pathways.[32] Concerning the (*R*)-enantiomer **3l** (Table 1, entry 12), this compound was totally metabolised by *Beauveria bassiana* and products could not be detected (TLC).

It was also of interest to determine if the addition of a second stereogenic centre into the docking/protecting group would have an effect on the course of the biohydroxylation. To this end, diastereoisomer **3n** was prepared and subjected to *Beauveria bassiana* in the usual manner. As can be seen from Table 1 (entry 14), only a complex mixture of products was afforded in low yield after exposure to this fungus and this was no longer investigated.

The results disclosed above suggest that extending the side-chain R^1 beyond a certain length reduces the regioselectivity of the hydroxylation considerably, even to the point that either mixtures are afforded, the substrate is completely metabolised or only side-chain hydroxylation takes place. Consequently, this was not investigated further. Existing hydroxylation models[5−7] for *Beauveria bassiana* state that the distance between the carbon which is hydroxylated and the carbonyl oxygen of a benzamide or carboxyl oxygen of a carbamate group is approximately 5.5 Å. It has already been mentioned that these models have to be used with caution because it is not known which enzymes are responsible for a particular conversion. However, in the case of these long side-chain substrates, it is not unreasonable to assume that two modes of binding which satisfy the 5.5 Å distance criterion are possible: one binding mode where hydroxylation takes place on the cyclopentane ring and another where hydroxylation takes place on the side-chain of the docking/protecting group.

Conclusion

The results presented show that docking/protecting groups can be successfully applied as chiral auxiliaries to increase the diastereomeric excess of the hydroxylated products obtained. More importantly, employing docking/protecting groups **2h** and **2i**, the absolute configuration of the hydroxylation product **6** could be chosen. In addition, yields of hydroxylated products could be increased and product characterisation with NMR and X-ray crystal-structure analysis was simplified.

Experimental Section

General Methods: All chemicals were purchased from either Aldrich or Fluka. When required, chemicals and solvents were purified according to Perrin and Armarego.[33] All chiral amino alcohols, apart from **2i**, **2j**, and **2k** which were prepared from the respective amino acids,[34] were commercially available. − Optical rotations were measured on a DIP-370 Digital Polarimeter (Japan Spectroscopic Co., Ltd). − Melting points (uncorrected) were determined in open capillaries using a Büchi 530. − ^{1}H and ^{13}C NMR spectra were recorded on either a Gemini 200 (Varian) or MSL 300 (Bruker). HETCOR, DEPT and COSY experiments were carried out as required. $CDCl_3$ was used as solvent and as internal stand-

ard unless otherwise stated. Before use, the $CDCl_3$ was filtered through a short plug of basic alumina to remove traces of acid. The minor isomer is shown in italics. − Mass spectra (EI, 70 eV) were recorded on a Kratos Profile HV-4 double-focussing magnetic sector instrument equipped with direct insertion (DI). Relative intensities are given in brackets. − Chiral HPLC was determined with a JASCO system containing pump 880-PU, UV-detector 875-UV (detection at 238 nm), and AXXIOM Model 727 chromatography software. The chiral column used was a CHIRALCEL OD-H unless otherwise stated (flow rate: 0.50 mL/min, eluent: *n*-heptane/2-propanol, 7:3 unless otherwise stated). For an improved separation, the column was cooled to 10 °C. − GC was performed with a HP 5890 series II plus equipped with a HP 5 (25m) and a FID. Chiral GC was measured on a Lipodex E (Macherey−Nagel). − LC was performed on Silica gel 60 (Merck, 70−230 mesh) using mixtures of ethyl acetate and petroleum ether unless otherwise stated. − TLC was performed on Silica gel 60 F254 aluminium plates (Merck) and compounds detected with UV (254 nm) and spraying with either reagent A (5% vanillin in concentrated H_2SO_4) or reagent B (10% H_2SO_4, 10% $(NH_4)_6Mo_7O_{24} \cdot 4\,H_2O$, and 0.8% $Ce(SO_4)_2 \cdot 4\,H_2O$ in water). The TLC plates were then developed on a hot plate. Unless otherwise stated, mixtures of petroleum ether/ethyl acetate were used as eluent. − Solvents needed for recrystallisation were filtered through basic alumina (ALDRICH, Basic Brockmann I, 150 mesh) prior to use.

Microorganism and Medium: The fungus *Beauveria bassiana* ATCC 7159 (DSM 1344) was obtained from DSM (Braunschweig, Germany). Stock cultures of the organism were maintained on PD (Difco) agar slants (per litre: 24 g potato-dextrose broth and 15 g agar), stored at 4 °C and subcultured every 4 weeks at room temperature. Medium E was employed for the fermentations. Medium E consisted of (per litre) 5 g of malt extract (Merck), 10 g of glucose, 5 g of peptone from meat (Merck), 2 g of yeast extract (Oxoid) and 2 g of KH_2PO_4.

General Procedure. − Fermentation Conditions and Product Isolation: Stage I cultures (70 mL) were inoculated with 1 cm^2 of a Petri-dish culture (1−2 weeks old) and incubated for 72 h in 300 mL baffled shaking flasks at 25 °C. Stage II cultures were inoculated (10%) aseptically with stage I culture and the fermentations were performed either in a Biostat M fermentor (Braun, 1.5 L-glass vessel, agitation was provided by 3 Rushton rotors and kept at 400 rpm) or in a Bioengineering AG model 1523 (16 L-stainless steel vessel with a working volume of 11 L, agitation was provided by 2 Rushton rotors and kept at 250−400 rpm). For both fermentors, the pH was measured with a combined glass electrode (Ingold, Urdorf, Switzerland) and kept constant at pH 7.0. Temperature was determined with a Pt-100 sensor and maintained at 25 °C. Dissolved oxygen was measured with a polarimetric electrode (Ingold). At the beginning of the stationary phase (generally after 32 h of growth) the substrate was added aseptically (usually 0.4918 mmol/L, the induction phase) after it had been dissolved in minimal amounts of EtOH. The second substrate addition (usually 2.459 mmol/L) occurred at the late stationary phase (generally after an additional 15 h). Typically, 60 to 160 h after the first addition of substrate, which is termed as the "total fermentation time", the hydroxylation was complete (TLC, GC). The concentrations of products and substrates were determined by gas chromatography. Samples were taken by aseptically removing 5 mL of the fermentation broth and extracting with ethyl acetate (2 mL). The organic phase was then measured directly without drying.

Immediately after the fermentation was complete, the culture broth was filtered and both the filtrate and biomass were extracted separately (filtrate: 3 × 300 mL ethyl acetate per litre; biomass: 3 × 150 mL). All organic phases were combined, dried over sodium sulfate, and evaporated under reduced pressure at 35 °C to yield a crude product. This was then purified by column chromatography employing mixtures of petroleum ether/ethyl acetate unless otherwise stated. Yields were calculated after having taken into consideration the amount of substrate and product lost through sample taking and the amount of starting material recovered after chromatography.

General Procedure. − Synthesis of 3b: In a manner similar to that described by Saavedra,[35] potassium carbonate (3.680 g, 26.6 mmol) was suspended in dry dichloromethane (10 mL) in a round-bottomed flask fitted with a drying tube. To this mixture, cyclopentanone **1** (1.800 g, 21.4 mmol) and (2*R*)-2-amino-1-propanol **3a** (1.000 g, 13.3 mmol) were added and the mixture was stirred at room temperature for 24 h. Subsequently, the heterogeneous reaction mixture was cooled (ice bath) and benzoyl chloride (1.870 g, 13.3 mmol) slowly added. After the addition, the mixture was allowed to reach room temperature. After 24 h, the mixture was filtered and the filtrate diluted with dichloromethane (100 mL). This was then quickly washed with aqueous HCl (5%, 1 × 100 mL), saturated aqueous $NaHCO_3$ (1 × 100 mL) as well as water (2 × 100 mL) and the organic phase was dried over Na_2SO_4. The pale yellow solution was filtered and the filtrate was concentrated down under reduced pressure to give an orange oil. Column chromatography (petroleum ether/ethyl acetate, 10:1) was then used to isolate the title product **3b** (2.450 g, 75% yield, for additional experimental data please see below) as a pale yellow solid.

General Procedure for Docking/Protecting Group Recycling. − Synthesis of 3b: In a round-bottomed flask, cyclopentanone **1** (1.180 g, 14.0 mmol) was dissolved in dry benzene (100 mL) and (2*R*)-2-benzoylamino-1-propanol **12**[36] (1.940 g, 10.8 mmol) as well as pyridinium tosylate (0.810 g, 3.24 mmol) added. The mixture was heated at reflux after a dropping funnel containing a small plug of glass wool and molecular sieves (4 Å) as well as a reflux condenser had been fitted to the round-bottomed flask. After 24 h, the mixture was set aside to cool, diethyl ether (100 mL) was added and the mixture was filtered. The filtrate was then washed with saturated aqueous $NaHCO_3$ (1 × 200 mL) as well as saturated aqueous NaCl (1 × 200 mL) and the organic phase was dried with Na_2SO_4. The solution was filtered and the filtrate was concentrated under reduced pressure to give a syrup. Column chromatography (cyclohexane/ethyl acetate, 20:1) was then used to isolate the title compound **3b** (1.110 g, 42% yield, for additional experimental data see below) as a pale yellow solid.

General Procedure for the Removal of the Docking/Protecting Group. − Synthesis of Ketone 6: Derivative **5b** (60 mg) was dissolved in acetonitrile (2 mL) and IR 120[H^+] (pre-washed twice with MeOH and once with water) was slowly added with vigorous stirring until a pH of 5−6 was reached (pH paper). Stirring was continued at room temperature until TLC had indicated that starting material was no longer present. Filtration of the reaction mixture to remove the ion-exchange resin and concentration of the filtrate under reduced pressure furnished a residue which was subsequently purified with column chromatography (petroleum ether/ethyl acetate, 6:1) to afford ketone **6** (21.3 mg, 61% yield, for additional experimental details see Table 1).

Substrates 3a−3n and 8a, 8b

Achiral Substrate 3a: The general procedure gave the title compound **3a** from **2a** (10.000 g) as a white solid (23.857 g, 63% yield). − M.p. 60.0−61.0 °C (from hexane /ethyl acetate). − ^1H NMR:

δ = 1.72 [m, 4 H, 8(8′)-H, 7(7′)-H], 1.91 & 2.54 [2 × br. s, 2 × 2 H, 6(6′)-H, 9(9′)-H], 3.52 & 3.88 [2 × t, 2 × 2 H, 2(2′)-H, 3(3′)-H, $J_{2,3}$ = 6.1 Hz], 7.38 (m, 5 H, CO*Ph*). − ^{13}C NMR: δ = 24.9, 35.3 (C-6, C-7, C-8, C-9), 49.0 (C-3), 63.9 (C-2), 104.9 (C-5), 126.8, 128.5, 130.0, 138.1, (CO*Ph*), 167.8 (*C*OPh).

(3*R*)-Me Substrate 3b: The general procedure furnished substrate **3b** from **2b** as a pale yellow solid (2.450 g, 75% yield). − M.p. 65.5−67.5 °C (from petroleum ether/ethyl acetate). − $[\alpha]_D^{20}$ = −79.8 (*c* = 2.1, CH_2Cl_2). − ^{1}H NMR: δ = 0.95 (d, 3 H, C*H*$_3$, *J* = 6.5 Hz,), 1.64−1.98 [m, 6 H, 6-H, 7(7′)-H, 8(8′)-H, 9-H], 2.37−2.71 [2 × br. m, 2 H, 6′-H, 9′-H], 3.60 (m, 1 H, 2-H), 4.00 (m, 2 H, 2′-H, 3-H), 7.40 (s, 5 H, CO*Ph*). − ^{13}C NMR: δ = 20.1 (*C*H$_3$), 24.7, 24.8 (C-7, C-8), 35.0, 36.5 (C-6, C-9), 54.1 (C-3), 70.0 (C-2), 105.0 (C-5), 126.2, 128.5, 129.4, 138.2, (CO*Ph*), 168.1 (*C*OPh).

(3*S*)-Me Substrate 3c: The title substance was prepared from **2c** (1.000 g) according to the general procedure above to give a pale yellow solid (2.920 g, 89% yield). − M.p. 65.5−67.5 °C (from petroleum ether/ethyl acetate). − $[\alpha]_D^{20}$ = +76.4 (*c* = 2.7, CH_2Cl_2). − ^{1}H NMR: δ = 0.93 (m, 3 H, C*H*$_3$), 1.57−2.03 [m, 6 H, 6-H, 7(7′)-H, 8(8′)-H, 9-H], 2.32−2.71 (2 × br. m, 2 H, 6′-H, 9′-H), 3.57 (m, 1 H, 2-H), 3.98 (m, 2 H, 2′-H, 3-H), 7.38 (s, 5 H, CO*Ph*). − ^{13}C NMR: δ = 20.1 (*C*H$_3$), 24.7, 24.8 (C-7, C-8), 35.0, 36.5 (C-6, C-9), 54.1 (C-3), 70.0 (C-2), 105.0 (C-5), 126.2, 128.5, 129.4, 138.2, (CO*Ph*), 168.0 (*C*OPh).

(3*R*)-Et Substrate 3d: The title compound was prepared from **2d** (1.009 g) as described above in the general procedure to afford a white waxy solid (2.240 g, 76% yield). − M.p. 48.0−49.0 °C (from petroleum ether/ethyl acetate). − $[\alpha]_D^{20}$ = −81.1 (*c* = 1.4, CH_2Cl_2). − ^{1}H NMR: δ = 0.65 (t, 3 H, CH_2CH_3, *J* = 7.4 Hz), 1.33 (m, 2 H, CH_2CH_3), 1.60−2.02 [m, 6 H, 6-H, 7(7′)-H, 8(8′)-H, 9-H], 2.31−2.71 (2 × br. m, 2 H, 6′-H, 9′-H), 3.76 (dd, 1 H, 2-H, $J_{2,2'}$ = 8.3 Hz, $J_{2,3}$ = 2.0 Hz), 3.85 (m, 1 H, 3-H), 3.95 (dd, 1 H, 2′-H, $J_{2',3}$ = 5.4 Hz), 7.40 (s, 5 H, CO*Ph*). − ^{13}C NMR: δ = 9.9 (CH_2CH_3), 24.8, 24.8, 26.5 (C-7, C-8, CH_2CH_3), 35.0, 36.4 (C-6, C-9), 59.6 (C-3), 67.3 (C-2), 104.7 (C-5), 126.3, 128.4, 129.4, 137.8 (CO*Ph*), 167.7 (*C*OPh).

(3*S*)-Et Substrate 3e: Substrate **3e** was prepared from **2e** (1.025 g) according to the general procedure to give a white waxy solid (2.129 g, 71% yield). − M.p. 49.0−50.0 °C (from petroleum ether/ethyl acetate). − $[\alpha]_D^{20}$ = +82.3 (*c* = 1.5, CH_2Cl_2). − ^{1}H NMR: δ = 0.63 (t, 3 H, CH_2CH_3, *J* = 7.4 Hz), 1.31 (m, 2 H, CH_2CH_3), 1.60−2.01 [m, 6 H, 6-H, 7(7′)-H, 8(8′)-H, 9-H], 2.31−2.71 (2 × br. m, 2 H, 6′-H, 9′-H), 3.75 (dd, 1 H, 2-H, $J_{2,2'}$ = 8.3 Hz, $J_{2,3}$ = 2.0 Hz), 3.85 (m, 1 H, 3-H), 3.95 (dd, 1 H, 2′-H, $J_{2',3}$ = 5.5 Hz), 7.39 (s, 5 H, CO*Ph*). − ^{13}C NMR: δ = 9.9 (CH_2CH_3), 24.8, 24.8, 26.4 (C-7, C-8, CH_2CH_3), 35.0, 36.3 (C-6, C-9), 59.6 (C-3), 67.3 (C-2), 104.9 (C-5), 126.3, 128.4, 129.4, 138.3 (CO*Ph*), 168.2 (*C*OPh).

(3*R*)-Ph Substrate 3f: Substrate **3f** was synthesised from **2f** (0.100 g) following the general procedure above to afford a white solid (0.170 g, 76% yield) which slightly discoloured upon expose to light and warmth. − M.p. 131.0−133.0 °C (from petroleum ether/ethyl acetate). − $[\alpha]_D^{20}$ = −189.1 (*c* = 1.5, CH_2Cl_2). − ^{1}H NMR: δ = 1.70−2.14 [m, 6 H, 6-H, 7(7′)-H, 8(8′)-H, 9-H], 2.60 & 2.84 (2 × m, 2 × 1 H, 6′-H, 9′-H), 3.82 (dd, 1 H, 2-H, $J_{2,2'}$ = 9.0 Hz, $J_{2,3}$ = 4.0 Hz), 4.25 (dd, 1 H, 2′-H, $J_{2',3}$ = 6.4 Hz), 4.80 (dd, 1 H, 3-H), 6.87−7.28 (m, 10 H, *Ph*, CO*Ph*). − ^{13}C NMR: δ = 24.9, 25.0 (C-7, C-8), 35.2, 35.8 (C-6, C-9), 62.9 (C-3), 71.9 (C-2), 106.1 (C-5), 126.1, 126.4, 127.5, 128.0, 128.4, 128.5, 129.1, 138.0, 141.3 (CO*Ph*, *Ph*), 169.1 (*C*OPh).

(3*S*)-Ph Substrate 3g: Substrate **3g** was synthesised from **2g** (0.100 g) following the general procedure above to afford a white solid (0.210 g, 94% yield) which slightly discoloured upon expose to light and warmth. − M.p. 128.0−131.0 °C (from petroleum ether/ethyl acetate). − $[\alpha]_D^{20}$ = +185.8 (*c* = 0.6, CH_2Cl_2). − ^{1}H NMR: δ = 1.64−2.19 [m, 6 H, 6-H, 7(7′)-H, 8(8′)-H, 9-H], 2.61 & 2.86 (2 × m, 2 × 1 H, 6′-H, 9′-H), 3.82 (dd, 1 H, 2-H, $J_{2,2'}$ = 9.0 Hz, $J_{2,3}$ = 4.0 Hz), 4.25 (dd, 1 H, 2′-H, $J_{2',3}$ = 6.4 Hz), 4.80 (dd, 1 H, 3-H), 6.86−7.28 (m, 10 H, *Ph*, CO*Ph*). − ^{13}C NMR: δ = 24.9, 25.0 (C-7, C-8), 35.2, 35.8 (C-6, C-9), 62.9 (C-3), 71.9 (C-2), 106.1 (C-5), 126.1, 126.4, 127.5, 128.0, 128.4, 128.5, 129.1, 138.0, 141.3 (CO*Ph*, *Ph*), 169.2 (*C*OPh).

(3*R*)-*i*Pr Substrate 3h: The title compound was synthesised from **2h** (5.184 g) according to the general procedure to furnish a white crystalline solid (11.159 g, 81% yield). − M.p. 79.5−80.5 °C (from petroleum ether/ethyl acetate). − $[\alpha]_D^{20}$ = −93.9 (*c* = 1.2, CH_2Cl_2). − ^{1}H NMR: δ = 0.62 & 0.80 [2 × d, 2 × 3 H, $CH(CH_3)_2$, *J* = 7.1 Hz], 1.43−2.02 [m, 7 H, 6-H, 7(7′)-H, 8(8′)-H, 9-H, $CH(CH_3)_2$], 2.39 & 2.65 (2 × m, 2 × 1 H, 6′-H, 9′-H), 3.89 [m, 3 H, 2(2′)-H, 3-H], 7.40 (s, 5 H, CO*Ph*). − ^{13}C NMR: δ = 16.3, 19.4 [$CH(CH_3)_2$], 24.8, 25.0 (C-7, C-8), 30.0 [$CH(CH_3)_2$] 35.2, 36.2 (C-6, C-9), 62.9 (C-3), 64.6 (C-2), 105.3 (C-5), 126.5, 128.4, 129.5, 138.4 (CO*Ph*), 168.6 (*C*OPh).

(3*S*)-*i*Pr Substrate 3i: Substrate **3i** was made from **2i**[34] (5.600 g) according to the general procedure to give a white solid (11.189 g, 75% yield). − M.p. 79.5−80.0 °C (from petroleum ether). − $[\alpha]_D^{20}$ = +95.7 (*c* = 1.1, CH_2Cl_2). − ^{1}H NMR: δ = 0.62 & 0.79 (2 × d, 2 × 3 H, $CH(CH_3)_2$, *J* = 7.1 Hz), 1.43−2.02 [m, 7 H, 6-H, 7(7′)-H, 8(8′)-H, 9-H, $CH(CH_3)_2$], 2.39 & 2.65 (2 × m, 2 × 1 H, 6′-H, 9′-H), 3.88 [m, 3 H, 2(2′)-H, 3-H], 7.39 (s, 5 H, CO*Ph*). − ^{13}C NMR: δ = 16.3, 19.4 [$CH(CH_3)_2$], 24.8, 25.0 (C-7, C-8), 30.0 [$CH(CH_3)_2$], 35.2, 36.2 (C-6, C-9), 62.9 (C-3), 64.6 (C-2), 105.3 (C-5), 126.5, 128.4, 129.5, 138.4 (CO*Ph*), 168.5 (*C*OPh).

(3*R*)-Pr Substrate 3j: The title compound was prepared from **2j**[34] (3.099 g) according to the general procedure to furnish a white solid (6.833 g, 83% yield). − M.p. 77.5−78.5 °C (from petroleum ether). − $[\alpha]_D^{20}$ = −100.7 (*c* = 1.3, CH_2Cl_2). − ^{1}H NMR: δ = 0.61 (t, 3 H, $CH_2CH_2CH_3$, *J* = 7.1 Hz), 0.83−1.52 (2 × m, 4 H, $CH_2CH_2CH_3$), 1.61−2.04 [m, 6 H, 6-H, 7(7′)-H, 8(8′)-H, 9-H], 2.44 & 2.63 (2 × m, 2 × 1 H, 6′-H, 9′-H), 3.74 (m, 1 H, 2-H), 3.92 (m, 2 H, 2′-H, 3-H), 7.39 (s, 5 H, CO*Ph*). − ^{13}C NMR: δ = 13.4 ($CH_2CH_2CH_3$), 18.8 ($CH_2CH_2CH_3$), 24.7, 24.8 (C-7, C-8), 34.9, 35.7, 36.4 ($CH_2CH_2CH_3$, C-6, C-9), 58.1 (C-3), 67.6 (C-2), 104.8 (C-5), 126.3, 128.4, 129.4, 138.3 (CO*Ph*), 168.1 (*C*OPh).

(3*S*)-Pr Substrate 3k: The title compound was prepared from **2k**[34] (2.859 g) according to the general procedure to furnish a white solid (6.396 g, 84% yield). − M.p. 76.5−78.0 °C (from petroleum ether). − $[\alpha]_D^{20}$ = +98.4 (*c* = 1.1, CH_2Cl_2). − ^{1}H NMR: δ = 0.61 (t, 3 H, $CH_2CH_2CH_3$, *J* = 7.1 Hz), 0.83−1.52 (2 × m, 4 H, $CH_2CH_2CH_3$), 1.61−2.04 [m, 6 H, 6-H, 7(7′)-H, 8(8′)-H, 9-H], 2.44 & 2.64 [2 × m, 2 × 1 H, 6′-H, 9′-H], 3.74 (m, 1 H, 2-H), 3.92 (m, 2 H, 2′-H, 3-H), 7.39 (s, 5 H, CO*Ph*). − ^{13}C NMR: δ = 13.4 ($CH_2CH_2CH_3$), 18.8 ($CH_2CH_2CH_3$), 24.7, 24.8 (C-7, C-8), 35.0, 35.7, 36.4 ($CH_2CH_2CH_3$, C-6, C-9), 58.1 (C-3), 67.6 (C-2), 104.8 (C-5), 126.3, 128.4, 129.4, 138.3 (CO*Ph*), 168.1 (*C*OPh).

(3*R*)-*i*Bu Substrate 3l: Substrate **3l** was prepared from **2l** (0.351 g) using the general procedure above to give a white crystalline solid (0.620 g, 72% yield). − M.p. 107.0−109.0 °C (from cyclohexane/ethyl acetate). − $[\alpha]_D^{20}$ = −100.0 (*c* = 1.2, CH_2Cl_2). − ^{1}H NMR: δ = 0.02 & 0.37 [2 × m, 2 × 3 H, $CH_2CH(CH_3)_2$], 0.65 [m, 1 H, $CH_2CH(CH_3)_2$], 0.92 [m, 1 H, $CH_2CH(CH_3)_2$], 1.18 [m, 1 H, $CH_2CH(CH_3)_2$], 1.27−1.73 [2 × m, 6 H, 6-H, 7(7′)-H, 8(8′)-H, 9-H], 2.12 & 2.33 (2 × m, 2 H, 6′-H, 9′-H), 3.39 (m, 1 H, 2-H) 3.60

(m, 2 H, 2′-H, 3-H), 7.08 (s, 5 H, CO*Ph*). − ^{13}C NMR: δ = 20.6, 23.5 [$CH_2CH(CH_3)_2$], 24.7, 24.8, 25.3 [C-7, C-8, $CH_2CH(CH_3)_2$], 35.0, 36.5 (C-6, C-9), 43.0 [$CH_2CH(CH_3)_2$], 57.1 (C-3), 67.8 (C-2), 104.5 (C-5), 126.3, 128.4, 129.3, 138.2 (CO*Ph*), 167.9 (*C*OPh).

(3*S*)-*i*Bu Substrate 3m: Compound **3m** was made from **2m** (7.000 g) as described in the general procedure to give a white crystalline compound (12.200 g, 71% yield). − M.p. 104.0−106.0 °C (from cyclohexane/ethyl acetate). − $[\alpha]_D^{20}$ = +99.0 (*c* = 1.2, CH_2Cl_2). − ^{1}H NMR: δ = 0.02 & 0.36 [2 × d, 2 × 3 H, $CH_2CH(CH_3)_2$, *J* = 6.4 Hz], 0.69 [m, 1 H, $CH_2CH(CH_3)_2$], 0.89 [m, 1 H, $CH_2CH(CH_3)_2$], 1.17 [m, 1 H, $CH_2CH(CH_3)_2$], 1.31−1.75 [2 × m, 6 H, 6-H, 7(7′)-H, 8(8′)-H, 9-H], 2.12 & 2.35 (2 × m, 2 H, 6′-H, 9′-H), 3.40 (br. d, 1 H, 2-H, $J_{2,2'}$ = 7.3 Hz), 3.60 (br. d, 2 H, 2′-H, 3-H), 7.07 (s, 5 H, CO*Ph*). − ^{13}C NMR: δ = 20.8, 23.6 [$CH_2CH(CH_3)_2$], 24.7, 24.9, 25.4 [C-7, C-8, $CH_2CH(CH_3)_2$], 34.9, 36.7 (C-6, C-9), 43.1 [$CH_2CH(CH_3)_2$], 57.3 (C-3), 67.9 (C-2), 104.7 (C-5), 126.5, 128.5, 129.5, 138.4 (CO*Ph*), 168.2 (*C*OPh).

(3*S*)-*s*Bu Substrate 3n: Diastereoisomer **3n** was prepared from **2n** (0.400 g) as described by the general procedure above to give a white crystalline solid (0.820 g, 84% yield). − M.p. 66.0−70.0 °C (from cyclohexane/ethyl acetate). − $[\alpha]_D^{20}$ = +99.6 (*c* = 1.2, CH_2Cl_2). − ^{1}H NMR: δ = 0.5 [t, 3 H, $CH(CH_3)CH_2CH_3$, *J* = 7.2 Hz], 0.76 [d, 3 H, $CH(CH_3)CH_2CH_3$, *J* = 7.0 Hz], 0.90 [m, 2 H, $CH(CH_3)CH_2CH_3$], 1.18 [br. m, 1 H, $CH(CH_3)CH_2CH_3$], 1.55−1.97 [m, 6 H, 6-H, 7(7′)-H, 8(8′)-H, 9-H], 2.35 & 2.62 (2 × m, 2 H, 6′-H, 9′-H), 3.82 [m, 2 H, 2(2′)-H], 3.97 [m, 1 H, 3-H], 7.36 (s, 5 H, CO*Ph*). − ^{13}C NMR: δ = 11.7 [$CH(CH_3)CH_2CH_3$], 13.5 [$CH(CH_3)CH_2CH_3$], 24.7, 25.0 (C-7, C-8), 26.6 [$CH(CH_3)CH_2CH_3$], 35.2, 35.9 (C-6, C-9), 36.8 [$CH(CH_3)CH_2CH_3$], 61.0 (C-3), 64.2 (C-2), 105.3 (C-5), 126.3, 128.4, 129.4, 138.3 (CO*Ph*), 168.4 (*C*OPh).

(2*S*)-Me Substrate 8a: Compound **8a** was prepared from **7a** (1.000 g) as described in the general procedure above to furnish a pale yellow oil (1.630 g, 50% yield). − $[\alpha]_D^{20}$ = +120.6 (*c* = 2.2, CH_2Cl_2). − ^{1}H NMR: δ = 1.27 (d, 3 H, CH_3, *J* = 5.9 Hz), 1.59−2.03 (m, 6 H, 6-H, 7(7′)-H, 8(8′)-H, 9-H], 2.35−2.75 (2 × br. m, 2 H, 6′-H, 9′-H), 3.19 (dd, 1 H, 3-H, $J_{2,3'} = J_{3,3'}$ = 9.5 Hz), 3.45 (dd, 1 H, 3′-H, $J_{2,3'}$ = 5.2 Hz), 4.04 (m, 1 H, 2-H), 7.33−7.51 (m, 5 H, CO*Ph*). − ^{13}C NMR: δ = 17.5 (CH_3), 24.5, 25.2 (C-7, C-8), 35.2, 36.1 (C-6, C-9), 55.6 (C-3), 70.8 (C-2), 105.0 (C-5), 126.6, 128.4, 129.8, 137.9 (CO*Ph*), 167.4 (*C*OPh).

(2*R*)-Me Substrate 8b: Substrate **8b** was made from **7b** (1.000 g) following the general procedure given above to afford a pale yellow oil (1.260 g, 39% yield). − $[\alpha]_D^{20}$ = −123.5 (*c* = 2.3, CH_2Cl_2). − ^{1}H NMR: δ = 1.27 (d, 3 H, CH_3, *J* = 5.9 Hz), 1.56−2.05 (m, 6 H, 6-H, 7(7′)-H, 8(8′)-H, 9-H], 2.36−2.75 (2 × br. m, 2 H, 6′-H, 9′-H), 3.20 (dd, 1 H, 3-H, $J_{2,3'} = J_{3,3'}$ = 9.5 Hz), 3.45 (dd, 1 H, 3′-H, $J_{2,3'}$ = 5.2 Hz), 4.03 (m, 1 H, 2-H), 7.33−7.51 (m, 5 H, CO*Ph*). − ^{13}C NMR: δ = 17.5 (CH_3), 24.5, 25.2 (C-7, C-8), 35.2, 36.1 (C-6, C-9), 55.6 (C-3), 70.8 (C-2), 105.0 (C-5), 126.6, 128.4, 129.8, 137.9 (CO*Ph*), 167.4 (*C*OPh).

Hydroxylated Products 4a−4e, 4h−4k as well as 9a, 9b and 13−15

Hydroxylated Product 4a: Employing 4 × 1 L shaking flasks (250 mL medium per flask) for the Stage II culture, substrate **3a** (0.400 g of substrate was added in one portion after 48 h of growth) was subjected (total fermentation time 48 h) to *Beauveria bassiana* to give a syrupy product, after chromatography, as a mixture of two isomers (0.256 g, 60% yield, chiral GC of **4a** and an NMR of the corresponding Mosher ester[12c] indicated an isomeric ratio of 2.3:1). − $[\alpha]_D^{20}$ = −2.9 (*c* = 2.3, CH_2Cl_2). − ^{1}H NMR: δ = 1.80, 1.96, 2.28 & 2.56 [4 × m, 6 H, 6-H, 8(8′)-H, 9(9′)-H, OH], 2.85 (dd, 1 H, 6′-H, *J* = 5.9 and 14.1 Hz), 3.53 & 3.92 [2 × t, 2 × 2 H, 2(2′)-H, 3(3′)-H, $J_{2,3}$ = 6.1 Hz], 4.49 (br. s, 1 H, 7-H), 7.36−7.49 (m, 5 H, CO*Ph*). − ^{13}C NMR: 33.8, 34.7 (C-8, C-9), 43.7 (C-6), 48.7 (C-3), 64.2 (C-2), 72.9 (C-7), 103.8 (C-5), 126.7, 128.6, 130.2, 137.6 (CO*Ph*), 169.0 (*C*OPh).

(3*R*)-Me Hydroxylated Product 4b: Treating substrate **3b** (Biostat M: first substrate addition, 0.110 g after 14 h; second substrate addition, 0.441 g after 11 h) with *Beauveria bassiana* as given above in the general procedure, furnished (total fermentation time 30 h) a mixture of isomers as a white solid (0.410 g, 84% yield, *de* = 90% as determined by NMR and HPLC). The isomers could be separated by column chromatography combined with recrystallisation.

4b MAJ: M.p. 106−108 °C (from petroleum ether/ethyl acetate). − $[\alpha]_D^{20}$ = −79.6 (*c* = 1.5, CH_2Cl_2). − ^{1}H NMR (assigned with the aid of HETCOR experiments): δ = 0.93 (d, 3 H, Me, $J_{3,Me}$ = 5.7 Hz), 1.77 (br. d, 1 H, 6-H, $J_{6,6'}$ = 13.9 Hz), 1.84−2.41 (m, 4 H, 8-H, 9-H, 9′-H or 8′-H, OH), 2.57−2.69 (m, 1 H, 8′-H or 9′-H), 2.75 (dd, 1 H, 6′-H, $J_{6',7}$ = 5.7 Hz), 3.63 (dd, 1 H, 2-H, $J_{2,3}$ = 5.1 Hz, $J_{2,2'}$ = 11.3 Hz), 3.98 (m, 2 H, 2′-H, 3-H), 4.42 (br. s, 1 H, 7-H), 7.37 (s, 5 H, CO*Ph*). − ^{13}C NMR (assigned with the aid of HETCOR and DEPT experiments): δ = 20.1 (Me), 34.6, 34.7 (C-8, C-9), 43.1 (C-6), 54.0 (C-3), 70.3 (C-2), 72.9 (C-7), 104.0 (C-5), 126.2, 128.6, 129.6, 137.7 (CO*Ph*), 168.2 (*C*OPh).

4b MIN: M.p. 86.5−88.0 °C (from *n*-hexane/CH_2Cl_2). − $[\alpha]_D^{20}$ = −37.9 (*c* = 1.8, THF). − ^{1}H NMR (assigned with the aid of HETCOR experiments): δ = 0.93 (d, 3 H, Me, $J_{3,Me}$ = 6.3 Hz), 1.73−2.05, 2.12−2.57 (2 × br. m, 6 H, 6-H, 8(8′)-H, 9(9′)-H, OH), 2.92 (dd, 1 H, 6′-H, $J_{6',7}$ = 6.1 Hz, $J_{6,6'}$ = 14.0 Hz), 3.62 (m, 1 H, 2-H), 4.01 (m, 2 H, 2′-H, 3-H), 4.48 (br. s, 1 H, 7-H), 7.41 (s, 5 H, CO*Ph*). − ^{13}C NMR (assigned with the aid of HETCOR and DEPT experiments): δ = 20.1 (Me), 33.6, 34.4 (C-8, C-9), 44.8 (C-6), 54.0 (C-3), 70.3 (C-2), 72.8 (C-7), 103.8 (C-5), 126.2, 128.6, 129.6, 137.8 (CO*Ph*), 168.3 (*C*OPh).

(3*S*)-Me Hydroxylated Product 4c: Substrate **3c** (Biostat M: first substrate addition, 0.114 g after 14 h; second substrate addition, 0.563 g after 12 h) was hydroxylated by *Beauveria bassiana* (total fermentation time 50 h) as described in the general procedure to give unchanged starting material (0.400 g) and a pale yellow syrup (0.050 g, 23% yield, *de* = 50% as determined by HPLC and NMR) after chromatography. − ^{1}H NMR (minor isomer in italics): δ = 0.94 (m, 3 H, Me), 1.74−2.70 [m, 6 H, 6-H, 8(8′)-H, 9(9′)-H, OH], *2.76* & 3.01 (2 × dd, 1 H, ratio: 1:3, 6′-H, $J_{6',7}$ = 5.9 Hz, $J_{6,6'}$ = 14.0 Hz), 3.63 (m, 1 H, 2-H), 4.02 (m, 2 H, 2′-H, 3-H), 4.47 (br. s, 1 H, 7-H), 7.38 (s, 5 H, CO*Ph*). − ^{13}C NMR (minor isomer in italics): δ = 20.1, *20.3* (Me), 33.8, 34.6, *34.7*, *34.9* (C-8, C-9), *43.4*, 45.0 (C-6), 54.2 (C-3), 70.5 (C-2), 73.0 (C-7), 104.0, *104.2* (C-5), 126.4, 128.7, 129.8, 138.1 (CO*Ph*), 168.5 (*C*OPh).

(3*R*)-Et Hydroxylated Product 4d: Substrate **3d** (Biostat M: first substrate addition, 0.156 g after 23 h, second substrate addition, 0.661 g after 12 h) was subjected to *Beauveria bassiana* (total fermentation time 165 h) to afford a pale yellow syrup (0.560 g, 82% yield, *de* = 81% as determined by HPLC). − ^{1}H NMR: δ = 0.64 (t, 3 H, CH_2CH_3, *J* = 7.4 Hz), 1.08−1.49 (br. m, 2 H, CH_2CH_3), 1.72−2.40 & 2.57−3.15 [2 × m, 4 H & 3 H, 6(6′)-H, 8(8′)-H, 9(9′)-H, OH], 3.74−4.08 [m, 3 H, 2(2′)-H, 3-H], 4.47 (br. m, 1 H, 7-H), 7.40 (s, 5 H, CO*Ph*) − ^{13}C NMR (minor isomer in italics): δ = 9.9 (CH_2CH_3), *26.3*, 26.4 (CH_2CH_3), 33.6, 34.5 (C-8, C-9), 43.1, *44.7* (C-6), 59.4 (C-3), *67.5*, 67.6 (C-2), *72.7*, 72.8 (C-7), 103.9 (C-5), 126.2, *128.4*, 128.4, *128.5*, 129.7, 137.7 (CO*Ph*), 168.3 (*C*OPh).

(3*S*)-Et Hydroxylated Product 4e: Substrate **3e** (Bioengineering AG model 1523: after 33 h 1.274 g was added for induction and, after an additional 18 h, 6.388 g was added) was subjected to a culture of *Beauveria bassiana* (total fermentation time 96 h) to furnish a syrup (4.220 g, 53% yield, *de* = 47% as determined by HPLC). − ^{1}H NMR: δ = 0.62 (t, 3 H, CH_2CH_3, *J* = 7.5 Hz), 1.29 (br. m, 2 H, CH_2CH_3), 1.72−2.69 [m, 6 H, 6-H, 8(8′)-H, 9(9′)-H, OH], *2.76* & 2.97 (2 × dd, 1 H, 6′-H, $J_{6,6'}$ = 13.8 Hz, $J_{6',7}$ = 5.8 Hz), 3.74−4.03 [m, 3 H, 2(2′)-H, 3-H], 4.49 (br. m, 1 H, 7-H), 7.40 (s, 5 H, CO*Ph*). − ^{13}C NMR (minor isomer in italics): δ = 9.8 (CH_2CH_3), 26.3, *26.5* (CH_2CH_3), 33.6, 34.5, *34.5* (C-8, C-9), *43.0*, 44.7 (C-6), 59.4 (C-3), 67.6, *67.6* (C-2), 72.9, *73.1* (C-7), 103.7, *103.9* (C-5), 126.2, *127.0*, 128.5, 129.7, 137.8 (CO*Ph*), 168.4 (*C*OPh).

The main isomer (**4e** MAJ) of this mixture was isolated by column chromatography as a crystalline solid. − M.p. 127−129 °C (from petroleum ether/ethyl acetate). − $[\alpha]_D^{20}$ = +67.9 (*c* = 1.2, CH_2Cl_2). − ^{1}H NMR: δ = 0.63 (t, 3 H, CH_2CH_3, *J* = 7.4 Hz), 1.31 (br. m, 2 H, CH_2CH_3), 1.72−2.61 [3 × m, 6 H, 6-H, 8(8′)-H, 9(9′)-H, OH], 2.96 (dd, 1 H, 6′-H, $J_{6,6'}$ = 14.0 Hz, $J_{6',7}$ = 6.0 Hz), 3.74−4.07 [m, 3 H, 2(2′)-H, 3-H], 4.49 (br. m, 1 H, 7-H), 7.42 (s, 5 H, CO*Ph*). − ^{13}C NMR: δ = 9.9 (CH_2CH_3), 26.3 (CH_2CH_3), 33.6, 34.5 (C-8, C-9), 44.7 (C-6), 59.4 (C-3), 67.6 (C-2), 72.9 (C-7), 103.7 (C-5), 126.2, 128.5, 129.7, 137.5 (CO*Ph*), 168.6 (*C*OPh).

(3*R*)-*i*Pr Hydroxylated Product 4h: Subjecting substrate **3h** (Biostat M: after 32 h 0.144 g were added for induction and, after an additional 16 h, 0.736 g were added) to *Beauveria bassiana* as described in the general procedure (total fermentation time 93 h) furnished the title compound as a pale yellow solid (0.354 g, 42%). The individual isomers were separated by chromatography combined with recrystallisation.

4h MAJ: M.p. 127.5−128.5 °C (from petroleum ether/CH_2Cl_2). − $[\alpha]_D^{20}$ = −98.6 (*c* = 1.2, CH_2Cl_2). − ^{1}H NMR: δ = 0.60 & 0.78 [2 × d, 2 × 3 H, $CH(CH_3)_2$, *J* = 6.9 Hz], 1.52 [br. m, 1 H, $CH(CH_3)_2$], 1.72−2.44 [3 × m, 5 H, 6-H, 8′-H, 9′-H, 8-H or 9-H, OH], 2.70 [m, 2 H, 6′-H, 8-H or 9-H], 3.91 [s, 3 H, 2(2′)-H, 3-H], 4.44 (br. s, 1 H, 7-H), 7.40 (s, 5 H, CO*Ph*). − ^{13}C NMR: δ = 16.4, 19.5 [$CH(CH_3)_2$], 30.1 [$CH(CH_3)_2$], 34.2, 34.4 (C-8, C-9), 43.0 (C-6), 62.8 (C-3), 65.0 (C-2), 73.1 (C-7), 104.3 (C-5), 126.4, 128.5, 129.7, 137.9 (CO*Ph*), 168.5 (*C*OPh).

4h MIN: M.p. 169.5−170.5 °C (from petroleum ether/EtOH). − $[\alpha]_D^{20}$ = −82.6 (*c* = 0.8, CH_2Cl_2). − ^{1}H NMR: δ = 0.61 & 0.77 [2 × d, 2 × 3 H, $CH(CH_3)_2$, *J* = 6.9 Hz], 1.51 [br. m, 1 H, $CH(CH_3)_2$], 1.71−2.58 [4 × m, 6 H, 6-H, 8(8′)-H, 9(9′)-H, OH], 2.98 (dd, 1 H, 6′-H, $J_{6,6'}$ = 13.9 Hz, $J_{6',7}$ = 5.9 Hz), 3.91 [m, 3 H, 2(2′)-H, 3-H], 4.50 (br. s, 1 H, 7-H), 7.40 (s, 5 H, CO*Ph*). − ^{13}C NMR: δ =16.3, 19.4 [$CH(CH_3)_2$], 29.9 [$CH(CH_3)_2$], 33.8, 34.6 (C-8, C-9), 44.5 (C-6), 62.8 (C-3), 64.9 (C-2), 72.9 (C-7), 104.0 (C-5), 126.4, 128.5, 129.8, 137.9 (CO*Ph*), 168.8 (*C*OPh).

(3*S*)-*i*Pr Hydroxylated Product 4i: Subjecting substrate **3i** (Bioengineering AG model 1523: after 26 h, 1.141 g was added for induction and, after an additional 14 h, 5.626 g was added) to *Beauveria bassiana* as described in the general procedure (total fermentation time 96 h) furnished the title compound as a pale yellow solid and as a mixture of isomers (2.678 g, 38%). The individual isomers could be separated by chromatography combined with recrystallisation.

4i MAJ: M.p. 127.0−128.0 °C (from petroleum ether/diethyl ether). − $[\alpha]_D^{20}$ = +93.5 (*c* = 0.9, CH_2Cl_2). − ^{1}H NMR: δ = 0.61 & 0.80 [2 × d, 2 × 3 H, $CH(CH_3)_2$, *J* = 7.0 Hz], 1.52 [br. m, 1 H, $CH(CH_3)_2$], 1.66−2.42 [m, 5 H, 6-H, 8′-H, 9′-H, 8-H or 9-H, OH], 2.71 [m, 2 H, 6′-H, 8-H or 9-H], 3.93 [s, 3 H, 2(2′)-H, 3-H], 4.44 (br. s, 1 H, 7-H), 7.40 (s, 5 H, CO*Ph*). − ^{13}C NMR: δ = 16.4, 19.5 [$CH(CH_3)_2$], 30.1 [$CH(CH_3)_2$], 34.2, 34.4 (C-8, C-9), 42.9 (C-6), 62.8 (C-3), 65.0 (C-2), 73.2 (C-7), 104.4 (C-5), 126.4, 128.5, 129.7, 137.9 (CO*Ph*), 168.3 (*C*OPh).

4i MIN: M.p. 174.0−174.5 °C (from petroleum ether/EtOH). − $[\alpha]_D^{20}$ = +79.6 (*c* = 1.1, CH_2Cl_2). − ^{1}H NMR: δ = 0.60 & 0.77 [2 × d, 2 × 3 H, $CH(CH_3)_2$, *J* = 6.9 Hz], 1.50 [br. m, 1 H, $CH(CH_3)_2$], 1.71−2.58 [4 × m, 6 H, 6-H, 8(8′)-H, 9(9′)-H, OH], 2.98 (dd, 1 H, 6′-H, $J_{6,6'}$ = 13.9 Hz, $J_{6',7}$ = 5.9 Hz), 3.91 [m, 3 H, 2(2′)-H, 3-H], 4.49 (br. s, 1 H, 7-H), 7.39 (s, 5 H, CO*Ph*). − ^{13}C NMR: δ = 16.3, 19.4 [$CH(CH_3)_2$], 29.8 [$CH(CH_3)_2$], 33.8, 34.6 (C-8, C-9), 44.5 (C-6), 62.8 (C-3), 64.9 (C-2), 72.9 (C-7), 104.0 (C-5), 126.4, 128.5, 129.8, 137.9 (CO*Ph*), 168.8 (*C*OPh).

(3*R*)-Pr Hydroxylated Product 4j: Subjecting substrate **3j** (Bioengineering AG model 1523: after 31 h, 0.930 g was added for induction and, after an additional 17 h, 3.967 g was added) to *Beauveria bassiana* as described in the general procedure (total fermentation time 169 h) furnished a dark brown syrup (4.949 g) after extraction. Column chromatography afforded the following products: **4j** (2.753 g, 54%) and **13** (0.075 g, 1.5%). In addition, two other products (11 mg and 20 mg) were also isolated and could not be identified owing to the presence of impurities and to the small amounts involved. Repeated chromatography of **4j** and subsequent recrystallisation furnished the individual isomers.

4j MAJ: Syrup. − $[\alpha]_D^{20}$ = −96.4 (*c* = 1.7, CH_2Cl_2). − ^{1}H NMR: δ = 0.61 (t, 3 H, $CH_2CH_2CH_3$, *J* = 7.0 Hz), 0.82−1.55 (m, 4 H, $CH_2CH_2CH_3$), 1.79 (br. d, 1 H, 6-H, $J_{6,6'}$ = 13.9 Hz), 1.85−2.11, 2.30 & 2.66 [3 × m, 3 H, 2 H & 1 H, 6-H, 8(8′)-H, 9(9′)-H, OH], 2.76 (dd, 1 H, 6′-H, $J_{6',7}$ = 5.7 Hz), 3.89 [m, 3 H, 2(2′)-H, 3-H], 4.45 (br. s, 1 H, 7-H), 7.39 (s, 5 H, CO*Ph*). − ^{13}C NMR: δ = 13.4 ($CH_2CH_2CH_3$), 18.8 ($CH_2CH_2CH_3$), 34.5, 35.6 (C-8, C-9, $CH_2CH_2CH_3$), 43.0 (C-6), 58.0 (C-3), 68.0 (C-2), 73.0 (C-7), 103.9 (C-5), 126.3, 128.5, 129.6, 137.7 (CO*Ph*), 168.2 (*C*OPh).

4j MIN: White crystalline solid. − M.p. 116.5−117.0 °C (from petroleum ether/diethyl ether). − $[\alpha]_D^{20}$ = −82.3 (*c* = 0.9, CH_2Cl_2). − ^{1}H NMR: δ = 0.60 (t, 3 H, $CH_2CH_2CH_3$, *J* = 7.0 Hz), 0.81−1.51, (m, 4 H, $CH_2CH_2CH_3$), 1.63−2.13, 2.27 & 2.51 [3 × m, 4 H, 1 H, 1 H, 6-H, 8(8′)-H, 9(9′)-H, OH], 2.96 (dd, 1 H, 6′-H, $J_{6,6'}$ = 14.1 Hz, $J_{6',7}$ = 6.0 Hz), 3.78 (dd, 1 H, 2 or 3-H, *J* = 1.6 Hz, *J* = 8.2 Hz), 3.95 (m, 2 H, 2′-H, 3 or 2-H), 4.50 (m, 1 H, 7-H), 7.42 (s, 5 H, CO*Ph*). − ^{13}C NMR: δ = 13.4 ($CH_2CH_2CH_3$), 18.8 ($CH_2CH_2CH_3$), 33.5, 34.5, 35.7 (C-8, C-9, $CH_2CH_2CH_3$), 44.7 (C-6), 58.0 (C-3), 68.0 (C-2), 72.9 (C-7), 103.6 (C-5), 126.3, 128.5, 129.6, 137.8 (CO*Ph*), 168.3 (*C*OPh).

(3*S*)-Pr Hydroxylated Products 4k: Subjecting substrate **3k** (Bioengineering AG model 1523: after 24.0 h, 1.259 g was added for induction and, after an additional 17.0 h, 4.400 g was added) to *Beauveria bassiana* as described in the general procedure (total fermentation time 88.0 h) furnished a dark brown syrup (9.583 g) after extraction. TLC indicated that a complex mixture had been obtained and this was not further investigated.

(2*S*)-Me Hydroxylated Product 9a: Treating substrate **8a** (Biostat M: first substrate addition, 0.109 g after 15 h; second substrate addition, 0.170 g after 10 h) with *Beauveria bassiana* as given above in the general procedure, furnished (total fermentation time 49 h) a mixture of isomers as a pale yellow oil (0.160 g, 71% yield, *de* = 83% as determined by NMR and HPLC). − $[\alpha]_D^{20}$ = +87.8 (*c* = 1.6, CH_2Cl_2). − ^{1}H NMR (minor isomer given in italics): δ = 1.26

(d, 3 H, CH_3, J = 6.0 Hz), 1.69−2.37 & 2.53−2.69 [2 × m, 4 H & 1 H, 6-H, 8(8′)-H, 9(9′)-H], 2.76 & *2.93* (2 × dd, 1 H, ratio: 11:1, 6′-H, $J_{6,6'}$ = 13.9 Hz, $J_{6',7}$ = 5.9 Hz), 3.19 (dd, 1 H, 3-H, $J_{2,3}$ = $J_{3,3'}$ = 9.6 Hz), 3.45 (dd, 1 H, 3′-H, $J_{3',2}$ = 5.3 Hz), 4.06 (m, 1 H, 2-H), 4.46 (m, 1 H, 7-H), 5.15 (br. s, 1 H, OH), 7.42 (m, 5 H, CO*Ph*). − ^{13}C NMR: δ = 17.4 (*C*H$_3$), 34.2 (C-8, C-9), 43.3 (C-6), 55.3 (C-3), 71.4 (C-2), 73.3 (C-7), 104.0 (C-5), 126.6, 128.4, 130.1, 137.3 (CO*Ph*), 167.7 (*C*OPh).

(2*R*)-Me Hydroxylated Product 9b: Treating substrate **8b** (Biostat M: first substrate addition, 0.110 g after 17 h; second substrate addition, 0.550 g after 14 h) with *Beauveria bassiana* as given above in the general procedure, furnished (total fermentation time 70 h) unchanged starting material (0.280 g) and a mixture of isomers as a pale yellow syrup (0.040 g, 20% yield, *de* = 53% as determined by NMR). − ^{1}H NMR (minor isomer in italics): δ = 1.23 (d, 3 H, CH_3, J = 5.9 Hz), 1.68−2.56 [m, 5 H, 6-H, 8(8′)-H, 9(9′)-H], *2.73* & 2.90 (2 × dd, 1 H, ratio: 1:3.3, 6′-H, $J_{6,6'}$ = 14.0 Hz, $J_{6',7}$ = 6.3 Hz), 3.17 (dd, 1 H, 3-H, $J_{2,3}$ = $J_{3,3'}$ = 9.7 Hz), 3.43 (dd, 1 H, 3′-H, $J_{3',2}$ = 5.3 Hz), 4.03 (m, 1 H, 2-H), 4.46 (m, 1 H, 7-H), 5.04 (br. s, 1 H, OH), 7.39 (m, 5 H, CO*Ph*). − ^{13}C NMR(minor isomer in italics): δ = 17.4 (*C*H$_3$), 33.8, 34.6 (C-8, C-9), *43.2*, 44.5 (C-6), 55.3 (C-3), 71.4 (C-2), 72.2, *73.3* (C-7), 103.5, *104.0* (C-5), 126.6, 128.4, 130.2, 137.2 (CO*Ph*), 167.8 (*C*OPh).

Hydroxylated Product 13: White crystalline solid. − M.p. 115.5−116.5 °C (from petroleum ether/diethyl ether). − $[\alpha]_D^{20}$ = −91.5 (*c* = 0.8, CH_2Cl_2). − ^{1}H NMR: δ = 0.97 [d, 3 H, $CH_2CH(OH)CH_3$, J = 6.2 Hz], 1.13−2.03 [4 × br. m, 9 H, $CH_2CH(OH)CH_3$, 6-H, 7(7′)-H, 8(8′)-H, 9-H], 2.37 & 2.68 [2 × br. m, 2 × 1 H, 6′-H, 9′-H], 3.65, 3.92 & 4.17 [3 × m, 4 H, $CH_2CH(OH)CH_3$, 2(2′)-H, 3-H], 7.40 (s, 5 H, CO*Ph*). − ^{13}C NMR (minor isomer in italics): δ = *23.4*, 23.8, 24.5, *24.6*, 24.9 [$CH_2CH(OH)CH_3$, C-7, C-8], 35.0, *35.0*, 36.3 (C-6, C-9), 42.6 [$CH_2CH(OH)CH_3$], 55.8 (C-3), 64.6, 68.0, *68.7* [$CH_2CH(OH)CH_3$, C-2], *104.5*, 105.1 (C-5), 126.2, 126.6, *128.5*, 129.5, *129.6*, 138.0 (CO*Ph*), 168.0 (*C*OPh).

Hydroxylated Product 14: Substrate **3m** (Biostat M: 0.760 g total; after 24 h of growth, 0.150 g was added for induction and, after an additional 12.5 h, 0.610 g was added to the fermentation) was subjected to a culture of *Beauveria bassiana* (total fermentation time 99 h) to afford a pale yellow oil, **14**, after work up and chromatography (0.085 g, 13% yield). − $[\alpha]_D^{20}$ = +81.4 (*c* = 1.1, CH_2Cl_2). − ^{1}H NMR: δ = 0.03 [d, 3 H, $CH_2CH(CH_3)CH_2OH$, J = 5.3 Hz], 0.62 [m, 1 H, $CH_2CH(CH_3)CH_2OH$], 0.98 [m, 1 H, $CH_2CH(CH_3)CH_2OH$], 1.30−1.67 [br. m, 7 H, 6-H, 7(7′)-H, 8(8′)-H, 9-H, $CH_2CH(CH_3)CH_2OH$], 2.11−2.32 (2 × m, 2 × 1 H, 6′-H, 9′-H), 2.87 [d, 2 H, $CH_2CH(CH_3)CH_2OH$, J = 6.2 Hz], 3.42 (br. d, 1 H, 2-H, $J_{2,2'}$ = 7.2 Hz), 3.63 (m, 2 H, 2′-H, 3-H), 7.09 (s, 5 H, CO*Ph*). − ^{13}C NMR: δ = 15.3 [$CH_2CH(CH_3)CH_2OH$], 24.8, 24.9 (C-7, C-8), 33.3 [$CH_2CH(CH_3)CH_2OH$], 35.0, 36.7 (C-6, C-9), 37.7 [$CH_2CH(CH_3)CH_2OH$], 57.1 (C-3), 67.8, 68.0 [C-2, $CH_2CH(CH_3)CH_2OH$], 104.9 (C-5), 126.5, 128.6, 129.6, 138.3 (CO*Ph*), 168.3 (*C*OPh).

Camphanoate Derivative 15:[31] Compound **14** (0.140 g, 0.46 mmol) was dissolved in dry CH_2Cl_2 (10 mL) and pyridine (0.040 g, 0.51 mmol) as well as catalytic amounts of 4-dimethylaminopyridine added. After the mixture had been stirred at room temperature for 15 min, (−)-camphanic chloride (0.110 g, 0.51 mmol) was added and stirring continued for 48 h. The reaction mixture was then washed with aqueous HCl (5%, 1 × 30 mL), saturated aqueous $NaHCO_3$ (1 × 30 mL) as well as saturated aqueous NaCl (1 × 30 mL) and the organic phase was dried with Na_2SO_4. The solution was filtered and the filtrate concentrated down under reduced pressure to give a syrup. Column chromatography (cyclohexane/ethyl acetate, 15:1) was then used to isolate **15** as colourless crystals (0.150 g, 68% yield). − M.p. 127.0−128.0 °C (from cyclohexane/diethyl ether). − $[\alpha]_D^{20}$ = +79.1 (*c* = 1.45, CH_2Cl_2). − ^{1}H NMR: δ = 0.36 [d, 3 H, 12-H, $J_{11,12}$ = 5.3 Hz], 0.91, 1.01, 1.09 [3 × s, 3 × 3 H, 22-H, C(CH_3)$_2$], 1.15−2.07 [br. m, 13 H, 6-H, 7(7′)-H, 8(8′)-H, 9-H, 10(10′)-H, 11-H, 20(20′)-H, 21(21′)-H], 2.39 & 2.64 (2 × m, 2 H, 6′-H, 9′-H), 3.62−3.97 [m, 5 H, 2(2′)-H, 3-H, 13(13′)-H], 7.44 (m, 5 H, CO*Ph*). − ^{13}C NMR: δ = 9.7 (C-22), 15.2 (C-12), 16.8, 18.1 [C(*C*H$_3$)$_2$], 24.6, 24.8 (C-7, C-8), 28.9, 29.9 (C-20, C-21), 30.7 (C-11), 34.8, 36.6 (C-6, C-9), 37.2 (C-10), 54.1, 54.8 [C-19, *C*(CH$_3$)$_2$], 56.6 (C-3), 67.3 (C-2), 70.0 (C-13), 91.1 (C-16), 104.0 (C-5), 126.4, 128.4, 129.9, 137.8 (CO*Ph*), 167.4, 171.2, 171.3 (*C*OPh, C-15, C-18).

Derivatised Products 5a−5e, 5h−5j as well as 10a and 10b

Derivatised Product 5a: Benzylation of alcohol **4a** (0.140 g) under standard conditions[28] afforded the title compound **5a** as a pale yellow syrup after column chromatography (0.140 g, 73% yield). − $[\alpha]_D^{20}$ = −10.5 (*c* = 3.5, CH_2Cl_2). − ^{1}H NMR: δ = 1.95 & 2.21−2.63 [2 × m, 5 H, 6-H, 8(8′)-H, 9(9′)-H], 2.87 (dd, 1 H, 6′-H, J = 7.1 and 14.2 Hz), 3.53 & 3.93 [2 × m, 2 × 2 H, 2(2′)-H, 3(3′)-H], 4.37 (m, 1 H, 7-H), 4.55 (s, 2 H, CH_2Ph), 7.20−7.56 (m, 10 H, CO*Ph*, CH_2*Ph*). − ^{13}C NMR: δ = 31.7, 34.0, (C-8, C-9), 41.9 (C-6), 48.6 (C-3), 64.2 (C-2), 71.0 (*C*H$_2$Ph), 79.2 (C-7), 102.9 (C-5), 126.7, 127.5, 127.8, 128.4, 128.5, 130.0, 137.5, 138.9 (CH_2*Ph*, CO*Ph*,), 167.7 (*C*OPh).

(3*R*)-Me Derivatised Product 5b: Benzylation of alcohol **4b**[28] (0.070 g) under standard conditions and column chromatography furnished the title compound **5b** as a white solid (0.080 g, 85% yield, 89% *de* NMR). Chromatography and recrystallisation (CH_2Cl_2/petroleum ether) furnished **5b** MAJ as fine colourless needles which were suitable for X-ray crystallographic analysis. − M.p. 85.0−86.0 °C . − $[\alpha]_D^{20}$ = −75.2 (*c* = 3.0, CH_2Cl_2). − ^{1}H NMR: (isomeric mixture, minor isomer in italics): δ = 0.95 (d, 3 H, CH_3, J = 6.6 Hz), 1.83−2.67 [m, 5 H, 6-H, 8(8′)-H, 9(9′)-H], 2.77 & *2.96* (2 × dd, 1 H, ratio: 18:1, 6′-H, $J_{6',7}$ = 6.7 Hz, $J_{6',6}$ = 14.4 Hz,), 3.64 (m, 1 H, 2-H), 4.03 (m, 2 H, 2′-H, 3-H), 4.33 (br. s, 1 H, 7-H), 4.54 (s, 2 H, CH_2Ph), 7.34 (m, 10 H, CO*Ph*, CH_2*Ph*). − ^{13}C NMR: δ = 20.1 (*C*H$_3$), 31.7, 35.3 (C-8, C-9), 41.9 (C-6), 54.0 (C-3), 70.4, 70.9 (C-2, *C*H$_2$Ph), 79.2 (C-7), 103.3 (C-5), 126.3, 127.5, 127.7, 128.4, 128.4, 129.7, 137.9, 138.9 (CH_2*Ph*, CO*Ph*,), 168.2 (*C*OPh).

(3*S*)-Me Derivatised Product 5c: Benzylation of alcohol **4c** (0.030 g) under standard conditions[28] and column chromatography furnished the title compound **5c** as a clear syrup (0.030 g, 74% yield, 33% *de* NMR). − ^{1}H NMR (minor isomer in italics): δ = 0.96 (m, 3 H, CH_3), 1.79−2.66 [m, 5 H, 6-H, 8(8′)-H, 9(9′)-H], *2.78* & 2.96 (2 × dd, 1 H, ratio: 1:2, 6′-H, $J_{6',7}$ = 7.3 Hz, $J_{6,6'}$ = 14.4 Hz), 3.56 (m, 1 H, 2-H), 4.03 (m, 2 H, 2′-H, 3-H), 4.33 (m, 1 H, 7-H), 4.54 (m, 1 H, CH_2Ph), 7.34 (m, 10 H, CO*Ph*, CH_2*Ph*). − ^{13}C NMR (minor isomer in italics): δ = 20.1 (*C*H$_3$), 31.5, *31.7*, 33.9, *34.1* (C-8, C-9), *41.9*, 43.0 (C-6), *54.0*, 54.1 (C-3), 70.3, *70.4*, *70.9*, 71.1 (C-2, *C*H$_2$Ph), 79.1, *79.2* (C-7), 103.0 (C-5), 126.2, 126.2, 127.4, 127.8, 128.3, 128.5, 129.6, 129.7, 138.0, 138.8 (CO*Ph*, CH_2*Ph*), 168.3 (*C*OPh).

(3*R*)-Et Derivatised Product 5d: Benzylation of alcohol **4d** (0.120 g, isomeric mixture) under standard conditions[28] and column chromatography afforded the title derivative as a pale yellow syrup (0.120 g, 75% yield, *de* = 75% as determined by NMR). − ^{1}H NMR (minor isomer in italics): δ = 0.64 (t, 3 H, CH_2CH_3, J =

7.4 Hz), 1.20−1.43 (br. m, 2 H, CH_2CH$_3$), 1.84−2.09 & 2.20−2.65 [2 × m, 5 H, 6-H, 8(8′)-H, 9(9′)-H], 2.76 & *2.98* (2 × dd, 1 H, ratio: 7:1, 6′-H, $J_{6',7}$ = 6.9 Hz, $J_{6,6'}$ = 14.1 Hz), 3.79 (dd, 1 H, 2-H, $J_{2,2'}$ = 8.6 Hz, $J_{2,3}$ = 2.6 Hz), 3.84 (m, 1 H, 3-H), 3.99 (dd, 1 H, 2′-H, $J_{2',3}$ = 5.5 Hz), 4.33 (br. s, 1 H, 7-H), 4.55 (m, 2 H, CH_2Ph), 7.22−7.47 (m, 10 H, CH$_2$*Ph*, CO*Ph*). − ^{13}C NMR (minor isomer in italics): δ = 9.9 (CH$_2$*C*H$_3$), 26.5, 31.8, *34.0*, 35.3, (C-8, C-9, *C*H$_2$CH$_3$), 42.1, *43.0* (C-6), 59.6, *59.7* (C-3), *67.8*, 67.9 (C-2), 71.0, *71.3* (*C*H$_2$Ph), *79.3*, 79.6 (C-7), 103.5 (C-5), 126.5, 127.6, 127.8, 128.5, 128.7, 129.7, 129.8, 138.2, 139.2 (CH$_2$*Ph*, CO*Ph*), 168.4 (*C*OPh).

(3*S*)-Et Derivatised Product 5e: The title compound was furnished from alcohol **4e** (0.179 g, isomeric mixture) after benzylation under standard conditions[28] as a pale yellow oil (0.169 g, 71% yield, *de* = 45% as determined by NMR). − ^{1}H NMR (minor isomer in italics): δ = 0.64 (t, 3 H, CH$_2$C*H*$_3$, *J* = 7.4 Hz), 1.13−1.50 (br. m, 2 H, CH_2CH$_3$), 1.66−2.66 [m, 5 H, 6-H, 8(8′)-H, 9(9′)-H], *2.74* & 2.97 (2 × dd, 1 H, ratio: 1:2.8, 6′-H, $J_{6',7}$ = 7.2 Hz, $J_{6,6'}$ = 14.1 Hz), 3.54−4.05 [m, 3 H, 2(2′)-H, 3-H], 4.35 (br. m, 1 H, 7-H), 4.56 (m, 2 H, CH_2Ph), 7.21−7.50 (m, 10 H, CH$_2$*Ph*, CO*Ph*). − ^{13}C NMR (minor isomer in italics): δ = *9.8*, 9.9 (CH$_2$*C*H$_3$), 26.4, *31.6*, 31.6, 33.8, *35.1* (C-8, C-9, *C*H$_2$CH$_3$), 41.9, *42.8* (C-6), *59.4*, 59.5 (C-3), 67.6, *67.7* (C-2), *70.9*, 71.1 (*C*H$_2$Ph), 79.1, *79.3* (C-7), 102.9 (C-5), 126.3, 127.4, 127.8, 128.4, 128.5, 129.6, 138.0, 138.9 (CH$_2$*Ph*, CO*Ph*), 168.3 (*C*OPh).

(3*R*)-*i*Pr Derivatised Product 5h: The title compound was obtained from **4h** (0.153 g, isomeric mixture) after benzylation under standard conditions[28] as a pale yellow oil (0.155 g, 77% yield, *de* = 80% as indicated by NMR). − ^{1}H NMR (minor isomer in italics): δ = 0.62 & 0.79 [2 × d, 2 × 3 H, CH(CH_3)$_2$, *J* = 6.9 Hz], 1.51 [br. m, 1 H, C*H*(CH$_3$)$_2$], 1.82−2.64 [m, 5 H, 6-H, 8(8′)-H, 9(9′)-H], 2.71 & *3.03* (2 × dd, 1 H, 6′-H, ratio: 9:1, $J_{6',7}$ = 6.5 Hz, $J_{6,6'}$ = 13.9 Hz), 3.92 [m, 3 H, 2(2′)-H, 3-H], 4.31 (br. m, 1 H, 7-H), 4.54 (s, 2 H, CH_2Ph), 7.21−7.60 (m, 10 H, CO*Ph*, CH$_2$*Ph*). − ^{13}C NMR (minor isomer in italics): δ = 16.3, *16.4*, 19.3, *19.4* [CH(*C*H$_3$)$_2$], *29.7*, 29.8, 31.5, *31.7*, 34.8 [C-8, C-9, *C*H(CH$_3$)$_2$], 42.1, *42.7* (C-6), 62.7, *62.8* (C-3), 65.0 (C-2), 70.9, *71.1* (*C*H$_2$Ph), *79.0*, 79.4 (C-7), 103.7 (C-5), 126.4, 127.0, 127.4, 127.6, 127.7, 127.8, 127.9, 128.1, 128.4, 128.5, 128.6, 138.0, 139.0 (minor isomer not assigned, CO*Ph*, CH$_2$*Ph*), 168.6 (*C*OPh).

(3*S*)-*i*Pr Derivatised Product 5i: The title compound was obtained from **4i** (0.190 g, isomeric mixture) after benzylation under standard conditions[28] as a pale yellow oil (0.199 g, 80% yield, *de* = 33% as indicated by NMR). − ^{1}H NMR (minor isomer in italics): δ = 0.62 & 0.79 [2 × d, 2 × 3 H, CH(CH_3)$_2$, *J* = 6.9 Hz], 1.51 [br. m, 1 H, C*H*(CH$_3$)$_2$], 1.72−2.64 [m, 5 H, 6-H, 8(8′)-H, 9(9′)-H], 2.71 & *3.03* (2 × dd, 1 H, 6′-H, ratio: 2:1, $J_{6',7}$ = 6.6 Hz, $J_{6,6'}$ = 13.9 Hz), 3.92 [m, 3 H, 2(2′)-H, 3-H], 4.32 (br. m, 1 H, 7-H), 4.55 (s, 2 H, CH_2Ph), 7.21−7.65 (m, 10 H, CO*Ph*, CH$_2$*Ph*). − ^{13}C NMR (minor isomer in italics): δ = 16.4, *16.6*, 19.6, *19.7* [CH(*C*H$_3$)$_2$], 30.0, *30.3*, 31.7, *31.8*, *34.1*, 35.0 [C-8, C-9, *C*H(CH$_3$)$_2$], 42.3, *42.8* (C-6), 62.9, *63.0* (C-3), 65.1, 65.2 (C-2), 71.1, *71.3* (*C*H$_2$Ph), *79.2*, 79.6 (C-7), *103.3*, 103.9 (C-5), 126.6, 126.9, 127.1, 127.2, 127.5, 127.5, 127.6, 127.7, 127.8, 127.8, 127.9, 127.9, 128.1, 128.2, 128.5, 128.6, 128.7, 138.2, 139.1 (minor isomer not assigned, CO*Ph*, CH$_2$*Ph*), 168.7, 168.8 (*C*OPh).

(3*R*)-Pr Derivatised Product 5j: The title compound was obtained from **4j** (0.124 g, isomeric mixture) after benzylation under standard conditions[28] as a pale yellow oil (0.106 g, 65% yield, *de* = 13% as indicated by NMR). − ^{1}H NMR (minor isomer in italics): δ = 0.52 (t, 3 H, CH$_2$CH$_2$C*H*$_3$, *J* = 6.6 Hz), 0.70−1.46 (br. m, 4 H, CH_2CH_2CH$_3$), 1.55−2.58 [m, 5 H, 6-H, 8(8′)-H, 9(9′)-H], 2.74 & *2.97* (2 × dd, 1 H, ratio: 1.3:1, 6′-H, $J_{6',7}$ = 6.9 Hz, $J_{6,6'}$ = 14.2 Hz), 3.80 [m, 3 H, 2(2′)-H, 3-H], 4.23 (br. s, 1 H, 7-H), 4.47 (m, 2 H, CH_2Ph), 7.12−7.45 (m, 10 H, CH$_2$*Ph*, CO*Ph*). − ^{13}C NMR (major isomer only): δ = 13.4 (CH$_2$CH$_2$*C*H$_3$), 18.7 (CH$_2$*C*H$_2$CH$_3$), 31.6, 35.1, 35.7 (C-8, C-9, *C*H$_2$CH$_2$CH$_3$), 41.8 (C-6), 57.9 (C-3), 68.1 (C-2), 70.9 (*C*H$_2$Ph), 79.3 (C-7), 103.2 (C-5), 126.3, 127.4, 127.7, 128.4, 128.5, 129.6, 137.9, 138.9 (CH$_2$*Ph*, CO*Ph*), 168.4 (*C*OPh).

(2*S*)-Me Derivatised Product 10a: Subjecting alcohol **9a** (0.090 g) to the standard benzylation procedure[28] furnished the title compound as a pale yellow oil (0.050 g, 41% yield, *de* = 89% as determined by NMR). − $[\alpha]_D^{20}$ = +62.7 (*c* = 2.7, CH$_2$Cl$_2$). − ^{1}H NMR: (minor isomer in italics): δ = 1.31 (d, 3 H, C*H*$_3$, *J* = 5.9 Hz), 1.84−2.39 & 2.52−2.73 [2 × m, 4 H & 1 H, 6-H, 8(8′)-H, 9(9′)-H], 2.81 & *2.96* (2 × dd, 1 H, ratio: 18:1, 6′-H, $J_{6',7}$ = 7.0 Hz, $J_{6,6'}$ = 13.8 Hz), 3.22 (dd, 1 H, 3-H, $J_{2,3}$ = $J_{3,3'}$ = 9.6 Hz), 3.47 (dd, 1 H, 3′-H, $J_{2,3'}$ = 9.6 Hz), 4.06 (m, 1 H, 2-H), 4.38 (m, 1 H, 7-H), 4.55 (s, 2 H, CH_2Ph), 7.21−7.57 (m, 10 H, CH$_2$*Ph*, CO*Ph*). − ^{13}C NMR: δ = 17.6 (*C*H$_3$), 31.5, 34.9 (C-8, C-9), 42.3 (C-6), 55.5 (C-3), 70.9, 71.1 (C-2, *C*H$_2$Ph), 79.8 (C-7), 103.2 (C-5), 126.8, 127.0, 127.5, 127.8, 128.4, 128.4, 128.8, 130.1, 137.6, 139.0 (CH$_2$*Ph*, CO*Ph*), 167.6 (*C*OPh).

(2*R*)-Me Derivatised Product 10b: Subjecting alcohol **9b** (0.070 g) to the standard benzylation procedure[28] furnished the title compound as a pale yellow oil (0.050 g, 53% yield, *de* = 73% as determined by NMR). − ^{1}H NMR: (minor isomer in italics): δ = 1.31 (d, 3 H, C*H*$_3$, *J* = 6.0 Hz), 1.77−2.70 [2 × m, 5 H, 6-H, 8(8′)-H, 9(9′)-H], *2.81* & 2.94 (2 × dd, 1 H, ratio: 1:6.3, 6′-H, $J_{6',7}$ = 7.7 Hz, $J_{6,6'}$ = 14.1 Hz), 3.22 (dd, 1 H, 3-H, $J_{2,3}$ = $J_{3,3'}$ = 9.5 Hz), 3.48 (dd, 1 H, 3′-H, $J_{2,3'}$ = 5.2 Hz), 4.08 (m, 1 H, 2-H), 4.40 (m, 1 H, 7-H), 4.54 (s, 2 H, CH_2Ph), 7.21−7.57 (m, 10 H, CH$_2$*Ph*, CO*Ph*). − ^{13}C NMR: δ = 17.5 (*C*H$_3$), 32.1, 33.9 (C-8, C-9), 42.8 (C-6), 55.3 (C-3), 71.3, 71.3 (C-2, *C*H$_2$Ph), 78.8 (C-7), 102.7 (C-5), 126.7, 126.7, 127.4, 127.8, 128.4, 128.4, 130.1, 137.5, 139.0 (CH$_2$*Ph*, CO*Ph*), 167.5 (*C*OPh).

Final Product Ketone 6

(*R*/*S*)-Ketone 6: The title compound was prepared from derivatised products **5a**−**e**, **5h**−**j**, **10a** and **10b** as described in the general procedure. Please refer to Table 1 for isolated yields. ^{1}H NMR spectroscopic data were in agreement with reported values.[37] The respective *ee* values were determined by chiral GC and the configuration established by comparison with reference compound (3*S*)-ketone **6** (results are listed in Table 1).

(3*S*)-Ketone 6: This chiral GC reference compound was prepared from (1*S*,4*R*)-4-benzyloxy-2-cyclopenten-1-ol as described in the supporting information.[29]

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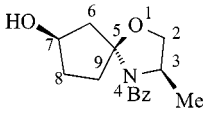

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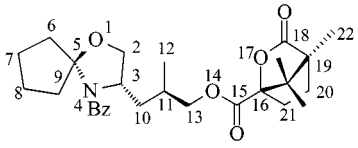

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