# A New Route to Protected Acyloins and Their Enzymatic Resolution with Lipases

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**Keywords:** Acyloins / Alkylation / Enzymatic catalysis / Hydrolases / Hydroxyalkanones / Kinetic resolution

A series of 16 different 3-acyloxy methyl ketones, the acyloin acetates and butyrates (±)-**5**, was synthesised by a straightforward new method through alkylation of *tert*-butyl 2-acyloxyacetoacetates **3**, followed by chemoselective dealkoxycarbonylation of the *tert*-butyloxycarbonyl group in the presence of other ester groups. Subsequent hydrolysis of (±)-**5** can be achieved with base to give racemic acyloins **6**, or with lipase catalysis to afford the corresponding non-racemic acyloins (*S*)-**6**. The remaining (*R*)-acyloin esters **5** can be racemised and resubjected to the procedure, or hydrolysed chemically. The kinetic resolution with two of the six tested enzymes, CAL-B and BCL (PS) lipase, proceeded selectively [enantiomeric ratio (*E*) values between 50 and > 200] and most of the acyloins (*S*)-**6** were obtained in very high enantiomeric excesses (up to > 99% *ee*).



## Introduction

The acyloin moiety is a key structural feature of many natural products.[1−4] Chiral α-hydroxy ketones (acyloins) are versatile synthetic intermediates in the asymmetric synthesis of a wide range of bioactive compounds. Reduction of the acyloin carbonyl group, for example, gives access to either the *threo* or the *erythro* 1,2-diols, which are highly valuable building blocks.[5] Wittig olefination allows the synthesis of chiral allylic alcohols, which have been applied in, for example, pheromone synthesis.[6] Furthermore, chiral α-hydroxy ketones have been used to synthesise *syn* or *anti* aldols with high diastereoselectivity by employment of boron-mediated aldol addition[7−9] or titanium enolates.[10,11] Baeyer−Villiger oxidation of chiral protected α-hydroxy ketones results in chiral acetals that can be converted into chiral secondary alcohols through Lewis acid-supported nucleophilic substitution with organocuprates.[12] Further applications of chiral acyloins can be found in the synthesis of chiral β-lactams and γ-butyrolactones.[13−15] These are only a few examples of the synthetic scope of optically pure acyloins.

Several chemical methods for the preparation of chiral α-hydroxy ketones are described in the literature. Useful methods include the enantioselective oxidation of chiral enolates,[16] the oxidation of non-chiral enolates with chiral oxidants,[17] or the use of DiTOX, a chiral dithiane oxide.[18] Further methods have extensively utilised the Sharpless asymmetric epoxidation to introduce chirality. The resulting optically pure epoxy alcohols can subsequently be converted into the corresponding alkynols and further transformed into acylprotected acyloins by use of a Ru catalyst.[19] Finally, L-amino acids from the chiral pool have been used as starting materials for the synthesis of some particular (3*S*)-3-hydroxy-2-ketones.[20]

In addition to the described classical chemical approaches to optically active acyloins, some biocatalytic routes to these compounds have also been reported. The most common approach so far has been the reduction of 1,2-diketones either with enzymes or by microbial reduction with whole-cell systems.[1,4,21,22] Frequently encountered drawbacks of these methods are overreduction to diols and also a lack of regioselectivity, yielding two regioisomeric acyloins. A reductive resolution of α-hydroxy ketones to give enantiopure *syn* diols and chiral acyloins, albeit one resulting in a relatively low isolated yield of the optically pure acyloin, has also been described.[23] Oxidative biocatalytic approaches towards optically pure acyloins have been discussed as well. Thus, enzyme oxidation of racemic *syn*

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or *anti* 1,2-diols allowed the isolation of enantiomerically enriched diols and acyloins.[24] However, the isolated yields, especially those of open-chain chiral acyloins, were rather disappointing. In general, it can be stated that chiral acyloins can be prepared with oxidoreductases either reductively or oxidatively, providing the products with high *ee*s, but that the methods suffer from drawbacks such as overreduction, regioselectivity problems, and low yields.

In addition to oxidoreductases, decarboxylases and lyases have also been used to produce optically active acyloins.[25] As an example, an acetoacetate decarboxylase-catalysed kinetic resolution of 2-ethyl-2-hydroxy-3-oxocarboxylate has been reported.[26] Recently, a phenylpyruvate decarboxylase from *Achromobacter eurydice* SC16386 was used in asymmetric acyloin condensations with different aldehydes.[27] A major drawback so far is that only a very limited range of different substrates is accepted by these enzymes.

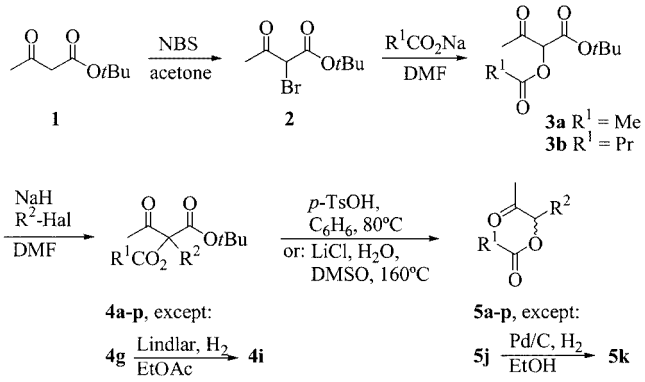
Although potentially a useful approach, the application of hydrolases for the preparation of α-hydroxy ketones has so far been limited to certain examples. Although kinetic resolutions of many secondary alcohols and their esters are well documented, only a few examples of α-hydroxy ketones, mostly of pseudo-*meso* precursors, are known to date.[28−31] The largest set of experimental data was collected by Hiyama et al., who screened 84 commercially available hydrolases in order to synthesise enantiomerically pure 2-hydroxy-1-indanone as a key precursor of chiral 1-amino-2-indanol, a structural element of a HIV-protease inhibitor.[31b]

During our synthetic studies towards epothilones B and D,[32] we were confronted with the need to introduce an optically pure α-hydroxy ketone functionality. We envisioned that a kinetic resolution of a racemic acyloin acetate with lipases might afford the desired optically pure α-hydroxy ketone. However, the lack of literature information on kinetic resolutions of acyloins prompted us to synthesise a series of 16 different 3-acyloxy-2-alkanones **5** (Scheme 1), and to screen them for selective hydrolysis with six different commercially available lipases. The results of our studies are presented in this paper.

## Results and Discussion

The acyloin esters **5a**−**p** used in our study were synthesised by application of simple acetoacetate chemistry, based on a similar procedure by Lawesson et al.[33] The original method proceeds through oxidation of alkylated acetoacetates with benzoyl peroxide followed by solvent-free dealkoxycarbonylation with *p*TsOH. Only benzoyl esters are accessible in this way, however. Furthermore, since oxidation is performed after introduction of the alkyl group, problems with other, oxidation-labile functionalities could arise. Another drawback in Lawesson's approach is that two steps are required after the alkylation to reach the desired intermediates **4**.

We therefore developed a more straightforward and variable synthesis of intermediates **4**, based on the introduction of the acyloxy group into the acetoacetate before alkylation.[34] Bromination of *tert*-butyl acetoacetate (**1**) with NBS to give the bromo derivative **2**, followed by nucleophilic substitution with sodium acetate in DMF, gave *tert*-butyl acetoxyacetoacetate (**3a**) in 69% over two steps (Scheme 1). In the same manner, *tert*-butyl-2-(butyryloxy)-acetoacetate (**3b**) was obtained by use of sodium butyrate as nucleophile, in 72% overall yield. This two-step procedure could be performed easily on a large scale, thus providing **3a** and **3b** as versatile starting materials for the synthesis of a variety of carboxylate-protected acyloins. Other acyloxy residues should be easily accessible by this route, simply through the use of other carboxylates in the substitution step. The fact that the acyloin oxygen is introduced through a carboxylate nucleophile is an advantage in terms of efficiency, because protection−deprotection steps are avoided. Compounds **3a** and **3b** can be alkylated smoothly by classical acetoacetate chemistry procedures, through deprotonation with NaH in DMF, followed by addition of alkyl, allyl, alkynyl or benzyl halides to yield the intermediates **4a**−**p** (Scheme 1). Alkylation with $K_2CO_3$ in a THF/DMF mixture was also possible, but resulted in lower yields. Selective dealkoxycarbonylation of **4a**−**p** was accomplished either through acid catalysis in benzene with *p*TsOH at 80 °C or by Krapcho dealkoxycarbonylation[35] with LiCl and water in DMSO at 160 °C. In this way, the 2-acyloxy substituent was not affected, whereas the *tert*-butylcarboxylate group was cleanly removed. Intermediate **4i** was obtained by hydrogenation of **4g** in the presence of Lindlar



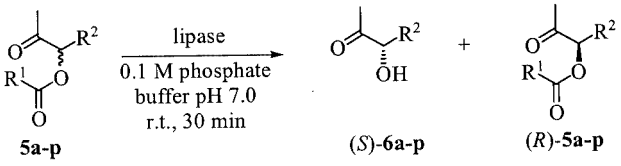

| Compd. no. 4, 5, or 6 | Substituent $R^1$ | $R^2$ |
|---|---|---|
| **a** | $CH_3$ | $CH_2CH_3$ |
| **b** | $CH_3$ | $(CH_2)_2CH_3$ |
| **c** | $CH_3$ | $(CH_2)_3CH_3$ |
| **d** | $CH_3$ | $(CH_2)_4CH_3$ |
| **e** | $CH_3$ | $(CH_2)_5CH_3$ |
| **f** | $CH_3$ | $CH_2CH{=}CH_2$ (allyl) |
| **g** | $CH_3$ | $CH_2C{\equiv}CCH_3$ |
| **h** | $CH_3$ | (*E*)-$CH_2CH{=}CHCH_3$ (*E*-crotyl) |
| **i** | $CH_3$ | (*Z*)-$CH_2CH{=}CHCH_3$ (*Z*-crotyl) |
| **j** | $CH_3$ | $CH_2CH{=}C(CH_3)_2$ (prenyl) |
| **k** | $CH_3$ | $CH_2CH_2CH(CH_3)_2$ |
| **l** | $CH_3$ | (*E*)-$CH_2C{=}C(CH_3)CH_2CH_2C{=}C(CH_3)_2$ (geranyl) |
| **m** | $CH_3$ | (*Z*)-$CH_2C{=}C(CH_3)CH_2CH_2C{=}C(CH_3)_2$ (neryl) |
| **n** | $CH_3$ | $CH_2C_6H_5$ (benzyl) |
| **o** | $CH_2CH_2CH_3$ | $CH_2CH{=}C(CH_3)_2$ (prenyl) |
| **p** | $CH_2CH_2CH_3$ | $CH_2C_6H_5$ (benzyl) |

Scheme 1. Synthesis of acyloin esters **5** and acyloins **6** from acetoacetate

catalyst, and acyloin acetate **5k** was obtained by hydrogenation of **5j** in the presence of palladium on charcoal.

The racemic acyloin esters **5a**−**p** thus obtained were hydrolysed with six commercially available lipases (Scheme 2). The screening was performed by using the enzymes in phosphate buffer (pH 7.0) at ambient temperature for 30 minutes. In each case, the corresponding free acyloins **6a**−**p** were the only detectable hydrolysis products; no acyloin shifts from, for example, 3-hydroxy-2-alkanone to 2-hydroxy-3-alkanone was observed. The structures of the acyloins **6a**−**p** were confirmed by comparison with literature data or by their spectroscopic data. No significant spontaneous hydrolysis was observed in aqueous buffer (phosphate buffer, pH ≈ 7, room temp.) in the absence of enzyme, except in the cases of the allyl derivative **5f** and the alkyne derivative **5g**, which were hydrolysed to extents of 2.6% (**5f**) and 4.3% (**5g**) within 30 minutes. We therefore concluded that the substrates showed sufficient stability under our hydrolysis conditions. In kinetic resolutions by lipases the enantioselectivity is usually described by the enantiomeric ratio (*E*), since this parameter is independent of the conversion. Thus, from the *ee* data obtained from chiral GC analysis, the *E* values (Table 1) were calculated according to Rakels and Straathof[36] or Chen et al.[37]




| | |
|---|---|
| *Burkholderia cepacia* | BCL (PS) |
| *Candida antarctica* B | CAL-B (CAB) |
| *Candida antarctica* A | CAL-A (CAA) |
| *Candida rugosa* | CRL (AYS) |
| *Rhizopus javanicus* | ROL (MJ) |
| Porcine pancreas Lipase | PPL |

Scheme 2. Enzymatic resolution of acyloin esters **5** with commercial lipases and their abbreviations (in brackets: alternative abbreviations commonly used)

The selectivities of the hydrolysis of **5a**−**p** by lipases from *Candida rugosa* (CRL), *Rhizopus oryzae* (ROL) and *Porcine pancreas* (PPL) were low (Table 1, $E < 5$), whereas *Candida antarctica* lipase A (CAL-A) catalysed hydrolysis of **5a**−**p** proceeded with low to moderate ($E < 36$) selectivities. These enzymes are therefore not suited for enantioselective kinetic resolution of acyloin acetates. On the other hand, better results were obtained for the hydrolysis of **5a**−**p** with lipases from *Burkholderia cepacia* (BCL) and *Candida antarctica* B (CAL-B), which sometimes showed comparable excellent selectivities and sometimes complemented each other. Thus, except for the hydrolysis of acyloin acetates with small side chains (ethyl, propyl and allyl; **5a**, **5b** and **5f** respectively), either lipase (BCL, CAL-B) or both of them were able to achieve excellent selectivities. From the data in Table 1 it can be deduced that BCL- or CAL-B-catalysed hydrolysis of acyloin acetates with longer alkyl chains proceeds with good selectivities. The longer the alkyl chain, the better the lipase can discriminate between the two side chains (i.e., alkyl and acyl residues). This observation is in agreement with the results of Kazlauskas et al., who showed, in a related study on lipase resolution of secondary alcohols, that the enantiomeric ratio (*E*) depends on the difference in the sizes of the two side chains.[38] Also in accordance with the Kazlauskas model, the tested enzymes showed no enantiodifferentiation of the small acyloin acetate **5a**, probably because the ethyl and acetyl moieties at C-3 are too similar in size. In line with these results is that CAL-B-catalysed hydrolysis of the propyl derivative **5b** already shows some stereodifferentiation, while the longer alkyl chain derivatives **5c**−**e** show excellent enantioselectivities. BCL-catalysed hydrolysis of the same derivatives **5b**−**e**, however, proceeded with only moderate selectivities. On the other hand, hydrolysis of the saturated and branched acyloin acetate **5k** (BCL) showed perfect selectivity. In this case the *E* value was > 200, superior even to CAL-B, with an $E > 150$.

The more rigid, unsaturated substrates **5h**, **5i**, and **5j** revealed an interesting feature. While CAL-B generally hydrolysed these acetoxy ketones with high enantioselectivity, remarkable differences were observed with BCL. The selectivities in the CAL-B-catalysed hydrolysis of *E*- and *Z*-crotyl-substituted acyloin acetates **5h** and **5i** increased from 116 to >200, respectively, while the BCL-catalysed hydrolysis literally switched from almost unselective (**5h**, $E = 12$) to enantioexclusive (**5i**, $E > 200$). The prenyl derivative **5j** is also hydrolysed with high selectivity by both enzymes. Comparison of, on one hand, the saturated butyl, pentyl and hexyl substrates **5c**−**e**, hydrolysed by BCL with rather

Table 1. Selectivities (*E* values) of lipase-catalysed hydrolysis of acyloin esters **5**; the corresponding chiral GC data and *ee* values are shown in Table 2 and 3, respectively

| Substrate | Lipase[a] | | | | | |
|---|---|---|---|---|---|---|
| | BCL | CAL-B | CAL-A | CRL | ROL | PPL |
| **5a** | 2 | 1 | 2 | 1 | 1 | 2 |
| **5b** | 25 | 19 | n.d.[b] | n.d.[b] | n.d.[b] | n.d.[b] |
| **5c** | 30 | 165 | 8 | 3 | 1 | 1 |
| **5d** | 55 | 110 | n.d.[b] | n.d.[b] | n.d.[b] | n.d.[b] |
| **5e** | 9 | 152 | 7 | 3 | 1 | 2 |
| **5f** | 26[c] | 18[c] | n.d.[b] | n.d.[b] | n.d.[b] | n.d.[b] |
| **5g** | 2[c] | 50[c] | 6[c] | 5[c] | 1[c] | 4[c] |
| **5h** | 12 | 116 | 36 | 1 | 2 | 2 |
| **5i** | >200 | >200 | 5 | 1 | 1 | 2 |
| **5j** | >200 | 166 | 20 | 1 | 2 | 1 |
| **5k** | >200 | 154 | 5 | 2 | 1 | 1 |
| **5l** | 41 | 62 | n.d.[b] | n.d.[b] | n.d.[b] | n.d.[b] |
| **5m** | 114 | 31 | 14 | 1 | − | − |
| **5n** | 177 | 13 | 15 | 1 | 1 | 3 |
| **5o** | >200 | >200 | 1 | 1 | n.d.[b] | n.d.[b] |
| **5p** | 104 | 7 | 4 | 1 | n.d.[b] | n.d.[b] |

[a] Enantiomeric ratio: $E = (k_{cat}/K_M)_(R)/(k_{cat}/K_M)_(S)$; calculated from $ee_P$, $ee_S$ according to Rakels et al.[36] or from $ee_P$ and conversion according to Chen et al.[37] [b] n.d. = not determined. [c] Corrected for spontaneous hydrolysis.

low selectivities, with the BCL-catalysed hydrolysis of the branched saturated substrate **5k** ($E > 200$) on the other, indicates that the increased selectivity is not a function of the unsaturation per se (i.e., *p*-orbitals, $sp^1$ or $sp^2$ carbon atoms), but of configurational or conformational properties. For comparison, conformationally restricted cyclic substrates, obtained from commercial 2-chlorocycloalkanones with acetate, were also hydrolysed. With all commercial lipases tested, the enantioselectivities were very low: the best results were $E = 27$ (BCL) and $E = 14$ (CAL-B) for 2-acetoxycyclopentanone and 2-acetoxycyclohexanone, respectively (data not shown in Tables, abs. configurations not assigned).

In summary, the observed selectivities can be interpreted in terms of a model of well differentiated substrates for the enzyme BCL (Figure 1). This enzyme shows optimum selectivities for the hydrolysis of substrates that contain a group $R^4$ other than H in a *cis* configuration (**5i**, **5j**, **5m** and **5l**) or *synperiplanar* (**5k**) with respect to the α-acetoxy ketone moiety. While the configuration is fixed in the case of a double bond, a linear saturated alkyl chain ($R^3 = H$) preferentially adopts a more stable *antiperiplanar* conformation. Branching at the δ-position ($R^3 = Me$), however, gives rise to an alkyl chain with $R^4$ close to a *synperiplanar* (or at least a *synclinal*) conformation, resulting in more selective BCL-catalysed hydrolysis. In line with these observations is that the longer diprenyl derivative **5l** (neryl) is clearly a better substrate for BCL than for CAL-B. The active site pocket in CAL-B might be somewhat smaller than in BCL. Finally, the alkyne derivative **5g** could not be differentiated by BCL, but CAL-B still showed reasonable enantioselectivity. A special case is the benzyl derivative **5n**, which was hydrolysed with good enantioselectivity with BCL but not with CAL-B. The butyrates **5o**, **5p** are also suitable, rapidly reacting substrates. They show the same tendency as the acetates, although somewhat more pronounced in one or the other direction. In consequence, a variation in the alkanoate may be useful to fine-tune enantioselectivity, reaction speed, or solubility of substrates.

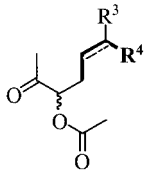



Figure 1. Acyloin substrate model for BCL

For the CAL-B lipase the most important selectivity factor seems to be the length of the alkyl or allyl chain. This is clearly revealed by the almost identical low *E* values for CAL-B-catalysed hydrolysis of **5f** (allyl) and **5b** (propyl) on one hand and the excellent selectivities observed with **5c**, **5h**, and **5i** on the other. At least a four-carbon chain seems to be required for a highly selective CAL-B-hydrolysis of acyloin acetates.

In conclusion, the BCL lipase is more suited for selective hydrolysis of larger unsaturated or saturated δ-branched substrates, while CAL-B is the enzyme of choice for selective hydrolysis of smaller substrates and unbranched saturated acyloins.

All enzymes preferentially hydrolysed the (*S*)-configured esters **5**, affording the (*S*)-acyloins **6** and leaving behind the (*R*)-*O*-acyl acyloins. The latter can easily be racemised and reintroduced into the lipase resolution process,[39] so that theoretically (after a few cycles) a 100% yield of the (*S*)-acyloins could be achieved. Access to the (*R*)-acyloins is possible through chemical hydrolysis of the (*R*)-acyloxy ketones. The direct generation of (*R*)-acyloins from racemic acyloxy ketones by use of (*R*)-selective lipases or esterases obtained from non-commercial sources is currently under investigation.

The absolute configurations of **6c** and **6n** were determined to be (*S*) by comparison of their optical rotation values to those obtained from the literature.[40a,40b] No literature data were available for any of the other acyloins, so we applied the method of Latypov et al.,[40c] in which the NMR spectra of (*R*)-2-methoxy-2-phenylacetic acid esters (MPA esters) of secondary alcohols were measured at two different temperatures. Changes in the chemical shifts of protons in the side-chains connected to the stereocenter reveal the absolute stereochemistry. Thus, after derivatisation of acyloins **6g**,[41] **6i**, **6l**[41] and **6m** to the corresponding MPA esters (details see Exp. Section) the absolute configuration could be determined as (*S*). This is in agreement with the Kazlauskas rule, which predicts the preferential hydrolysis of the (*S*)-configured acyloin esters with different types of hydrolases.[38] The other absolute configurations (**6a**, **6b**, **6d**, **6e**, **6f**, **6h**, **6j**, **6k**) were assigned from the GC retention times, the (*S*)-alcohols being eluted prior to the (*R*)-alcohols.

## Conclusion

A series of 16 different acyloinacetates and butyrates (±)-**5** was synthesised by a new and straightforward method through alkylation of **3** and selective dealkoxycarbonylation, resulting in acyloxy acetoacetates **4**. Subsequent hydrolytic kinetic resolution with six different lipases gave the (*S*)-acyloins **6**. It was found that only two of the tested enzymes, CAL-B and BCL, were able to resolve most of the tested acyloin esters selectively. Two general rules could be defined for the selective hydrolysis of α-acetoxy ketones by CAL-B and BCL lipase: (i) when CAL-B lipase was used, an increase in the chain length of substituent $R^2$ to more than three carbon atoms allowed excellent resolution, especially of smaller and unbranched saturated acyloins, and (ii) substrates suited for BCL lipase must bear an unsaturated carbon chain or at least a saturated four-carbon chain with a branching substituent at the δ-position. An increased length of the carbon chain had no negative influence on the selectivities; the geranyl- and neryl-derived substrates **5l** and **5m**, for example, were still resolved well. However, un-

branched substrates were less suitable for BCL-lipase-catalysed hydrolysis.

For other substrates, such as benzyl- or methylalkynyl-derived substrates, one of the two lipases always proved to be sufficiently selective. Therefore, any acyloin acetate with a residue $R^2$ larger than propyl could be resolved selectively by use of either CAL-B or BCL.

## Experimental Section

**General Remarks:** NMR spectra were recorded in $CDCl_3$ with a Bruker ARX 200, a Bruker ARX 250, or a Varian MERCURY-VX 400 machine. Chemical shifts of $^1H$ NMR and $^{13}C$ NMR spectra are referenced to tetramethylsilane ($\delta = 0$ ppm). Coupling constants are given in Hz and the $^{13}C$ multiplicities were determined by the use of a DEPT-135 pulse sequence. IR spectroscopy was performed on a Mattson Instruments 6030 Galaxy Series FT-IR, all compounds were measured as thin oil films between NaCl plates. Mass spectrometry (MS) was performed with a Finnigan MAT-90 mass spectrometer operating at an ionisation potential of 70 eV. High-resolution mass spectrometry (HRMS) was performed with a Finnigan MAT-90 mass spectrometer with isobutene as ionisation gas. TLC was carried out with silica gel Merck-60 (F254 on aluminium with fluorescence indicator), and compounds were visualised by UV (extinction at $\lambda = 254$ nm or fluorescence at $\lambda = 366$ nm) and/or by staining with Cer-MOP [a solution of molybdatophosphoric acid (5 g), cerium(IV)sulfate (2 g) and concd. $H_2SO_4$ (16 mL) in 180 mL water]. Compounds were purified by flash chromatography on Baker (40 μ, 60 Å) or Merck 60 (230−400 mesh) silica gel. Volatile compounds were purified by (kugelrohr) distillation. Petroleum ether with a boiling range of 40−60 °C was used. Chiral GC analysis was carried out with a Varian Star 3400 Cx chromatograph with FID and a (2,6-*O*-methyl-5-*O*-pentyl)-β-cyclodextrin OV 1701 column (11 m × 0.25 mm, 0.25 μm film, $H_2$). The injector port temperature was 170 °C and the detector was maintained at 200 °C. The split ratio was 100/1 and the column pressure 10 psi. Lipases were either purchased or donated by Amano, Nagoya, Japan (CRL = Amano AY, BCL = Amano PS) or Roche, Penzberg, Germany [CAL-A (Chirazyme L-5), CAL-B (Chirazyme L-2), PPL]. Enzyme preparations were used as obtained by the suppliers. Processes are not optimised.

### Synthesis of Acyloin Esters 5a−5p

**Synthesis of *tert*-Butyl 2-Acetoxyacetoacetate (3a):** *N*-Bromosuccinimide (58.7 g, 330 mmol) was added portionwise to a stirred solution of *tert*-butyl acetoacetate (**1**) (49.0 mL, 47.5 g, 300 mmol) in acetone (30 mL). The resulting suspension was stirred for one hour at room temp. and filtered. The filtrate was concentrated in vacuo before being dissolved in petroleum ether (300 mL) and washed three times with water (100 mL). The solution was then dried with $Na_2SO_4$ and filtered. Removal of the solvent in vacuo gave the bromoacetoacetate **2** (71.1 g, 300 mmol, quant.) as a slightly yellow oil. $^1H$ NMR (200 MHz): $\delta = 1.50$ (s, 9 H), 2.42 (s, 3 H), 4.70 (s, 1 H) ppm. $^{13}C$ NMR (50 MHz): $\delta = 26.12$ (q), 27.50 (q), 50.56 (d), 84.27 (s), 163.80 (s), 196.45 (s) ppm. IR: $\tilde{\nu} = 735$ (s), 845 (w), 912 (m), 1140 (s), 1258 (m), 1287 (m), 1308 (m), 1371 (m), 1395 (m), 1425 (w), 1456 (w), 1478 (w), 1726 (s), 2938 (m), 2982 (m) $cm^{-1}$. MS (CI): *m*/*z* (%) = 103 (87), 105 (61), 115 (98), 129 (77), 131 (76), 149 (78), 159 (70), 227 (64), 229 (58), 237 (100) [$MH^+$], 239 (100) [$MH^+$]. HRMS: calculated for $C_8H_{14}BrO_3$ [$MH^+$]: 237.01263; found 237.01056.

Compound **2** (59.27 g, 250 mmol) was added to a suspension of sodium acetate (30.76 g, 375 mmol) in DMF (250 mL). After the mixture had been stirred at ambient temperature for 90 min, water (415 mL) was added and the mixture was extracted three times with ethyl acetate (325 mL). The combined organic layers were washed three times with water (325 mL) and once with brine (325 mL) and then dried with $Na_2SO_4$. After filtration, the solvent was removed in vacuo and the resulting oil was purified by distillation (12 mbar, 128 °C) to give **3a** (36.52 g, 169 mmol, 68%). $^1H$ NMR (200 MHz): $\delta = 1.50$ (s, 9 H), 2.22 (s, 3 H), 2.34 (s, 3 H), 5.41 (s, 1 H) ppm. $^{13}C$ NMR (50 MHz): $\delta = 20.46$ (q), 27.32 (q), 27.83 (q), 78.38 (d), 84.04 (s), 163.36 (s), 169.55 (s), 197.84 (s) ppm. IR: $\tilde{\nu} = 841$ (w), 1094 (m), 1152 (s), 1221 (s), 1250 (s), 1395 (w), 1420 (w), 1456 (w), 1748 (s), 2938 (m), 2980 (m) $cm^{-1}$. MS (CI): *m*/*z* (%) = 117 (19), 143 (12), 161 (100), 205 (43), 207 (12), 217 (18) [$MH^+$]. HRMS: calculated for $C_{10}H_{17}O_5$ [$MH^+$]: 217.10760; found 217.10460. $C_{10}H_{17}O_5$: calcd. C 55.55, H 7.46; found C 55.39, H 7.54.

**Synthesis of *tert*-Butyl 2-(Butyryloxy)acetoacetate (3b):** The bromoacetoacetate **2** (59.27 g, 250 mmol) was treated with sodium butyrate (45 g, 410 mmol) as described above for the synthesis of **3a**. The usual workup, followed by distillation at 95 °C and 1.0 mbar, gave **3b** (44 g, 180 mmol, 72%). $^1H$ NMR (400 MHz): $\delta = 0.99$ (t, $J = 7.4$ Hz, 3 H), 1.50 (s, 9 H), 1.72 (tq, $J = 7.0$, $J = 7.4$ Hz, 2 H), 2.33 (s, 3 H), 2.47 (t, $J = 7.0$ Hz, 2 H), 5.41 (s, 1 H) ppm. $^{13}C$ NMR (100 MHz): $\delta = 13.49$ (q), 18.20 (t), 27.24 (q), 27.76 (q), 35.47 (t), 78.09 (d), 83.86 (s), 163.36 (s), 172.14 (s), 197.95 (s) ppm.

**General Method for the Alkylation of *tert*-Butyl 2-Acyloxyacetoacetates (3) to give *tert*-Butyl 2-Acetyl-2-acyloxyalkanoates (4):** The acyloxyacetoacetate (**3a** or **3b**, 1.00 equiv.) was added at 0 °C to a suspension of NaH in DMF (2.0 mL/mmol, 1.10−1.30 equiv.). After 15 min an alkyl or allyl bromide or chloride (1.00 equiv.) was slowly added at 0 °C and the mixture was stirred overnight at room temp. The mixture was then diluted with $Et_2O$ (10 mL/mmol) and washed with $H_2O$ (3 × 4.0 mL/mmol) and brine (4.0 mL/mmol). The organic layer was dried with $Na_2SO_4$, filtered and concentrated in vacuo to yield 2-alkylated acetoacetates **4a**−**p**. The products were mostly of sufficient purity for the subsequent dealkoxycarbonylation step; otherwise kugelrohr distillation was the fastest purification method.

**General Method A for the Selective Dealkoxycarbonylation of *tert*-Butyl 2-Acetyl-2-acyloxyalkanoates (4) with *para*-Toluenesulfonic Acid To Give 3-Acyloxy-2-alkanones (5):** The appropriate compound **4** (1.0 equiv.) and *p*TsOH·$H_2O$ (0.1 equiv.) were dissolved in benzene (3.0 mL/mmol), and the mixture was stirred at 78 °C for 3−5 h. The obtained light brown solution was filtered through a small column of silica, which was flushed with ethyl acetate. The benzene/ethyl acetate solution was concentrated in vacuo, and the remaining yellow oil was purified by kugelrohr distillation or flash chromatography on silica with ethyl acetate/petroleum ether mixtures.

**General Method B for the Selective Dealkoxycarbonylation of *tert*-Butyl 2-Acetyl-2-acyloxyalkanoates (4) with LiCl in DMSO To Give 3-Acyloxy-2-alkanones (5):** The appropriate 2-alkylated acetoacetate **4** (1.0 equiv.), $H_2O$ (1.1 equiv.) and LiCl (1.1 equiv.) were dissolved in DMSO (2.3 mL/mmol), and the mixture was heated to 145−160 °C and stirred at 160 °C for 5 h and at room temp. overnight. After dilution with $H_2O$ (4.5 mL/mL DMSO), the mixture was extracted with $Et_2O$ (3 × 3.3 mL/mL DMSO). The combined organic layers were washed with $H_2O$ (3 × 1.0 mL/mL $Et_2O$) and brine (1.0 mL/mL $Et_2O$), dried with $Na_2SO_4$, filtered and concentrated in vacuo. Crude products were purified by flash chromatography.

***tert*-Butyl 2-Acetoxy-2-ethyl-3-oxobutanoate (4a):** Acetoacetate **3a** (1.08 g, 5.00 mmol), NaH (156 mg, 6.5 mmol) and ethyl bromide (373 μL, 549 mg, 5.00 mmol) in DMF (10 mL) were treated as described in the general alkylation method to give **4a** (970 mg, 3.97 mmol, 79%) as a slightly yellow oil. $^1$H NMR (200 MHz): δ = 0.85 (t, *J* = 9.5 Hz, 3 H), 1.43 (s, 9 H), 2.10 (q, *J* = 9.5 Hz, 2 H), 2.15 (s, 3 H), 2.30 (s, 3 H) ppm. $^{13}$C NMR (50 MHz): δ = 7.55 (q), 20.42 (q), 26.86 (q), 27.08 (t), 27.56 (q), 82.99 (s), 88.39 (s), 166.09 (s), 169.41 (s), 200.94 (s) ppm. IR: ṽ = 897 (w), 910 (w), 928 (w), 972 (w), 1022 (m), 1059 (m), 1103 (m), 1115 (w), 1184 (w), 1236 (s), 1260 (m), 1375 (m), 1433 (m), 1460 (m), 1730 (s), 1744 (s), 2942 (m), 2974 (m) cm$^{-1}$. MS (CI): *m*/*z* (%) = 101 (14), 129 (24), 161 (16), 171 (8), 189 (100), 206 (7), 217 (9), 229 (6), 245 (4). HRMS: calculated for $C_{12}H_{21}O_5$ [MH$^+$]: 245.13890; found 245.13559.

**3-Acetoxypentan-2-one (5a):** Compound **4a** (1.40 g, 5.73 mmol) and *p*-TsOH·$H_2O$ (109 mg, 0.57 mmol) were stirred in benzene (18.0 mL) as described in dealkoxycarbonylation method A. Kugelrohr distillation gave **5a** (486 mg, 3.4 mmol, 59%) as a colourless oil. $^1$H NMR (200 MHz): δ = 1.35 (s, 9 H), 2.08 (s, 3 H), 2.13 (s, 3 H), 3.40 (s, 2 H), 6.90−7.40 (m, 5 H) ppm. $^{13}$C NMR (50 MHz): δ = 20.69 (q), 27.21 (q), 27.47 (q), 38.69 (t), 83.23 (s), 88.40 (s), 127.03 (d), 128.17 (d), 129.93 (d), 134.33 (d), 165.24 (s), 169.38 (s), 202.11 (s) ppm. IR: ṽ = 700 (w), 845 (w), 1030 (w), 1084 (w), 1155 (m), 1229 (m), 1252 (m), 1273 (m), 1370 (m), 1456 (w), 1751 (s), 2936 (m), 2978 (m), 3003 (w) cm$^{-1}$. MS (CI): *m*/*z* (%) = 43 (39), 45 (22), 57 (34), 91 (19), 119 (10), 145 (9), 173 (9), 189 (14), 190 (78), 191 (18), 233 (45), 246 (22), 251 (100), 252 (11), 307 (44) [MH$^+$]. HRMS: calculated for $C_{17}H_{23}O_5$ [MH$^+$]: 307.15454; found 307.15070.

***tert*-Butyl 2-Acetoxy-2-acetylpentanoate (4b):** Acetoacetate **3a** (7.12 g, 32.9 mmol), NaH (900 mg, 37.5 mmol) and propyl bromide (4.05 g, 32.9 mmol) in DMF (64 mL) were treated as described in the general alkylation method to give **4b** (6.00 g, 23.2 mmol, 71%) as a slightly yellow oil after kugelrohr distillation at 160 °C and 1.0 mbar. $^1$H NMR (300 MHz): δ = 0.93 (t, *J* = 7.4 Hz, 3 H), 1.25−1.45 (m, 2 H), 1.47 (s, 9 H), 2.05−2.11 (m, 2 H), 2.16 (s, 3 H), 2.34 (s, 3 H) ppm. $^{13}$C NMR (75 MHz): δ = 14.11 (q), 16.92 (t), 20.71 (q), 27.03 (q), 28.20 (q), 35.99 (t), 83.13 (s), 88.26 (s), 166.10 (s), 169.38 (s), 200.87 ppm.

**3-Acetoxyhexan-2-one (5b):** Compound **4b** (6.00 g, 23.2 mmol) and *p*-TsOH·$H_2O$ (393 mg, 2.07 mmol) were stirred in benzene (60 mL) as described in dealkoxycarbonylation method A. Kugelrohr distillation at 1.0 mbar and 150 °C, followed by column chromatography (diethyl ether/petroleum ether, 1:8), gave **5b** (2.00 g, 12.6 mmol, 54%) as a colourless oil. $^1$H NMR (400 MHz): δ = 0.94 (t, *J* = 7.3 Hz, 3 H), 1.38−1.46 (m, 2 H), 1.67−1.77 (m, 2 H), 2.15 (s, 3 H), 2.16 (s, 3 H), 5.00 (dd, *J* = 7.6, *J* = 5.3 Hz, 1 H) ppm. $^{13}$C NMR (100 MHz): δ = 13.77 (q), 18.59 (t), 20.74 (q), 26.15 (q), 32.31 (t), 78.49 (d), 170.44 (s), 205.18 (s) ppm.

***tert*-Butyl 2-Acetoxy-2-acetylhexanoate (4c):** The acetoacetate **3a** (1.08 g, 5.00 mmol), NaH (156 mg, 6.5 mmol) and butyl bromide (538 μL, 685 mg, 5.00 mmol) in DMF (10 mL) were treated as described in the general alkylation method to give **4c** (1026 mg, 3.77 mmol, 75%) as a slightly yellow oil. $^1$H NMR (200 MHz): δ = 0.81 (t, *J* = 7.1 Hz, 3 H), 0.99−1.47 (m, 4 H), 1.40 (s, 9 H), 1.98−2.11 (m, 2 H), 2.10 (s, 3 H), 2.28 (s, 3 H) ppm. $^{13}$C NMR (50 MHz): δ = 13.73 (q), 20.58 (q), 22.41 (t), 25.40 (t), 26.91 (q), 27.67 (q), 33.65 (t), 83.11 (s), 88.22 (s), 166.26 (s), 169.52 (s), 201.11 (s) ppm. IR: ṽ = 845 (m), 1018 (m), 1047 (m), 1140 (s), 1163 (s), 1202 (m), 1250 (s), 1279 (s), 1317 (s), 1370 (s), 1395 (m), 1420 (m), 1435 (m), 1456 (m), 1744 (s), 2872 (m), 2934 (m), 2961 (m) cm$^{-1}$. MS (CI): *m*/*z* (%) = 201 (14), 203 (15), 217 (29), 261 (100), 263 (41), 273 (17). HRMS: calculated for $C_{14}H_{25}O_5$ [MH$^+$]: 273.17020; found 273.16759.

**3-Acetoxyheptan-2-one (5c):** Compound **4c** (731 mg, 2.68 mmol) and *p*TsOH·$H_2O$ (51 mg, 0.27 mmol) were stirred in benzene (9.0 mL) as described in dealkoxycarbonylation method A. Kugelrohr distillation at 1.0 mbar and 60 °C gave **5c** (415 mg, 2.41 mmol, 90%) as a colourless oil. $^1$H NMR (200 MHz): δ = 0.85 (t, *J* = 4.8 Hz, 3 H), 1.10−1.45 (m, 4 H), 1.50−1.90 (m, 2 H), 2.10 (s, 2 × 3 H), 4.90 (m, 1 H) ppm. $^{13}$C NMR (50 MHz): δ = 13.64 (q), 20.51 (q), 22.16 (t), 25.94 (q), 27.12 (t), 29.80 (t), 78.57 (d), 170.49 (s), 205.30 (s) ppm. IR: ṽ = 1028 (m), 1049 (m), 1078 (m), 1115 (m), 1181 (w), 1240 (s), 1375(m), 1435 (m), 1456 (m), 1730 (s), 1744 (s), 2872 (m), 2934 (m), 2959 (m) cm$^{-1}$. MS (CI): *m*/*z* (%) = 143 (26), 157 (11), 169 (13), 173 (100) [MH$^+$]. HRMS: calculated for $C_9H_{17}O_3$ [MH$^+$]: 173.11777; found 173.11535.

***tert*-Butyl 2-Acetoxy-2-acetylheptanoate (4d):** The acetoacetate **3a** (7.12 g, 32.9 mmol), NaH (900 mg, 37.5 mmol) and pentyl bromide (4.97 g, 32.9 mmol) in DMF (64 mL) were treated as described in the general alkylation method to give **4d** (6.40 g, 22.3 mmol, 68%) as a slightly yellow oil after kugelrohr distillation at 185 °C and 1.0 mbar. $^1$H NMR (400 MHz): δ = 0.88 (t, *J* = 6.7 Hz, 3 H), 1.26−1.31 (m, 6 H), 1.47 (s, 9 H), 2.08 (m, 2 H), 2.16 (s, 3 H), 2.33 (s, 3 H) ppm. $^{13}$C NMR (100 MHz): δ = 13.97 (q), 20.73 (q), 22.38 (t), 23.05 (t), 27.04 (q), 27.81 (q), 31.62 (t), 33.91 (t), 83.15 (s), 88.29 (s), 166.13 (s), 169.41 (s), 200.88 (s) ppm.

**3-Acetoxyoctan-2-one (5d):** Compound **4d** (6.40 g, 22.3 mmol) and *p*TsOH·$H_2O$ (402 mg, 2.11 mmol) were stirred in benzene (65 mL) as described in dealkoxycarbonylation method A. Kugelrohr distillation at 1.0 mbar and 125 °C, followed by column chromatography (ethyl acetate/petroleum ether, 1:4), gave **5d** (1.6 g, 8.59 mmol, 39%) as a colourless oil. $^1$H NMR (400 MHz): δ = 0.89 (t, *J* = 6.7 Hz, 3 H), 1.28−1.41 (m, 6 H), 1.72−1.79 (m, 2 H), 2.15 (s, 3 H), 2.16 (s, 3 H), 4.98 (dd, *J* = 7.7, *J* = 4.8 Hz, 1 H) ppm. $^{13}$C NMR (100 MHz): δ = 14.01 (q), 20.74 (q), 22.43 (t), 24.89 (t), 26.15 (q), 30.25 (t), 31.41 (t), 78.68 (d), 170.42 (s), 205.15 (s) ppm.

***tert*-Butyl 2-Acetoxy-2-acetyloctanoate (4e):** Acetoacetate **3a** (1.08 g, 5.00 mmol), NaH (156 mg, 6.5 mmol) and hexyl bromide (702 μL, 825 mg, 5.00 mmol) in DMF (10 mL) were treated as described in the general alkylation method to give **4e** (1063 mg, 3.54 mmol, 71%) as a slightly yellow oil. $^1$H NMR (200 MHz): δ = 0.80 (m, 3 H), 1.1−1.3 (m, 8 H), 1.40 (s, 9 H), 1.95−2.13 (m, 2 H), 2.10 (s, 3 H), 2.28 (s, 3 H) ppm. $^{13}$C NMR (50 MHz): δ = 13.93 (q), 20.58 (q), 22.41 (t), 23.22 (t), 26.92 (q), 27.68 (q), 29.03 (t), 31.38 (t), 33.85 (t), 83.15 (s), 88.29 (s), 166.28 (s), 169.57 (s), 201.11 (s) ppm. IR: ṽ = 758 (w), 845 (w), 1157 (m), 1244 (m), 1395 (m), 1420 (w), 1435 (w), 1456 (m), 1748 (s), 2861 (m), 2930 (m), 2957 (m) cm$^{-1}$. MS (CI): *m*/*z* (%) = 113 (21), 142 (14), 156 (15), 157 (10), 158 (16), 184 (12), 227 (30), 245 (100), 246 (13), 289 (34), 301 (13). HRMS: calculated for $C_{16}H_{29}O_5$ [MH$^+$]: 301.20151; found 301.19881.

**3-Acetoxynonan-2-one (5e):** Compound **4e** (2.19 g, 7.29 mmol) and *p*TsOH·$H_2O$ (139 mg, 0.73 mmol) were stirred in benzene (22.0 mL) as described in dealkoxycarbonylation method A. kugelrohr distillation at 0.8 mbar and 80 °C and subsequent flash chromatography (column dimensions: 2.0 × 20.0 cm, diethyl ether/petroleum ether, 1:6) gave **5e** (419 mg 2.10 mmol, 29%) as a colourless oil. $^1$H NMR (200 MHz): δ = 0.75−1.00 (m, 3 H), 1.10−1.50 (m, 8 H), 1.60−1.85 (m, 2 H), 2.13 (s, 2 × 3 H), 4.95 (m, 1 H) ppm. $^{13}$C NMR (50 MHz): δ = 13.85 (q), 20.51 (q), 22.35 (t), 24.96 (t), 25.94 (q), 28.71 (t), 30.09 (t), 31.35 (t), 78.60 (d), 170.52 (s),

205.33 (s) ppm. IR: $\tilde{\nu}$ = 1044 (m), 1074 (w), 1121 (w), 1175 (w), 1236 (s), 1373 (m), 1433 (m), 1458 (m), 1732 (s), 1744 (s), 2859 (m), 2930 (m), 2953 (m) $cm^{-1}$. MS (CI): *m*/*z* (%) = 113 (28), 142 (12), 158 (15), 171 (29), 185 (16), 201 (100) [$MH^+$], 202 (12). HRMS: calculated for $C_{11}H_{21}O_3$ [$MH^+$]: 201.14906; found 201.14587.

***tert*-Butyl 2-Acetoxy-2-acetylpent-4-enoate (4f):** The acetoacetate **3a** (3.56 g, 16.4 mmol), NaH (0.43 g, 18.0 mmol) and allyl bromide (1.98 g, 16.4 mmol) in DMF (32 mL) were treated as described in the general alkylation method to give **4f** (3.57 g, 13.9 mmol, 85%) as a slightly yellow oil after kugelrohr distillation at 2.0 mbar and 135 °C. $^1$H NMR (250 MHz): δ = 1.46 (s, 9 H), 2.15 (s, 3 H), 2.31 (s, 3 H), 2.89 (t, *J* = 1.1 Hz, 1 H), 2.92 (t, *J* = 1.1 Hz, 1 H), 5.08−5.10 (m, 1 H), 5.14−5.17 (m, 1 H), 5.58−5.72 (m, 1 H) ppm. $^{13}$C NMR (62.5 MHz): δ = 20.65 (q), 26.90 (q), 27.75 (q), 37.94 (t), 83.41 (s), 87.81 (s), 119.76 (t), 130.66 (d), 165.59 (s), 169.36 (s), 200.79 (s) ppm.

**3-Acetoxy-5-hexen-2-one (5f):** Compound **4f** (2.50 g, 9.75 mmol) and *p*-TsOH·$H_2O$ (186 mg, 0.98 mmol) were stirred in benzene (30 mL) as described in dealkoxycarbonylation method A. Kugelrohr distillation at 0.6 mbar and 80 °C gave **5f** (1.29 g, 8.27 mmol, 85%) as a colourless oil. $^1$H NMR (250 MHz): δ = 2.14 (s, 3 H), 2.16 (s, 3 H), 2.48−2.57 (m, 2 H), 5.05−5.18 (m, 3 H), 5.65−5.80 (m, 1 H) ppm. $^{13}$C NMR (62.5 MHz): δ = 20.64 (q), 26.54 (q), 34.81 (t), 77.87 (d), 118.80 (t), 131.99 (d), 170.42 (s), 204.78 (s) ppm.

***tert*-Butyl 2-Acetoxy-2-acetylhex-4-ynoate (4g):** The acetoacetate **3a** (3.24 g, 15.0 mmol), NaH (660 mg, 16.5 mmol) and 1-chlorobut-2-yne (2.00 g, 15.0 mmol) in DMF (30 mL) were treated as described in the general alkylation method to give **4g** (3.83 g, 14.3 mmol, 95%) as a slightly yellow oil. $^1$H NMR (200 MHz): δ = 1.39 (s, 9 H), 1.69 (t, *J* = 2.6 Hz, 3 H), 2.15 (s, 3 H), 2.31 (s, 3 H), 3.01 (m, 2 H) ppm. $^{13}$C NMR (50 MHz): δ = 3.40 (q), 20.72 (q), 23.87 (t), 26.80 (q), 27.55 (q), 71.88 (s), 78.96 (s), 83.49 (s), 86.85 (s), 164.71 (s), 169.31 (s), 200.88 (s) ppm.

**3-Acetoxy-5-heptyn-2-one (5g):** Compound **4g** (1.61 g, 6.00 mmol) and *p*-TsOH·$H_2O$ (114 mg, 0.60 mmol) were stirred in benzene (20 mL) as described in dealkoxycarbonylation method A. Flash chromatography (column dimensions: 2.0 × 20.0 cm, ethyl acetate/petroleum ether, 1:4) gave **5g** (922 mg, 5.48 mmol, 91%) as a colourless oil. $^1$H NMR (200 MHz): δ = 1.71 (s, 3 H), 2.11 (s, 3 H), 2.17 (s, 3 H), 2.57 (m, 2 H), 5.00 (t, *J* = 6.0 Hz, 1 H) ppm. $^{13}$C NMR (50 MHz): δ = 3.22 (q), 20.43 (q), 20.97 (t), 26.90 (q), 72.52 (s), 76.33 (d), 78.69 (s),170.05 (s), 204.16 (s) ppm. IR: $\tilde{\nu}$ = 873 (w), 926 (w), 967 (w), 1059 (w), 1148 (w), 1174 (m), 1242 (s), 1374 (s), 1426 (w), 1732 (s), 1746 (s), 2923 (m), 3451 (w) $cm^{-1}$. MS (CI): *m*/*z* (%) = 43 (76), 57 (100), 109 (56), 127 (12), 169 (62) [$MH^+$], 170 (8). HRMS: calculated for $C_9H_{13}O_3$ [$MH^+$]: 169.08672; found 169.08647.

***tert*-Butyl (4*E*)-2-Acetoxy-2-acetylhex-4-enoate (4h):** The acetoacetate **3a** (4.98 g, 23.0 mmol), NaH (0.61 g, 25.4 mmol) and crotyl chloride (2.08 g, 23.0 mmol) in DMF (45 mL) were treated as described in the general alkylation method to give (4*E*)-**4h** (0.368 g, 1.4 mmol, 6%) as a slightly yellow oil after kugelrohr distillation at 1.0 mbar and 140 °C. $^1$H NMR (200 MHz): δ = 1.40 (s, 9 H), 1.58 (d, *J* = 9.5 Hz, 3 H), 2.10 (s, 3 H), 2.25 (s, 3 H), 2.73 (d, *J* = 9.5 Hz, 2 H), 5.02−5.65 (m, 2 H) ppm. $^{13}$C NMR (50 MHz): δ = 17.94 (q), 20.61 (q), 26.89 (q), 27.70 (q), 37.01 (t), 83.21 (s), 87.98 (s), 122.76 (d), 130.53 (d), 165.75 (s), 169.48 (s), 200.93 (s) ppm. IR: $\tilde{\nu}$ = 845 (w), 970 (w), 1040 (w), 1059 (w), 1076 (w), 1130 (m), 1157 (m), 1194 (m), 1227 (m), 1254 (s), 1370 (m), 1395 (w), 1431 (m), 1454 (w), 1746 (s), 2857 (w), 2891 (w), 2934 (m), 2978 (m) $cm^{-1}$. MS (CI): *m*/*z* (%) = 127 (11), 139 (13), 154 (16), 155 (12), 167 (11), 171 (10), 215 (100), 216 (12), 259 (22), 271 (1). HRMS: calculated for $C_{14}H_{23}O_5$ [$MH^+$]: 271.15289; found 271.15454.

**(5*E*)-3-Acetoxy-5-hepten-2-one (5h):** Compound **4h** (330 mg, 1.22 mmol) and *p*TsOH·$H_2O$ (23 mg, 0.12 mmol) were stirred in benzene (4.0 mL) as described in dealkoxycarbonylation method A. Kugelrohr distillation at 1.5 mbar and 60 °C gave 133 mg (0.78 mmol, 64%) of a 10:1 mixture of the (4*E*) isomer **5h** and the (4*Z*) isomer **5i**, respectively. $^1$H NMR (200 MHz): δ = 1.55−1.70 (m, 3 H), 2.09 (s, 2 × 3 H), 2.25−2.55 (m, 2 H), 4.85−5.08 (m, 1 H), 5.20−5.65 (m, 2 H) ppm. $^{13}$C NMR (50 MHz): δ = 17.75 (q), 20.47 (q), 26.39 (q), 33.51 (t), 78.16 (d), 124.08 (d), 129.36 (d), 170.31 (s), 204.88 (s) ppm. IR: $\tilde{\nu}$ = 1044 (m), 1074 (w), 1121 (w), 1175 (w), 1236 (s), 1373 (m), 1433 (m), 1458 (m), 1732 (s), 1744 (s), 2859 (m), 2930 (m), 2953 (m) $cm^{-1}$. MS (CI): *m*/*z* (%) = 107 (11), 111 (16), 123 (34), 135 (10), 141 (17), 143 (9), 149 (9), 155 (19), 171 (100) [$MH^+$]. HRMS: calculated for $C_9H_{15}O_3$ [$MH^+$]: 171.10213; found 171.09980.

**(4*Z*)-*tert*-Butyl 2-Acetoxy-2-acetylhex-4-enoate (4i):** The 2-acetoxyhexynoate **4g** (630 mg, 2.32 mmol) and Lindlar catalyst (120 mg) were stirred under hydrogen in ethyl acetate (50 mL) for 24 h. The reaction suspension was filtered through Celite® and the filtrate was concentrated in vacuo to give (4*Z*)-**4i** (628 mg, 2.32 mmol, 99%) as a slightly yellow oil. $^1$H NMR (200 MHz): δ = 1.39 (s, 9 H), 1.53 (d, *J* = 6.8 Hz, 3 H), 2.08 (s, 3 H), 2.24 (s, 3 H), 2.80−2.90 (m, 2 H), 5.13−5.26 (m, 1 H), 5.48−5.64 (m, 1 H) ppm. $^{13}$C NMR (50 MHz): δ = 12.78 (q), 20.50 (q), 26.78 (q), 27.54 (q), 31.10 (t), 83.11 (s), 87.67 (s), 121.68 (d), 128.54 (d), 165.70 (s), 169.34 (s), 200.99 (s) ppm. IR: $\tilde{\nu}$ = 845 (m), 905 (w), 969 (m), 1058 (m), 1077 (m), 1130 (s), 1158 (s), 1193 (m), 1226 (s), 1253 (s), 1370 (s), 1395 (m), 1431 (m), 1455 (m), 1478 (w), 1742 (s), 2935 (m), 2979 (m), 3432 (w) $cm^{-1}$.

**(5*Z*)-3-Acetoxy-5-hepten-2-one (5i):** Compound **4i** (433 mg, 1.60 mmol) and *p*TsOH·$H_2O$ (30 mg, 0.16 mmol) were stirred in benzene (6 mL) as described in dealkoxycarbonylation method A. Flash chromatography (column dimensions: 2.0 × 20.0 cm, ethyl acetate/petroleum ether, 1:4) gave **5i** (205 mg, 1.20 mmol, 75%) as a colourless oil. $^1$H NMR (200 MHz): δ = 1.54 (d, *J* = 7.6 Hz, 3 H), 2.05 (s, 3 H), 2.08 (s, 3 H), 2.45 (m, 2 H), 4.95 (t, *J* = 6.3 Hz, 1 H), 5.20−5.40 (m, 1 H), 5.40−5.70 (m, 1 H), ppm. $^{13}$C NMR (50 MHz): δ = 12.65 (q), 20.43 (q), 26.33 (t), 27.83 (t), 77.93 (d), 123.15 (d), 127.81 (d), 170.25 (s), 204.94 (s) ppm. IR: $\tilde{\nu}$ = 934 (w), 969 (w), 1041 (m), 1074 (m), 1173 (w), 1239 (s), 1373 (s), 1432 (m), 1732 (s), 1746 (s), 2923 (w), 3023 (w), 3454 (w) $cm^{-1}$. MS (CI): *m*/*z* (%) = 71 (42), 85 (84), 111 (48), 127 (52), 169 (44) 171 (100) [$MH^+$]. HRMS: calculated for $C_9H_{13}O_3$ [$MH^+$]: 171.10213; found 171.10180.

***tert*-Butyl 2-Acetoxy-2-acetyl-5-methoxyhex-4-enoate (4j):** Acetoacetate **3a** (3.94 g, 18.2 mmol), NaH (0.48 g, 20.0 mmol) and 3-methyl-2-butenyl bromide (prenyl bromide, 2.71 g, 18.2 mmol) in DMF (45 mL) were treated as described in the general alkylation method to give **4j** (5.02 g, 17.6 mmol, 97%) as a slightly yellow oil after kugelrohr distillation at 1.5 mbar and 145 °C. $^1$H NMR (200 MHz): δ = 1.40 (s, 9 H), 1.55 (s, 3 H), 1.65 (s, 3 H), 2.10 (s, 3 H), 2.25 (s, 3 H), 2.75 (t, *J* = 7.1 Hz, 2 H), 4.95 (t, *J* = 7.1 Hz, 1 H) ppm. $^{13}$C NMR (50 MHz): δ = 17.84 (q), 20.56 (q), 25.79 (q), 26.88 (q), 27.58 (q), 32.57 (t), 83.00 (s), 87.87 (s), 115.77(d), 136.38 (s), 165.90 (s), 169.48 (s), 201.10 (s) ppm. IR: $\tilde{\nu}$ = 845 (w), 1022 (w), 1051 (w), 1074 (w), 1119 (w), 1157 (m), 1235 (m), 1258 (m), 1317 (w), 1370 (m), 1435 (w), 1454 (w), 1746 (m), 2864 (w), 2876 (w), 2930 (m), 2976 (m), 3030 (w) $cm^{-1}$. MS (CI): *m*/*z* (%) = 153

(12), 169 (10), 185 (61), 197 (7), 211 (8), 213 (11), 215 (8), 225 (16), 229 (100), 230 (35), 241 (36), 246 (11), 273 (99), 274 (57), 275 (100), 276 (36), 285 (98), 286 (43), 302 (11). HRMS: calculated for $C_{15}H_{25}O_5$ [$MH^+$]: 285.17020; found 285.16679.

**3-Acetoxy-6-methyl-5-hepten-2-one (5j):** Compound **4j** (850 mg, 2.99 mmol), LiCl (139 mg, 3.29 mmol) and $H_2O$ (59 μL, 59 mg, 3.29 mmol) in DMSO (7.5 mL) were treated at 160 °C for 5 h as described in dealkoxycarbonylation method B. The remaining yellow oil was purified by flash chromatography (column dimensions: 2.0 × 20.0 cm, ethyl acetate/petroleum ether, 1:4) to yield **5j** (133 mg, 0.78 mmol, 64%). $^1$H NMR (200 MHz): δ = 1.59 (s, 3 H), 1.68 (s, 3 H), 2.08 (s, 3 H), 2.10 (s, 3 H), 2.40 (t, 2 H), 4.93 (t, 1 H), 5.05 (t, 1 H) ppm. $^{13}$C NMR (50 MHz): δ = 17.66 (q), 20.48 (q), 25.56 (q), 26.37 (q), 29.06 (t), 78.28 (d), 117.21 (d), 135.67 (s), 170.33 (s), 205.12 (s) ppm. IR: ṽ = 733 (w), 845 (w), 1051 (m), 1113 (w), 1167 (m), 1242 (s), 1321 (w), 1375 (m), 1435 (m), 1732 (s), 1744 (s), 2861 (w), 2918 (m), 2971 (m) cm$^{-1}$. MS (CI): *m*/*z* (%) = 97 (28), 99 (25), 107 (31), 107 (31), 109 (30), 111 (24), 123 (25), 125 (100), 137 (23), 141 (23), 143 (19), 151 (22), 185 ($MH^+$, 25). HRMS: calculated for $C_{10}H_{17}O_3$ [$MH^+$]: 185.11777; found 185.11188.

**3-Acetoxy-6-methylheptan-2-one (5k):** The heptenone **5j** (300 mg, 1.63 mmol) and Pd/C catalyst (5%, 60 mg) were stirred under hydrogen in abs. ethanol (10 mL) at room temp. After 30 minutes the suspension was filtered through Celite® and the filtrate was concentrated in vacuo to give **5k** (302 mg, 1.62 mmol, 99%) as a colourless oil. $^1$H NMR (200 MHz): δ = 0.82 (d, *J* = 6.9 Hz, 2 × 3 H), 1.00−1.40 (m, 1 H), 1.40−1.60 (m, 2 H), 1.60−1.80 (m, 2 H), 2.07 (s, 3 H), 2.08 (s, 3 H), 4.85−4.92 (m, 1 H) ppm. $^{13}$C NMR (50 MHz): δ = 20.42 (q), 21.98 (q), 22.26 (q), 25.87 (d), 27.55 (q), 27.99 (t), 33.86 (t), 78.71 (d), 170.37 (s), 205.18 (s) ppm. MS (CI): *m*/*z* (%) = 85 (18), 115 (16), 134 (20), 148 (28), 167 (16) 187 (100) [$MH^+$]. HRMS: calculated for $C_9H_{13}O_3$ [$MH^+$]: 187.13213; found 187.13342.

**(4E)-*tert*-Butyl 2-Acetoxy-2-acetyl-5,9-dimethyldeca-4,8-dienoate (4l):** Acetoacetate **3a** (10.8 g, 50 mmol), NaH (2.32 g, 58 mmol, 60% suspension in mineral oil) and geranyl bromide (10.9 g, 50 mmol) in DMF (100 mL) were treated as described in the general alkylation method to give (4*E*)-**4l** (17.6 g, 50 mmol, 100%) as a slightly yellow oil. $^1$H NMR (200 MHz): δ = 1.46 (s, 9 H) 1.60 (s, 6 H), 1.68 (s, 3 H), 2.00−2.05 (m, 4 H), 2.15 (s, 3 H), 2.31 (s, 3 H), 2.84−2.89 (m, 2 H), 5.00−5.05 (m, 2 H) ppm. $^{13}$C NMR (50 MHz): δ = 16.01 (q), 17.46 (q), 20.44 (q), 25.48 (q), 26.21 (t), 26.83 (q), 27.61 (q), 32.36 (t), 39.60 (t), 82.81 (s), 87.82 (s), 115.66 (d), 123.72 (d), 131.27 (s), 139.81 (s), 165.77 (s), 169.27 (s), 201.04 (s) ppm. IR: ṽ = 734 (w), 845 (w), 1072 (w), 1116 (w), 1157 (s), 1196 (w), 1235 (m), 1257 (s), 1369 (s), 1456 (w), 1733 (s), 1748 (s), 1756 (s), 2929 (m), 2935 (m), 2976 (m) cm$^{-1}$. MS (EI): *m*/*z* (%) = 352 (0.01) [$M^+$], 296, 236, 193, 167, 153, 69, 57, 43 (100.0).

**(5*E*)-3-Acetoxy-6,10-dimethyl-5,9-undecadien-2-one (5l):** Compound **4l** (10.55 g, 30.0 mmol), LiCl (1.40 g, 33.0 mmol) and $H_2O$ (549 μL, 549 mg, 33.0 mmol) were treated in DMSO (75 mL) at 150 °C for 5 h as described in dealkoxycarbonylation method B. The remaining yellow oil was purified by kugelrohr distillation at 150 °C and 0.5 mbar to yield **5l** (6.24 g, 25 mmol, 82%).

$^1$H NMR (200 MHz): δ = 1.59 (s, 3 H), 1.62 (s, 3 H), 1.67 (s, 3 H), 2.02−2.06 (m, 4 H), 2.12 (s, 3 H), 2.15 (s, 3 H), 2.49 (m, 2 H), 5.00 (dd, *J* = 6.3, *J* = 6.3 Hz, 1 H), 5.00−5.20 (m, 2 H) ppm. $^{13}$C NMR (50 MHz): δ = 15.87 (q), 17.40 (q), 20.34 (q), 25.40 (q), 26.16 (t), 26.32 (q), 28.97 (t), 33.48 (t), 78.19 (d), 117.18 (d), 123.68 (d), 131.21 (s), 139.10 (s), 170.15 (s), 204.97 (s) ppm. IR: ṽ = 667 (w), 845 (w), 895 (w), 932 (w), 1051 (m), 1167 (m), 1242 (m), 1321 (w), 1373 (s), 1436 (m), 1730 (s), 1745 (s), 2858 (m), 2879 (m), 2921 (m), 2974 (m) cm$^{-1}$. MS (EI): *m*/*z* (%) = 253.0 (100) [M + H]$^+$, 209 (42), 193.0 (24) [M + H − AcOH]$^+$.

**(4Z)-*tert*-Butyl 2-Acetoxy-2-acetyl-5,9-dimethyldeca-4,8-dienoate (4m):** The acetoacetate **3a** (19.5 g, 90 mmol), NaH (2.59 g, 108 mmol) and neryl bromide (19.6 g, 90 mmol) in DMF (180 mL) were treated as described in the general alkylation method to give (4*Z*)-**4m** (30.3 g, 86 mmol, 96%) as a slightly yellow oil. $^1$H NMR (200 MHz): δ = 1.46 (s, 9 H) 1.60 (s, 3 H), 1.68 (s, 3 H), 1.70 (s, 3 H), 2.00−2.05 (m, 4 H), 2.16 (s, 3 H), 2.31 (s, 3 H), 2.82−2.87 (m, 2 H), 5.00−5.09 (m, 2 H) ppm. $^{13}$C NMR (50 MHz,): δ = 17.56 (q), 20.60 (q), 23.52 (q), 25.61 (q), 26.32 (t), 26.95 (q), 27.63 (q), 31.90 (t), 32.30 (t), 83.08 (s), 87.83 (s), 116.22 (d), 123.75 (d), 131.84 (s), 140.07 (s), 165.96 (s), 169.53 (s), 201.06 (s) ppm. IR: ṽ = 845 (w), 1024 (w), 1072 (w), 1086 (w), 1115 (w), 1157 (s), 1236 (s), 1256 (s), 1314 (w), 1370 (s), 13895 (w), 1437 (w), 1452 (w), 1746 (s), 2861 (w), 2882 (w), 2932 (m), 2976 (m) cm$^{-1}$. MS (CI, isobut.): *m*/*z* (%) = 353 (13) [M + H]$^+$, 298 (21), 297 (100), 279 (14), 255 (10), 253 (13), 237 (27), 219 (20), 209 (65), 193 (10), 175 (6), 153 (7), 137 (16). HRMS: calculated for $C_{17}H_{31}O_5$ [$MH^+$]: calcd. 353.23282; found 353.23245.

**(5*Z*)-3-Acetoxy-6,10-dimethyl-5,9-undecadien-2-one (5m):** Compound **4m** (1.661 g, 4.71 mmol), LiCl (220 mg, 5.18 mmol) and $H_2O$ (93 μL, 93 mg, 5.18 mmol) were treated in DMSO (12.5 mL) at 140 °C for 3h 45 min and at 160 °C for 3h 30 min as described in dealkoxycarbonylation method B. The remaining yellow oil was purified by flash chromatography (column dimensions: 3.5 × 20.0 cm, ethyl acetate/petroleum ether, 1:5) to give 817 mg (3.24 mmol, 69%) of **5m**. $^1$H NMR (200 MHz): δ = 1.61 (s, 3 H), 1.68 (s, 3 H), 1.71 (s, 3 H), 1.90−2.10 (m, 4 H), 2.13 (s, 3 H), 2.15 (s, 3 H), 2.45−2.51 (m, 2 H), 4.93−5.00 (m, 1 H), 5.08−5.15 (m, 2 H) ppm. $^{13}$C NMR (50 MHz): δ = 17.47 (q), 20.48 (q), 23.28 (q), 25.53 (q), 26.21 (t), 26.38 (q), 28.79 (t), 31.80 (t), 78.39 (d), 117.90 (d), 123.67 (d), 131.74 (s), 139.27 (s), 170.36 (s), 205.03 (s) ppm. IR: ṽ = 853 (w), 877 (w), 932 (w), 949 (w), 1047 (s), 1070 (m), 1163 (m), 1177 (m), 1189 (m), 1239 (s), 1374 (m), 1446 (w), 1745 (s), 2288 (m), 2891 (m), 2915 (m), 2922 (m), 2929 (m), 2937 (m), 2965 (m) cm$^{-1}$. MS (ESI): *m*/*z* (%) = 527.4 (42) [2M + Na]$^+$, 275.1 (38) [M + Na]$^+$, 253.1 (6) [M + H]$^+$, 193.1 (4) [M + H − AcOH]$^+$.

***tert*-Butyl 2-Acetoxy-2-benzyl-3-oxobutanoate (4n):** The acetoacetate **3a** (749 mg, 3.46 mmol), NaH (108 mg, 4.5 mmol) and benzyl bromide (411 μL, 592 mg, 3.46 mmol) in DMF (7 mL) were treated as described in the general alkylation method to give **4n** (956 mg, 3.12 mmol, 90%) as a colourless oil. $^1$H NMR (200 MHz): δ = 1.35 (s, 9 H), 2.08 (s, 3 H), 2.13 (s, 3 H), 3.40 (m, 2 H), 6.90−7.40 (m, 5 H) ppm. $^{13}$C NMR (50 MHz): δ = 20.81 (q), 27.33 (q), 27.59 (q), 38.81 (t), 83.35 (s), 88.52 (s), 127.15 (d), 128.29 (d), 130.05 (d), 134.45 (s), 165.36 (s), 169.50 (s), 202.23 (s) ppm. IR: ṽ = 700 (w), 845 (w), 1030 (w), 1084 (w), 1155 (m), 1229 (m), 1252 (m), 1273 (m), 1370 (m), 1456 (w), 1751 (s), 2936 (m), 2978 (m), 3003 (w) cm$^{-1}$. MS (CI): *m*/*z* (%) = 43 (39), 45 (22), 57 (34), 91 (19), 119 (10), 145 (9), 173 (9), 189 (14), 190 (78), 191 (18), 233 (45), 246 (22), 251 (100), 252 (11), 307 (44). HRMS: calculated for $C_{17}H_{23}O_5$ [$MH^+$]: 307.15454; found 307.15070.

**3-Acetoxy-4-phenylbutan-2-one (5n):** Compound **4n** (919 g, 3.00 mmol) was decarboxylated as described in dealkoxycarbonylation method B. Purification by flash chromatography (column dimensions: 2.0 × 20.0 cm, ethyl acetate/petroleum ether, 1:4) gave **5n** (287 mg, 1.39 mmol, 46%) as a slightly yellow oil. $^1$H NMR

(200 MHz): δ = 2.03 (s, 2 × 3 H), 2.85−3.15 (m, 2 H), 5.08−5.23 (m, 1 H), 7.08−7.35 (m, 5 H) ppm. $^{13}$C NMR (50 MHz): δ = 20.38 (q), 26.64 (q), 36.45 (t), 78.90 (d), 126.87 (d), 128.40 (d), 129.13 (d), 135.74 (s), 170.16 (s), 205.09 (s) ppm. IR: $\tilde{\nu}$ = 702 (m), 735 (w), 748 (w), 1047 (m), 1070 (m), 1175 (m), 1240 (s), 1373 (m), 1433 (m), 1454 (m), 1497 (m), 1730 (s), 1744 (s), 2926 (w), 3030 (w) cm$^{-1}$. MS (CI): *m*/*z* (%) = 91 (13), 131 (19), 145 (32), 146 (84), 147 (79), 207 ($MH^+$, 100), 208 (14). HRMS: calculated for $C_{12}H_{15}O_3$ [$MH^+$]: 207.10211; found 207.10001.

***tert*-Butyl 2-Acetyl-2-butyryloxy-5-methylhex-4-enoate (4o):** Acetoacetate **3b** (8.04 g, 32.9 mmol), NaH (900 mg, 37.5 mmol) and prenyl bromide (1.23 g, 16.5 mmol) in DMF (64 mL) were treated as described in the general alkylation method to give **4o** (1.52 g, 12.5 mmol, 76%) as a slightly yellow oil after kugelrohr distillation at 1.0 mbar and 140 °C. $^1$H NMR (400 MHz): δ = 1.00 (t, *J* = 7.4 Hz, 3 H), 1.45 (s, 9 H), 1.60 (s, 3 H), 1.69 (s, 3 H), 1.67−1.73 (m, 2 H), 2.31 (s, 3 H), 2.38−2.42 (m, 2 H), 2.78−2.92 (m, 2 H), 5.41 (m, 1 H) ppm. $^{13}$C NMR (100 MHz): δ = 13.61 (q), 17.93 (q), 18.27 (t), 25.89 (q), 27.66 (q), 27.80 (q), 32.59 (t), 35.79 (q), 83.00 (s), 87.75 (s), 115.90 (d), 136.37 (s), 166.02 (s), 172.10 (s), 201.50 (s) ppm.

**3-Butyryloxy-6-methyl-5-hepten-2-one (5o):** Compound **4o** (7.34 g, 23.5 mmol) and *p*-TsOH·$H_2O$ (437 mg, 2.30 mmol) were stirred in benzene (100 mL) as described in dealkoxycarbonylation method A. Kugelrohr distillation at 1.0 mbar and 145 °C gave a colourless oil, which was further purified by column chromatography (ethyl acetate/petroleum ether, 1:3) to afford **5o** (1.04 g, 4.90 mmol, 15%). $^1$H NMR (400 MHz): δ = 0.97 (t, *J* = 7.3 Hz, 3 H), 1.62 (s, 3 H), 1.71 (s, 3 H), 1.65−1.72 (m, 2 H), 2.16 (s, 3 H), 2.36−2.41 (m, 2 H), 2.45−2.50 (m, 2 H), 4.99−5.03 (m, 1 H), 5.07−5.13 (m, 1 H) ppm. $^{13}$C NMR (100 MHz): δ = 13.55 (q), 17.82 (q), 18.30 (t), 25.71 (q), 26.56 (q), 29.26 (t), 35.82 (t), 78.16 (d), 117.46 (d), 135.73 (s), 173.13 (s), 205.47 ppm.

***tert*-Butyl 2-Benzyl-2-butyryloxy-3-oxo-butanoate (4p):** The acetoacetate **3b** (4.02 g, 16.5 mmol), NaH (450 mg, 18.8 mmol) and benzyl bromide (2.82 g, 16.5 mmol) in DMF (32 mL) were treated as described in the general alkylation method to give **4p** (4.70 g, 14.1 mmol, 85%) as a slightly yellow oil after distillation at 2 mbar and 175 °C. $^1$H NMR (400 MHz): δ = 0.99 (t, *J* = 7.4 Hz, 3 H), 1.40 (s, 9 H), 1.64−1.71 (m, 2 H), 2.18 (s, 3 H), 2.33−2.39 (m, 2 H), 3.47 (d, *J* = 14.4 Hz, 1 H), 3.53 (d, *J* = 14.0 Hz, 1 H), 7.08−7.11 (m, 2 H), 7.22−7.31 (m, 3 H) ppm. $^{13}$C NMR (100 MHz): δ = 13.64, 18.14, 27.45, 27.58, 35.93, 38.83, 83.23, 88.30, 127.09, 128.23, 130.06, 134.48, 165.42, 172.01, 202.54 ppm.

**3-Butyryloxy-4-phenylbutan-2-one (5p):** Compound **4p** (4.70 g, 14.1 mmol) and *p*-TsOH·$H_2O$ (278 mg, 1.46 mmol) were stirred in benzene (50 mL) as described in dealkoxycarbonylation method A. Kugelrohr distillation at 1.0 mbar and 140 °C gave **5p** (2.20 g, 9.39 mmol, 67%) as a colourless oil. $^1$H NMR (400 MHz): δ = 0.89 (t, *J* = 7.4 Hz, 3 H), 1.57−1.66 (m, 2 H), 2.08 (s, 3 H), 2.28−2.37 (m, 2 H), 2.99 (dd, AB, *J* = 14.1, *J* = 8.6 Hz, 1 H), 3.12 (dd, AB, *J* = 14.1, *J* = 4.7 Hz, 1 H), 5.22 (s, dd, *J* = 8.6, *J* = 5.1 Hz, 1 H), 7.20−7.33 (m, 5 H) ppm. $^{13}$C NMR (100 MHz): δ = 13.49 (q), 18.18 (t), 26.82 (q), 35.73 (t), 36.65 (t), 78.76 (d), 126.93 (d), 128.47 (d), 129.23 (d), 135.84 (s), 172.96 (s), 205.47 (s) ppm.

### Hydrolysis of Acyloin Esters 5a−5p

**General Procedure for the Chemical Hydrolysis of Acyloin Esters 5a−n:** A saturated aqueous solution of $K_2CO_3$ (80 μL per mmol ester) was added dropwise to esters **5a−n** in methanol (0.13 M). After completion of hydrolysis (usually after 5−10 min) the reaction was quenched by the addition of brine (1.5 times the amount of methanol), followed by a fivefold extraction with the same amount of diethyl ether. The combined organic layers were washed once with brine (3 times the amount of methanol), dried with $Na_2SO_4$, filtered and concentrated in vacuo. If necessary, flash chromatography was used to purify the racemic α-hydroxy ketone.

**(±)-3-Hydroxynonan-2-one [(±)-6e]:** 3-Acetoxynonan-2-one (**5e**, 60 mg, 0.30 mmol) was hydrolysed as described in the general chemical hydrolysis method to give (±)-**6e** as a slightly yellow oil (42 mg, 0.27 mmol, 88%). $^1$H NMR (200 MHz): δ = 0.70−1.00 (m, 3 H), 1.00−1.65 (m, 8 H), 1.65−1.90 (m, 2 H), 2.13 (s, 3 H), 3.00−3.80 (br., −OH, 1 H), 4.05−4.20 (m, 1 H) ppm. $^{13}$C NMR (50 MHz): δ = 13.86 (q), 22.38 (t), 24.52 (t), 25.00 (q), 28.94 (t), 31.47 (t), 33.67 (t), 76.68 (d), 209.88 (s) ppm.

**(±)-(5*Z*)-3-Hydroxy-5-hepten-2-one [(±)-6i]:** (5*Z*)-3-Acetoxyhept-5-en-2-one (**5i**, 43 mg, 0.25 mmol) was hydrolysed as described in the general chemical hydrolysis method to give (±)-**6i** as a slightly yellow oil (31 mg, 0.24 mmol, 96%). $^1$H NMR (200 MHz): δ = 1.58 (d, *J* = 7.4 Hz, 3 H), 2.14 (s, 3 H), 2.30−2.60 (m, 2 H), 3.10−3.70 (br., −OH, 1 H), 4.20 (m, 1 H), 5.15−5.40 (m, 1 H), 5.40−5.70 (m, 1 H) ppm. $^{13}$C NMR (50 MHz): δ = 12.87 (q), 25.20 (q), 30.91 (t), 76.29 (d), 123.49 (d), 127.54 (d), 209.32 (s) ppm.

**(±)-3-Hydroxy-6-methyl-5-hepten-2-one [(±)-6j]:** 3-Acetoxy-6-methyl-5-hepten-2-one (**5j,** 48 mg, 0.26 mmol) was hydrolysed as described in the general chemical hydrolysis method to give (±)-**6j** as a slightly yellow oil (28 mg, 0.20 mmol, 77%) after flash chromatography (ethyl acetate/petroleum ether, 1:4). $^1$H NMR (200 MHz): δ = 1.55 (s, 3 H), 1.65 (s, 3 H), 2.15 (s, 3 H), 2.17−2.55 (m, 2 H), 3.40 (br., −OH, 1 H), 4.15 (m, 1 H), 5.05 (m, 1 H) ppm. $^{13}$C NMR (50 MHz): δ = 17.85 (q), 25.24 (q), 25.65 (q), 32.13 (t), 77.52 (d), 117.52 (d), 135.45 (s), 209.58 (s) ppm.

**(±)-3-Hydroxy-6-methylheptan-2-one [(±)-6k]:** 3-Acetoxy-6-methylheptan-2-one (**5k**, 47 mg, 0.25 mmol) was hydrolysed as described in the general chemical hydrolysis method to give (±)-**6k** as slightly yellow oil (32 mg, 0.22 mmol, 88%). $^1$H NMR (200 MHz): δ = 0.82 (s, 3 H), 0.85 (s, 3 H), 0.90−1.65 (m, 3 H), 1.65−1.95 (m, 2 H), 2.14 (s, 3 H), 3.10−3.50 (br., −OH, 1 H), 4.00−4.20 (m, 1 H) ppm. $^{13}$C NMR (50 MHz): δ = 22.08 (q), 22.44 (q), 25.01 (q), 27.75 (d), 31.21 (t), 33.41 (t), 76.81 (d), 210 (s) ppm.

**(±)-(5*Z*)-3-Hydroxy-6,10-dimethyl-5,9-undecadien-2-one [(±)-6m]:** (5*E*)-3-Acetoxy-6,10-dimethyl-5,9-undecadien-2-one (**5m,** 63 mg, 0.25 mmol) was hydrolysed as described in the general chemical hydrolysis method to give (±)-**6m** as a slightly yellow oil (47 mg, 0.22 mmol, 89%). $^1$H NMR (200 MHz): δ = 1.58 (s, 3 H), 1.65 (s, 3 H), 1.69 (s, 3 H), 2.00−2.05 (m, 4 H), 2.16 (s, 3 H), 2.20−2.60 (m, 2 H), 3.00−3.60 (br., −OH, 1 H), 4.18 (m, 1 H), 4.90−5.20 (m, 2 H) ppm. $^{13}$C NMR (50 MHz): δ = 13.95 (q), 23.29 (q), 25.29 (q), 25.54 (q), 26.20 (t), 31.89 (t), 31.96 (t), 76.59 (d), 118.19 (d), 123.74 (d), 131.77 (t), 139.15 (s), 209.53 (s) ppm.

**General Procedure for the Hydrolase Screening for Enantioselective Acyloin−Ester Cleavage:** Racemic acyloin acetates **5** (5 μL) were hydrolysed (in triplicate) with each lipase (BCL, CAL-B, CAL-A, CRL, ROL, and PPL, ca. 20 mg) in phosphate buffer (0.1 M, pH 7.0, 0.7 mL) by shaking the mixture at ambient temperature (300 strokes per minute). After 30 minutes, acetone (0.3 mL) was added to stop the enzymatic hydrolysis. After twofold extraction with ethyl acetate (0.4 mL; phase separation was achieved by centrifugation at 8000 g for 5 min), the combined organic layers were dried with $Na_2SO_4$ and then centrifuged (8000 g/5 min). The supernatant was decanted and analysed by TLC and chiral GC (Table 2) meth-

Table 2. Chiral GC data

| Acyloxy ketone/acyloin | Conditions[a] [°C] | Retention times acyloins **6a−p** [min] (absol. config.) | Retention times of acyloxy ketones **5a−p** [min] (absol. config.) |
|---|---|---|---|
| **5a/6a** | 40 (iso) | 2.8 (*R*), 3.6 (*S*) | 10.1 (*R*), 11.2 (*S*) |
| **5b/6b** | 70 (iso) | 1.5 (*R*), 1.9 (*S*) | 3.1 (*R*), 3.6 (*S*) |
| **5c/6c** | 80 (iso) | 1.9 (*R*), 2.4 (*S*) | 3.6 (*R*), 4.1 (*S*) |
| **5d/6d** | 70/10′-6/min-110 | 6.5 (*R*), 7.4 (S) | 12.1 (*R*), 13.1 (*S*) |
| **5e/6e** | 95/1′-4/min-110 | 3.0 (*R*), 3.3 (*S*) | 4.5 (*R*), 4.7 (*S*) |
| **5f/6f** | 70 (iso) | 1.4 (*R*), 1.8 (*S*) | 3.0 (*R*), 3.3 (*S*) |
| **5g/6g** | 80 (iso) | 2.8 (*R*), 3.6 (*S*) | 6.0 (*R*), 6.0 (*S*) |
| **5h/6h** | 70 (iso) | 3.1 (*R*), 4.3 (*S*) | 6.3 (*R*), 7.2 (*S*) |
| **5i/6i** | 70 (iso) | 3.8 (*R*), 4.9 (*S*) | 6.8 (*R*), 7.8 (*S*) |
| **5j/6j** | 80 (iso) | 3.7 (*R*), 4.5 (*S*) | 6.4 (*R*), 7.1 (*S*) |
| **5k/6k** | 75 (iso) | 3.8 (*R*), 4.5 (*S*) | 7.0 (*R*), 8.1 (*S*) |
| **5l/6l** | 105 (iso) | 15.9 (*R*), 17.0 (*S*) | 28.8 (*R*), 30.0 (*S*) |
| **5m/6m** | 100 (iso) | 20.1 (*R*), 21.5 (*S*) | 32.2 (*R*), 33.7 (*S*) |
| **5n/6n** | 100 (iso) | 10.7 (*R*), 12.3 (*S*) | 13.1 (*R*), 14.0 (*S*) |
| **5o/6o** | 80(iso) | 10.5 (*R*), 12.4 (*S*) | 14.1 (*R*), 15.0 (*S*) |
| **5p/6p** | 100(iso) | 15.4 (*R*), 16.6 (*S*) | 27.5 (*R*), 29.4 (*S*) |

[a] For details see general remarks of the Exp. Sect.

ods. Control experiments without addition of enzyme were performed for each acyloin acetate **5**.

**General Procedure for the Preparative Resolution of Acyloins 5c, 5g, 5j, 5l, 5m and 5n with Lipase:** The acyloin ester was dissolved in phosphate buffer (pH 7.0, 0.1 M), after which the lipase powder [if not indicated otherwise, ca. 25% (wt.) of the acyloin ester] was added and the reaction vessel was continuously shaken at 300 strokes per minute at ambient temperature. After appropriate conversion (TLC or GC monitoring), acetone was added (half the volume of buffer) and the mixture was extracted five times with ethyl acetate (1.5 times the volume of buffer used). The combined organic layers were washed with brine (twice the volume of buffer used), dried with $Na_2SO_4$, filtered and concentrated in vacuo. The alcohol and ester were separated by flash chromatography.

**(*S*)-3-Hydroxyheptan-2-one [(*S*)-6c]:** 3-Acetoxyheptanone (**5c**, 100 mg, 0.58 mmol) was selectively hydrolysed with *Candida antartica* B lipase (6 mg) in buffer (10 mL) by the general procedure for the preparative resolution described above. The reaction was worked up after 3.75 h, and flash chromatography (ethyl acetate/petroleum ether, 1:6) gave (in order of elution) the unchanged optically enriched ester **5c** (35 mg, 0.20 mmol, 35%) and the (*S*)-alcohol **6c** (20 mg, 0.15 mmol, 26%).

**Compound (*R*)-5c:** $R_f$ value (ethyl acetate/hexane, 1:4): 0.48. $[\alpha]_D^{25}$ = +9.6 (*c* = 1.805; $CHCl_3$; *ee* = 78%).

**Compound (*S*)-6c:** $R_f$ value (ethyl acetate/hexane, 1:4): 0.33. $[\alpha]_D^{25}$ = +69.9 (*c* = 0.410; $CHCl_3$; *ee* = 82%).

**(*S*)-3-Hydroxy-5-heptyn-4-one [(*S*)-6g]:** Compound **5g** (124 mg, 0.74 mmol) was selectively hydrolysed with *Candida antarctica* lipase B (34 mg) in buffer (15 mL) by the general procedure for the preparative resolution described above. The reaction was worked up after 3 h, and flash chromatography (ethyl acetate/petroleum ether, 1:5) gave (in order of elution) the unchanged optically enriched ester **5g** (51 mg, 0.37 mmol, 41%) and the (*S*)-alcohol **6g** (33 mg, 0.26 mmol, 35%).

**Compound (*R*)-5g:** $R_f$ value (ethyl acetate/hexane, 1:4): 0.48. $[\alpha]_D^{25}$ = −2.8 (*c* = 5.10; $CHCl_3$; *ee* = 85%).

**Compound (*S*)-6g:** $R_f$ value (ethyl acetate/hexane, 1:4): 0.33. $[\alpha]_D^{25}$ = +60.9 (*c* = 3.30; $CHCl_3$; *ee* = 89%). $^1$H NMR (200 MHz): δ = 1.72 (t, *J* < 2 Hz, 3 H), 2.28 (s, 3 H), 2.55−2.65 (m, 2 H), 3.61 (d, *J* = 6 Hz, 1 H, OH), 4.22 (m, 1 H) ppm. $^{13}$C NMR (50 MHz): δ = 3.37 (q), 24.24 (t), 25.54 (q), 72.93 (d), 75.16 (d), 79.13 (s), 208.17 (s) ppm.

**(*S*)-3-Hydroxy-6-methyl-5-hepten-4-one [(*S*)-6j]:** Heptenone **5j** (200 mg, 1.09 mmol) was selectively hydrolysed with Amano lipase BCL (63 mg) in buffer (15 mL) by the general procedure for the preparative resolution described above. The reaction was worked up after 6 h, and flash chromatography (ethyl acetate/petroleum ether, 1:8) gave (in order of elution) the unchanged optically pure ester **5j** (103 mg, 0.56 mmol, 52%) and the (*S*)-alcohol **6j** (71 mg, 0.50 mmol, 46%).

**Compound (*R*)-5j:** $R_f$ value (ethyl acetate/hexane, 1:4): 0.50. $[\alpha]_D^{25}$ = −15.5 (*c* = 2.030; $CHCl_3$; *ee* = 99%).

**Compound (*S*)-6j:** $R_f$ value (ethyl acetate/hexane, 1:4): 0.22. $[\alpha]_D^{2}$ = +64.5 (*c* = 0.979; $CHCl_3$; *ee* = 99%). $^1$H NMR (200 MHz): δ = 1.61 (s, 3 H), 1.69 (s, 3 H), 2.16 (s, 3 H), 2.2−2.7 (m, 2 H), 3.40 (d, *J* = 4.9 Hz, −OH), 4.20 (q, *J* = 5.2 Hz, 1 H), 5.07 (t, *J* = 7.1 Hz, 1 H) ppm. $^{13}$C NMR (50.3 MHz): δ = 17.86 (q), 25.24 (q), 25.66 (q), 32.15 (t), 76.57 (d), 117.51 (d), 135.49 (s), 209.51 (s) ppm.

**(3*S*,5*E*)-3-Hydroxy-6,10-dimethyl-5,9-undecadien-2-one [(*S*)-6l]:** Compound (5*E*)-**5l** (150 mg, 0.59 mmol) was selectively hydrolysed with Amano lipase BCL (38 mg) in buffer (15 mL) by the general procedure for the preparative resolution described above. The reaction was worked up after 4 h, and flash chromatography (ethyl acetate/petroleum ether, 1:5) gave (in order of elution) the unchanged ester (*R*)-**5l** (10 mg, 0.04 mmol, 7%) and the (*S*)-alcohol **6l** (38 mg, 0.18 mmol, 31%).

**Compound (*S*)-6l:** $R_f$ value (ethyl acetate/hexane, 1:4): 0.38. $[\alpha]_D^{25}$ = +20.2 (*c* = 3.80; $CHCl_3$; *ee* = 30%). $^1$H NMR (200 MHz): δ = 1.59 (s, 3 H), 1.64 (s, 3 H), 1.67 (s, 3 H), 2.00−2.10 (m, 2 H), 2.18 (s, 3 H), 2.25−2.70 (m, 2 H), 4.24 (m, 1 H), 4.90−5.25 (m, 2 H) ppm.

**(3*S*,5*Z*)-3-Hydroxy-6,10-dimethyl-5,9-undecadien-2-one [(*S*)-6m]:** Compound (5*Z*)-**5m** (200 mg, 0.79 mmol) was selectively hydrolysed with Amano BCL (63 mg) in buffer (15 mL) by the general procedure for the preparative resolution described above. The reaction was worked up after 6 h, and flash chromatography (ethyl acetate/petroleum ether, 1:8) gave (in order of elution) the unchanged optically pure ester (*R*)-**5m** (107 mg, 0.42 mmol, 54%) and the (*S*)-alcohol **6m** (70 mg, 0.33 mmol, 42%).

**Compound (*R*)-5m:** $R_f$ value (ethyl acetate/hexane, 1:4): 0.52. $[\alpha]_D^{25}$ = −19.7 (*c* = 1.560; $CHCl_3$; *ee* = 97%).

**Compound (*S*)-6m:** $R_f$ value (ethyl acetate/hexane, 1:4): 0.38. $[\alpha]_D^{25}$ = +63.7 (*c* = 2.115; $CHCl_3$; *ee* = 95%). $^1$H NMR (200 MHz): δ = 1.60 (s, 3 H), 1.67 (s, 3 H), 1.71 (s, 3 H), 2.00−2.07 (m, 4 H), 2.18 (s, 3 H), 2.25−2.65 (m, 2 H), 3.10−3.60 (br., OH), 4.17−4.23 (m, 1 H), 5.05−5.20 (m, 2 H) ppm. $^{13}$C NMR (50 MHz): δ = 17.47 (q), 23.30 (q), 25.29 (q), 25.54 (q), 26.20 (t), 31.89 (t), 31.96 (t), 76.60 (d), 118.19 (d), 123.74 (d), 131.77 (s), 139.15 (s), 209.53 (s) ppm. IR: $\tilde{\nu}$ = 734 (w), 1093 (m), 1173 (w), 1252 (w), 1356 (m), 1377 (m), 1449 (m), 1716 (s), 2857 (m), 2924 (s), 2965 (s), 3476 (m) $cm^{-1}$.

**(*S*)-3-Hydroxy-4-phenylbutan-2-one [(*S*)-6n]:** Butanone **5n** (150 mg, 0.73 mmol) was selectively hydrolysed with Amano lipase BCL (38 mg) in buffer (15 mL) by the general procedure for the preparative resolution described above. The reaction was worked up after 3 h, and flash chromatography (ethyl acetate/petroleum ether, 1:8) gave (in order of elution) the unchanged optically enriched ester **5n** (76 mg, 0.37 mmol, 50%) and the (*S*)-alcohol **6n** (51 mg, 0.31 mmol, 43%).

**Compound (*R*)-5n:** $R_f$ value (ethyl acetate/hexane, 1:4): 0.48. $[\alpha]_D^{25}$ = −3.0 (*c* = 2.325; $CHCl_3$; *ee* = 85%).

**Compound (*S*)-6n:** $R_f$ value (ethyl acetate/hexane, 1:4): 0.33. $[\alpha]_D^{25}$ = +64.1 (*c* = 0.820; $CHCl_3$; *ee* = 89%). $^1$H NMR (200 MHz): δ = 2.19 (s, 3 H), 2.87 (dd, *J* = 14.1, *J* = 7.2 Hz, 1 H), 3.13 (dd, *J* = 14.1, *J* = 4.7 Hz, 1 H), 4.41 (m, 1 H), 7.0−7.4 (m, 5 H) ppm. $^{13}$C NMR (50 MHz): δ = 25.73 (q), 39.76 (t), 77.49 (d), 126.80 (d), 128.41 (d), 129.09 (d), 136.26 (s), 208.94 (s) ppm. IR: $\tilde{\nu}$ = 700 (s), 743 (m), 841 (w), 873 (w), 917 (w), 969 (w), 1030 (w), 1092 (s), 1175 (w), 1246 (w), 1358 (m), 1418 (w), 1455 (m), 1497 (m), 1603 (w), 1713 (s), 2924 (m), 3029 (m), 3062 (w), 3086 (w), 3445 (m) $cm^{-1}$.

**General Procedure for the Derivatisation of Alcohols 6 as *O*-Methylmandelates for the Determination of the Absolute Configuration:** (See also main text). EDCI (two equiv.) was added to a solution of equimolar amounts of acyloin **6**, (*R*)-methoxyphenylacetic acid and DMAP, and the mixture was stirred for 16 h at ambient temperature. Diethyl ether (3 × 10 mL) was then added, and the resulting suspension was washed with demineralised water (5 mL) and brine (2 × 5 mL). The organic layer was dried with $Na_2SO_4$, filtered and concentrated in vacuo. The remaining residue was purified (e.g., by flash chromatography on silica with diethyl ether/pentane, 1:4) to afford analytical samples of the corresponding MPA esters, which were pure enough for temperature-dependent NMR experiments to determine the absolute configuration. In this way, **6g**, **6i**, **6l**, and **6m** were shown to have (*S*) configurations.

**Selected Typical Data for MTPA Esters**

**Compound 7c:** Colourless oil, $R_f$ = 0.34. $^1$H NMR (400 MHz): δ = 0.76 (t, *J* = 7.2 Hz, 3 H), 0.90−1.15 (m, 4 H), 1.57−1.78 (m, 2 H), 2.10 (s, 3 H), 3.45 (s, 3 H), 4.90 (s, 1 H), 4.99 (m, 1 H), 7.30−7.50 (m, 5 H) ppm.

**Compound 7j:** Colourless oil, $R_f$ = 0.39. $^1$H NMR (400 MHz: δ = 1.48 (s, 3 H), 1.57 (s, 3 H), 2.09 (s, 3 H), 2.40 (m, 2 H), 3.44 (s, 3 H), 4.80 (m, 1 H), 4.88 (s, 1 H), 4.98 (m, 1 H), 7.30−7.45 (m, 5 H) ppm.

**Compound 7l:** Colourless oil, $R_f$ = 0.39. $^1$H NMR (400 MHz): δ = 1.47 (s, 3 H), 1.58 (s, 3 H), 1.68 (s, 3 H), 1.80−2.00 (m, 4 H), 2.10 (s, 3 H), 2.40 (m, 2 H), 3.44 (s, 3 H), 4.35 (m, 1 H), 4.38 (s, 1 H), 5.00 (m, 2 H), 7.30−7.45 (m, 5 H) ppm.

**Compound 7m:** Slightly yellow oil. $^1$H NMR (400 MHz): δ = 1.43 (s, 3 H), 1.58 (s, 3 H), 1.68 (s, 3 H), 1.85−2.00 (m, 4 H), 2.10 (s, 3 H), 2.30−2.50 (m, 2 H), 3.45 (s, 3 H), 4.82 (m, 1 H), 4.90 (s, 1 H), 4.98 (m, 1 H), 5.05 (m, 1 H), 7.30−7.50 (m, 5 H) ppm.

Table 3. Representation of the enantiomeric excesses of acyloin esters (*R*)-**5** and acyloins (*S*)-**6** achievable with the three most suitable enzymes tested; for each substrate, the best *ee* values are printed in bold (n.d. = not determined)

| *ee* Values Substrate/Product | Enzyme BCL | CAL-B | CAL-A |
|---|---|---|---|
| **5a/6a** | 9:27 | 13:14 | 6:**35** |
| **5b/6b** | 58:87 | 12:**89** | n.d. |
| **5c/6c** | **100**:66 | **100**:87 | 19:73 |
| **5d/6d** | 54:94 | 11:**98** | n.d. |
| **5e/6e** | **99**:34 | **99**:93 | 19:71 |
| **5f/6f** | 43:**89** | 9:**89** | n.d. |
| **5g/6g** | 0:8 | **100**:91 | 7:66 |
| **5h/6h** | **99**:27 | 95:**94** | 76:88 |
| **5i/6i** | 100:100 | **100**:95 | 33:69 |
| **5j/6j** | 99:99 | **98**:94 | 19:89 |
| **5k/6k** | **100**:96 | 77:**97** | 15:61 |
| **5l/6l** | **100**:88 | 28:**96** | n.d. |
| **5m/6m** | **95**:94 | 55:89 | 52:78 |
| **5n/6n** | **97**:95 | 14:84 | 15:85 |
| **5o/6o** | **99**:98 | 55:**99** | n.d./0 |
| **5p/6p** | **97**:92 | 5:75 | 99:11 |

## Acknowledgments

The authors gratefully acknowledge F. de Kanter (VUA) for recording the NMR spectra and R. Schmitz (VUA) for his crucial help in the lab and on the chiral GC. Furthermore, we would like to express our thanks to G. Schmidt (IPB) for the synthesis of the derivatives **5b**, **5j**, **5o**, and **5p**, and to J. Schmidt (IPB) and H. Zappey (VUA) for mass spectra.

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[41] Derivatisation of **6g** and **6l** as (*R*)-MPA esters according to Latypov[40c] produced a somewhat diminished *der*, In the case of **6g** this was due to relatively high spontaneous hydrolysis (ca. 4.3% within 30 min). For **6l** the *E* value was rather low, resulting in a diastereomeric mixture of (*R*)-MTPA esters. However, it was still possible to assign the absolute configuration.

Received June 4, 2003

  