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## Microbial Hydroxylation of 2-Cycloalkylbenzoxazoles. Part II. Determination of Product Structures and Enhancement of Enantiomeric Excess

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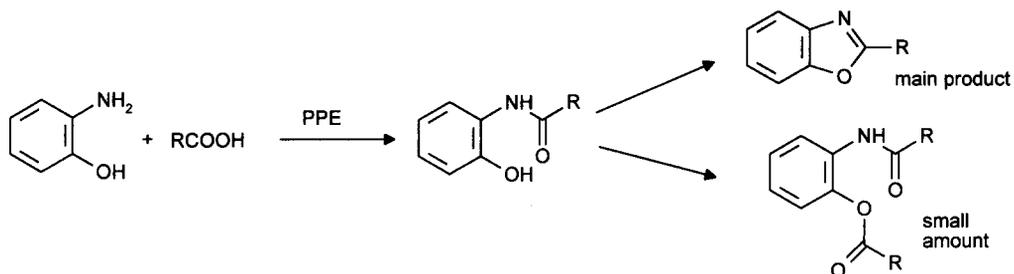
**Abstract:** The determinations of product structures obtained in the microbial hydroxylations of various 2-cycloalkyl-1,3-benzoxazoles using *Cunninghamella blakesleeana* DSM 1906 and *Bacillus megaterium* DSM 32 are described. The initially low e.e. of 3-(benz-1,3-oxazol-2-yl)cyclopentan-1-ol **6**, 2-(benz-1,3-oxazol-2-yl)cyclohexan-1-ol **14** and 4-(2-benz-1,3-oxazol-2-yl)cycloheptan-1-ol **21** can be enhanced to 98 % using lipase catalyzed resolution.

### INTRODUCTION

In the preceding publication<sup>1</sup> we described substrate specificities and stereoselectivities of the hydroxylations of benzoxazoles with *Cunninghamella blakesleeana* DSM 1906 and *Bacillus megaterium* DSM 32. Here we want to report how we determined the structures of the products of the fermentations and how we established the absolute configuration of some hydroxylated benzoxazoles.

### PREPARATION OF BENZOXAZOLES

Benzoxazoles can be prepared in one step by reacting carboxylic acids with 2-aminophenol in the presence of PPE (polyphosphoric acid ethyl ester)<sup>2</sup>. The published procedure<sup>3</sup> does not employ a solvent and a reaction temperature of 110° C for 30 minutes is required. Yields are from 40 - 85 % for a wide range of cycloalkyl- and alkylcarboxylic acids. Through the use of dichloromethane as solvent and conducting the reaction at reflux temperature the transformation can be carried out under milder conditions. This gave slightly higher (5 - 10 %) yields compared with the former procedure and the workup was also simplified as less quantities of extraction solvents were needed. The reaction involves the intermediate formation of the amide, which then cyclizes in the highly acidic reaction mixture losing a molecule of water to furnish the desired benzoxazole. As a byproduct small amounts (< 5%) of the diacylated 2-aminophenol were obtained.



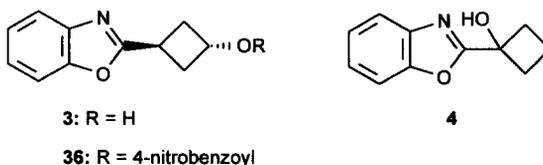
Unfortunately this procedure of benzoxazole formation is limited to unsubstituted carboxylic acids. Substituents such as OH, OBn, and even OMe were always eliminated during the course of the reaction forming olefins (see 2-cyclohexylbenzoxazole section below). The benzothiazoles **30**<sup>4</sup> and **33** were prepared using the analogous reaction with 2-aminothiophenol. Benzoxazoles prepared for this study are shown below:

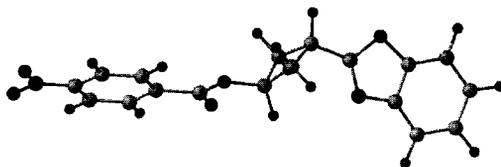
Compound Nr.	1	2	5	12	19	23	30	33	
	n	2	3	4	5	6	7	4	5
	X	O	O	O	O	O	O	S	S
Compound Nr.	9		15		16		17		
R									
Compound Nr.	26		27		28		29		
R							1-adamantyl		

## PRODUCT STRUCTURE ELUCIDATION

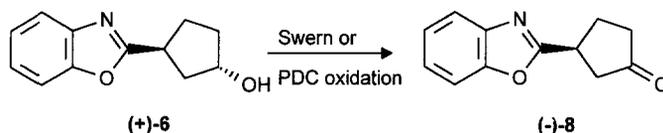
### 2-Cyclobutyl-1,3-benzoxazole **2**

Hydroxylation of 2-cyclobutyl-1,3-benzoxazole **2** produced two achiral alcohols **3** and **4** (Scheme 2), which could be easily identified by NMR-spectroscopy. <sup>13</sup>C-NMR spectra of both compounds suggested a symmetrical distribution of substituents on the cyclobutane ring. Compound **4** contained a tertiary alcohol for which only one structure is possible. Alcohol **3**, however, is a secondary alcohol and therefore could exist in two different relative configurations. Esterification of **3** with 4-nitrobenzoic acid gave crystalline 4-nitrobenzoate **36**. An X-ray structure showed the *trans*-relationship between the benzoxazole moiety and the hydroxyl function.



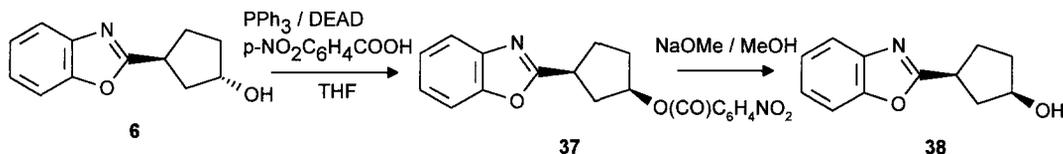
Figure 1. X-ray structure of **36** (drawn in SYBYL)**2-Cyclopentyl-1,3-benzoxazole 5**

Three products were obtained from the fermentation of 2-cyclopentyl-1,3-benzoxazole **5**, namely two alcohols **6** and **7** and a ketone **8**. Inspection of the  $^1\text{H-NMR}$  spectrum of **8** showed an isolated methylene group with coupling to one single proton. Chemical oxidation (Swern-oxidation<sup>5</sup> or PDC<sup>6</sup>) showed that alcohol **6** can be converted into ketone **8**.

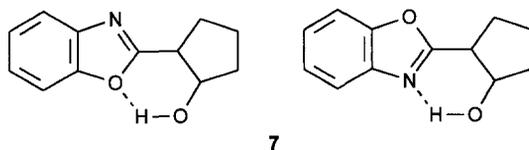


Interestingly, the sense of the specific rotation of the chemically oxidized product **8** was opposite to that of **8** produced *via* the microbial reaction as described in part I.<sup>1</sup>

Alcohol **7** could be either the *cis*-isomer of **6** or a regioisomer. For structure elucidation alcohol **6** was converted into its diastereomer **38** *via* the following sequence:

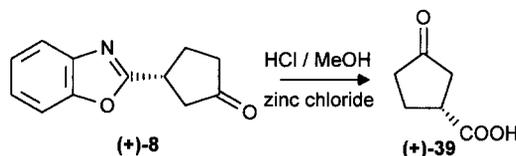


A Mitsunobu reaction<sup>7</sup> of **6** with *p*-nitrobenzoic acid as acidic component and nucleophile gave *p*-nitrobenzoate **37**, being the epimer of the starting alcohol. Ester cleavage using catalytic amounts of sodium methoxide gave alcohol **38**, which had different spectral properties both from **6** and **7**. This proved the structure of alcohol **7**. Alcohol **6**, in turn, was diastereomerically pure because its NMR-spectrum did not contain a trace of **38**.<sup>8</sup> Another interesting feature of the hydroxylated products, which was quite helpful in structure assignments, was the relatively low polarity on TLC compared with other alcohols if an intramolecular hydrogen bridge between the hydroxyl group and one of the electronegative atoms in the benzoxazole could be formed.



### Absolute Configuration of 6 and 8

Cleavage of the microbially produced ketone (+)-8 using the benzoxazole cleavage procedure described in part III<sup>9</sup> gave 3-oxocyclopentylcarboxylic acid (+)-39.



The configuration of (-)-39 was already assigned by Azerad *et al.*<sup>10</sup> as being *S*. As a control experiment the chemically produced ketone (-)-8 was also cleaved using the same procedure leading to (*S*)-(-)-39, proving the assignment above. In analogy to the structures of the hydroxylated compounds, which were already obtained, the relationship between the benzoxazole group and the hydroxyl function in 6 was assumed to be *trans*. This would then lead to a (1*S*,3*S*) absolute configuration for 6. In order to prove this an X-ray determination of a chirally protected derivative<sup>11</sup> of 6 was undertaken. For this purpose either enantiomerically pure alcohol 6 was needed or a separation of the diastereomers formed after derivatization with the chiral reagent, presumably *via* crystallization or chromatographical separation, had to be carried out. The first choice for a chiral derivative was enantiomerically pure *O*-methyl mandelic acid, which in addition would probably also allow assignment of the absolute configuration using the procedure described by Trost.<sup>12</sup> Unfortunately, the diastereomeric *O*-methyl mandelates were only separable with considerable effort on normal phase silica gel chromatography and not crystalline. We then found that an enhancement of the initially 30 % e.e. of alcohol 6 can be effected using a lipase catalyzed hydrolysis of the corresponding acetate 40. Two lipases<sup>13,14</sup> were tested: the enzyme from *Candida rugosa* was found to be less selective, providing a faster reaction than that from *Pseudomonas fluorescens*, which produced enantiomerically pure 6 at a somewhat slower rate. Esterification of enantiomerically pure 6 with (1*S*)-camphanic acid produced a crystalline derivative 41 suitable for X-ray analysis.

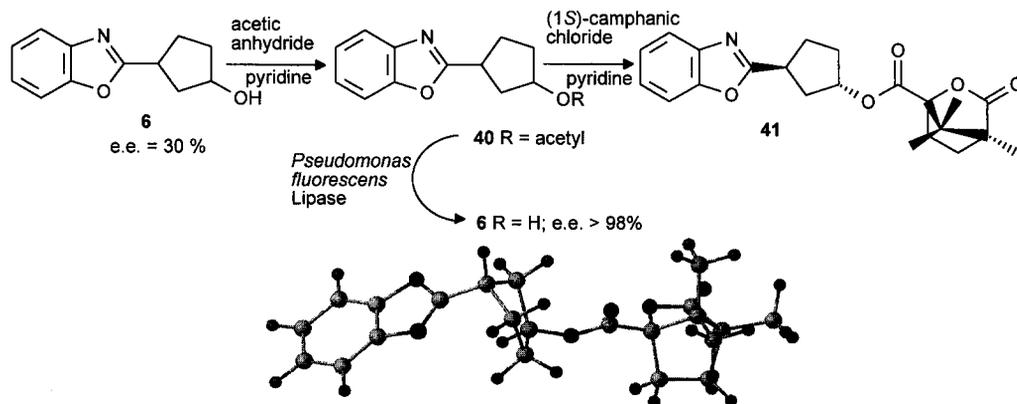
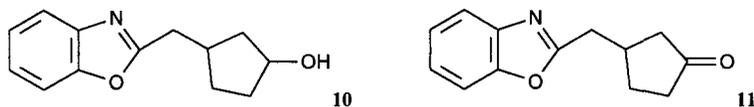


Figure 2. X-ray structure of 41 (drawn in SYBYL)

Camphanoate **41** showed the expected (1*S*,3*S*)-stereochemistry suggested above. The procedure described is useful for the preparation of larger amounts of enantiomerically pure alcohol **6**.

### 2-Cyclopentylmethyl-1,3-benzoxazole **9**



The same reasoning as applied above allowed the determination of the structures of alcohol **10** and ketone **11**, which were the two products obtained from 2-cyclopentylmethyl-1,3-benzoxazole **9** with *C. blakesleeana*. Since the alcohol was a mixture of diastereomers according to its <sup>13</sup>C-NMR spectrum and the ketone showed almost no optical rotation no further attempts were made in structure elucidation.

### 2-Cyclohexyl-1,3-benzoxazole **12**

A less complicated situation than with substrate **5** can be found with the products of 2-cyclohexyl-1,3-benzoxazole **12**. Two alcohols **13** and **14** were formed with the major component being **13**. Only four signals in the <sup>13</sup>C-NMR spectrum of alcohol **13** for the carbons in the six-membered ring suggested a symmetrical distribution of substituents. Assignment of *cis*- or *trans*-relationship could not be made from the NMR-spectra. A crystalline acetate **42** was prepared from alcohol **13** which was investigated using X-ray crystallography.

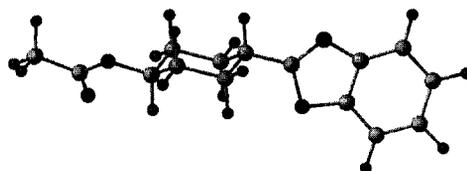


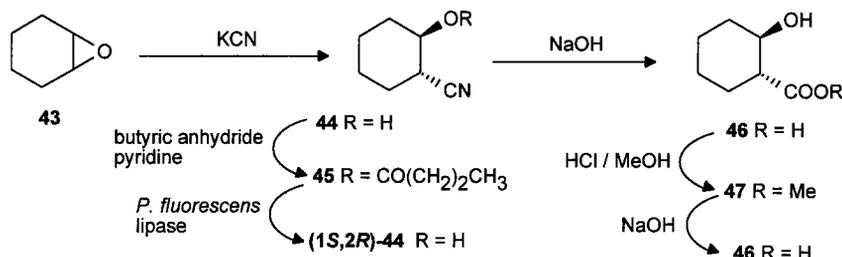
Figure 3. X-ray structure of **42** (drawn in SYBYL)

Again **13** was found to be the *trans*-isomer. Alcohol **14** had a high *R<sub>f</sub>*-value on TLC in accordance with a substitution pattern analogous to alcohol **7**. This assumption was proved by a 2D NMR homonuclear COSY experiment, which revealed coupling between the proton on the tertiary carbon atom and the proton attached to the carbon bearing the hydroxyl group. Furthermore, **14** had a very high specific rotation and high e.e. (65 %) for a hydroxylation reaction, which justified determination of the absolute configuration.

### Absolute Configuration of **14**

In the first strategy, independent synthesis of alcohol **14** from chiral starting materials of known absolute configuration was attempted assuming a *trans*-relationship between hydroxyl group and benzoxazole moiety. Cyclohexene oxide **43** was used as a starting material and converted into *trans*-2-cyanocyclohexanol **44** via ring opening of the epoxide with KCN.<sup>15</sup> Acylation of **44** with butyric anhydride gave **45**, which could be

resolved by *Pseudomonas fluorescens* lipase to give (1*S*,2*R*)-**44** in > 95 % e.e.<sup>16</sup> Saponification of the nitrile gave the hydroxyacid **46** as mixture of several products. Obviously the hydrolysis did not proceed as smoothly as described by Yang *et al.*<sup>15</sup> To allow purification **46** was esterified with methanolic hydrochloric acid to give methyl ester **47**, which could be easily separated from its contaminants by chromatography. Saponification of **47** now afforded pure hydroxyacid **46**.



Unfortunately the formation of the benzoxazole **14** from **46** failed with both procedures reported above resulting in the elimination of the hydroxyl group and formation of 2-(cyclohex-1-enyl)-1,3-benzoxazole. Differently protected hydroxyacids **46** (OBn, OMe instead of OH) behaved in a similar manner.

Therefore the strategy successfully employed for alcohol **6** was applied. Acetylation gave acetate **48** which could be resolved using *Pseudomonas fluorescens* lipase. Esterification of enantiomerically pure **14** with (1*S*)-camphanic acid was unproblematic to yield camphanoate **49**, which readily crystallized.

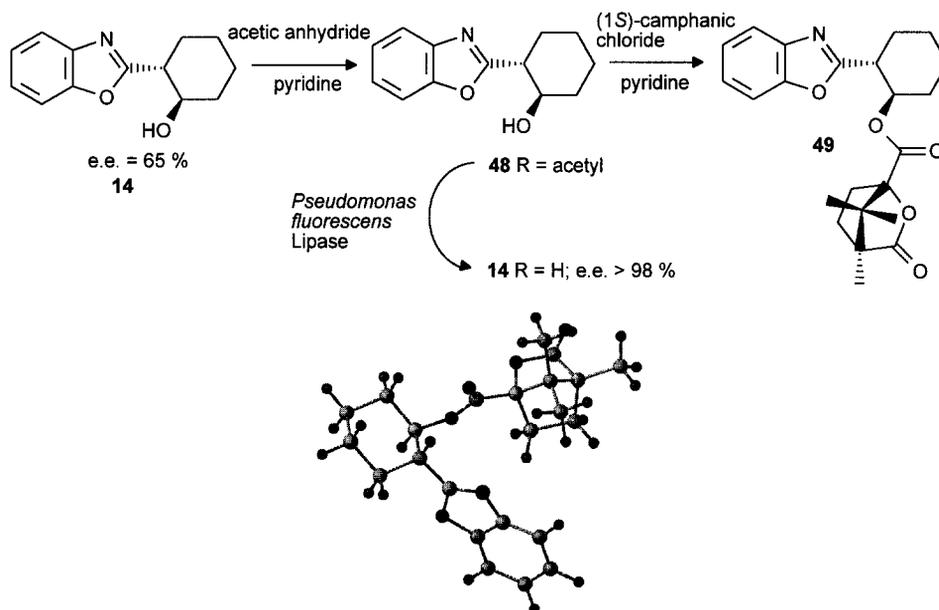


Figure 4. X-ray structure of **49** (drawn in SYBYL)

The absolute configuration of (-)-**14** thus was determined as (1*R*,2*R*) in contrast to that obtained for alcohol **6**.

**2-(Cyclohex-3-enyl)-1,3-benzoxazole 17**

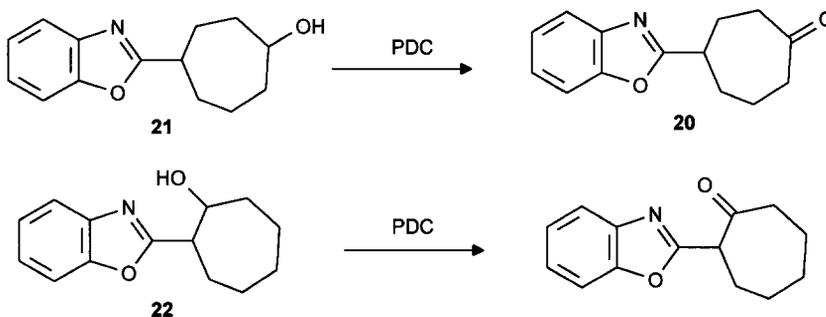
The main product obtained by conversion of 2-(cyclohex-3-enyl)-1,3-benzoxazole **17** with *B. megaterium* was the racemic epoxide **18** verified by HPLC-analysis. The diastereoselection, however, is quite high as proved by the following reaction.



Chemical epoxidation using MCPBA gave a mixture of the diastereomeric epoxides in a ratio of 1:1, which could be easily separated by chromatography. Comparison of this mixture with the biotransformation product showed that the latter contained only one diastereomer, the stereochemistry of which was assumed to be *trans* by analogy to the alcohol **13**.

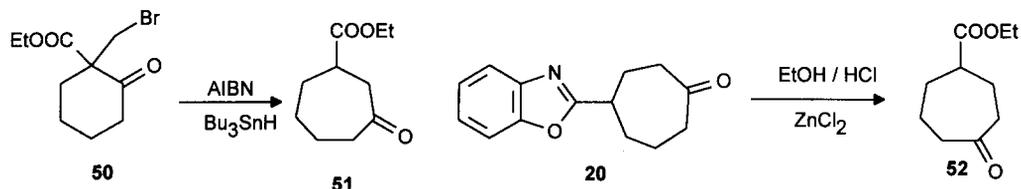
**2-Cycloheptyl-1,3-benzoxazole 19**

Two alcohols **21** and **22** and a ketone **20** were found as the biotransformation products of 2-cycloheptyl-1,3-benzoxazole **19**. Higher conformational flexibility of the seven-membered ring and a higher number of methylene groups as potential reaction centers made the structure determination more difficult. The best strategy was to focus on the ketones,<sup>17</sup> because they contained only one chiral center. Thereby the number of isomers is reduced. Consequently chemical oxidation (PDC) of **21** gave **20**, but oxidation of **22** gave another ketone, which could not be found in the biotransformation mixture.



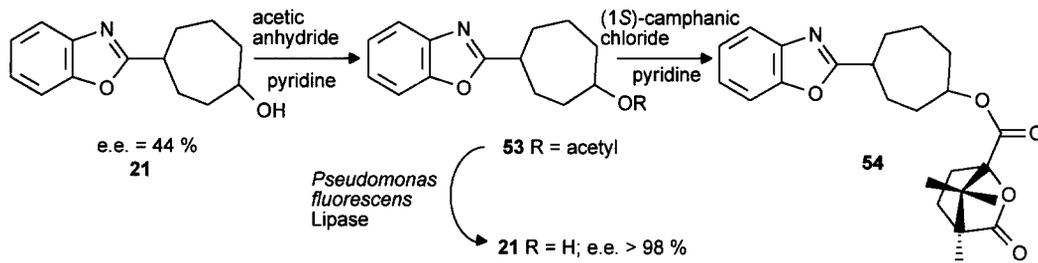
The structure of alcohol **22** was assigned from the <sup>1</sup>H-NMR spectrum (coupling between the proton on the tertiary carbon atom and the proton on the hydroxylated carbon) and the high R<sub>F</sub>-value on TLC in analogy to the alcohols **7** and **14**. This fact remarkably reduced the number of isomeric structures possible for **20/21**. Since **21** could not be a tertiary alcohol because of its <sup>13</sup>C-NMR spectrum and the possibility to oxidize it to ketone **20**, decision between the only hydroxylation positions left was done by comparison with the literature:

Ethyl 3-oxocycloheptanecarboxylate **51** could be prepared from the bromomethyl adduct of ethyl 2-oxocyclohexanecarboxylate **50** via a free radical ring enlargement.<sup>18</sup>



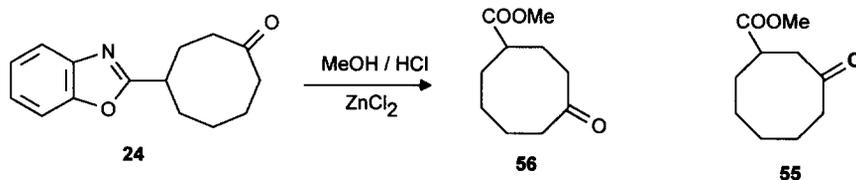
Acidic cleavage of the benzoxazole **20** gave an ethyl ester **52**, which had a similar but different NMR-spectrum compared to **51** under exactly the same conditions (300 MHz-spectrometer;  $\text{CDCl}_3$  as solvent). Therefore the structure of **20** was assigned as shown above.

Acetylation of **21** (44 % e.e.) gave acetate **53**, which also was a good substrate for *Pseudomonas fluorescens* lipase and resolved to an alcohol of very high e.e. (> 95 %). Unfortunately, the crystals obtained from the camphanoate **54** were not suitable for X-ray determination of the absolute configuration of **21**.



### 2-Cyclooctyl-1,3-benzoxazole **24**

Microbial hydroxylation of **24** gave products which were much less selectively hydroxylated. The alcohols **25** obtained from both microorganisms are mixtures of diastereomers. The position of the hydroxylation was determined using the same line of thought as for 2-cycloheptylbenzoxazole. Chemical oxidation of alcohol **25** gave ketone **24** proving that their formation in the biotransformation was interconnected. Since **25** was not hydroxylated at C-2 and also reaction at C-5 could be ruled out, because this would be a symmetrical distribution of substituents on the eight-membered ring giving different NMR-spectra to the one obtained, only C-3 or C-4 remained as potential reaction centers. Methyl 3-oxocyclooctanecarboxylate **55** is known from literature<sup>18</sup> and gave different spectra compared to the product **56** obtained from acidic alcoholysis of ketone **24**.



Therefore the hydroxylation position of **24/25** was determined as C-4. No further attempts were made to assign the stereochemistries of the diastereomeric mixtures.

**Acknowledgment:** We want to express our cordial thanks to U. Wagner and W. Mosler (Institute of Physical Chemistry, University of Graz) for the determination of the X-ray structures. Furthermore we thank C. Illaszewicz and G. Gradnig for the measurement of some of the NMR-spectra and M. Friedrich, S. Heumann and S. Zöchling for technical assistance. Funding within the framework of the European Community Program Human Capital and Mobility, project Biooxygenations, contract no. ERB CHRXCT 930259, the Christian Doppler Society and Chemie Linz GmbH is gratefully acknowledged.

## EXPERIMENTAL

**Analytical Methods:** *Melting points* (uncorrected): Büchi 530. *Optical rotation*: DIP-370 Digital Polarimeter (Japan Spectroscopic Co., Ltd.).  $^1\text{H}$ ,  $^{13}\text{C}$ -NMR: Gemini 200 (Varian), MSL 300 (Bruker) solvent as internal standard. Assignment of signals in the benzoxazole region especially C-5' and C-6' might also be reversed.  $^{19}\text{F}$ -NMR: MSL 300 (Bruker),  $\text{CCl}_3\text{F}$  as external standard. *MS*: Profile (Kratos), EI (70 eV) and CI. *Elemental analyses*: Microanalytical Laboratory of the Institute for Organic Chemistry, University of Graz. *GC*: Hewlett Packard HP 5890 Series II with autosampler HP 7673 and integrator HP 3396 A, quartz capillary column: 1 m x 0.32 mm, 0.52  $\mu\text{m}$  HP1 and 25 m x 0.32 mm, 0.52  $\mu\text{m}$  HP5, carrier gas He, FID. *HPLC*: JASCO system containing pump 880-PU, UV-detector 875-UV and AXXIOM Model 727 chromatography software; chiral column: CHIRALPAK AD from DAICEL with the eluent heptane / 2-propanol 95:5. For better separation the column was cooled to 10° C. Detection of benzoxazoles was at 230 nm. *LC*: Silica gel 60, 70-230 mesh (Merck) *TLC*: Silica gel 60 F<sub>254</sub> aluminum plates (Merck), Detection: a. UV (254 nm), b. spraying reagent A (5% vanillin in concentrated.  $\text{H}_2\text{SO}_4$ ) or spraying reagent B (10%  $\text{H}_2\text{SO}_4$ , 10%  $(\text{NH}_4)_6\text{Mo}_7\text{O}_{24} \times 4 \text{H}_2\text{O}$  and 0.8%  $\text{Ce}(\text{SO}_4)_2 \times 4 \text{H}_2\text{O}$  in water) and developing on a heat plate (600 °C). *Lipases*: *Candida rugosa* was obtained from SIGMA, *Pseudomonas fluorescens* from AMANO.

### General Procedure for Benzoxazole Preparation (Method A)

2-Amino-phenol (10 mmole) is added at once to 10 g preheated polyphosphate ethyl ester (PPE) in a round-bottomed flask at 110° C. When the 2-amino-phenol is dissolved, resulting in a homogeneous red solution, the respective carboxylic acid (10 mmole) is added and the solution is stirred for 30 min. at the same temperature. TLC (eluent: ethylacetate/hexanes 1:1) shows several products with the benzoxazole being the least polar. Then the reaction mixture is allowed to cool to room temperature, ice-water (50 mL) is added and the mixture is neutralized with saturated sodium bicarbonate solution. Extraction with ethyl acetate (3x100 mL), drying ( $\text{Na}_2\text{SO}_4$ ) and evaporation under reduced pressure gives the crude benzoxazole, which is further purified by column chromatography (eluent: ethyl acetate/hexanes 1:8) and kugelrohr-distillation.

### General Procedure for Benzoxazole Preparation (Method B)

A solution of 2-aminophenol (10 mmol), PPE (10 g) and carboxylic acid (10 mmol) in dichloromethane (50 mL) is refluxed overnight. Then the reaction mixture is cooled with ice, water (100 mL) is added and solid  $\text{NaHCO}_3$  is added carefully until pH 7 is reached. Separation of the phases and extraction of the water phase with dichloromethane (3 x 100 mL) gives a combined organic layer, which is dried ( $\text{Na}_2\text{SO}_4$ ) and evaporated. Further purification of the crude product is done by column chromatography and kugelrohr distillation.

### General Procedure for Acylations (Method C)

A solution of the respective alcohol (1 mmole), acylating agent (anhydride or acid chloride 1.1 mmole), pyridine (1.1 mmole) and a catalytic amount of 4-dimethylaminopyridine in dichloromethane (25 mL) is allowed to stand at r.t. overnight. The reaction mixture is then washed with 1 N HCl, saturated  $\text{NaHCO}_3$  solution and brine. Drying ( $\text{Na}_2\text{SO}_4$ ) and evaporation gives a crude product, which is purified by flash chromatography.

### General Procedure for Enzymatic Resolutions (Method D)

The respective ester (10 mmole) is added to a stirred solution of phosphate buffer (0.1 M; 150 mL) and

enzyme (500 mg) at pH 7.0 on a pH-Stat. The pH is kept constant by the continuous addition of base. After 40 % conversion (measured by consumption of 0.25 N NaOH) the reaction mixture is extracted with dichloromethane, dried ( $\text{Na}_2\text{SO}_4$ ) and evaporated, followed by chromatographic separation.

#### General Procedure for Swern Oxidations (Method E)<sup>5</sup>

A solution of oxalyl chloride (1.2 mmole) in dichloromethane (5 mL) is cooled to  $-80\text{ }^\circ\text{C}$ , DMSO (1.3 mmole) in dichloromethane (2 mL) is added slowly via a syringe. The solution is stirred for 20 minutes or until the evolution of gas ( $\text{CO}/\text{CO}_2$ ) has ceased. The alcohol (1 mmole) in dichloromethane (5 mL) is added at  $-80\text{ }^\circ\text{C}$  and the reaction mixture is stirred for further 20 minutes and then allowed to warm to  $-50\text{ }^\circ\text{C}$ . At this temperature triethylamine (3 mmole) is added whereupon the resulting solution is slowly warmed to r.t. Extraction of the dichloromethane phase with HCl (1N) and  $\text{NaHCO}_3$  (saturated solution) gives after drying ( $\text{Na}_2\text{SO}_4$ ) and evaporation a crude product, which is usually purified by flash chromatography.

#### General Procedure for PDC Oxidations (Method F)<sup>6</sup>

The alcohol (1 mmole) is dissolved in dichloromethane (10 mL) and pyridinium dichromate (PDC; 1.5 mmole) is added. The resulting suspension is stirred at r.t. for 20 h. Then dry ether (30 mL) is added, the mixture is filtered over a layer of silica gel (5 g), the filtrate is extracted with HCl (1N) and  $\text{NaHCO}_3$  (saturated solution), dried ( $\text{Na}_2\text{SO}_4$ ) and evaporated. Chromatographic separation yields the pure product.

#### General Procedure for Alcoholic Benzoxazole Cleavage (Method G)

The benzoxazole (2 mmole) is dissolved in the respective alcohol (25 mL), aqueous HCl (4 N, 25 mL) and zinc chloride (5 mmole) are added. The resulting solution is refluxed for four hours. Then water (50 mL) is added and the reaction mixture is extracted with dichloromethane (5 x 30 mL). The dichloromethane phase is dried ( $\text{Na}_2\text{SO}_4$ ) and evaporated. Column chromatography yields the pure ester.

#### General Procedure for Fermentations (Method H)

Transformations with *Cunninghamella blakesleeana* were performed in 1-L shaking flasks containing 250 mL of Czapek-Dox medium or medium E. After 2 days of growth an ethanolic solution of substrate (0.3 g/L) was added to the culture. Biohydroxylations of 2-cyclopentyl-, 2-cyclohexyl-, 2-cycloheptyl- and 2-cyclooctyl-1,3-benzoxazole were done in a bioreactor as described elsewhere.<sup>19</sup>

Biohydroxylations with *Bacillus megaterium* were done in 1-L shaking flasks containing 250 mL of buffered medium E. 2-cyclohexyl-1,3-benzoxazole was transformed in a bioreactor (Bioengineering L1523) containing 11 L of medium K. Substrate (0.3 g/L) was added after 16 hours of growth (5.0 g/L of biomass).

After 2 - 4 days the culture broth was extracted twice with ethyl acetate. The organic phase was evaporated after drying with  $\text{Na}_2\text{SO}_4$ . Products were separated by column chromatography.

Medium E consisted (per liter) of 15 g of malt extract (Merck), 10 g of glucose, 5 g of peptone (Merck), and 2 g of yeast extract (Oxoid). Czapek-Dox medium contained (per liter) 2 g of  $\text{NaNO}_3$ , 1 g of  $\text{KH}_2\text{PO}_4$ , 0.5 g of  $\text{MgSO}_4 \cdot 7\text{H}_2\text{O}$ , 0.5 g KCl, 0.1 g of  $\text{Fe(III)NH}_4$ -citrate, 20 g of glucose, and 1 g of yeast extract (Oxoid). Medium K was made of 4.5 g/L  $\text{Na}_2\text{SO}_4 \cdot 2\text{H}_2\text{O}$ , 1.5 g/L  $\text{KH}_2\text{PO}_4$ , 3.5 g/L  $(\text{NH}_4)_2\text{SO}_4$ , 0.2 g/L  $\text{MgSO}_4 \cdot 7\text{H}_2\text{O}$ , 0.05 g/L  $\text{Fe(III)-NH}_4$ -citrate, 0.02 g/L  $\text{CaCl}_2 \cdot 2\text{H}_2\text{O}$ , 1 g/L Na-acetate, 1 g/L yeast extract, 20 g/L glucose, 1 mL/L trace solution.

#### General Procedure for MCPBA-Epoxidations (Method I)

A solution of the olefin (1 mmole) in dichloromethane (10 mL) is cooled with ice and *m*-chloroperbenzoic acid (MCPBA; 1.2 mmole) is added. The resulting suspension is stirred for 4 h, cooled with ice, solid *m*-chlorobenzoic acid is removed by filtration, the filtrate is washed with  $\text{NaHSO}_3$ -solution (2M, 10 mL),  $\text{NaHCO}_3$ -solution (saturated, 10 mL) and brine (10 mL), dried ( $\text{Na}_2\text{SO}_4$ ) and evaporated. Chromatographic purification yields the pure epoxide.

#### Physical Data of Substrates

##### 2-Cyclopentylcarbonylamino phenyl cyclopentylcarboxylate: Diacylated Byproduct of the 2-Cyclopentyl-1,3-benzoxazole 5 Preparation

Method A; Method B; Yield: 2 %; <sup>1</sup>H-NMR ( $\text{CDCl}_3$ ): ppm 1.53-2.12 (m, 16 H); 2.64 (p, J = 8 Hz, 1H, H-1); 3.02 (p, J = 8 Hz, 1H, H-1'); 7.03-7.39 (m, 4H); 8.12 (d, J = 8 Hz, 1H, NH). <sup>13</sup>C-NMR ( $\text{CDCl}_3$ ): ppm 26.00

(C-3, C-4); 26.11 (C-3', C-4'); 30.13 (C-2, C-5); 30.36 (C-2', C-5'); 43.95 (C-1); 46.93 (C-1'); 122.0 (C-3''); 123.0 (C-6''); 124.5 (C-5''); 126.3 (C-4''); 130.2 (C-2''); 140.9 (C-1''); 174.5 (CO); 174.6 (CO').

### 2-Cyclopropyl-1,3-benzoxazole 1<sup>20</sup>

Method A; Yield: 53 %; <sup>1</sup>H-NMR (CDCl<sub>3</sub>): ppm 0.95-1.35 (m, 4H, H-2, H-3); 2.05-2.25 (m, 1H, H-1); 7.20 (m, 2H, H-5', H-6'); 7.47 (m, 1H, H-4'); 7.65 (m, 1H, H-7'). <sup>13</sup>C-NMR (CDCl<sub>3</sub>): ppm 8.96 (C-2, C-3), 9.18 (C-1), 109.89 (C-4'), 118.94 (C-7'), 123.83 (C-6'), 123.96 (C-5'), 141.65 (C-9'), 150.47 (C-8'), 168.43 (C-2').

### 2-Cyclobutyl-1,3-benzoxazole 2

Method A; Yield: 51%; <sup>1</sup>H-NMR (CDCl<sub>3</sub>): ppm 2.00-2.15 (m, 2H, H-3), 2.41-2.55 (m, 4H, H-2, H-4), 3.72-3.82 (m, 1H, H-1), 7.18 (m, 2H, H-5', H-6'), 7.43 (m, 1H, H-4'), 7.63 (m, 1H, H-7'). <sup>13</sup>C-NMR (CDCl<sub>3</sub>): ppm 18.79 (C-3), 27.06 (C-2, C-4), 33.44 (C-1), 110.30 (C-4'), 120.35 (C-7'), 124.07 (C-6'), 124.44 (C-5'), 141.40 (C-9'), 150.78 (C-8'), 169.38 (C-2').

### 2-Cyclopentyl-1,3-benzoxazole 5

Method A; Yield: 51%; Method B; Yield: 70%; <sup>1</sup>H-NMR (CDCl<sub>3</sub>): ppm 1.57-2.16 (m, 8H, H-2, H-3, H-4, H-5), 3.32 (t, J = 8Hz, 1H, H-1), 7.18 (m, 2H, H-5', H-6'), 7.38 (m, 1H, H-4'), 7.64 (m, 1H, H-7'). <sup>13</sup>C-NMR (CDCl<sub>3</sub>): ppm 25.74 (C-3, C-4), 31.41 (C-2, C-5), 38.97 (C-1), 110.22 (C-4'), 119.58 (C-7'), 123.98 (C-6'), 124.30 (C-5'), 141.54 (C-9'), 150.93 (C-8'), 170.54 (C-2').

### 2-Cyclopentylmethyl-1,3-benzoxazole 9

Method A; Yield: 52%; <sup>1</sup>H-NMR (CDCl<sub>3</sub>): ppm 1.18-1.36 (m, 2H, H-6), 1.47-1.71 (m, 4H, H-4, H-5), 1.75-1.92 (m, 2H, H-3), 2.43 (m, 1H, H-2), 2.89 (d, J = 8Hz, 2H, H-1), 7.21 (m, 2H, H-5', H-6'), 7.42 (m, 1H, H-4'), 7.67 (m, 1H, H-7'). <sup>13</sup>C-NMR (CDCl<sub>3</sub>): ppm 25.06 (C-4, C-5), 32.57 (C-3, C-6), 34.53 (C-2), 38.16 (C-1), 110.24 (C-4'), 119.62 (C-7'), 124.01 (C-6'), 124.36 (C-5'), 141.61 (C-9'), 150.90 (C-8'), 166.94 (C-2').

### 2-Cyclohexyl-1,3-benzoxazole 12

Method A; Yield: 49%; Method B; Yield: 65 %; mp 34-35°C (Lit.:<sup>21</sup> 37-38°C); <sup>1</sup>H-NMR (CDCl<sub>3</sub>): ppm 0.90-1.11 (m, 2H, H-4), 1.35-1.51 (m, 4H, H-3, H-5), 1.80-1.92 (m, 4H, H-2, H-6), 2.51-2.62 (m, 1H, H-1), 6.95 (m, 2H, H-5', H-6'), 7.13 (m, 1H, H-4'), 7.43 (m, 1H, H-7'). <sup>13</sup>C-NMR (CDCl<sub>3</sub>): ppm 25.03 (C-4), 25.29 (C-3, C-5), 29.09 (C-2, C-6), 37.28 (C-1), 109.62 (C-4'), 119.10 (C-7'), 123.69 (C-6', C-5'), 141.00 (C-9'), 150.12 (C-8'), 169.50 (C-2').

### 2-Cyclohexylmethyl-1,3-benzoxazole 15

Method A; Yield: 49%; <sup>1</sup>H-NMR (CDCl<sub>3</sub>): ppm 1.32-1.91 (m, 10H, H-3, H-4, H-5, H-6, H-7), 2.15-2.25 (m, 2H, H-1), 2.92-3.01 (m, 1H, H-2), 7.28 (m, 2H, H-5', H-6'), 7.48 (m, 1H, H-4'), 7.68 (m, 1H, H-7'). <sup>13</sup>C-NMR (CDCl<sub>3</sub>): ppm 25.84 (C-3, C-4, C-5, C-6, C-7), 30.72 (C-2), 38.16 (C-1), 110.46 (C-4'), 119.84 (C-7'), 124.15 (C-6'), 124.50 (C-5'), 141.50 (C-9'), 150.86 (C-8'), 170.04 (C-2').

### 2-(2-Cyclohexylethyl)-1,3-benzoxazole 16

Method A; Yield: 52%; <sup>1</sup>H-NMR (CDCl<sub>3</sub>): ppm 0.81-0.95 (m, 2H, H-6), 1.11-1.34 (m, 4H, H-5, H-7), 1.64-1.85 (m, 7H, H-2, H-3, H-4, H-8), 2.81-2.96 (m, 2H, H-1), 7.18 (m, 2H, H-5', H-6'), 7.38 (m, 1H, H-4'), 7.63 (m, 1H, H-7'). <sup>13</sup>C-NMR (CDCl<sub>3</sub>): ppm 25.99 (C-6), 26.06 (C-4, C-5, C-7, C-8), 32.24 (C-3), 34.00 (C-2), 37.09 (C-1), 110.00 (C-4'), 119.38 (C-7'), 123.81 (C-6'), 124.11 (C-5'), 141.03 (C-9'), 150.80 (C-8'), 167.33 (C-2').

**2-Cyclohex-3-enyl-1,3-benzoxazole 17**

Method A; Yield: 54 %; <sup>1</sup>H-NMR (CDCl<sub>3</sub>): ppm 1.93 (m, 1H, H-5b), 2.20 (m, 3H, H-5a, H-6), 2.51 (d, 2H, H-2), 3.18 (m, 1H, H-1), 5.75 (s, 2H, H-3, H-4), 7.26 (m, 2H, H-5', H-6'), 7.45 (m, 1H, H-4'), 7.67 (m, 1H, H-7'). <sup>13</sup>C-NMR (CDCl<sub>3</sub>): ppm 24.62 (C-6), 26.66 (C-5), 28.97 (C-2), 34.39 (C-1), 110.41 (C-4'), 119.85 (C-7'), 124.12 (C-6'), 124.54 (C-5'), 125.22 (C-4), 127.01 (C-3), 141.53 (C-9'), 150.82 (C-8'), 170.08 (C-2').

**2-Cycloheptyl-1,3-benzoxazole 19**

Method B; Yield: 85 %; <sup>1</sup>H-NMR (CDCl<sub>3</sub>): ppm 1.40-2.30 (m, 12H, H-2 - H-7), 3.12 (m, 1H, H-1); 7.30 (m, 2H, H-5', H-6'); 7.47 (m, 1H, H-4'); 7.70 (m, 1H, H-7'). <sup>13</sup>C-NMR (CDCl<sub>3</sub>): ppm 26.31 (C-4, C-5), 28.42 (C-3, C-6), 32.31 (C-2, C-7), 39.7 (C-1), 110.2 (C-4'), 119.6 (C-7'), 123.9 (C-6'), 124.3 (C-5'), 141.3 (C-9'), 150.6 (C-8'), 171.3 (C-2').

**2-Cyclooctyl-1,3-benzoxazole 23**

Method B; Yield: 76 %; <sup>1</sup>H-NMR (CDCl<sub>3</sub>): ppm 1.50-1.90 (m, 10H, H-3 - H-7); 1.95-2.25 (m, 4H, H-2, H-8); 3.15 (m, 1H, H-1); 7.21 (m, 2H, H-5', H-6'); 7.47 (m, 1H, H-4'); 7.65 (m, 1H, H-7'). <sup>13</sup>C-NMR (CDCl<sub>3</sub>): ppm 25.19 (C-4, C-6), 26.06 (C-5), 27.01 (C-3, C-7), 29.81 (C-2, C-8), 38.31 (C-1), 110.25 (C-4'), 119.60 (C-7'), 123.95 (C-6'), 124.31 (C-5'), 141.28 (C-9'), 150.63 (C-8'), 171.55 (C-2').

**2-Decyl-1,3-benzoxazole 26**

Method A; Yield: 58%; <sup>1</sup>H-NMR (CDCl<sub>3</sub>): ppm 0.88 (t, J = 4 Hz, 3H, H-9), 1.29 (m, 12H, H-3, H-4, H-5, H-6, H-7, H-8), 1.87 (m, 2H, H-2), 2.92 (t, J = 7 Hz, 2H, H-1), 7.23 (m, 2H, H-5', H-6'), 7.44 (m, 1H, H-4'), 7.65 (m, 1H, H-7'). <sup>13</sup>C-NMR (CDCl<sub>3</sub>): ppm 14.23 (C-10), 26.97 (C-9), 28.84-29.72 (C-8-C-2), 32.08 (C-1), 110.40 (C-4'), 119.71 (C-7'), 124.20 (C-6'), 124.56 (C-5'), 141.64 (C-9'), 151.03 (C-8'), 167.59 (C-2').

**2-Dec-9-enyl-1,3-benzoxazole 27**

Method A; Yield: 62%; <sup>1</sup>H-NMR (CDCl<sub>3</sub>): ppm 1.34 (m, 8H, H-4, H-5, H-6, H-7), 1.87 (m, 2H, H-3), 2.05 (m, 2H, H-2), 2.93 (t, J = 7 Hz, 2H, H-1), 4.93 (m, 2H, H-9), 5.78 (m, 1H, H-8), 7.23 (m, 2H, H-5', H-6'), 7.46 (m, 1H, H-4'), 7.68 (m, 1H, H-7'). <sup>13</sup>C-NMR (CDCl<sub>3</sub>): ppm 26.93 (C-8), 28.80-29.68 (C-7-C-2), 33.92 (C-1), 110.39 (C-4'), 114.31 (C-10), 119.71 (C-7'), 124.20 (C-6'), 124.54 (C-5'), 139.26 (C-9), 141.88 (C-9'), 152.07 (C-8'), 167.52 (C-2').

**2-Styryl-1,3-benzoxazole 28**

Method A; Yield: 32%; mp 77,5-78°C (Lit.:<sup>21</sup> 83°C) <sup>1</sup>H-NMR (CDCl<sub>3</sub>): ppm 6.95-7.12 (m, 1H, H-1), 7.31-7.61 (m, 7H, H-4, H-5, H-6, H-7, H-8, H-5', H-6'), 7.70-7.82 (m, 3H, H-2, H-4', H-7'). <sup>13</sup>C-NMR (CDCl<sub>3</sub>): ppm 110.46 (C-4'), 114.17 (C-2), 120.06 (C-7'), 124.63 (C-6'), 125.32 (C-5'), 127.70 (C-6), 129.09 (C-5, C-7), 129.87 (C-1), 135.37 (C-4, C-8), 139.58 (C-3), 142.45 (C-9'), 151.60 (C-8'), 162.93 (C-2').

**2-(1-Adamantyl)-1,3-benzoxazole 29**

Method A; Yield: 52%; mp 92-3 °C; <sup>1</sup>H-NMR (CDCl<sub>3</sub>): ppm 1.79 (m, 6H, 3xCH<sub>2</sub>), 2.12 (m, 9H, 3xCH, 3xCH<sub>2</sub>), 7.26 (m, 2H, H-5', H-6'), 7.47 (m, 1H, H-4'), 7.69 (m, 1H, H-7'). <sup>13</sup>C-NMR (CDCl<sub>3</sub>): ppm 28.21 (3xCH<sub>2</sub>), 36.72 (3xCH<sub>2</sub>), 39.71 (C-1), 40.53 (3xCH), 110.5 (C-4'), 119.9 (C-7'), 124.1 (C-6'), 124.4 (C-5'), 141.7 (C-9'), 150.7 (C-8'), 173.2 (C-2').

**2-Cyclopentyl-1,3-benzothiazole 30**

Method A modified (2-aminothiophenol); Yield: 51%; <sup>1</sup>H-NMR (CDCl<sub>3</sub>): ppm 1.57-2.16 (m, 8H, H-2, H-3, H-4, H-5), 3.32 (t, J = 8Hz, 1H, H-1), 7.23 (m, 2H, H-5', H-6'), 7.81 (m, 1H, H-4'), 7.94 (m, 1H, H-7'). <sup>13</sup>C-

NMR (CDCl<sub>3</sub>): ppm 25.74 (C-3, C-4), 31.41 (C-2, C-5), 38.97 (C-1), 121.8 (C-4'), 123.5 (C-7'), 124.4 (C-6'), 125.6 (C-5'), 134.2 (C-9'), 153.9 (C-8'), 171.0 (C-2').

### 2-Cyclohexyl-1,3-benzothiazole 33

Method A modified (2-aminothiophenol); Yield: 49%; <sup>1</sup>H-NMR (CDCl<sub>3</sub>): ppm 1.19-1.91 (m, 8H, H-2, H-3, H-5, H-6), 2.20 (d, 2H, H-4), 3.07 (m, 1H, H-1), 7.21 (t, J = 7 Hz, 1H, H-5'), 7.41 (t, J = 7 Hz, 1H, H-6'), 7.80 (d, J = 8 Hz, 1H, H-4'), 7.96 (d, J = 8 Hz, 1H, H-7'). <sup>13</sup>C-NMR (CDCl<sub>3</sub>): ppm 25.9 (C-4), 26.2 (C-3, C-5), 33.6 (C-2, C-6), 43.6 (C-1), 121.7 (C-4'), 122.8 (C-7'), 124.6 (C-6'), 125.9 (C-5'), 134.8 (C-9'), 153.4 (C-8'), 171.6 (C-2').

### Biotransformation Products

#### *trans*-3-(Benz-1,3-oxazol-2-yl)cyclobutan-1-ol 3<sup>20</sup>

Method H (*Bacillus megaterium*); Yield: 14%; <sup>1</sup>H-NMR (CDCl<sub>3</sub>): ppm 2.44-2.87 (m, 4H, H-2, H-4), 3.71 (m, 1H, H-1), 4.02 (sb, 1H, OH), 4.78 (p, J = 8 Hz, 1H, H-3), 7.32 (m, 2H, H-5', H-6'), 7.47 (m, 1H, H-4'), 7.69 (m, 1H, H-7').

#### 1-(Benz-1,3-oxazol-2-yl)cyclobutan-1-ol 4

Method H (*Bacillus megaterium*); Yield: 6%; <sup>1</sup>H-NMR (CDCl<sub>3</sub>): ppm 1.95-2.15 (m, 2H, H-3), 2.45-2.83 (m, 4H, H-2, H-4), 4.39 (sb, 1H, OH), 7.32 (m, 2H, H-5', H-6'), 7.45 (m, 1H, H-4'), 7.67 (m, 1H, H-7'). <sup>13</sup>C-NMR (CDCl<sub>3</sub>): ppm 22.60 (C-3), 37.51 (C-2, C-4), 65.82 (C-1), 110.65 (C-4'), 119.74 (C-7'), 124.46 (C-6'), 124.86 (C-5'), 141.45 (C-9'), 151.17 (C-8'), 169.95 (C-2').

#### 3-(Benz-1,3-oxazol-2-yl)cyclopentan-1-ol 6

Method H (*Bacillus megaterium*; *Cunninghamella blakesleeana*); Yield: 20-40 %; (1*S*,3*S*)-6: [α]<sub>D</sub><sup>20</sup> +6.2 (c 2.0, dichloromethane); e.e. 30 %; Method D: Yield: 29 % (1*S*,3*S*)-6: [α]<sub>D</sub><sup>20</sup> +18.9 (c 2.0, dichloromethane); e.e. >98 %; <sup>1</sup>H-NMR (CDCl<sub>3</sub>): ppm 1.79 (m, 1H, H-4a), 1.97-2.26 (m, 4H, H-2a, H-4b, H-5), 2.38 (m, 1H, H-2b), 3.73 (t, J = 4z, 1H, H-1), 4.02 (sb, 1H, OH), 4.58 (m, 1H, H-3), 7.25 (m, 2H, H-5', H-6'), 7.43 (m, 1H, H-4'), 7.63 (m, 1H, H-7'). <sup>13</sup>C-NMR (CDCl<sub>3</sub>): ppm 29.10 (C-4), 35.12 (C-5), 36.80 (C-2), 40.91 (C-1), 73.36 (C-3), 110.48 (C-4'), 119.60 (C-7'), 124.31 (C-6'), 124.70 (C-5'), 141.19 (C-9'), 150.94 (C-8'), 170.40 (C-2'). MS: 39(10), 64(13), 91(10), 120(10), 133(15), 146(100), 159(10), 185(10), 203(30); M<sup>+</sup>

#### 2-(Benz-1,3-oxazol-2-yl)cyclopentan-1-ol 7

Method H (*Bacillus megaterium*; *Cunninghamella blakesleeana*); Yield: 6 %; (+)-7: [α]<sub>D</sub><sup>20</sup> +19.2 (c 0.5, dichloromethane); e.e. 33 %; mp 81-82 °C; <sup>1</sup>H-NMR (CDCl<sub>3</sub>): ppm 1.80-2.38 (m, 6H, H-3, H-4, H-5) 3.28 (m, 1H, H-1), 3.54 (sb, 1H, OH), 4.63 (m, 1H, H-2), 7.28 (m, 2H, H-5', H-6'), 7.42 (m, 1H, H-4'), 7.65 (m, 1H, H-7'). <sup>13</sup>C-NMR (CDCl<sub>3</sub>): ppm 22.34 (C-4), 28.87 (C-3), 34.34 (C-5), 48.02 (C-1), 77.28 (C-2), 110.65 (C-4'), 119.76 (C-7'), 124.50 (C-6'), 124.90 (C-5'), 141.17 (C-9'), 150.91 (C-8'), 170.23 (C-2'). MS: 39(10), 63(18), 91(5), 117(8), 133(15), 146(100), 160(10), 175(20), 203(20); M<sup>+</sup>

#### 3-(Benz-1,3-oxazol-2-yl)cyclopentan-1-one 8

Method H (*Cunninghamella blakesleeana*); Yield: 0 - 23 %; (1*R*)-8: [α]<sub>D</sub><sup>20</sup> +1.6 (c 0.5, dichloromethane); e.e. 64 %; Method E: Yield: 72 %; Method F: Yield: 70 %; (1*S*)-8: [α]<sub>D</sub><sup>20</sup> -0.8 (c 0.5, dichloromethane); e.e. 33 % mp 72-73 °C; <sup>1</sup>H-NMR (CDCl<sub>3</sub>): ppm 2.32-2.63 (m, 4H, H-4, H-5), 2.78 (d, J = 8 Hz, 2H, H-2), 3.69 (p, J = 8 Hz, 1H, H-1), 7.33 (m, 2H, H-5', H-6'), 7.48 (m, 1H, H-4'), 7.69 (m, 1H, H-7'). <sup>13</sup>C-NMR (CDCl<sub>3</sub>):

ppm 28.11 (C-4), 36.16 (C-5), 37.78 (C-2), 42.64 (C-1), 110.72 (C-4'), 120.14 (C-7'), 124.67 (C-6'), 125.21 (C-5'), 141.36 (C-9'), 151.19 (C-8'), 167.70 (C-2'), 215.95 (C-3).

### 3-(Benz-1,3-oxazol-2-ylmethyl)cyclopentan-1-ol 10

Method H (*Cunninghamella blakesleeana*); Yield: 33%;  $[\alpha]_{\text{D}}^{20}$  0;  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ ): ppm 1.20-2.18 (m, 6H, H-3, H-5, H-6), 2.47+2.73 (m, 1H, H-2), 2.89+3.03 (d,  $J = 8\text{Hz}$ , 2H, H-1), 4.38 (m, 1H, H-4), 5.12 (sb, 1H, OH), 7.37 (m, 2H, H-5', H-6'), 7.45 (m, 1H, H-4'), 7.63 (m, 1H, H-7').  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ ): ppm 30.17+30.46 (C-6), 34.57+34.89 (C-5), 35.21+35.67 (C-3), 35.79+36.13 (C-2), 41.69+42.46 (C-1), 73.36+73.58 (C-4), 110.46 (C-4'), 119.70 (C-7'), 124.28 (C-6'), 124.67 (C-5'), 141.56 (C-9'), 151.08 (C-8'), 166.58 (C-2').

### 3-(Benz-1,3-oxazol-2-ylmethyl)cyclopentan-1-one 11

Method H (*Cunninghamella blakesleeana*); Yield: 14%; (-)-11:  $[\alpha]_{\text{D}}^{20}$  -8.8 (c 1.8, dichloromethane);  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ ): ppm 1.70 (m, 1H, H-6a), 1.95-2.38 (m, 4H, H-3a, H-5, H-6b), 2.53 (dd,  $J_1 = 7\text{Hz}$ ,  $J_2 = 18\text{Hz}$ , 1H, H-3b), 2.81 (m, 1H, H-2), 3.07 (d,  $J = 8\text{Hz}$ , 2H, H-1), 7.26 (m, 2H, H-5', H-6'), 7.42 (m, 1H, H-4'), 7.65 (m, 1H, H-7').  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ ): ppm 29.36 (C-6), 34.05 (C-5), 34.67 (C-3), 38.39 (C-2), 44.76 (C-1), 110.53 (C-4'), 119.90 (C-7'), 124.47 (C-6'), 124.95 (C-5'), 141.42 (C-9'), 150.97 (C-8'), 165.27 (C-2'), 217.78 (C-4).

### trans-4-(Benz-1,3-oxazol-2-yl)cyclohexan-1-ol 13

Method H (*Cunninghamella blakesleeana*; *Bacillus megaterium*); Yield: 16%; mp 119-120 °C;  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ ): ppm 1.40-2.33 (m, 8H, H-2, H-3, H-5, H-6) 2.87 (m, 1H, H-1), 3.42 (sb, 1H, OH), 3.71 (m, 1H, H-4), 7.28 (m, 2H, H-5', H-6'), 7.44 (m, 1H, H-4'), 7.67 (m, 1H, H-7').  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ ): ppm 28.75 (C-3, C-5), 34.80 (C-2, C-6), 37.16 (C-1), 69.86 (C-4), 110.47 (C-4'), 119.78 (C-7'), 124.28 (C-6'), 124.70 (C-5'), 141.29 (C-9'), 150.77 (C-8'), 169.70 (C-2').

### 2-(Benz-1,3-oxazol-2-yl)cyclohexan-1-ol 14

Method H (*Bacillus megaterium*); Yield: 17%; (1R,2R)-14:  $[\alpha]_{\text{D}}^{20}$  -49.3 (c 1.0, dichloromethane); e.e. 65 %; Method D; Yield: 26 %; (1R,2R)-14:  $[\alpha]_{\text{D}}^{20}$  -86.1 (c 1.0, dichloromethane); e.e. >98 %; mp 152-153 °C;  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ ): ppm 1.40-1.58 (m, 4H, H-5, H-6) 1.87 (m, 2H, H-4), 2.10-2.38 (m, 2H, H-3), 2.89 (m, 1H, H-1), 3.85 (sb, 1H, OH), 4.03 (m, 1H, H-2), 7.31 (m, 2H, H-5', H-6'), 7.49 (m, 1H, H-4'), 7.69 (m, 1H, H-7').  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ ): ppm 24.70 (C-6), 25.42 (C-5), 29.34 (C-4), 34.02 (C-3), 46.38 (C-1), 71.93 (C-2), 110.70 (C-4'), 119.91 (C-7'), 124.53 (C-6'), 124.92 (C-5'), 141.06 (C-9'), 150.73 (C-8'), 168.69 (C-2'). MS: 39(10), 63(10), 91(5), 120(5), 133(20), 146(100), 160(10), 189(30), 217(10):  $\text{M}^+$

### 3-(Benz-1,3-oxazol-2-yl)cyclohexeneoxide 18

Method H (*Bacillus megaterium*); Yield: 18%;  $[\alpha]_{\text{D}}^{20}$  0 (c 1.0, dichloromethane); e.e. 0 %; mp 79-80 °C; Method I; Yield: 82 %;  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ ): ppm 1.63 (m, 1H, H-5b), 1.98 (m, 3H, H-5a, H-6), 2.25 (m, 1H, H-2a), 2.54 (dd,  $J_1 = 4\text{Hz}$ ,  $J_2 = 15\text{Hz}$ , 1H, H-2b), 3.13 (m, 2H, H-3, H-4), 3.80 (m, 1H, H-1), 7.23 (d, 2H, H-5', H-6'), 7.43 (d, 1H, H-4'), 7.68 (d, 1H, H-7').  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ ): ppm 22.93 (C-6), 24.51 (C-5), 28.65 (C-2), 30.72 (C-1), 51.49 (C-4), 52.27 (C-3), 110.46 (C-4'), 119.78 (C-7'), 124.25 (C-6'), 124.72 (C-5'), 141.24 (C-9'), 150.83 (C-8'), 169.40 (C-2').

### 4-(Benz-1,3-oxazol-2-yl)cycloheptan-1-one 20

Method H (*Cunninghamella blakesleeana*; *Bacillus megaterium*); Yield: 17 %; (+)-20:  $[\alpha]_{\text{D}}^{20}$  +39.4 (c 1.0; dichloromethane); e.e. 64 %; Yield: 6 %; (-)-20:  $[\alpha]_{\text{D}}^{20}$  -12.2 (c 1.0; dichloromethane); e.e. 19 %; Method F; Yield: 90 %; (+)-20:  $[\alpha]_{\text{D}}^{20}$  +16.1 (c 1.0, dichloromethane) e.e. 44 %; mp 94-95 °C;  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ ):

ppm 1.55-2.78 (m, 10H, H-2, H-3, H-5, H-6, H-7); 3.22 (tt,  $J_1 = 4$  Hz,  $J_2 = 9$  Hz, 1H, H-1); 7.32 (m, 2H, H-5', H-6'); 7.49 (m, 1H, H-4'); 7.68 (m, 1H, H-7').  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ ): ppm 22.4 (t); 27.8 (t); 33.9 (t); 41.2 (t); 41.7 (t) (C-2 - C-3; C-5 - C-7); 43.6 (C-1); 110.5 (C-4'); 119.8 (C-7'); 124.2 (C-6'); 124.8 (C-5'); 140.4 (C-9'); 150.2 (C-8'); 169.3 (C-2'); 213.3 (C-4).

#### 4-(Benz-1,3-oxazol-2-yl)cycloheptan-1-ol 21

Method H (*Cunninghamella blakesleeana*; *Bacillus megaterium*); Yield: 22 %; (+)-**21**:  $[\alpha]_{\text{D}}^{20} +7.9$  (c 1.0; dichloromethane); e.e. 44 %; Method D; Yield: 30 %; (+)-**21**:  $[\alpha]_{\text{D}}^{20} +18.0$  (c 1.0; dichloromethane); e.e. >98 %;  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ ): ppm 1.53-2.32 (m, 11H, H-2, H-3, H-5, H-6, H-7, OH); 3.23 (m, 1H, H-1); 3.95 (m, 1H, H-4); 7.25 (m, 2H, H-5', H-6'); 7.49 (m, 1H, H-4'); 7.65 (m, 1H, H-7').  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ ): ppm 20.3 (t); 26.2 (t); 31.9 (t); 35.3 (t); 37.7 (t) (C-2 - C-3; C-5 - C-7); 39.4 (C-1); 72.3 (C-4); 110.4 (C-4'); 119.7 (C-7'); 124.1 (C-6'); 124.5 (C-5'); 140.5 (C-9'); 150.3 (C-8'); 170.8 (C-2').

#### 2-(Benz-1,3-oxazol-2-yl)cycloheptan-1-ol 22

Method H (*Cunninghamella blakesleeana*; *Bacillus megaterium*); Yield: 5 %; Yield: 1 %;  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ ): ppm 1.44-2.23 (m, 11H, H-3, H-4, H-5, H-6, H-7, OH); 3.45 (p,  $J = 8$  Hz, 1H, H-1); 4.21 (tt,  $J_1 = 8$  Hz,  $J_2 = 11$  Hz, 1H, H-2); 7.28 (m, 2H, H-5', H-6'); 7.43 (m, 1H, H-4'); 7.63 (m, 1H, H-7').

#### 4-(Benz-1,3-oxazol-2-yl)cyclooctan-1-one 24

Method H (*Cunninghamella blakesleeana*; *Bacillus megaterium*); Yield: 7 %; (+)-**24**:  $[\alpha]_{\text{D}}^{20} +10.5$  (c 1.0; dichloromethane) e.e. 7 %; yield: 3 %; Method F: (-)-**24**: e.e. 15 %;  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ ): ppm 1.6-2.7 (m, 12H, H-2, H-3, H-5, H-6, H-7, H-8), 3.20 (m, 1H, H-1), 7.27 (m, 2H, H-5', H-6'), 7.48 (m, 1H, H-4'), 7.57 (m, 1H, H-7').  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ ): ppm 24.8 (t), 26.8 (t), 27.2 (t), 28.5 (t), 31.8 (t), 38.9 (t) (C-2 - C-3; C-5 - C-8), 41.2 (C-1), 110.6 (C-4'), 120.0 (C-7'), 124.4 (C-6'), 124.8 (C-5'), 141.3 (C-9'), 150.9 (C-8'), 169.5 (C-2'), 216.7 (C-4).

#### 4-(Benz-1,3-oxazol-2-yl)cyclooctan-1-ol 25

Method H (*Cunninghamella blakesleeana*; *Bacillus megaterium*); Yield: 9 %;  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ ): ppm 1.5-2.3 (m, 12H, H-2, H-3, H-5, H-6, H-7, H-8), 3.1-3.4 (m, 2H, H-1, OH), 3.95 (m, 1H, H-4), 7.27 (m, 2H, H-5', H-6'), 7.47 (m, 1H, H-4'), 7.66 (m, 1H, H-7').  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ ): ppm 22.5 (t), 22.9 (t), 25.8 (t), 28.6 (t), 33.2 (t), 34.8 (t) (C-2 - C-3; C-5 - C-8), 39.0 (C-1), 71.9 (C-4), 110.5 (C-4'), 119.8 (C-7'), 124.2 (C-6'), 124.6 (C-5'), 141.3 (C-9'), 150.8 (C-8'), 170.9 (C-2').

#### 3-(Benz-1,3-thiazol-2-yl)cyclopentan-1-ol 31

Method H (*Bacillus megaterium*); Yield: 12 %;  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ ): ppm 1.70-2.51 (m, 6H, H-2, H-4, H-5); 2.91-3.62 (m, 1H, OH); 3.93 (m, 1H, H-1); 4.60 (m, 1H, H-3); 7.31-7.47 (m, 2H, H-5', H-6'); 7.8 (d,  $J = 8$  Hz, 1H, H-4'); 7.97 (d,  $J = 8$  Hz, 1H, H-7').  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ ): 31.66 (C-4), 35.33 (C-5), 42.32 (C-2), 43.42 (C-1), 73.49 (C-3), 121.58 (C-4'), 122.66 (C-7'), 124.75 (C-6'), 126.00 (C-5'), 134.92 (C-9'), 153.35 (C-8'), 176.30 (C-2').

#### 2-(Benz-1,3-thiazol-2-yl)cyclopentan-1-ol 32

Method H (*Bacillus megaterium*); Yield: 5 %;  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ ): ppm 1.65-2.45 (m, 6H, H-3, H-4, H-5); 3.21-3.62 (m, 1H, OH); 3.43 (dd,  $J_1 = 8.3$  Hz,  $J_2 = 16$  Hz, 1H, H-1); 4.47 (dd,  $J_1 = 7.3$ ,  $J_2 = 14.5$ , 1H, H-2); 7.3-7.47 (m, 2H, H-5', H-6'); 7.81 (d,  $J = 8$  Hz, 1H, H-4'); 7.97 (d,  $J = 8$  Hz, 1H, H-7').

#### 3-(Benz-1,3-thiazol-2-yl)cyclopentan-1-one 34

Method H (*Bacillus megaterium*); Yield: 3 %;  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ ): ppm 2.33-2.71 (m, 4H, H-4, H-5); 2.80 (dd,  $J_1 = 8.3$  Hz,  $J_2 = 2.5$  Hz, 1H, H-2); 3.94 (m, 1H, H-1); 7.31-7.47 (m, 2H, H-5', H-6'); 7.82 (d,  $J = 8$  Hz, 1H, H-4'); 7.97 (d,  $J = 8$  Hz, 1H, H-7').

**Determination of Product Structures****3-(Benz-1,3-oxazol-2-yl)cyclobut-1-yl-4-nitrobenzoate 36<sup>20</sup>**

Method C; Yield: 95 %; mp 148-149 °C; X-ray; <sup>1</sup>H-NMR (CDCl<sub>3</sub>): 2.75-2.90 (m, 2H, H-2, H-4); 2.97-3.15 (m, 2H, H-2, H-4); 3.92 (dt, 1H, H-1); 5.66 (dt, 1H, H-3); 7.33 (m, 2H, H-5', H-6'); 7.51 (m, 1H, H-4'); 7.69 (m, 1H, H-7'); 8.2-8.36 (m, 4H, p-Nitroaryl-H). <sup>13</sup>C-NMR (CDCl<sub>3</sub>): 27.86 (C-2, C-4), 34.54 (C-1), 69.43 (C-3), 110.53 (C-4'), 119.81 (C-7'), 123.65 (p-Nitroaryl), 124.43 (C-6'), 124.92 (C-5'), 130.18 (p-Nitroaryl), 130.84 (p-Nitroaryl), 135.38 (p-Nitroaryl), 139.57 (C-9'), 150.8 (C-8'), 164.1 (Carboxy), 168.3 (C-2').

**3-(Benz-1,3-oxazol-2-yl)cyclopent-1-yl-4-nitrobenzoate 37**

2-(3-Hydroxycyclopentyl)benzoxazole (10 mg; 0.0492 mmole) is dissolved in THF (0.45 mL), triphenylphosphine (26 mg; 0.0984 mmole), diethylazodicarboxylate (17 mg; 0.0984 mmole) and 4-nitrobenzoic acid (16.5 mg; 0.0984 mmole) are added. The solution is allowed to stand at r.t. for 24 h. Evaporation and flash chromatography of the residue (ethyl acetate / hexanes 1:8) yields 14 mg of ester.

<sup>1</sup>H-NMR(CDCl<sub>3</sub>): 2.12-2.68 (m, 6H, H-2, H-4, H-5); 3.63 (m, 1H, H-1); 5.58 (m, 1H, H-3); 7.29 (m, 2H, H-5', H-6'); 7.41 (dd, 1H, H-4'); 7.58 (dd, 1H, H-7'); 8.03 (d, 2H, p-Nitroaryl-H); 8.14 (d, 2H, p-Nitroaryl-H).

**cis-3-(Benz-1,3-oxazol-2-yl)cyclopentan-1-ol 38**

Nitrobenzoate **37** (16 mg; 0.0454 mmole) is dissolved in dry methanol (2 mL) and 5 drops of a solution of sodium (50 mg) dissolved in methanol (5 mL) are added. The solution is allowed to stand at r.t. for 4 h. Evaporation of the solvent until one third is still left, addition of dichloromethane (4 mL), extraction with 1 N HCl, saturated bicarbonate-solution and water, drying (Na<sub>2</sub>SO<sub>4</sub>) and evaporation gives 20 mg of a yellow oil, which is purified by flash chromatography.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>): ppm 1.98-2.44 (m, 6H, H-2, H-4, H-5); 3.55 (m, 1H, H-1); 3.73 (sb, 1H, OH); 4.48 (m, 1H, H-3); 7.25 (m, 2H, H-5', H-6'); 7.47 (dt, 1H, H-4'); 7.65 (dt, 1H, H-7') <sup>13</sup>C-NMR (CDCl<sub>3</sub>): ppm 30.2 (C-4); 36.0 (C-2); 37.5 (C-5); 40.5 (C-1); 73.7 (C-3); 110.6 (C-4'); 119.8 (C-7'); 124.5 (C-6'); 124.8 (C-5'); 141.88 (C-9') 152.07 (C-8'); 167.5 (C-2').

**3-Oxocyclopentanecarboxylic acid 39<sup>10</sup>**

Method G; Yield: 43 %; (*R*)-**39**: [α]<sub>D</sub><sup>20</sup> +15.0 (c 1.0; MeOH) e.e. 64 %; Lit:<sup>10</sup> (*S*)-**39**: [α]<sub>D</sub><sup>20</sup> -21 (c 0.75; CH<sub>3</sub>OH; e.e. 85-90 %); <sup>1</sup>H-NMR (CDCl<sub>3</sub>): ppm 2.05-2.35 (m, 4H, H-4, H-5); 2.45 (t, 2H, H-2); 3.05-3.20 (m, 1H, H-1); 3.72 (s, 3H, OCH<sub>3</sub>). <sup>13</sup>C-NMR (CDCl<sub>3</sub>): ppm 26.75 (C-4), 37.58 (C-5), 40.99 (C-2), 41.34 (C-1), 52.27 (OCH<sub>3</sub>), 174.87 (COO), 216.37 (C-3).

**3-(Benz-1,3-oxazol-2-yl)cyclopent-1-yl-acetate 40**

Method C; Yield: 82%; mp 48-49 °C; Method D; Yield: 65%; (*1S,3S*)-**40**: [α]<sub>D</sub><sup>20</sup> +8.6 (c 3.0; dichloromethane); e.e. 10 %; <sup>1</sup>H-NMR (CDCl<sub>3</sub>): ppm 1.82-1.93 (m, 1H, H-5a); 2.03 (s, 3H, Ac); 2.05-2.39 (m, 5H; H-2, H-4, H-5b); 3.63 (p, J = 8 Hz; 1H, H-1); 5.37 (m, 1H, H-3); 7.21 (m, 2H, H-5', H-6'); 7.43 (dt, 1H, H-4'); 7.67 (dt, 1H, H-7'). <sup>13</sup>C-NMR (CDCl<sub>3</sub>): ppm 21.4 (Ac); 29.4 (C-5); 32.4 (C-4); 37.2 (C-2); 38.1 (C-1); 76.4 (C-3); 110.5 (C-4'); 119.8 (C-7'); 124.3 (C-6'); 124.7 (C-5'); 141.5 (C-9'); 151.1 (C-8'); 169.4 (C-2'); 170.7 (AcCO).

**3-(Benz-1,3-oxazol-2-yl)cyclopent-1-yl-(1*S*)-camphanoate 41**

Method C; Yield: 88 %; mp 141-142 °C; X-ray; <sup>1</sup>H-NMR (CDCl<sub>3</sub>): ppm 0.97 (s, 3H, camph); 1.06 (s, 3H, camph); 1.13 (s, 3H, camph); 1.69 (m, 1H, camph); 1.88-2.50 (m, 9H, H-5, H-4, H-2, camph); 3.68 (p, J = 8 Hz; 1H, H-1); 5.53 (m, 1H, H-3); 7.28 (m, 2H, H-5', H-6'); 7.43 (m, 1H, H-4'); 7.65 (m, 1H, H-7'). <sup>13</sup>C-NMR (CDCl<sub>3</sub>): ppm 9.9 (camph); 17.0 (camph); 17.1 (camph); 29.2 (t); 29.4 (t); 30.9 (t); 32.6 (t); 37.2 (t); 38.1 (C-1); 54.4 (s); 55.1 (s); 76.8 (C-3); 91.2 (s); 110.6 (C-4'); 119.9 (C-7'); 124.5 (C-6'); 124.9 (C-5'); 141.5 (C-9'); 151.2 (C-8'); 167.3 (camph); 169.1 (C-2'); 178.3 (camph).

**4-(Benz-1,3-oxazol-2-yl)cyclohex-1-yl-acetate 42**

Method C; Yield: 87 %; mp 83-4 °C; X-ray; <sup>1</sup>H-NMR (CDCl<sub>3</sub>): 1.53 (dq, 2H, H-2a, H-6a); 1.82 (m, 2H, H-2b, H-6b); 2.08 (s, 3H, Ac); 2.15 (m, 2H, H-3a, H-5a); 2.32 (m, 2H, H-3b, H-5b); 2.97 (ddt, 1H, H-1); 4.81 (ddt, 1H, H-4); 7.28 (m, 2H, H-5', H-6') 7.48 (m, 1H, H-4'); 7.56 (m, 1H, H-7'). <sup>13</sup>C-NMR (CDCl<sub>3</sub>): 21.5

(AcCH<sub>3</sub>); 28.3 (C-2, C-6); 30.9 (C-3, C-5); 37.0 (C-1); 72.2 (C-4); 110.5 (C-4'); 119.9 (C-7'); 124.4 (C-6'); 124.8 (C-5'); 141.5 (C-9'); 150.9 (C-8'); 169.2 (C-2'); 170.6 (AcCO).

#### **trans-2-Hydroxycyclohexanecarbonitrile 44**

This compound was prepared according to the literature procedure.<sup>15</sup> Method D; Yield: 38 %; (**1S,2R**)-**44**: [ $\alpha$ ]<sub>D</sub><sup>20</sup> -47.2 (c 3.0; dichloromethane); e.e. 86 %; (**1S,2R**)-**44**: [ $\alpha$ ]<sub>D</sub><sup>20</sup> -55.4 (c 3.0; dichloromethane); e.e. >98 %<sup>16</sup>

#### **trans-2-Butanoyloxycyclohexanecarbonitrile 45**

Method C; Yield: 97 %; Method D; Yield: 46 %; (**1R,2S**)-**45**: [ $\alpha$ ]<sub>D</sub><sup>20</sup> +41.1 (c 6.0; dichloromethane); e.e. 60 %; <sup>1</sup>H-NMR (CDCl<sub>3</sub>): 0.89 (t, 3H, CH<sub>3</sub>); 1.21-1.41 (m, 3H); 1.48-1.76 (m, 5H); 2.03 (m, 2H, CH<sub>2</sub>-Bu); 2.25 (dt, 2H, CH<sub>2</sub>-Bu); 2.52 (dt, 1H, H-1); 4.81 (dt, 1H, H-2). <sup>13</sup>C-NMR (CDCl<sub>3</sub>): ppm 13.4 (CH<sub>3</sub>); 18.5 (CH<sub>2</sub>-Bu); 22.9 (CH<sub>2</sub>-Bu); 23.7 (C-4); 28.0 (C-3); 30.4 (C-5); 33.8 (C-6); 36.3 (C-1); 71.3 (C-2); 119.9 (CN); 172.4 (BuCOO).

#### **trans-2-Hydroxycyclohexanecarboxylic acid 46**

A solution of **44** (1.00 g; 7.99 mmole) and potassium hydroxide (2.17 g; 38.7 mmole) in ethanol (25 mL; 95 %) is refluxed for 16 h. Then the reaction mixture is cooled with ice and acidified with 6 N HCl to pH 2. Water is added to a volume of 150 mL and this solution is extracted with chloroform, dried (Na<sub>2</sub>SO<sub>4</sub>) and evaporated. The crude product **46** is then reesterified refluxing it in methanol containing 8 % gaseous hydrochloric acid overnight. Evaporation of the solvent and flash chromatography (ethyl acetate / hexanes 1:8) gives *trans*-2-hydroxycyclohexanecarboxylic acid methyl ester **47** (600 mg; 48 %). The ester is then dissolved in 2 N NaOH solution (12 mL; 23.4 mmole) and stirred for ten minutes. Acidification using 6 N HCl and extraction with ether gives after drying (Na<sub>2</sub>SO<sub>4</sub>) and evaporation *trans*-2-hydroxycyclohexanecarboxylic acid **46** (575 mg) which crystallizes in the refrigerator. mp 101-102 °C; <sup>1</sup>H-NMR (CDCl<sub>3</sub>): 1.12-1.47 (m, 4H, H-4, H-5); 1.71 (m, 2H, H-3); 2.01 (m, 2H, H-6); 2.27 (m, 1H, H-1) 3.73 (m, 1H, H-2); 6.30 (bs, 2H, OH). <sup>13</sup>C-NMR (CDCl<sub>3</sub>): 23.8 (C-5); 24.3 (C-4); 28.3 (C-3); 33.9 (C-6); 49.9 (C-1); 71.3 (C-2); 179.3.6 (CO).

#### **2-(Benz-1,3-oxazol-2-yl)cyclohex-1-yl-acetate 48**

Method C; Yield: 83 %; Method D; yield: 68 %; <sup>1</sup>H-NMR (CDCl<sub>3</sub>): ppm 1.30-1.48 (m, 3H); 1.75-1.88 (m, 6H); 2.12-2.19 (m, 2H); 3.12 (dt, J<sub>1</sub> = 4Hz, J<sub>2</sub> = 11 Hz, 1H); 5.21 (m, 1H); 7.26 (m, 2H); 7.39 (m, 1H); 7.63 (m, 1H). <sup>13</sup>C-NMR (CDCl<sub>3</sub>): ppm 21.1 (q); 24.1 (t); 24.8 (t); 29.8 (t); 31.5 (t); 43.5 (d); 73.8 (d); 110.6 (d); 120.0 (d); 124.3 (d); 124.8 (d); 141.5 (s); 150.9 (s); 167.3 (s); 170.1 (s).

#### **2-(Benz-1,3-oxazol-2-yl)cyclohex-1-yl-(1S)-camphanoate 49**

Method C; Yield: 82 %; mp 165-166 °C; X-ray; <sup>1</sup>H-NMR (CDCl<sub>3</sub>): ppm 0.57 (s, 3H, camph); 0.92 (s, 3H, camph); 1.03 (s, 3H, camph); 1.39-1.52 (m, 4H); 1.78-1.95 (m, 4H); 2.17-2.35 (m, 4H); 3.25 (m, 1H, H-1); 5.38 (m, 1H, H-2); 7.28 (m, 2H, H-5', H-6'); 7.47 (m, 1H, H-4'); 7.63 (m, 1H, H-7').

#### **Ethyl 4-Oxocycloheptanecarboxylate 52**

Method G; Yield: 52 %; <sup>1</sup>H-NMR (CDCl<sub>3</sub>): ppm 1.23 (t, J = 7 Hz, 3H, CH<sub>3</sub>); 1.57-2.18 (m, 7H); 2.42-2.61 (m, 4H); 4.12 (q, J = 7 Hz, 2H, OCH<sub>2</sub>). <sup>13</sup>C-NMR (CDCl<sub>3</sub>): ppm 14.4 (CH<sub>3</sub>); 22.6 (t); 26.6 (t); 32.8 (t); 41.7 (t); 43.7 (t) (C-2 - C-4; C-5 - C-7); 46.7 (C-1); 60.7 (OCH<sub>2</sub>); 175.1 (COO); 213.5 (C-4).

For comparison: **Ethyl 3-oxocycloheptanecarboxylate 51**<sup>18</sup>

<sup>1</sup>H-NMR (CDCl<sub>3</sub>): ppm 1.25 (t, 3H, J = 7.1 Hz); 1.44-2.13 (m, 6H), 2.42-2.57 (m, 2H), 2.65-2.72 (m, 2H), 2.80 (q, 1H, J<sub>AB</sub> = 15.5 Hz, J<sub>vic</sub> = 10.8 Hz), 4.14 (q, 2H, J = 7.1 Hz). <sup>13</sup>C-NMR (CDCl<sub>3</sub>): ppm 14.03, 23.78, 28.14, 33.08, 41.09, 43.75, 45.38, 60.6, 174.3, 211.9.

#### **4-(Benz-1,3-oxazol-2-yl)cyclohept-1-yl-acetate 53**

Method C; <sup>1</sup>H-NMR (CDCl<sub>3</sub>): 1.70-2.35 (m, 10H, H-2, H-3, H-5, H-6, H-7); 2.07 (s, 3H, H-Acetyl); 3.24 (m, 1H, H-1); 5.03 (m, 1H, H-4); 7.25-7.35 (m, 2H, H-5', H-6'); 7.48 (m, 1H, H-4'); 7.67 (m, 1H, H-7').

#### **4-(Benz-1,3-oxazol-2-yl)cyclohept-1-yl-(1S)-camphanoate 54**

Method C; <sup>1</sup>H-NMR (CDCl<sub>3</sub>): ppm 0.98 (s, 3H, camph); 1.08 (s, 3H, camph); 1.14 (s, 3H, camph); 1.61-2.52 (m, 14H); 3.25 (m, 1H, H-1); 5.20 (m, 1H, H-4); 7.29-7.38 (m, 2H, H-5', H-6'); 7.51 (m, 1H, H-4'); 7.69 (m,

1H, H-7').

**Methyl 4-Oxocyclooctanecarboxylate 56**

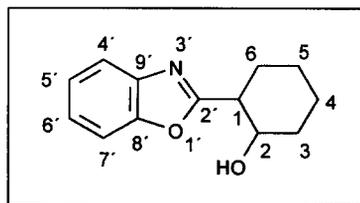
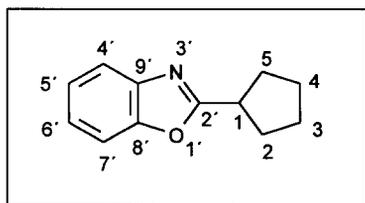
Method G; Yield: 55 %; <sup>1</sup>H-NMR (CDCl<sub>3</sub>): ppm 1.40-2.51 (m, 13H); 3.68 (s, 3H, OCH<sub>3</sub>). <sup>13</sup>C-NMR (CDCl<sub>3</sub>): ppm 24.88 (t), 25.12 (t), 28.11 (t), 31.69 (t), 34.24 (t), 42.23 (t) (C-2 - C-3, C-5 - C-8), 49.79 (C-1), 51.58 (OCH<sub>3</sub>), 174.12 (COO), 212.65 (C-4).

For comparison: **Methyl 3-oxocycloheptanecarboxylate 55**<sup>18</sup>

<sup>1</sup>H-NMR (CDCl<sub>3</sub>): ppm 1.39-2.04 (m, 8H), 2.42 (m, 2H), 2.56 (dd, 1H, J<sub>AB</sub> = 12.5 Hz, J<sub>vic</sub> = 2.2 Hz), 2.79 (t, 1H, J = 12.9 Hz), 3.69 (s, 3H, OCH<sub>3</sub>). <sup>13</sup>C-NMR (CDCl<sub>3</sub>): ppm 23.0, 24.5, 27.0, 29.5, 42.4, 42.5, 42.6, 51.6, 174.6, 214.2.

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