EPC-Synthesis of β-Amino Acid Derivatives through Lithiated Hydropyrimidines

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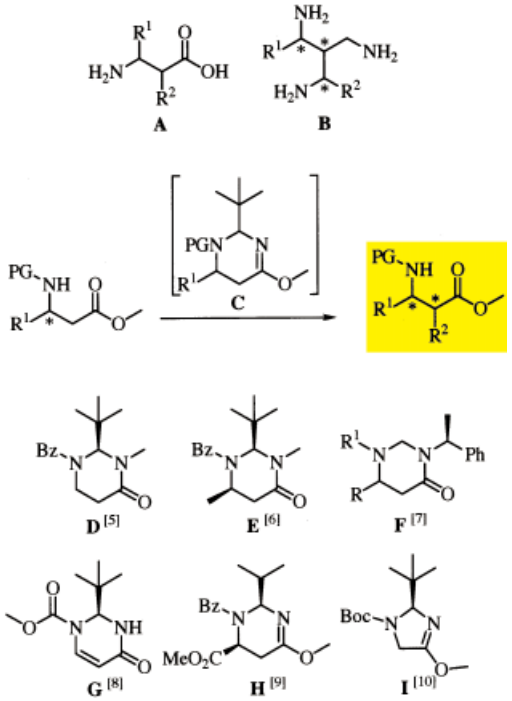
Racemic and enantiopure 2-*tert*-butyltetrahydropyrimidinones (from pivalaldehyde and 3-aminocarboxylic acids) are converted to Alloc-, Boc-, and Z-protected cyclic imino esters (**7**–**10**, Schemes 2–4). These are deprotonated to Li enaminates (**K**, **L**). Reactions with electrophiles (*prim*., *sec*. alkyl, allyl, benzyl, propargyl halides, aldehydes, imines, enoates) give good yields and are highly diastereoselective (products **11**–**42,** Schemes 5–10). A two-step cleavage (removal of protecting group and hydrolysis) under very mild conditions converts the heterocyclic products to α-branched β-amino acid methyl esters (**43**–**61**, Schemes 11–13). The structure of the products is determined by NMR spectroscopy (Figure 1), by chemical correlation (Scheme 14), and by X-ray analysis (Figure 2, 3, 7, Table 1). A structure of the Li enaminates is proposed (Figure 4). Mechanistic models are derived for the reactions occurring with formation of two stereogenic centers with relative topicity *like* (Figures 5, 6).

1. Introduction

The interest in β-amino acid derivatives stems from two lines of research in our group. We have recently embarked in an investigation of β-peptides containing exclusively 3-aminocarboxylic acid residues **A**, with side chains R in 2- or/and 3-position,[1] and thus we needed to have versatile and multiple access to enantiopure β-amino acids.[2] A longer lasting interest in this type of structure originates in our work on chiral dendrimers[3] where we want to use chiral triamines **B** as core building blocks, and these we intended to prepare through diastereoselective aminoalkylation in the 2-position of 3-aminocarbamides.In the present contribution we describe, in full detail, the results of an effort of several years[4] in which we elaborated a new methodology for α-alkylation of β-amino acids, including the achiral 3-aminopropanoic acid, through chiral Li enaminates derived from tetrahydropyrimidines **C** (with and without a substituent R^1 in the 6-position). There was need for improvement of previously used methods: the Li enolates of tetrahydropyrimidinones **D**−**F** (Scheme 1) do not always exhibit the required reactivities and diastereoselectivities in their reactions with electrophiles, especially in additions to trigonal centers creating two new stereogenic centers.[11]

Furthermore, the hydrolysis of products arising from such reactions with electrophiles requires stringent conditions (for the eventual hydrolysis of carbamide groups to the free β-amino acid). This holds, at least partially, also for applications of the Michael acceptor **G** which, like the cyclic iminoester **H**, is prepared from aspartic acid. As first shown in a preparative application by Schöllkopf,[12] "lactim ethers", such as **C**, **H** and **I**, are readily cleaved to give methyl esters under mildly acidic conditions. A strong motivation for us to study lithiated iminoesters **C** came from our successful developement of the chiral, non-auxiliary-based glycine derivative **I** (BDI) as a versatile reagent for



Scheme 1. Dihydro- and tetrahydropyrimidinone derivatives for β-amino acid synthesis; PG = protecting group, Bz = benzoyl, Boc = *tert*-butyloxycarbonyl

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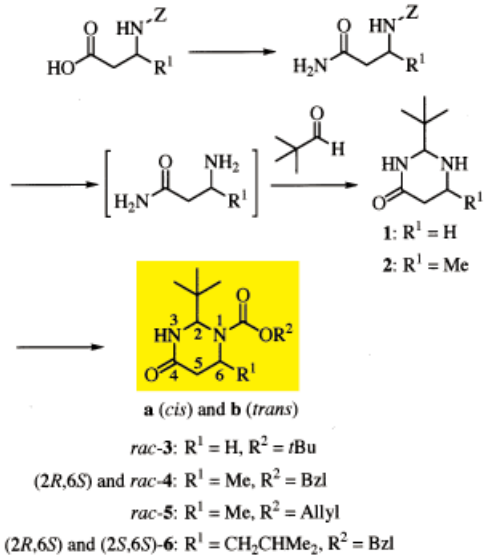
the preparation of α-amino acids (including those with acid-sensitive side chains).

2. Preparation of the Starting Materials

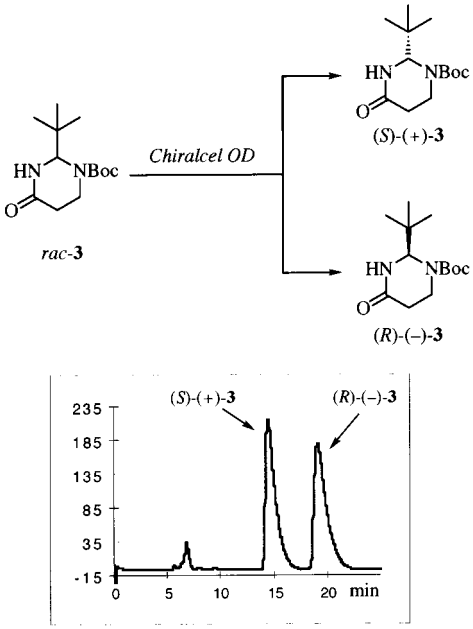
The amides of 3-aminopropanoic,[13] *rac*- and (*S*)-3-aminobutanoic[14] and (*S*)-3-amino-5-methylhexanoic acid[15] were prepared from the corresponding Z-protected acids and converted in situ to aminals with pivalaldehyde, providing tetrahydropyrimidinones (**1**, **2**), the basic nitrogen of which was alkoxycarbonylated (protected, → **3**−**6**), as shown in Scheme 2 (cf. the procedure for preparation of analogous 1-benzoyl-3-methyl derivatives;[6,16] Boc-protection was only possible with the propionic acid derivative **1**). The major products **4**−**6** have *cis* configuration **a**; *trans* isomers **b** are readily separated and have been characterized (see Experimental Section and configurational assignment in section 5).[17,18]



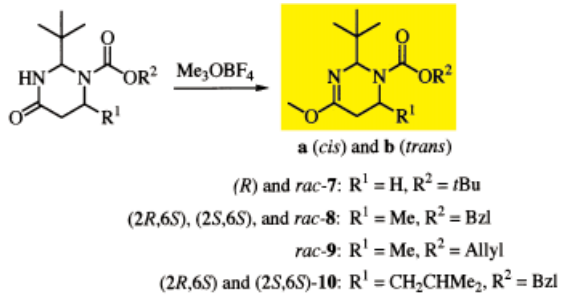
Scheme 2. Preparation of tetrahydropyrimdinones with various carbamate protecting groups in the 1-position; the non-racemic forms of **4**−**6** are derived from (*S*)-alanine and (*S*)-leucine; the major products **4**−**6** have *cis* configuration **a**. Z = benzyloxycarbonyl, Bzl = benzyl

While the 6-methyl- and 6-isobutyltetrahydropyrimidinones **4** and **6** were obtained in enantiopure form from the corresponding amino acids,[14,15], the propionic acid derivatives (*R*)- and (*S*)-**3** had to be prepared by resolution. We chose to use the method of preparative chromatographic resolution on a chiral column which readily provided multi-gram amounts of both enantiomers (Scheme 3).

With the *rac* and enantiopure pyrimidinone derivatives at hand, we prepared the cyclic methyl iminoesters **7**−**10** by treatment with Meerwein salt (Scheme 4). The 1-Alloc-, 1-Boc, and 1-Z-protected 2-*tert*-butyl-4-methoxytetrahydropyrimidines (BMP) thus prepared could be readily purified and characterized. These *cis* isomers **8a**−**10a** derived from the major cyclization products **4a**−**6a** were used exclusively for the reactions described in the following sections.[19]



Scheme 3. Preparative chromatographic enantiomer separation of the 3-aminopropionic acid derivative *rac*-**3**; analytic and preparative resolution on *Chiralcel OD*; for assignment of absolute configuration (*R*) and (*S*) to the dextrorotatory and laevorotatory enantiomer see sections 3, 4



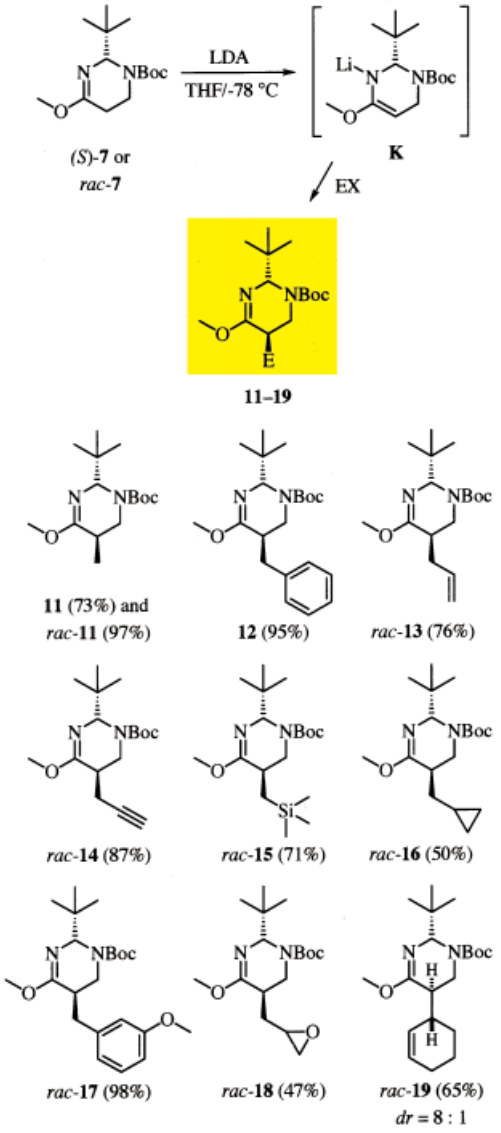
Scheme 4. Conversion of the Alloc-, Boc-, and Z-protected tetrahydropyrimidinones to the cyclic imino esters **7**−**10** with Meerwein salt; all reactions outlined in the following schemes were performed with the *cis* isomers **a**. Allyloxycarbonyl derivatives such as **9** and its precursor **5** are designated as *Alloc*-protected

Whereas the pyrimidone precursors are crystalline solids, the iminoesters **7**−**10** are colorless oils (after chromatography). They have been kept for long periods of time in stoppered flasks without decomposition (even at room temperature).

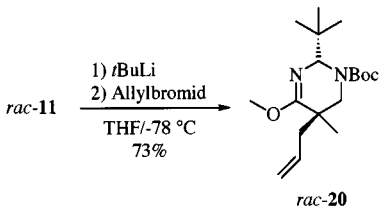
3. Lithiation of Hydro-Pyrimidines 7−10 and Reactions with Electrophiles

Lithium enaminates such as **K** and **L** were usually generated from the BMPs **7**−**10** by treatment with lithium diisopropylamide (LDA) in tetrahydrofuran (THF) at dry-ice temperature. The results of reactions (carried out mostly with *rac* starting materials, for **8**−**10** of *cis* configuration[20]) with electrophiles are outlined in Schemes 5−10, in which the yields all refer to analytically pure samples.

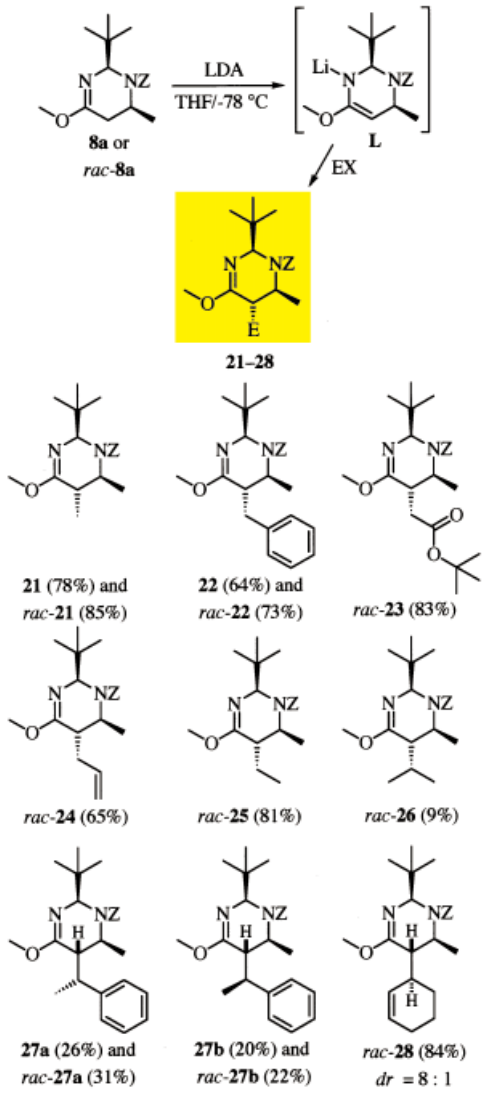
Alkylations (Schemes 5, 6, 7, 8) are high-yielding reactions with primary alkyl, allyl, propargyl, benzyl, and carbalkoxymethyl halides. The yields are somewhat better with the aminopropionic acid derivative **7** (products **11**−**19**) than with the heterocycles **8**−**10** bearing a substituent in the 6-position (products **21**−**31**).



Scheme 5. Products of alkylation of the Li enaminate **K**; the diastereoisomers **11**−**17** shown are formed with > 98% selectivity; when *rac*-**7** was used as starting material, only one enantiomer of the corresponding product is shown; the yields refer to chromatographed, analytically pure products

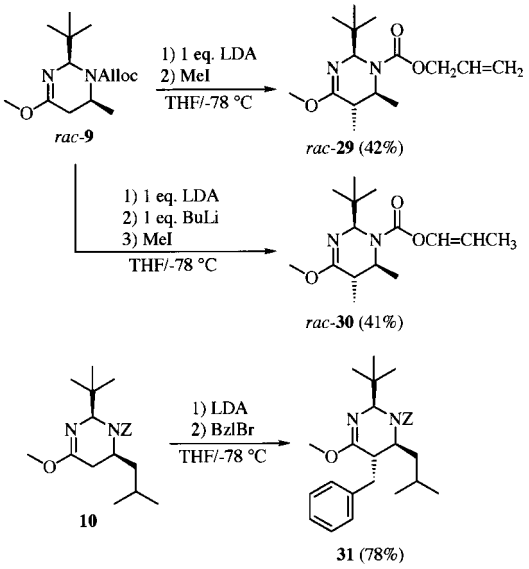


Scheme 6. Introduction of a second substituent in the 5-position of *rac*-**11**; only *one* diastereoisomer is formed; for configurational assignment see section 5

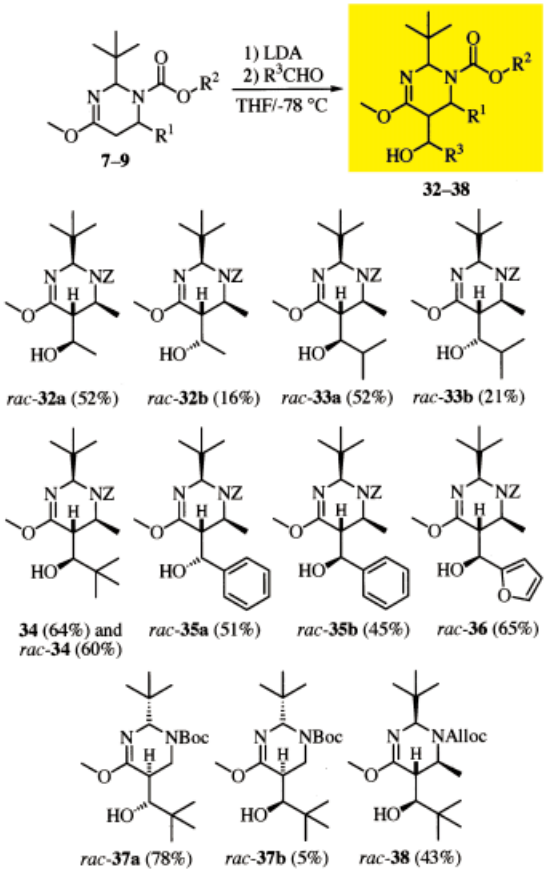


Scheme 7. Alkylation of the (2*R*,6*S*)- and *rac*-dihydropyrimidine **8a** (Z = CO_2Bzl) through the enaminate **L**; only one entantiomer of *rac*-products is shown; the products **21**−**26** are formed as single diastereoisomers. For the configuration of the carbocyclic stereocenter in **28** see Scheme 14 and Figure 2: the yields refer to chromatographed analytically pure samples

A second alkylation could be performed, starting with the 6-unsubstituted BMP **7** which was first methylated (→ **11**) and then allylated, with formation of the 5,5-geminally disubstituted product **20** (Scheme 6).[21] Secondary halides reacted well only when allylic (compare the yields of **19**, **26**, **27**, and **28**). The most remarkable assets of these alkylations are of stereochemical nature: (i) the alkyl groups are introduced in the 4-position exclusively from the face of the ring opposite to that bearing the 2-*tert*-butyl group; in no case did we detect a second diastereoisomer by high-field NMR spectroscopy of the crude products[22] obtained with simple halides R−CH_2X; (ii) there was efficient kinetic resolution in the reaction with *rac*-3-bromocyclohexene, providing major diastereoisomer **19** and **28** with 89% stereoselectivity; *rac*-epibromohydrin, gave a diastereoisomer **18** predominating in a ratio of 3:1; with *rac*-1-bromo-1-phenylethane the



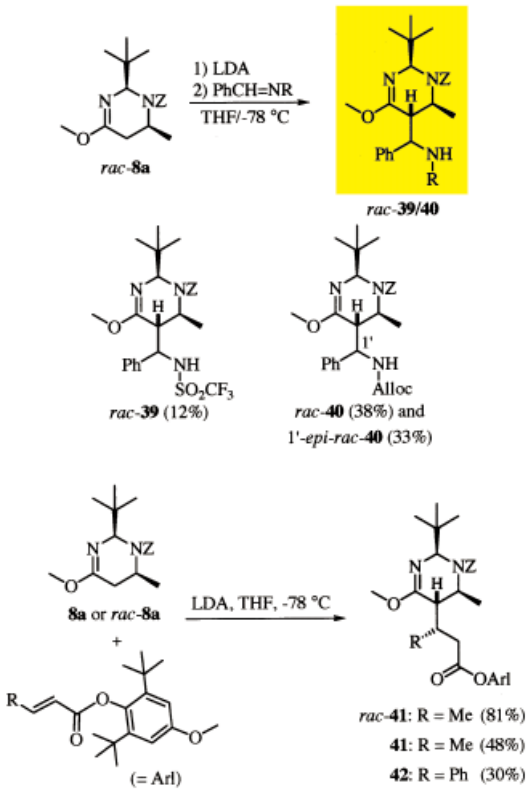
Scheme 8. Alkylation of the allyloxycarbonyl(Alloc)-protected heterocycle **9** and of the leucine-derived heterocycle **10; o**nly one enantiomer of the Alloc-protected pyrimidine is shown, only one diastereoisomer is formed in the three reactions. Note that excess base leads to an allylic shift from allyl to enol ester in the protecting group (the configuration of the C,C-double bond in **30** was not determined; broad NMR signals from rotamers!)



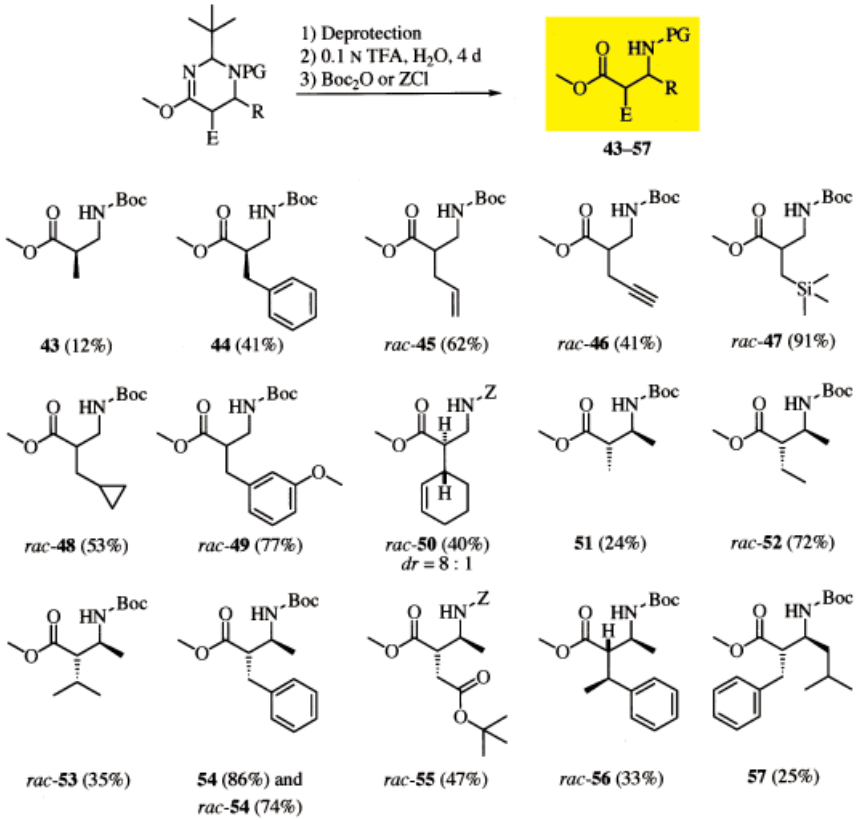
Scheme 9. Aldol additions of Li enaminates from the dihydropyrimidines **7**, **8**, and **9**; only one enantiomer of *rac*-products is shown; the diastereoselectivity with respect to the exocyclic stereocenters is much higher with aliphatic than with aromatic aldehydes; the diastereoisomers were separated by chromatography, and the yields refer to analytically pure materials (mostly recrystallized). For determination of the configuration see section 5; **a** and **b** designate the products formed with rel. topicity *like* and *unlike*, respectively

rate with which the enantiomers reacted differed only marginally (see **27a**/**27b**). The assignment of configurations to the alkylation products **11**−**31** as pictured in Schemes 5−8 is discussed in section 5.

The products of *addition* of various BMP Li enaminates to aldehydes (→ **32**−**38**), aldimines (→ **39**, **40**), and enoates (→ **41**, **42**) are shown in Schemes 9 and 10. The yields of purified materials are somewhat lower than in the alkylations. Of the four possible diastereoisomers we have been able to detect only two[22] (exception **39**), chromatographic separation of which posed no problem. As with the structurally similar Li enolates of 1,3-dioxan-4-ones[23] and of hydropyrimidin-4-ones[16] the stereoselectivity is higher in the additions to aliphatic aldehydes (2.5:1−16:1) than it is with aromatic aldehydes (1:1.3 for PhCHO, → **35**; 3:1 for furfural, → **36**).[24] While the addition to *N*-trifluoromethylsulfonyl benzaldimine was not productive, the *N*-alloc imine gave a ca. 70% yield of the two diastereoisomers (ca. 1.3:1; **40**). The Michael addition to enoate esters with sterically protected but electronically effective carbonyl groups[25,26] occur with high stereoselectivity to give the 2-aminoethyl-3-substituted glutaric acid derivatives **41** and **42** (Scheme 10). From the configurational assignments made in section 5 and shown in Schemes 9 and 10 we derive attack of the



Scheme 10. *Mannich*-type products and *Michael* adducts from the Li enaminate **L** and imines or enoates; only one enantiomer of *rac*-compounds is shown. More than two diastereoisomers of the triflamide **39** are formed; the configuration of **39**, **40**, and *epi*-**40** was not assigned, for **41** see Figure 2. The glutaric acid derivatives **41** and **42** are formed with a diastereoselectivity of > 9:1. The yields of **41** and **42** refer to **8** (excess enoate employed), the yield of *rac*-**41** to the enoate (excess *rac*-**8a**)

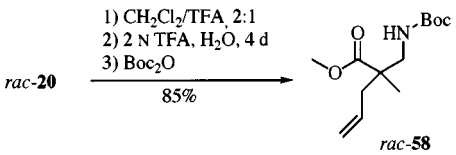


Scheme 11. Conversion of the heterocyclic derivatives of type **11**−**19**, **21**−**28** and **31** to Boc- or Z-protected β-amino acid methyl esters (**43**−**57**), the stereocenter of simple *rac*-products is not specified; only one enantiomer of *rac*-products with two or three stereocenters is drawn; the yields refer to chromatographed, analytically pure materials. *Deprotection* refers to treatment with trimethylsilyl triflate (for Boc) or Pd/C-H_2 (for Z)

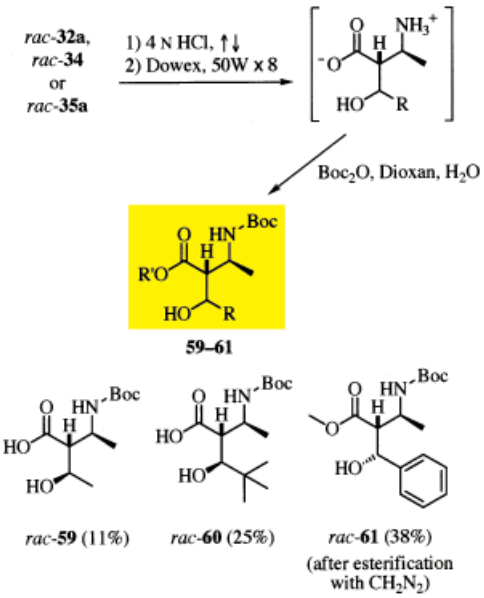
lithiated BMPs by the electrophiles exclusively from the face *trans* to the *tert*-butyl group, while the newly formed exocyclic stereocenters give rise to more or less epimer formation.

4. Cleavage of the BMP Derivatives and Isolation of Boc- or Z-protected β-Amino Acid Methyl Esters

Direct hydrolytic cleavage of the Boc- or Z-protected 4-methoxytetrahydropyrimidenes to Boc- or Z-protected β-amino acid methyl esters was not feasible: with dilute acid the lactim was converted to a lactam moiety, and under strongly acidic conditions partial racemization or epimerization in the α-carbonyl postition is observed, and, also, acid sensitive groups in the side chains do not survive. Thus, as with the α-amino acid derivatives obtained from Boc-BDI[10] (**I** in Scheme 1 above), we chose a two-step pro-



Scheme 12. Preparation of the 2-aminomethyl-2-methylpent-4-enoic acid derivative *rac*-**58** from *rac*-**20**



Scheme 13. Hydrolysis of adducts of type **32**−**38** to β-amino-β′-hydroxycarboxylic acid derivatives **59**−**61**; partial epimerization in the α-carbonyl position takes place in refluxing dilute HCl; the yields refer to analytically pure major epimers, the relative configuration of which are assumend to be identical to those of the heterocyclic starting materials; only one enantiomer of the racemic products is shown

cedure for the cleavage of the alkyl-substituted 6-ring heterocycles: The protecting group PG was first removed with silyl triflate, with CF_3CO_2H (TFA), or with H_2/Pd-C, and then the ring was cleaved under mildly acidic conditions (TFA in water at 0°C), to give the methyl esters of the β-amino acids. These were then N-protected for purification and full characterization,[27] see the products **43**–**58** in Schemes 11 and 12. The aldol adducts were hydrolyzed in one step by refluxing aqueous HCl, with losses caused by epimerization; for characterization, the resulting β-hydroxy-β′-aminocarboxylic acid derivatives were, again, protected (**59**–**61** in Scheme 13).

5. Structure Determination and Configurational Assignment

In the previous sections we have assigned absolute and relative configurations to the products (shown in the various Schemes), without proof. Actually, these assignments are derived from a multitute of measurements: (i) optical comparison with authentic samples (**43**,[1,28] providing assignment to (*S*)-(+)- and (*R*)-(−)-**3**); for **27a**/**b** configurational assignment was derived from optical comparison of the unreacted benzylic bromide (see exp. section); (ii) nuclear Overhauser effects in the NMR spectra (Figure 1); (iii) similarities and anologies in the coupling and chemical shift

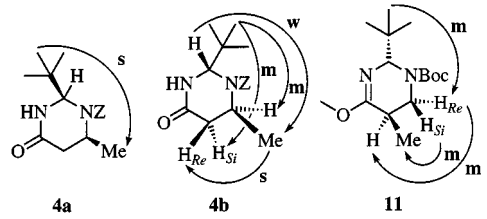
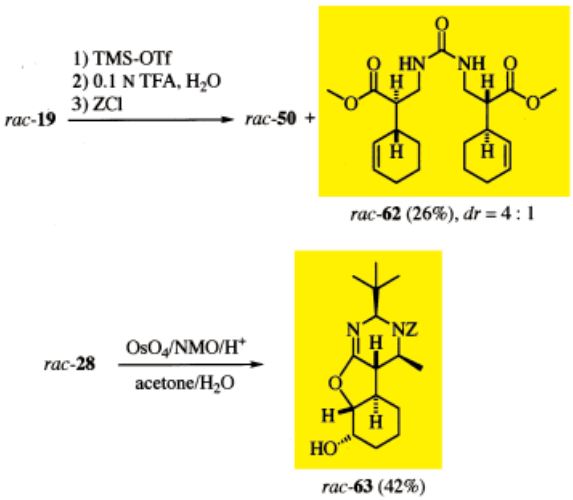


Figure 1. Nuclear Overhauser effects for configurational assignment in the dihydropyrimidinones **4** and in the cyclic iminoester **11**; the NOE intensities are classified as strong (s), medium (m) and weak (w)



Scheme 14. Conversions of the cyclohexenyl derivatives **19** and **28** for configurational assignment of the carbocyclic stereogenic centers (NMO = *N*-methylmorpholine *N*-oxide), for X-ray crystal structures of **62** and **63** see Figure 2, for a mechanistic proposal derived from these structures see Figure 5

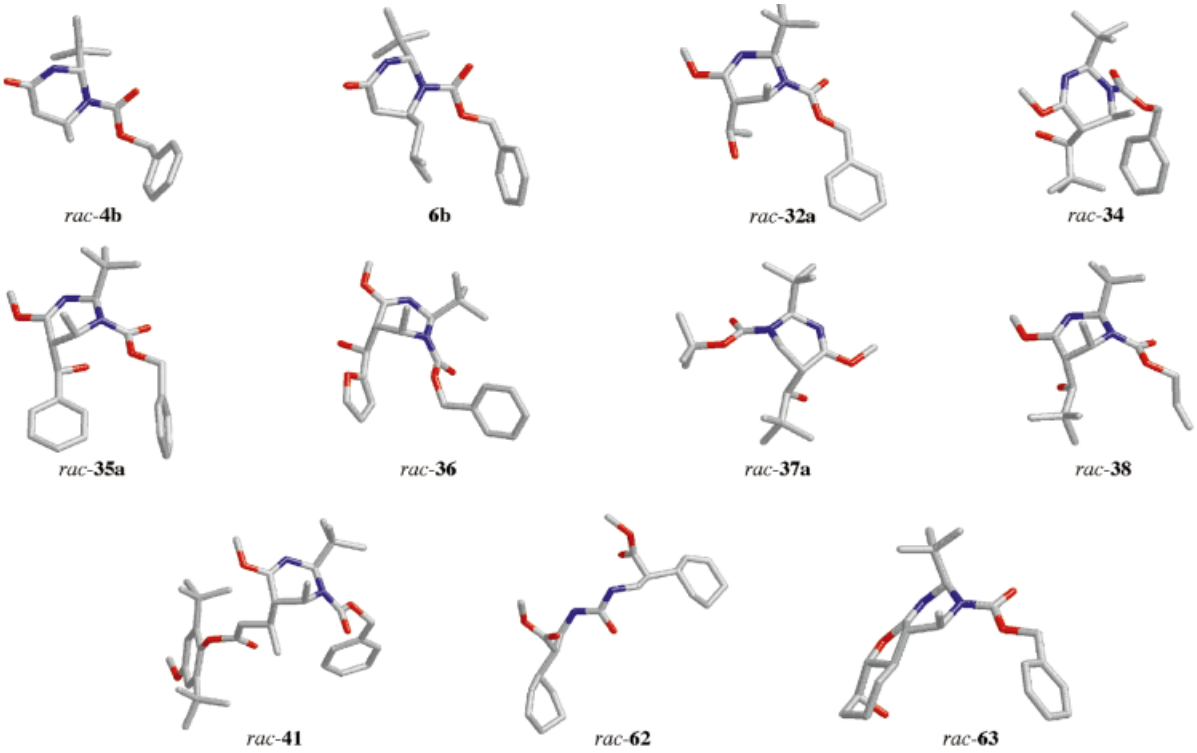


Figure 2. *RasMol* presentations of the single-crystal X-ray structures of some products obtained through Li enaminates of Type **K**, **L**; these structures provide configurational assignments, and thus information about the course of reactions (see Figure 5 and 6)

patterns of the NMR spectra; (iv) most importantly: eleven crystal structures of products (Figure 2), some of which have been obtained by derivatization of the originally formed compounds (Scheme 14 and Table 1 in the Experimental Section).

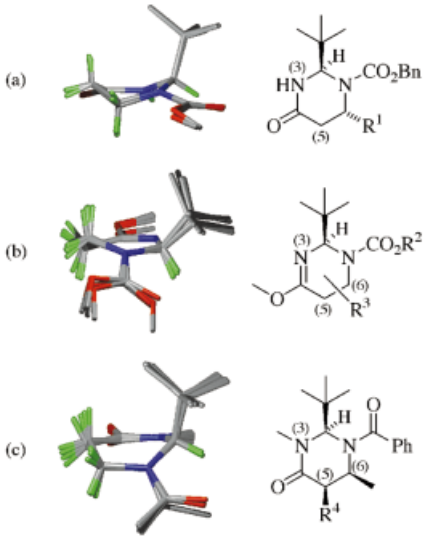


Figure 3. Superposition of crystal structures of 2-*tert*-butylhydropyrimidinone derivatives; the superpositions have been generated by MolMol[30]. (a) Z-Protected tetrahydropyrimidinones *rac*-**4b** and **6b**. (b) Dihydropyrimidines *rac*-**32a**, *rac*-**34**, *rac*-**35a**, *rac*-**36**, *rac*-**37a**, *rac*-**38**, and *rac*-**41**. (c) Two pairs of epimers of benzoyl derivatives with R^4 = CH(OH)Ph and CH(OH)CH$(CH_3)_2$ (taken from ref.[16]). R^3 in (b) indicates substituents in 5- and/or 6-position of the ring; all heterocycles have *sofa*-type conformations, with C(5), C(6), and C(2) out oft the plain formed by the other five ring atoms in (a), (b) and (c), respectively. The *tert*-butyl group is in a *quasi-axial* position in (c), while the C−$(CH_3)_3$ bond forms a ca. 45° angle with the main plain of the sofa in (a) and (b). The C(6)−N(1)−C(2)−C$(CH_3)_3$/C(4)−N(3)−C(2)−C$(CH_3)_3$ mean dihedral angels (in°) are 110/90, 110/140, 85/95 in (a), (b), and (c), respectively. The packing patterns of some of the structures have crystallographically interesting features which can be retrieved from the Cambridge Crystallographic Data Centre (one example is shown in Figure 7)

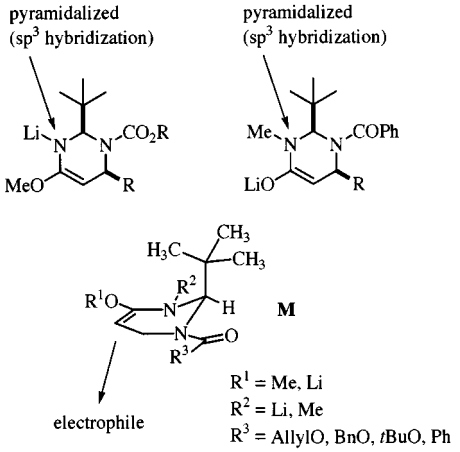


Figure 4. Proposed structures of the Li enaminates and Li enolates derived from hydropyrimidinones; both Li derivatives contain the ketene N,O-acetal structural element, the nitrogen atom of which should be highly pyramidalized.[18,31] A conformation **M** carrying an *axial tert*-butyl group, would be compatible with the high face selectivity of electrophilic attack, common to the two types of Li derivatives

It is interesting to note that all hydropyrimidine derivatives studied by us, so far, have *sofa* conformations of the six-membered rings. Depending upon the particular structure, different carbon atoms of the rings are out of plane with respect to the avarage plane containing the five other ring atoms: C(5) in the precursor tetrahydropyrimidinones (Figure 3a), C(6) in our methoxy derivatives (Figure 3b), and C(2) in the previously studied[29] benzoyl-protected tetrahydropyrimidinones (Figure 3c). In the precursors to Li enolates of the latter series, the *tert*-butyl groups occupy *axial* positions on the out-of-plane carbon atoms, while in the former lactim ether series they are in *quasi-equatorial* positions, and in all three series, the acylated nitrogens are pyramidalized, albeit to a much lesser extent than in the 5-ring analogs.[18] Since the Li enolates and the Li enaminates react with similarly high selectivity from the face *trans* to the *tert*-butyl group, we suggest that the structures in the two series of Li nucleophiles are also similar, with the *tert*-butyl groups in an *axial* disposition, as pictured in **M** of Figure 4 (cf. Figure 5).

6. Stereochemical Course of the Reactions

It was to be expected that the reactions of Li enaminate with electrophiles, just like all other previously studied[10][18] transformations of Li nucleophiles generated from five- and six-ring pivalaldehyde O,O-, O,S-, N,O-, and N,N-acetals, should occur from the face opposite to that occupied by the *tert*-butyl group.

More interesting was the stereochemical course, i.e. the relative topicity, of reactions occurring with combinations of trigonal centers.[32] The first reaction of this type are the alkylations of Li enaminates **K** and **L** with bromocyclohexene, for which we have no experimental evidence as to whether they occur by an S_N2 or an S_N2' mechanism (Figure 5); the product configuration (Scheme 14, Figure 2) is compatible with the relative topicity *like* as pictured on the right side of Figure 5; since we do not recognize a clear-cut *like/unlike* bias for the S_N2 mechanism we tend to favor the *syn*-S_N2' mechanism[33] in which the bulk of the cyclohexenyl ring would point away from the heterocycle. The second reaction in which two trigonal centers are combined is the addition to aldehydes and imines which appears to be diastereoselective only with certain aliphatic aldehydes to give the products with relative configuration *like*, see **N** and **O** in Figure 6; the topicity does not reverse when going from Li enolates to Li enaminates derived from pyrimidines, as it does with the imidazol derivatives.[10,34] Finally, there is the Michael addition to enoates which also yields products arising from a *like* combination, see **P** in Figure 6.

Thus, all three types of selective reactions involving formation of two new stereogenic centers with the Li enaminates **K**/**L** occur with relative topicity *like*, reflecting a preferred approach trajectory with the larger substituent on the trigonal center of the electrophile to be near the methoxy substituent rather than close to the carbamate group of the lithiated heterocycle.

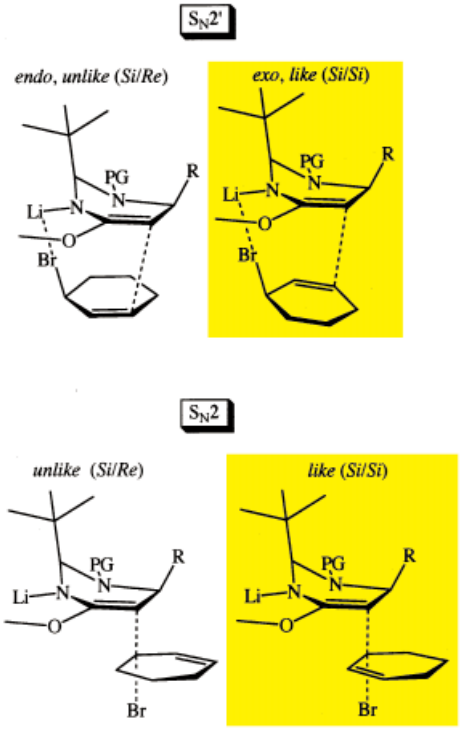


Figure 5. S_N2' and S_N2 approaches of a Li enaminate of Type **K**, **L** to 3-bromo-cyclohexene; the observed product configuration (see Figure 2 and Scheme 14) is such that the two centers must have combined with relative topicity like which would result from the "*exo*" S_N2' mode (*syn* mechanism[33]) or from an S_N2 inversion mechanism as pictured on the right side of the figure

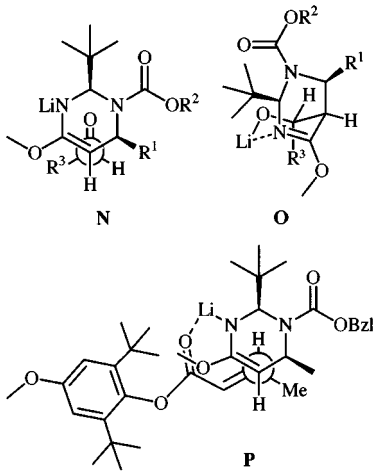


Figure 6. Approach trajectories **N**, **P** and primary adduct **O** of the aldol and *Michael* additions of Li enaminates of type **K**, **L**; **N** and **O** refer to products **32**–**38**, **P** to product **41**; the relative topicity, with which the trigonal centers of the nucleophile (Li enaminate) and of the electrophile (aldehyde or enoate) combine preferentially is *like* (as in the case of cyclohexenylation!, cf. Figure 5)

7. Conclusions

A new route to α-branched β-amino acids has been developed which is amenable to the preparation of products with acid-sensitive side-chain functional groups. With the 3-aminopropionic acid derivatives **3** and **7** (from resolution) and with compounds **4**, **6**, **8**, and **10** (arising from homologation of α-amino acids) it is possible to prepare β^3- and $\beta^{2,3}$-amino acid esters with one, two, and three stereocenters in racemic form or in either one of the enantiomeric forms (see products **43**–**61**).

The Li enaminates **K**, **L** are highly nucleophilic species, but they appear to be accessible only from precursors with a single substituent either in the 4- or in the 5-position. The enantiomer-differentiating ability of the Li enaminates in the allylation with bromocyclohexene and in the reaction with bromohydrine is remarkable (and might be large enough to be useful for the preparation of enantioenriched bromocyclohexene by kinetic resolution!). If our interpretation of the stereochemical course of the reactions creating two new stereocenters is correct (models in Figures 4, 5, and 6), the outcome of reactions of the Li enaminates with other electrophiles (not tested here) could be predicted. Some of the β-amino acid esters described herein will be welcome building blocks for our β-peptide syntheses, especially the ones carrying functional groups in the side chain (such as **45**, **46**, **47**, **50**, **55**, and **59**–**61** in Schemes 11 and 13).

Experimental Section

General Methods: THF used for alkylations was freshly distilled from potassium/benzophenone ketyl under an inert gas atmosphere of Ar. Flasks, stirring bars and hypodermic needles used for the generation and reactions of organolithium reagents were dried for ca. 12 h at 150°C and allowed to cool in a desiccator with P_2O_5. The side arms of the reaction flasks were connected to an Ar line by three-way taps. An excess pressure of Ar was established. – The electrophiles used for the reactions were passed through a short column of basic Al_2O_3 prior to injection. – Diisopropylamine and triethylamine were distilled from CaH_2 under Ar and stored over molecular sieves (4 Å), solvents for chromatography and work-up were distilled, all other solvents were purchased from Fluka. – Thin layer chromatography (TLC) analyses were performed on silica gel plates (Merck 60 F_{254}, 0.25 mm thickness), components were detected by UV light and/or by dipping into a solution of 5.25 g of *N,N,N′,N′*-tetramethyl-4,4′-methylenebis(aniline) (TDM), 10.20 g of KI, 3.4 mg of ninhydrin, 23.6 mL of CH_3CO_2H and 310 mL of H_2O followed by dipping into hot water or into a solution of 12.5 g phosphomolybdic acid hydrate, 5 g $Ce(SO_4)_2$, 30 mL conc. H_2SO_4, and 470 mL H_2O or into a solution of 9.2 mL anisaldehyde, 3.75 mL AcOH, 12.5 mL H_2SO_4 and 340 mL EtOH. – For flash chromatography (FC) Fluka silica gel 60, 230–400 mesh was used. – Melting points were determined in open capillaries in a Büchi 510 apparatus with Anschütz thermometers and are uncorrected. – $[\alpha]_D$: Perkin-Elmer 241 polarimeter using a 1.00 dm cell at room temp. (ca. 22°C); concentration *c* (in g/100 mL) and solvent in parenthesis. – IR: Perkin-Elmer FT-IR 1600. – ^1H NMR and ^{13}C NMR: AMX 400 (400 MHz/100 MHz) or a Gemini 300 (300 MHz/75 MHz). $CDCl_3$ and $[D_6]$DMSO were used as solvent and chemical shifts are reported in ppm downfield from tetramethysilane (δ = 0). Coupling constants *J* are given in Hertz (Hz); multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. Carbon multiplicities were assigned by DEPT techniques. – MS: Hitachi-Perkin-Elmer RMU-6M (EI, 70 eV), VG Tribrid (FAB), Finnigan MAT TSQ 7000 (ESI). For FAB MS spectra 3-

nitrobenzyl alcohol (3-NOBA) or glycerin were used as matrix. – Elemental analyses were performed by the "Mikroelementaranalytisches Laboratorium der ETH Zürich".

General Procedures (GP)

Synthesis of 6-Alkyl-2-*tert*-butyltetrahydropyrimidin-4-ones from the Corresponding β-Amino Acid (GP1): At −20°C 1 equiv. of the β-amino acid was dissolved in THF and 1.2 equiv. of NEt_3 and ethyl chloroformate were added. Then the white suspension was cooled below −50°C and via a needle gaseous NH_3 was added for 1 h. After another 3 h, the solvent was removed by rotary evaporation. To the white solid water was added and the resulting suspension was filtered and washed three times with water. The white powder was dried for 12 h at 0.05 Torr. Then the crude product was suspended in MeOH and Pd on activated charcoal (10 mass% of amide) was added. After 12 h under a H_2 atmosphere, the Pd was filtered off, the MeOH was evaporated and the β-amino acid amide was dissolved in CH_2Cl_2, 2 equiv. pivalaldehyde was added and the mixture was heated to reflux with an inversed Dean−Stark trap for 12 h. The solvent was removed and the crude product was purified by recrystallization. The ratio of the two diastereoisomers was determined by ^{1}H-NMR.

Protection of 6-Alkyl-2-*tert*-butyltetrahydropyrimidin-4-ones with Chloroformate Derivatives (GP2):[35] At room temp. the 6-alkyl-2-*tert*-butyltetrahydropyrimidin-4-one was dissolved in CH_2Cl_2 and 1.5 equiv. *N,O*-bis(trimethylsilyl)acetamide dissolved in CH_2Cl_2 was added. After 1 h the solution was cooled to 0°C and 1.3 equiv. benzyl or allyl chloroformate (*Z*-chloride or *Alloc*-chloride) was added. After 20 h at 0°C satd. $NaHCO_3$ was added and the aqueous layer was extracted three times with CH_2Cl_2, and the combined organic layer were washed with satd. NaCl solution and dried with anhydrous $MgSO_4$. The solvent was removed by rotary evaporation and the crude product was purified by FC and/or recrystallization. The ratio of the two diastereoisomers was determined in the ^{1}H-NMR spectra of the crude product.

***O*-Alkylation of the *N*(1)-Carbamate Protected 6-Alkyl-2-*tert*-butyltetrahydorpyrimidin-4-ones with Meerwein's Salt (GP3):** A solution of the tetrahydropyrimidinone derivative in CH_2Cl_2 was cooled to 0°C and 1.2 equiv. of trimethyloxonium tetrafluoroborate (crushed) was added. After 12 h at 0°C satd. $NaHCO_3$ was added and the aqueous layer was extracted two times with CH_2Cl_2, the combined organic layers washed with satd. NaCl solution and dried with anhydrous $MgSO_4$. The solvent was removed by rotary evaporation and the crude product purified by FC.

Alkylations of *tert*-Butyl (*S*)- and *rac*-2-*tert*-Butyl-4-methoxy-5,6-dihydro-2*H*-pyrimidine-1-carboxylate (GP4): A solution of 1 equiv. of *rac*- or (*S*)-**7** (usually ca. 10 mmol) in THF (30 mL) was cooled to −78°C. A freshly prepared and precooled (ca. −50°C) solution of LDA (1.2 equiv.) in THF (8 mL) was added slowly. The reaction solution was stirred at −78°C for 1 h. The corresponding electrophile (1−4 equiv.), dissolved in THF (10 mL) and precooled, was then added slowly (T < −70°C) to the reaction mixture using a cannula. After 4 h at −78°C the reaction mixture was warmed up to room temp. within 1 h and satd. NH_4Cl solution (75 mL) was added. The aqueous layer was extracted three times with Et_2O (100 mL), and the combined organic layers washed with satd. NaCl solution (150 mL) and dried with anhydrous $MgSO_4$. The solvent was removed by rotary evaporation and the crude product was purified by FC.

Alkylations of the Z- and Alloc-protected Dihydropyrimidines (GP5): A solution of 1 equiv. of the tetrahydropyrimidine (usually ca. 10 mmol) in THF (30 mL) was cooled to −78°C. A freshly prepared and precooled (ca. −50°C) solution of LDA (1.0 equiv.) in THF (8 mL) was added slowly. The reaction solution was stirred at −78°C for 1 h. The corresponding electrophile (1−4 equiv.), dissolved in THF (10 mL) and precooled (ca. −60°C) was then added slowly (T < −70°C) using a cannula. After 4 h at −78°C the reaction mixture was warmed up to −30°C within ca. 1 h and satd. NH_4Cl solution (75 mL) was added. The aqueous layer was extracted three times with Et_2O (100 mL), and the combined organic layers washed with satd. NaCl solution (150 mL) and dried with anhydrous $MgSO_4$. The solvent was removed by rotary evaporation and the crude product was purified by FC.

Hydroxyalkylation and Hydroxyamination of the Dihydropyrimidines (GP6): A solution of 1 equiv. of a tetrahydropyrimidine (usually ca. 10 mmol) in THF (30 mL) was cooled to −78°C. A freshly prepared and precooled (−78°C) solution of 1.0 equiv. LDA in THF (10 mL) was added slowly. The reaction solution was stirred at −78°C for 1 h and then the corresponding aldehyde (2−4 equiv.) or imine (2 equiv.) dissolved and precooled (−78°C) in THF, was added using a cannula. After stirring the reaction mixture for 30 min at −78°C, satd. NH_4Cl solution (50 mL) was added. The aqueous layer was extracted three times with Et_2O (100 mL), and the combined organic layers were washed with satd. NaCl solution (150 mL) and dried with anhydrous $MgSO_4$. The solvent was removed by rotary evaporation and the crude product was purified by FC and recrystallization. The ratio of the two diastereoisomers was determined by ^{1}H NMR.

Michael Additions with Benzyl (2*R*,6*S*)-2-*tert*-Butyl-4-methoxy-6-methyl-5,6-dihydro-2*H*-pyrimidine-1-carboxylate (GP7): A solution of 1 equiv. *rac*-**8a** or (2*R*,6*S*)-**8** (5−10 mmol) in THF (30 mL) was cooled to −78°C. A freshly prepared and precooled (−78°C) solution of LDA (1.0−1.5 equiv.) in THF (15 mL) was added slowly. The reaction solution was stirred at −78°C for 1 h. The corresponding Michael acceptor (0.75−1.5 equiv.) dissolved and precooled in THF (10 mL) was then added using a cannula. After stirring the reaction solution at −78°C for 6−48 h, satd. NH_4Cl solution (75 mL) was added. The aqueous layer was extracted three times with Et_2O (100 mL), and the combined organic layers were washed with satd. NaCl solution (150 mL) and dried with anhydrous $MgSO_4$. The solvent was removed by rotary evaporation and the crude product was purified by FC.

Hydrolysis of 5-Monosubstituted Boc-Protected Dihydropyrimidines and Protection to the Corresponding Boc- or Z-Protected 3-Amino Acid Methyl Esters (GP8): A solution of the dihydropyrimidine in CH_2Cl_2 was cooled to −15°C. TMS-OTf (6 equiv.) was added using a syringe and the reaction solution was stirred for 12 h at −15°C. The reaction solution was diluted with an equal volume of satd. $NaHCO_3$ solution, extracted five times with CH_2Cl_2 and the combined organic layers dried with anhydrous Na_2SO_4. The solvent was removed by rotary evaporation and the crude product dissolved in THF. 0.1 N CF_3CO_2H/H_2O (3 equiv.) was added and the reaction solution stirred at 4°C for 4 d. The mixture was set to pH > 10 with a 10%-NH_3 solution, saturated with NaCl and the aqueous layer was extracted three times with CH_2Cl_2. The combined organic layers were dried with anhydrous Na_2SO_4. The solvent was partially removed by rotary evaporation and Boc_2O or Benzyl chloroformate and NEt_3 were added, and the solution was stirred at room temp. for 12 h. The reaction mixture was washed with half a volume of satd. $NaHCO_3$ solution and dried with anhydrous $MgSO_4$. The solvent was removed by rotary evaporation and the crude product was purified by FC.

Hydrolysis of 5-Monosubstituted Z-Protected Dihydropyrimidines and Protection to the Corresponding Boc- or Z-Protected 3-Amino

Acid Methyl Esters (GP9): The dihydropyrimidine derivatives were dissolved in MeOH, Pd on activated charcoal (10%) was added and under a H_2-atmosphere the reaction mixture was stirred for 12 h at room temp. The Pd was filtered off , the solvent was removed by rotary evaporation and the crude product was dissolved in THF. Then 0.1 N CF_3CO_2H/H_2O (3 equiv.) was added and the reaction solution stirred at 4°C for 4 d. The mixture was set to pH > 10 with a 10%-NH_3 solution, satd. with NaCl and the aqueous layer extracted three times with CH_2Cl_2. The combined organic layers were dried with anhydrous $MgSO_4$. The solvent was partionally removed by rotary evaporation and Boc_2O, or Benzyl chloroformate and NEt_3 was added and the solution was stirred at room temp. for 12 h. The reaction mixture was washed with half a volume of satd. $NaHCO_3$ solution and dried with anhydrous Na_2SO_4. The solvent was removed by rotary evaporation and the crude product was purified by FC.

Hydrolysis of Aldol-Addition Products to the Corresponding β-Amino-β′-hydroxycarboxylic Acids (GP10): A sample of aldol addition product was heated in 4 N HCl at reflux for 6 h. The reaction solution was extracted with Et_2O and the layers were separated. The aqueous layer was evaporated on a rotary evaporator and the crude product was purified by ion exchange chromatography on a Dowex 50W×8 column with a 1%-NH_3 solution as eluent. The resulting solids (*dr* ≈ 3:1) were recrystallized ($MeOH/CH_2Cl_2$, *dr* 95:5) and protected with Boc_2O and NaOH in H_2O/dioxane. The crude product was purified by recrystallization.

Synthesis of the Tetrahydropyrimidinones 1−6

***rac*-2-*tert*-Butyltetrahydropyrimidin-4-one (*rac*-1):** According to GP1 Z-3-amino propionic acid (50 g, 224 mmol) was converted to *rac*-**1** (23.8 g, 68%), a white solid, which was purified by recrystallization from hexane and AcOEt, m.p. 124−125°C. − IR ($CHCl_3$): $\tilde{\nu}$ = 3403 m, 2963 m, 2873 w, 1662 s, 1480 m, 1414 w, 1367 w, 1305 m, 1114 w, 1050 w, 1014 w, 828 w, 658 w. − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.96 (s, 9 H, *t*Bu), 1.25 [s, 1 H, HN(1)], 2.30−2.35 [m, 2 H, H-C(5)], 2.87−2.95 [m, 1 H, H-C(6)], 3.28−3.33 [m, 1 H, H-C(6)], 3.95 [s, 1 H, H-C(2)], 6.10 [s, 1 H, HN(3)]. − ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 24.93 (Me), 32.74 (CH_2), 34.25 (C), 41.51 (CH_2), 76.47 (CH), 171.58 (C). − EI-MS; *m/z* (%): 157.1 (32) [M + 1]$^+$, 141.1 (96), 124.1 (10), 112.1 (71), 99.1 (100), 82.1 (25), 72.1 (91), 57.1 (14), 44.1 (8). − $C_8H_{16}N_2O$ (156.23): calcd. C 61.51, H 10.32, N 17.93; found C 61.54, H 10.42, N 17.89.

rac*-2-*tert*-Butyl-6-methyltetrahydropyrimidin-4-one (*rac*-2): rac-**3-Aminobutanamide[36] (37.6 g, 427 mmol) was dissolved in CH_2Cl_2 and pivalaldehyde (90 mL, 854 mmol) was added. After heating to reflux with an inversed Dean−Stark trap for 12 h the solvent was removed. Purification of the crude product by recrystallization (hexane/AcOEt) gave *rac*-**2** (29.1 g, 41%) as a white solid, m.p. 148−150°C. − IR (KBr): $\tilde{\nu}$ = 3277 w, 3202 m, 2956 m, 1653 s, 1481 m, 1401 m, 1328 w, 1290 w, 1142 w, 1087 w, 841 m. − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.96 (s, 9 H, *t*Bu), 1.19 (d, *J* = 6.4, 3 H, Me), 1.92 [A***B*X*, J_{AB} = 17.3, J_{AX} = 11.5, 1 H, H-C(5)], 2.41 [A***B***X, J_{AB} = 17.3, J_{BX} = 4.0, 1 H, H-C(5)], 2.95−3.07 [m, 1 H, H-C(6)], 3.98 [d, *J* = 5.9, 1 H, H-C(2)], 6.18 (s, 1 H, HN). − ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 21.94 (Me), 24.85 (*t*Bu), 34.08 (C), 40.38 (CH_2), 47.70 (CH), 75.81 (CH), 171.79 (C). − EI-MS; *m/z* (%): 171.1 (9) [M + 1]$^+$, 155.1 (42), 138.1 (6), 126.1 (32), 113.0 (100), 96.1 (28), 86.0 (66), 69.0 (26), 57.0 (13), 44.0 (18). − $C_9H_{18}N_2O$ (170.25): calcd. C 63.49, H 10.66, N 16.45; found C 63.47, H 10.50, N 16.34.

***tert*-Butyl *rac*-2-*tert*-Butyl-4-oxotetrahydropyrimidine-1-carboxylate (*rac*-3):** To a solution of *rac*-**1** (23.8 g, 152 mmol) in CH_2Cl_2 (400 mL) Boc_2O (66.4 g, 305 mmol) was added. After 2 d heating to reflux the solvent was removed by rotary evaporation. Purification of the crude product by FC (AcOEt) and recrystallization (hexane/AcOEt) gave *rac*-**3** (35.5 g, 91%) as white solid, m.p. 153−154°C. − IR ($CHCl_3$): $\tilde{\nu}$ = 3411 m, 2978 s, 1665 s, 1471 m, 1415 m, 1369 m, 1320 m, 1159 m, 1075 w, 982 m, 820 w, 658 w. − ^{1}H NMR ($CDCl_3$, 400 MHz) 2 conformers: δ = 1.00 (s, 9 H, *t*Bu), 1.48 (s, 9 H, *t*Bu), 2.34 [br, 2 H, H-C(5)], 3.23 [br, 1 H, H-C(6)], 4.15, 4.34 [br, 1 H, H-C(6)], 5.12, 5.26 [br, 1 H, H-C(2)], 6.50, 6.74 (br, 1 H, HN). − ^{1}H NMR ([D_6]DMSO, 300 MHz, 90°C): δ = 0.91 (s, 9 H, *t*Bu), 1.41 (s, 9 H, *t*Bu), 2.15−2.20 [m, 2 H, H-C(5)], 3.15−3.25 [m, 1 H, H-C(6)], 3.97−4.08 [m, 1 H, H-C(6)], 5.00 [d, *J* = 3.1, 1 H, H-C(2)], 7.61 (br, 1 H, HN). − ^{13}C NMR ($CDCl_3$, 100 MHz) 2 conformers: δ = 26.06 (*t*Bu), 28.28 (*t*Bu), 31.25, 31.57 (CH_2), 36.88, 38.21 (CH_2), 70.67, 71.55 (CH), 81.39 (C), 154.62 (C), 171.04 (C). − EI-MS; *m/z* (%): 257.2 (1.6) [M + 1]$^+$, 199.1 (15), 143.0 (100), 99.0 (19), 57.1 (24). − $C_{13}H_{24}N_2O_3$ (256.34): calcd. C 60.91, H 9.44, N 10.93; found C 61.12, H 9.37, N 10.95.

Enantiomer Resolution of *tert*-Butyl *rac*-2-*tert*-Butyl-4-oxotetrahydropyrimidin-1-carboxylate (*rac*-3) by Preparative HPLC: The chromatographic system for the analytical resolution of *rac*-**3** consisted of a Knauer HPLC pump 64 was used together with a Knauer injection valve V7226, Knauer Integration Package *EuroChrom 2000* and a Chiralcel OD column (250 × 4 mm) hexane/*i*PrOH (94:6, v/v) (detection wavelength, 216 nm; flow-rate, 1 mL/min; room temp.; injected volume, 20 µl; sample concentration, 10 mg/mL; t_0 = 5.50 min, t_1 = 14.38, t_2 = 19.02 min, k_1' = 1.61, k_2' = 2.46, α = 1.52). The semi-preparative separation of the enantiomers was performed on a Chiralcel OD (178 g CSP, 200 × 40 mm I. D., detection wavelength, 205 nm; flow-rate, 30 mL/min; room temp.; injected volume, 2 mL; sample concentration, 50 mg/mL; by E. Küsters, Chemical Development, Novartis Pharma Inc.).

***tert*-Butyl (*S*)-(+)-2-*tert*-Butyl-4-oxotetrahydropyrimidin-1-carboxylate [(*S*)-(+)-3]:** M.p. 154−155°C. − $[\alpha]_D$ = +116.8 (≥ 99.5% *ee*, determined by HPLC).

***tert*-Butyl (*R*)-(−)-2-*tert*-Butyl-4-oxotetrahydropyrimidin-1-carboxylate [(R)-(−)-3]:** M.p. 152−154°C. − $[\alpha]_D$ = −116.0 (99.4% *ee*).

Benzyl *rac*-(2*R*,6*S*)- and *rac*-(2*S*,6*S*)-2-*tert*-Butyl-6-methyl-4-oxotetrahydropyrimidine-1-carboxylate (*rac*-4 and *rac*-4b): The protection of *rac*-**2** (13.7 g, 80.4 mmol) with benzyl chloroformate (13.6 mL, 96.5 mmol) was performed according to *GP2*. Purification and separation of the diastereoisomers (*dr* = 4:1) by FC (AcOEt/pentane, 4:1) and recrystallization (Et_2O) gave *rac*-**4a** (14.5 g, 57%) and *rac*-**4b** (2.5 g, 10%) as white solids.

rac-**4a**: M.p. 105.5−106.5°C. − IR (KBr): $\tilde{\nu}$ = 3202 m, 3065 m, 2972 s, 1682 s, 1483 w, 1430 w, 1394 w, 1394 m, 1309 m, 1097 s, 995 w, 982 w, 775 m, 747 m, 699 w, 663 w. − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.00 (s, 9 H, *t*Bu), 1.39 (d, *J* = 6.2, 3 H, Me), 2.51 [d, *J* = 9.9, 2 H, H-C(5)], 4.21−4.30 [m, 1 H, H-C(6)], 5.17 (s, 2 benzylic H), 5.33 [br, *J* = 4.8, 1 H, H-C(2)], 7.30−7.39 (m, 6 H, 5 arom. H, HN). − ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 23.00 (Me), 26.61 (*t*Bu), 36.62 (CH_2), 38.81 (C), 47.74 (CH), 67.98 (CH_2), 72.77 (CH), 128.01 (CH), 128.24 (CH), 128.56 (CH), 135.98 (C), 156.80 (C), 170.51 (C). − EI-MS; *m/z* (%): 305.3 (0.04) [M + 1]$^+$, 247.2 (21), 203.2 (16), 112.1 (2), 91.1 (100), 65.1 (5). − $C_{17}H_{24}N_2O_3$ (304.39): calcd. C 67.08, H 7.95, N 9.20; found C 67.36, H 8.21, N 9.31.

rac-**4b**, M.p. 98−99°C. − IR ($CHCl_3$): $\tilde{\nu}$ = 3417 w, 2973 w, 1682 s, 1456 w, 1379 w, 1325 m, 1274 m, 1102 m, 1064 w, 643 w. − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.97 (s, 9 H, *t*Bu), 1.32 (d, *J* = 6.4, 3 H, Me), 2.25 [***A***B*X*, J_{AB} = 16.7, J_{AX} = 4.1, 1 H, H-C(5)], 2.84

[A***B***X, J_{AB} = 16.7, J_{BX} = 5.5, 1 H, H-C(5)], 4.22−4.29 [m, 1 H, H-C(6)], 5.14 (***CD***, *J* = 12.2, 1 benzylic H), 5.18 (*C**D***, *J* = 12.2, 1 benzylic H), 5.18 [d, *J* = 4.0, 1 H, H-C(2)], 7.08 (d, *J* = 4.0, 1 H, HN), 7.30−7.39 (m, 5 arom. H). − ^{13}C NMR($CDCl_3$, 100 MHz): δ = 21.04 (Me), 26.70 (*t*Bu), 37.86 (CH_2), 40.16 (C), 48.27 (CH), 67.64 (CH_2), 72.25 (CH), 128.26 (CH), 128.28 (CH), 128.56 (CH), 135.91 (C), 156.40 (C), 171.24 (C). − EI-MS; *m/z* (%): 305.3 (0.08) $[M + 1]^+$, 247.2 (25), 203.2 (20), 112.1 (3), 91.1 (100), 65.1 (3). − $C_{17}H_{24}N_2O_3$ (304.39): calcd. C 67.08, H 7.95, N 9.20; found C 67.34, H 7.91, N 9.16.

Benzyl (2*R*,6*S*)-2-*tert*-Butyl-6-methyl-4-oxotetrahydropyrimidine-1-carboxylate (4a): According to *GP1* (*S*)-*Z*-3-aminobutyric acid (49.5 g, 222 mmol) was converted to the corresponding unprotected tetrahydropyrimidinone (24.6 g, 144 mmol) and according to *GP2* the obtained crude product was converted with Z-chloride (24.4 mL, 173 mmol) to **4a** (25.4 g, 38%, *dr* = 4:1). Purification by FC (AcOEt/pentane 4:1) and recrystallization gave a white solid, m.p. 120.5−121.5°C. − $[\alpha]_D$ = +99.2 (*c* = 1.00, $CHCl_3$). − IR ($CHCl_3$): $\tilde{\nu}$ = 3414 m, 2972 m, 1675 s, 1464 w, 1384 m, 1308 s, 1072 m, 1013 w, 965 w, 892 w, 658 w. − ^{1}H NMR($CDCl_3$, 400 MHz): δ = 1.00 (s, 9 H, *t*Bu), 1.40 (d, *J* = 6.2, 3 H, Me), 2.51 [d, *J* = 9.9, 2 H, H-C(5)], 4.22−4.31 [m, 1 H, H-C(6)], 5.17 (s, 2 benzylic H), 5.33 [br d, *J* = 4.8, 1 H, H-C(2)], 7.26−7.39 (m, 6 H, 5 arom. H, HN). − ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 23.00 (Me), 26.61 (*t*Bu), 36.66 (CH_2), 38.81 (C), 47.74 (CH), 67.99 (CH_2), 72.79 (CH), 128.01 (CH), 128.24 (CH), 128.56 (CH), 136.00 (C), 156.50 (C), 170.47 (C). − EI-MS; *m/z* (%): 305.3 (0.15) $[M + 1]^+$, 247.2 (46), 203.2 (35), 112.1 (4), 91.1 (100). − $C_{17}H_{24}N_2O_3$ (304.39): calcd. C 67.08, H 7.95, N 9.20; found C 67.08 H 7.82, N 9.18.

Allyl *rac*-(2*R*,6*S*)-2-*tert*-Butyl-6-methyl-4-oxotetrahydropyrimidine-1-carboxylate (*rac*-5): The protection of *rac*-**2** (20.7 g, 122 mmol) with *Alloc*-chloride (16.8 mL, 158 mmol) was performed according to *GP2*. Purification and separation of the diastereoisomers (*dr* = 4:1) by FC (AcOEt/pentane, 4:1) and recrystallization (Et_2O/pentane) gave *rac*-**5** (14.5 g, 48%) as a white solid, m.p. 90−91°C. − IR (KBr): $\tilde{\nu}$ = 3189 m, 3088 m, 2968 s, 1679 s, 1444 m, 1388 m, 1314 m, 1202 w, 1117 m, 972 m, 775 m, 678 w. − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.02 (s, *t*Bu), 1.41 (d, *J* = 6.2, 3 H, Me), 2.52 [d, *J* = 9.7, 2 H, H-C(5)], 4.21−4.30 [m, 1 H, H-C(6)], 4.62−4.64 [m, 2 allylic H)], 5.23−5.36 [m, 3 H, H_2C=, H-C(2)], 5.89−5.99 (m, 1 H, HC=), 7.27 [br, HN(3)]. − ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 22.98 (Me), 26.66 (*t* Bu), 36.70 (CH_2), 38.86 (C), 47.78 (CH), 66.82 (CH_2), 72.80 (CH), 118.14. (CH_2), 132.43 (CH), 157.48 (C), 170.59 (C). − EI-MS; *m/z* (%): 255.3 (0.44) $[M + 1]^+$, 197.2 (100), 153.2 (12). − $C_{13}H_{22}N_2O_3$ (254.33): calcd. C 61.39, H 8.72, N 11.01; found C 61.52, H 8.69, N 11.00.

Benzyl (2*R*,6*S*)- and (2*S*,6*S*)-2-*tert*-Butyl-6-isobutyl-4-oxotetrahydropyrimidine-1-carboxylate (6a and 6b): According to *GP1* (*S*)-3-amino-5-methylhexanoic acid (21.1 g, 75.5 mmol) was converted to the corresponding unprotected tetrahydropyrimidinone (10.2 g, 48 mmol) and according to *GP2* this tetrahydropyrimidinone was converted with *Z*-chloride (24.4 mL, 173 mmol) to **6**. Purification and separation of the diastereoisomers (*dr* = 3:1) by FC (Et_2O) and recrystallization (Et_2O/pentane) gave (2*R*,6*S*)-**6** (4.5 g, 17%) as a pale yellow oil and and (2*S*,6*S*)-**6** as a white solid (3.7 g, 14%).

6a: $[\alpha]_D$ = +65.1 (*c* = 1.01, $CHCl_3$). − IR ($CHCl_3$): $\tilde{\nu}$ = 3414 m, 2962 m, 1673 s, 1468 w, 1410 m, 1395 m, 1309 s, 1080 m, 984 w. − ^{1}H NMR ($CDCl_3$, 400 MHz): 0.81 (br, 3 H, Me), 0.88 (d, *J* = 6.5, 3 H, Me), 1.00 (s, *t*Bu), 1.39−1.86 [m, 3 H, H-C(2′), 2 H-C(1′)], 2.42 [***ABX***, J_{AB} = 16.8, J_{AX} = 10.1, 1 H, H-C(5)], 2.59 [***ABX***, J_{AB} = 16.8, J_{BX} = 7.7, 1 H, H-C(5)], 4.18−4.28 [m, 1 H, H-C(6)], 5.14 (***AB***, *J* = 12.1, 1 benzylic H), 5.16 (*A**B***, *J* = 12.1, 1 benzylic H), 5.34 ([*d*, *J* = 3.7, 1 H, H-C(2)], 7.30−7.39 (m, 6 H, 5 arom. H, HN). − ^{13}C NMR ($CDCl_3$, 400 MHz): δ = 20.82 (Me), 23.91 (Me), 24.75 (CH), 26.64 (*t*Bu), 34.98 (CH_2), 38.66 (C), 46.52 (CH_2), 50.12 (CH), 68.17 (CH_2), 72.59 (CH), 128.37 (CH), 128.42 (CH), 128.57 (CH), 135.88 (C), 156.50 (C), 170.57 (C). − EI-MS; *m/z* (%): 347.3 (0.3) $[M + 1]^+$, 289.2 (41), 245.2 (41), 91.1 (100). − $C_{20}H_{30}N_2O_3$ (346.47): calcd. C 69.33, H 8.73, N 8.09; found C 69.09, H 8.89, N 8.03.

6b: m.p. 119−120°C. − $[\alpha]_D$ = −40.8 (*c* = 0.98, $CHCl_3$). − IR ($CHCl_3$): $\tilde{\nu}$ = 3414 m, 2962 m, 1680 s, 1455 w, 1386 m, 1325 m, 1276 m, 1072 m. − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.79 (d, *J* = 6.3, 3 H, Me), 0.85 (d, *J* = 6.2, 3 H, Me), 0.98 (s, 3 H, *t*Bu), 1.48−1.63 [m, 3 H, H-C(2′), 2 H-C(1′)], 2.39 [***ABX***, J_{AB} = 16.9, J_{AX} = 6.0, 1 H, H-C(5)], 2.66 [***ABX***, J_{AB} = 16.9, J_{BX} = 4.5, 1 H, H-C(5)], 3.92−3.98 [m, 1 H, H-C(6)], 5.13 (***CD***, *J* = 12.1, 1 benzylic H), 5.17 (*C**D***, *J* = 12.1, 1 benzylic H), 5.18 [d, *J* = 4.0, 1 H, H-C(2)], 6.86 (d, *J* = 4.0, HN), 7.30−7.39 (m, 5 arom. H). − ^{13}C NMR ($CDCl_3$, 400 MHz): δ = 21.30 (Me), 23.60 (Me), 25.46 (CH), 26.72 (*t*Bu), 35.40 (CH_2), 39.42 (C), 43.11 (CH_2), 50.86 (CH), 67.73 (CH_2), 72.71 (CH), 128.39 (CH), 128.55 (CH), 128.58 (CH), 135.87 (C), 156.52 (C), 171.50 (C). − EI-MS; *m/z* (%): 347.3 (3.8) $[M + 1]^+$, 289.2 (100), 245.2 (95), 91.1 (76). − $C_{20}H_{30}N_2O_3$ (346.47): calcd. C 69.33, H 8.73, N 8.09; found C 69.32, H 8.95, N 8.07.

Conversion of the Pyrimidinones to the Cyclic Imino Esters 7−10

***tert*-Butyl *rac*-2-*tert*-Butyl-5,6-dihydro-4-methoxy-2*H*-pyrimidine-1-carboxylate (*rac*-7):** The alkylation of *rac*-**3** (24.0 g, 93.6 mmol) was performed according to *GP3*. Purification of the crude product by FC (pentane/Et_2O, 9:1) gave *rac*-**7** (22.7 g, 90%) as a colorless oil. − IR (film): $\tilde{\nu}$ = 2974 s, 1708 s, 1481 m, 1404 m, 1369 m, 1332 m, 1286 w, 1234 m, 1160 m, 1080 w, 1020 m, 954 m, 863 w, 780 w, 690 w. − ^{1}H NMR ($CDCl_3$, 400 MHz) 2 conformers: δ = 0.98 (s, 9 H, *t*Bu), 1.47 (s, 9 H, *t*Bu), 2.04−2.31 [m, 2 H, H-C(5)], 2.97 [br, 1 H, H-C(6)], 3.67 (s, 3 H, MeO), 4.13, 4.33 [br, 1 H, H-C(6)], 5.23, 5.33 [br, 1 H, H-C(2)]. − ^{1}H NMR ([D_6]DMSO, 300 MHz, 90°C): δ = 0.92 (s, 9 H, *t*Bu), 1.42 (s, 9 H, *t*Bu), 2.07−2.13 [m, 2 H, H-C(5)], 2.89−2.99 [m, 1 H, H-C(6)], 3.59 (s, 3 H, MeO), 4.06−4.14 [m, 1 H, H-C(6)], 5.16 [s, 1 H, H-C(2)]. − ^{13}C NMR ($CDCl_3$, 100 MHz) 2 conformers: δ = 25.48, 25.90 (CH_2), 27.05 (*t*Bu), 28.41 (*t*Bu), 35.90, 37.32 (CH_2), 38.21 (C), 52.10 (Me), 73.58, 74.35 (CH), 80.23 (C), 155.16 (C), 160.02 (C). − EI-MS; *m/z* (%): 271.2 (32) $[M + 1]^+$, 213.1 (67), 197.1 (32), 157.1 (100), 113.1 (79), 57.1 (68), 41.1 (22). − $C_{14}H_{26}N_2O_3$ (256.34): calcd. C 62.19, H 9.69, N 10.36; found C 62.03, H 9.48, N 10.57.

***tert*-Butyl (*S*)-2-*tert*-Butyl-4-methoxy-5,6-dihydro-2*H*-pyrimidine-1-carboxylate [(*S*)-7]:** The alkylation of (*S*)-**3** (6.0 g, 23.4 mmol) was performed according to *GP3*. Purification of the crude product by FC (pentane/Et_2O, 9:1) gave (*S*)-**7** (5.2 g, 83%) as a colorless oil, with the same analytical datas as *rac*-**7** and $[\alpha]_D$ = +93.1 (*c* = 1.58, $CHCl_3$).

Benzyl *rac*-(2*R*,6*S*)-2-*tert*-Butyl-4-methoxy-6-methyl-5,6-dihydro-2*H*-pyrimidine-1-carboxylate (*rac*-8a): The alkylation of *rac*-**4a** (23.8 g, 78.2 mmol) was performed according to *GP3*. Purification of the crude product by FC (pentane/Et_2O 17:3) gave *rac*-**8a** (16.0 g, 65%) as a colorless oil. − IR (film): $\tilde{\nu}$ = 2955 m, 1699 s, 1439 w, 1390 w, 1363 w, 1303 m, 1212 m, 1068 w, 1001 w, 924 w, 864 w, 775 w, 750 w, 698 m. − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.97 (s, 9 H, *t*Bu), 1.32 (d, *J* = 6.5, 3 H, Me), 2.06 [***ABX***, J_{AB} = 16.9, J_{AX} = 7.2, 1 H, H-C(5)], 2.42 [***ABX***, J_{AB} = 16.9, J_{BX} = 8.4, 1 H, H-C(5)], 3.67 (s, MeO), 4.32−4.45 [m, H-C(6)], 5.12 (***CD***, *J* = 12.3, 1 benzylic H), 5.16 (*C**D***, *J* = 12.3, 1 benzylic H), 5.56 [s, 1 H, H-C(2)], 7.28−7.37 (m, 5 arom. H). − ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 23.23 (Me), 27.07 (*t*Bu), 30.54 (CH_2), 38.47 (C), 45.19 (CH),

52.29 (Me), 67.30 (CH_2), 76.54 (CH), 127.96 (CH), 127.99 (CH), 128.44 (CH), 136.56 (C), 156.51 (C), 160.65 (C). − EI-MS; *m/z* (%): 319.2 (1.43) $[M + 1]^+$, 303.1 (0.5), 275.1 (0.5), 261.1 (81), 217.0 (83), 91.0 (100), 65.0 (5), 41.0 (3). − $C_{18}H_{26}N_2O_3$ (318.42): calcd. C 67.90, H 8.23; N 8.80; found C 67.90, H 8.01, N 8.88.

Ethoxy-Analog of *rac*-8a: Benzyl *rac*-(2*R*,6*S*)-2-*tert*-Butyl-4-ethoxy-6-methyl-5,6-dihydro-2*H*-pyrimidine-1-carboxylate : The alkylation of *rac*-**4a** (5.00 g, 16.4 mmol) with triethyloxonium tetrafluoroborate (3.45 g, 17.2 mmol) was performed according to *GP3*. Purification of the crude product by FC (pentane/Et_2O 3:1) gave benzyl *rac*-(2*R*,6*S*)-2-*tert*-butyl-4-ethoxy-6-methyl-5,6-dihydro-2*H*-pyrimidine-1-carboxylate (3.76 g, 69%) as a colorless oil. − IR ($CHCl_3$): $\tilde{\nu}$ = 2975 m, 1694 s, 1481 w, 1455 w, 1376 m, 1307 m,1072 w, 1031 w, 902 w. − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.97 (s, 9 H, *t*Bu), 1.26 [t, *J* = 7.1, 3 H, Me-CH_2OC(4)], 1.31 (d, *J* = 6.5, 3 H, Me), 2.05 [***ABX***, J_{AB} = 16.9, J_{AX} = 7.3, 1 H, H-C(5)], 2.40 [***ABX***, J_{AB} = 16.9, J_{BX} = 8.4, 1 H, H-C(5)], 4.06 (***C****DY*$_3$, J_{CD} = 10.7, J_{CY} = 7.1, 1 H, HC-OC(4)], 4.15 (C***D***Y$_3$, J_{CD} = 10.7, J_{DY} = 7.1, 1 H, HC-OC(4)], 4.33−4.40 [m, H-C(6)], 5.11 (***EF***, J_{EF} = 12.3, 1 benzylic H), 5.16 (*EF*, J_{EF} = 12.3, 1 benzylic H), 5.53 [s, H-C(2)], 7.37−7.28 (m, 5 arom. H). − ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 14.32 (Me), 27.15 (Me), 30.84 (CH_2), 38.56 (C), 45.28 (CH), 60.56 (CH_2), 67.32 (CH_2), 76.59 (CH), 127.98 (CH), 128.02 (CH), 128.47 (CH), 136.64 (C), 156.58 (CO), 160.19 (CN). − EI-MS; m/z (%): 333.2 (0.54) $[M + 1]^+$, 275.1 (41), 231.1 (24), 203.1 (8), 91.1 (100), 65.1 (2). − $C_{19}H_{28}N_2O_2$ (332.44): calcd. C 68.65, H 8.49, N 8.43; found C 68.38, H 8.63, N 8.49.

Benzyl (2*R*,6*S*) and (2*S*,6*S*)-2-*tert*-Butyl-4-methoxy-6-methyl-5,6-dihydro-2*H*-pyrimidine-1-carboxylate (8a and 8b): The alkylation of a mixture of (2*R*,6*S*)-**4** and (2*S*,6*S*)-**4** (21.3 g, 70.0 mmol) was performed according to *GP3*. Purification of the crude product by FC (pentane/Et_2O, 17:3) gave **8a** (15.3 g, 69%) and **8b** (2.4, 11%) as colorless oils.

8a: $[\alpha]_D$ = +45.5 (*c* = 0.99, $CHCl_3$). − IR (film): $\tilde{\nu}$ = 2955 m, 1698 s, 1439 w, 1362 w, 1304 m, 1212 m, 1069 w, 1001 w, 924 w, 775 w, 698 m. − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.97 (s, 9 H, *t*Bu), 1.32 (d, *J* = 6.5, 3 H, Me), 2.06 [***ABX***, J_{AB} = 17.0, J_{AX} = 7.2, 1 H, H-C(5)], 2.42 [***ABX***, J_{AB} = 17.0, J_{BX} = 8.4, 1 H, H-C(5)], 3.67 (s, 3 H, MeO), 4.36−4.41 [m, 1 H, H-C(6)], 5.12 (***C****D*, *J* = 12.3, 1 benzylic H), 5.16 [*C****D***, *J* = 12.3, 1 benzylic H), 5.56 (s, H-C(2)], 7.27−7.37 (m, 5 arom. H). − ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 23.28 (Me), 27.10 (*t*Bu), 30.60 (CH_2), 38.49 (C), 45.22 (CH), 52.31 (Me), 67.34 (CH_2), 76.58 (CH), 127.99 (CH), 128.02 (CH), 128.47 (CH), 136.60 (C), 156.55 (C), 160.68 (C). − EI-MS; *m/z* (%): 318.2 (0.03, M^+), 261.1 (10), 217.0 (12), 91.0 (32), 83.9 (86), 49.0 (100). − $C_{18}H_{26}N_2O_3$ (318.42): calcd. C 67.90, H 8.23, N 8.80; found C 67.97, H 8.29, N 8.72.

8b: $[\alpha]_D$ = −17.0 (*c* = 1.06, $CHCl_3$). − IR ($CHCl_3$): $\tilde{\nu}$ = 2974 m, 1690 s, 1439 m, 1364 m, 1293 m, 1258 m, 1095 m, 1000 m, 929 w. − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.97 (s, 9 H, *t*Bu), 1.38 (d, *J* = 6.7, 3 H, Me), 2.16 [***ABX***, J_{AB} = 16.3, J_{AX} = 7.3, 1 H, H-C(5)], 2.36 [***ABX***, J_{AB} = 16.3, J_{BX} = 4.7, 1 H, H-C(5)], 3.68 (s, 3 H, MeO), 3.82−3.90 [m, 1 H, H-C(6)], 5.10 (***C****D*, *J* = 12.3, 1 benzylic H)], 5.14 (*C****D***, *J* = 12.3, 1 benzylic H), 5.43 [s, 1 H, H-C(2)], 7.28−7.38 (m, 5 arom. H). − ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 20.47 (Me), 27.33 (*t*Bu), 33.12 (CH_2), 38.76 (C), 47.21 (CH), 52.39 (Me), 66.87 (CH_2), 76.91 (CH), 127.93 (CH), 127.97 (CH), 128.43 (CH), 136.56 (C), 156.58 (C), 161.30 (C). − EI-MS; *m/z* (%): 319.3 (0.03) $[M + 1]^+$, 261.2 (35), 217.2 (45), 91.1 (100), 86.0 (46), 84.0 (76), 49.0 (84). − $C_{18}H_{26}N_2O_3$ (318.42): calcd. C 67.90, H 8.23, N 8.80; found C 67.70, H 8.42, N 8.78.

Benzyl *rac*-(2*S*,6*S*)-2-*tert*-Butyl-4-methoxy-6-methyl-5,6-dihydro-2*H*-pyrimidine-1-carboxylate (*rac*-8b): The alkylation of *rac*-**4b** (8.85 g, 29.1 mmol) was performed according to *GP3*. Purification of the crude product by FC (pentane/Et_2O, 17:3) gave *rac*-**8b** (6.1 g, 65%) as a colorless oil. − IR (film): $\tilde{\nu}$ = 2953 s, 1682 s, 1438 m, 1364 m, 1286 m, 1226 m, 1164 m, 1094 m, 1000 m, 929 w, 776 m, 751 w, 698 m. − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.97 (s, 9 H, *t*Bu), 1.38 (d, *J* = 6.7, 3 H, Me), 2.16 [***ABX***, J_{AB} = 16.3, J_{AX} = 7.3, 1 H, H-C(5)], 2.36 [***ABX***, J_{AB} = 16.3, J_{BX} = 4.7, 1 H, H-C(5)], 3.67 (s, MeO), 3.79−3.90 (*m*, H-C(6)], 5.10 (***C****D*, *J* = 12.6, 1 benzylic H), 5.14 (*C****D***, J_{AB} = 12.6, 1 benzylic H), 5.43 [s, 1 H, H-C(2)], 7.27−7.37 (m, 5 arom. H). − ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 20.50 (Me), 27.36 (*t*Bu), 33.15 (CH_2), 38.79 (C), 47.24 (CH), 52.41 (Me), 66.90 (CH_2), 77.04 (CH), 127.95 (CH), 127.99 (CH), 128.46 (CH), 136.59 (C), 156.61 (C), 161.33 (C). − EI-MS; *m/z* (%): 319.1 (1.66) $[M + 1]^+$, 261.0 (65), 217.0 (74), 91.0 (100), 57.0 (13), 41.0 (14). − $C_{18}H_{26}N_2O_3$ (318.42): calcd. C 67.90, H 8.23, N 8.80; found C 67.78, H 8.22, N 8.89.

Allyl *rac*-(2*R*,6*S*)-2-*tert*-Butyl-4-methoxy-6-methyl-5,6-dihydro-2*H*-pyrimidine-1-carboxylate (*rac*-9): The alkylation of *rac*-**5** (3.00 g, 11.8 mmol) was performed according to *GP3*. Purification of the crude product by FC (pentane/Et_2O, 4:1) gave *rac*-**9** (1.84 g, 58%) as a colorless oil. − IR ($CHCl_3$): $\tilde{\nu}$ = 2973 m, 1694 s, 1440 w, 1393 w, 1363 w, 1311 m, 1075 w, 1000 w, 931 w, 864 w. − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.98 (s, 9 H, *t*Bu), 1.32 (d, *J* = 6.6, 3 H, Me), 2.07 [***ABX***, J_{AB} = 16.9, J_{AX} = 7.1, 1 H, H-C(5)], 2.43 [***ABX***, J_{AB} = 16.9, J_{BX} = 8.4, 1 H, H-C(5)], 3.68 (s, 3 H, MeO), 4.34−4.43 [m, 1 H, H-C(6)], 4.55−4.65 (m, 2 allylic H), 5.19−5.34 (m, 2 H, H_2C=), 5.54 [s, 1 H, H-C(2)], 5.89−5.99 (m, HC=). − ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 23.20 (Me), 27.07 (*t* Bu), 30.56 (CH_2), 38.44 (C), 45.13 (CH), 52.27 (Me), 66.14 (CH_2), 76.49 (CH), 117.44 (CH_2), 132.93 (CH), 156.39 (C), 160.60 (C). − EI-MS; *m/z* (%): 269.1 (5.2) $[M + 1]^+$, 211.0 (100), 167.1 (32), 99.1 (9), 84.1 (22). − $C_{14}H_{24}N_2O_3$ (268.36): calcd. C 62.66, H 9.01, N 10.44; found C 62.41, H 8.73, N 10.46.

Benzyl (2*R*,6*S*)-2-*tert*-Butyl-6-isobutyl-4-methoxy-5,6-dihydro-2*H*-pyrimidine-1-carboxylate [(2*R*,6*S*)-10]: The alkylation of (2*R*,6*S*)-**6** (6.22 g, 18.0 mmol) was performed according to *GP3*. Purification of the crude product by FC (pentane/Et_2O, 17:3) gave (2*R*,6*S*)-**10** (4.13 g, 64%) as a colorless oil. − $[\alpha]_D$ = +25.9 (*c* = 1.27, $CHCl_3$). − IR ($CHCl_3$): $\tilde{\nu}$ = 2959 m, 1690 s, 1440 w, 1365 w, 1306 m, 1085 m, 1024 w, 963 w. − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.81−0.93 (m, 6 H, 2 Me), 0.97 (s, 9 H, *t*Bu), 1.23−1.30 [m, 1 H, H-C(2′)], 1.53−1.67 [m, 2 H, H-C(1′)], 2.03 [***ABX***, J_{AB} = 16.8, J_{AX} = 5.3, 1 H, H-C(5)], 2.41 [***ABX***, J_{AB} = 16.8, J_{BX} = 8.3, 1 H, H-C(5)], 3.67 (s, 3 H, MeO), 4.42 [br, 1 H, H-C(6)], 5.10 (***C****D*, *J* = 12.2, 1 benzylic H), 5.17 (*C****D***, *J* = 12.2, 1 benzylic H), 5.52 [s, 1 H, H-C(2)], 7.27−7.37 (m, 5 arom. H). − ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 21.66 (Me), 23.32 (Me), 24.98 (CH), 27.09 (*t*Bu), 29.36 (CH_2), 38.23 (C), 46.10 (CH_2), 47.39 (CH), 52.25 (Me), 67.42 (CH_2), 76.08 (CH), 128.04 (CH), 128.17 (CH), 128.45 (CH), 136.51 (C), 156.78 (C), 159.93 (C). − EI-MS; *m/z* (%): 361.2 (0.6) $[M + 1]^+$, 303.2 (87), 259.1 (100), 91.0 (52). − $C_{21}H_{32}N_2O_3$ (360.50): calcd. C 69.97, H 8.95, N 7.77; found C 70.03, H 8.86, N 7.64.

Benzyl (2*S*,6*S*)-2-*tert*-Butyl-6-isobutyl-4-methoxy-5,6-dihydro-2*H*-pyrimidine-1-carboxylate [(2*S*,6*S*)-10]: The alkylation of (2*S*,6*S*)-**6** (1.78 g, 5.1 mmol) was performed according to *GP3*. Purification of the crude product by FC (pentane/Et_2O, 9:1) gave (2*S*,6*S*)-**10** (0.89 g, 48%) as a colorless oil. − $[\alpha]_D$ = −5.7 (*c* = 1.00, $CHCl_3$). − IR ($CHCl_3$): $\tilde{\nu}$ = 2959 s, 1687 s, 1438 w, 1365 w, 1298 m, 1161 w, 1106 w, 979 w, 855 w. − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.83 (d, *J* = 6.5, 3 H, Me), 0.90 (d, *J* = 6.4, 3 H, Me), 1.01 (s, 9 H,

*t*Bu), 1.47−1.63 [m, 2 H, H-C(1′)], 1.90−1.98 [m, 1 H, H-C(2′)], 2.18 [***ABX***, J_{AB} = 16.4, J_{AX} = 4.2, 1 H, H-C(5)], 2.26 [***ABX***, J_{AB} = 16.4, J_{BX} = 9.4, 1 H, H-C(5)], 3.44−3.51 [m, 1 H, H-C(6)], 3.66 (s, 3 H, MeO), 5.07 (***C****D*, *J* = 12.3, 1 benzylic H), 5.13 (*C****D***, *J* = 12.3, 1 benzylic H), 5.39 [s, 1 H, H-C(2)], 7.27−7.37 (m, 5 arom. H). − ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 22.33 (Me), 23.25 (Me), 25.44 (CH), 27.48 (*t*Bu), 31.53 (CH_2), 37.72 (C), 42.65 (CH_2), 49.81 (CH), 52.37 (Me), 66.96 (CH_2), 77.93 (CH), 127.96 (CH), 128.03 (CH), 128.45 (CH), 136.58 (C), 156.71 (C), 161.11 (C). − EI-MS; *m/z* (%): 361.3 (0.1) $[M + 1]^+$, 303.2 (65), 259.2 (100), 91.1 (82). − $C_{21}H_{32}N_2O_3$ (360.50): calcd. C 69.97, H 8.95, N 7.77; found C 70.12, H 9.12, N 7.71.

Alkylation of the Boc-Protected Pyrimidines (11−19)

tert*-Butyl *rac*-(2*S*,5*R*)-2-*tert*-Butyl-4-methoxy-5-methyl-5,6-dihydro-2*H*-pyrimidine-1-carboxylate (*rac*-11):** The alkylation of *rac*-**7** (2.00 g, 7.4 mmol) with MeI (1.4 mL, 22.2 mmol) was performed according to *GP4*. Purification of the crude product by FC (pentane/Et_2O, 9:1) gave *rac*-**11** (2.09 g, 99%) as a colorless oil. − IR (film): $\tilde{\nu}$ = 2973 s, 1682 s, 1462 m, 1364 m, 1328 m, 1272 w, 1216 w, 1146 m, 1099 m, 1042 m, 1004 m, 951 m, 916 m, 874 m, 772 w. − ^{1}H NMR ($CDCl_3$, 400 MHz) 2 conformers: δ = 0.97 (s, 9 H, *t*Bu), 1.09 (d, *J* = 7.2, 3 H, Me), 1.46, 1.47 (s, 9 H, *t*Bu), 2.19−2.31 [m, 2 H, H-C(5)], 3.15, 3.19 [ABX***, $J_{AB}(1)$ = 13.5, $J_{AX}(1)$ = 4.0, $J_{AB}(2)$ = 13.7, $J_{AX}(2)$ = 3.9, 1 H, H-C(6)], 3.64, 3.65 (s, 3 H, MeO), 3.93, 4.15 [***ABX***, $J_{AB}(2)$ = 13.7, $J_{BX}(2)$ = 0, $J_{AB}(1)$ = 13.5, $J_{BX}(1)$ = 0, 1 H, H-C(6)], 5.25, 5.37 [s, 1 H, H-C(2)]. − ^{13}C NMR ($CDCl_3$, 100 MHz) 2 conformers: δ = 16.12, 16.26 (Me), 26.79, 27.01 (*t*Bu), 28.36 (*t*Bu), 31.48, 31.59 (CH), 38.32, 38.50 (C), 42.07, 43.50 (CH_2), 52.16 (Me), 73.47, 74.37 (CH), 79.45, 79.98 (C), 155.37, 156.01 (C), 162.68, 163.63 (C). − EI-MS; *m/z* (%): 285.2 (0.7) $[M + 1]^+$, 227.1 (20), 171.0 (100), 127.1 (63), 69.0 (14), 57.0 (87), 41.0 (42), 29.0 (18). − $C_{15}H_{26}N_2O_3$ (284.40): calcd. 63.35 C, 9.92 H, 9.85 N; found 63.60 C, 9.65 H, 10.04 N.

***tert*-Butyl (2*S*,5*R*)-2-*tert*-Butyl-4-methoxy-5-methyl-5,6-dihydro-2*H*-pyrimidine-1-carboxylate (11):** The alkylation of (*S*)-**7** (1.50 g, 5.5 mmol) with MeI (1.38 mL, 22.2 mmol) was performed according to *GP4*. Purification of the crude product by FC (pentane/Et_2O, 9:1) gave **11** (1.15 g, 73%) as a colorless oil, with the same analytical datas as *rac*-**11**. − $[\alpha]_D$ = +95.2 (*c* = 1.31, $CHCl_3$).

***tert*-Butyl (2*S*,5*R*)-5-Benzyl-2-*tert*-butyl-4-methoxy-5,6-dihydro-2*H*-pyrimidine-1-carboxylate (12):** The alkylation of (*S*)-**7** (1.50 g, 5.5 mmol) with benzyl bromide (1.98 mL, 16.6 mmol) was performed according to *GP4*. Purification of the crude product by FC (pentane/Et_2O, 9:1) gave **12** (1.90 g, 95%) as a colorless oil. $[\alpha]_D$ = +69.7 (*c* = 1.24, $CHCl_3$). − IR ($CHCl_3$): $\tilde{\nu}$ = 3007 w, 2976 m, 1688 s, 1454 w, 1409 m, 1366 m, 1282 m, 1162 s, 1086 m, 959 m, 916 m, 882 m. − ^{1}H NMR ($CDCl_3$, 400 Mhz) 2 conformers: δ = 0.98 (s, 9 H, *t*Bu), 1.46, 1.52 (s, 9 H, *t*Bu), 2.29−2.56 [m, 2 H, H-C(5), H-C(1′)], 2.81−3.09 [m, 2 H, H-C(1′), H-C(6)], 3.65, 3.68 (s, 3 H, MeO), 3.93, 4.24 (*[d*, *J*(1) = 14.0, *J*(2) = 13.8, 1 H, H-(6)], 5.31, 5.46 [s, 1 H, H-C(2)], 7.19−7.36 (m, 5 arom. H). − ^{13}C NMR ($CDCl_3$, 100 MHz) 2 conformers: δ = 26.90, 27.06 (*t*Bu), 28.39 (*t*Bu), 35.90, 36.06 (CH_2), 38.23, 39.40 (CH), 38.30, 38.72 (C), 38.60, 39.73 (CH_2), 52.22 (Me), 73.18, 74.28 (CH), 79.84, 80.01 (C), 126.26, 126.31 (CH), 128.23, 128.37 (CH), 129.02, 129.48 (CH), 139.48, 139.51 (C), 154.95, 155.56 (C), 161.17, 162.16 (C). − EI-MS; *m/z* (%): 303.2 (17) $[M - 57]^+$, 247.1 (100), 203.1 (14), 91.1 (34), 57.1 (78). − $C_{21}H_{32}N_2O_3$ (360.50): calcd. 69.97 C, 8.95 H, 7.77 N; found 70.06 C, 8.75 H, 7.70 N.

tert*-Butyl *rac*-(2*S*,5*R*)-5-Allyl-2-*tert*-butyl-4-methoxy-5,6-dihydro-2*H*-pyrimidine-1-carboxylate (*rac*-13):** The alkylation of *rac*-**7** (4.06 g, 15.0 mmol) with allyl bromide (3.81 mL, 45.0 mmol) was performed according to *GP4*. Purification of the crude product by FC (pentane/Et_2O, 9:1) gave *rac*-**13** (3.54 g, 76%) as a colorless oil. − IR ($CHCl_3$): $\tilde{\nu}$ = 2972 m, 1686 s, 1480 w, 1410 m, 1366 m, 1335 w, 1276 m, 1163 s, 1145 s, 1080 w, 1042 w, 994 w, 950 w, 867 w. − ^{1}H NMR ($CDCl_3$, 400 MHz) 2 conformers: δ = 0.97 (s, 9 H, *t*Bu), 1.46, 1.47 (s, 9 H, *t*Bu), 1.96−2.30 [m, 3 H, H-C(6), 2 H-C(1′)], 3.00, 3.10 [ABX***, $J_{AB}(1)$ = 13.7, $J_{AX}(1)$ = 4.2, $J_{AB}(2)$ = 13.9, $J_{AX}(2)$ = 3.8, 1 H, H-C(6)], 3.65, 3.66 (s, 3H MeO), 4.09, 4.30 [***ABX***, $J_{AB}(2)$ = 13.9, $J_{BX}(2)$ = 0, $J_{AB}(1)$ = 13.7, $J_{BX}(1)$ = 0, 1 H, H-C(5)], 5.04−5.13 (m, 2 H, H_2C=), 5.24, 5.38 [s, 1 H, H-C(2)], 5.75−5.85 (m, 1 H, HC=). − ^{13}C NMR ($CDCl_3$, 100 MHz) 2 conformers: δ = 26.83, 27.02 (*t*Bu), 28.36 (*t*Bu), 34.06, 34.61 (CH_2), 36.79, 36.82 (CH), 38.53, 38.60 (C), 39.07, 40.10 (CH_2), 52.14, 52.16 (Me), 73.21, 74.22 (CH), 79.66, 79.95 (CH), 116.89 (CH_2), 135.26, 135.72 (C), 155.01, 155.48 (C), 161.21, 162.10 (C). − EI-MS; *m/z* (%): 309.0 (0.2) $[M - 1]^+$, 197.1 (100), 153.1 (28), 86.0 (14), 84.0 (21), 57.1 (12). − $C_{17}H_{30}N_2O_3$ (310.44): calcd. C 65.77, H 9.74, N 9.02; found C 65.79, H 9.74, N 9.03.

tert*-Butyl *rac*-(2*S*,5*R*)-2-*tert*-Butyl-4-methoxy-5-propargyl-5,6-dihydro-2*H*-pyrimidine-1-carboxylate (*rac*-14):** The alkylation of *rac*-**7** (2.70 g, 10.0 mmol) with propargyl bromide (2.25 mL, 30.0 mmol) was performed according to *GP4*. Purification of the crude product by FC (pentane/Et_2O, 9:1) gave *rac*-**14** (2.67 g, 87%) as a pale yellow oil. − IR ($CHCl_3$): $\tilde{\nu}$ = 3308 m, 3008 w, 2976 m, 1690 s, 1479 w, 1409 m, 1366 m, 1336 w, 1279 w, 1163 m, 1048 m, 954 w, 854 w. − ^{1}H NMR ($CDCl_3$, 400 MHz) 2 conformers: δ = 0.98 (s, 9 H, *t*Bu), 1.48, 1.49 (s, 9 H, *t*Bu), 2.01 (t, *J* = 2.6, 1 H, H-C≡), 2.13−2.46 [m, 3 H, H-C(5), 2 H-C(1′)], 3.10, 3.16 [ABX***, $J_{AB}(1)$ = 13.9, $J_{AX}(1)$ = 3.8, $J_{AB}(2)$ = 14.1, $J_{AX}(2)$ = 3.5, 1 H, H-C(6)], 3.64, 3.67 (s, 3 H, MeO), 4.37, 4.50 [***ABX***, $J_{AB}(2)$ = 14.1, $J_{BX}(2)$ = 0, $J_{AB}(1)$ = 13.9, $J_{BX}(1)$ = 0, 1 H, H-C(6)], 5.25, 5.37 [s, 1 H, H-C(2)]. − ^{13}C NMR ($CDCl_3$, 100 MHz) 2 conformers: δ = 19.72, 20.46 (CH_2), 26.81, 27.07 (*t*Bu), 28.23, 28.38 (*t*Bu), 35.83, 36.33 (CH), 38.89, 38.54 (C), 39.66, 40.22 (CH_2), 52.35 (Me), 69.74, 69.79 (CH), 73.39, 74.40 (CH), 79.95, 80.16 (C), 81.40, 81.90 (C), 155.11, 155.50 (C), 159.84, 160.58 (C). − EI-MS; *m/z* (%): 309.2 (4.4) $[M + 1]^+$, 251.1 (36), 195.1 (100), 151.1 (59), 57.1 (15). − $C_{17}H_{28}N_2O_3$ (308.42): calcd. C 66.20, H 9.15, N 9.08; found C 66.39, H 8.98, N 9.27.

tert*-Butyl *rac*-(2*S*,5*R*)-2-*tert*-Butyl-4-methoxy-5-trimethylsilanylmethyl-5,6-dihydro-2*H*-pyrimidine-1-carboxylate (*rac*-15):** The alkylation of *rac*-**7** (1.08 g, 4.0 mmol) with trimethylsilylmethyl iodide (0.6 mL, 4.0 mmol) was performed according to *GP4*. Purification of the crude product by FC (pentane/Et_2O, 19:1) gave *rac*-**15** (1.01 g, 71%) as a colorless oil. − IR ($CHCl_3$): $\tilde{\nu}$ = 2974 m, 1686 s, 1479 w, 1407 m, 1366 m, 1330 m, 1051 m, 931 m, 847 m. − ^{1}H NMR ($CDCl_3$, 400 MHz) 2 conformers: δ = 0.04 (s, 9 H, Me_3Si), 0.62−0.74 [m, 2 H, H-C(1′)], 0.96 (s, 9 H, *t*Bu), 1.47 (s, 9 H, *t*Bu), 2.16−2.25 [m, 1 H, H-C(5)], 3.05, 3.16 [ABX***, $J_{AB}(1)$ = 13.3, $J_{AX}(1)$ = 3.8, $J_{AB}(2)$ = 13.5, $J_{AX}(2)$ = 3.5, 1 H, H-C(6)], 3.61, 3.63 (s, 3 H, MeO), 3.89, 4.15 [***ABX***, $J_{AB}(2)$ = 13.5, $J_{BX}(2)$ = 0, $J_{AB}(1)$ = 13.3, $J_{BX}(1)$ = 0, 1 H, H-C(6)], 5.23, 5.37 [s, 1 H, H-C(2)]. − ^{13}C NMR ($CDCl_3$, 100 MHz) 2 conformers: δ = −1.28, −1.16 (Me_3Si), 18.47, 18.59 (CH_2), 26.74, 26.96 (*t*Bu), 28.34, 28.45 (*t*Bu), 32.48, 32.56 (CH), 38.54, 38.65 (C), 42.93, 44.52 (CH_2), 51.94 (Me), 73.22, 74.10 (CH), 79.51, 79.81 (C), 155.50, 156.03 (C), 162.98, 164.09 (C). − EI-MS; *m/z* (%): 357.3 (0.4) $[M + 1]^+$, 299.2 (31), 243.1 (100), 199.1 (47), 73.0 (27), 57.1 (56). − $C_{18}H_{36}N_2O_3Si$ (356.58): calcd. C 60.63, H 10.18, N 7.86; found C 60.55, H 10.27, N 7.78.

***tert*-Butyl *rac*-(2*S*,5*R*)-2-*tert*-Butyl-5-cyclopropylmethyl-4-methoxy-5,6-dihydro-2*H*-pyrimidine-1-carboxylate (*rac*-16):** The alkylation of

rac-**7** (3.0 g, 11.1 mmol) with (bromomethyl)cyclopropane (2.65 mL, 27.7 mmol) was performed according to *GP4*. Purification of the crude product by FC (pentane/Et_2O, 92:8) gave *rac*-**16** (1.79 g, 50%) as a colorless oil. − IR ($CHCl_3$): $\tilde{\nu}$ = 2976 m, 1686 s, 1460 w, 1408 m, 1366 m, 1334 m, 1281 m, 1150 m, 1084 w, 1019 w, 953 w, 913 w, 868 m. − ^{1}H NMR ($CDCl_3$, 400 MHz) 2 conformers: δ = −0.04−0.19 (m, 2 H, H_2C), 0.35−0.53 (m, 2 H, H_2C), 0.73−0.93 [m, 1 H, H-C(2′)], 0.97 (s, 9 H, *t*Bu), 1.01−1.61 [m, 2 H, H-C(1′)], 1.47 (s, 9 H, *t*Bu), 2.17−2.27 [m, 1 H, H-C(5)], 3.04, 3.12 [***ABX***, $J_{AB}(1)$ = 13.6, $J_{AX}(1)$ = 4.1, $J_{AB}(2)$ = 13.8, $J_{AX}(2)$ = 3.7, 1 H, H-C(6)], 3.62, 3.64 (s, 3 H, MeO), 4.17, 4.40 [***ABX***, $J_{AB}(2)$ = 13.8, $J_{BX}(2)$ = 0, $J_{AB}(1)$ = 13.6, $J_{BX}(1)$ = 0, 1 H, H-C(6)], 5.22, 5.35 [s, 1 H, H-C(2)]. − ^{13}C NMR ($CDCl_3$, 100 MHz) 2 conformers: δ = 3.93, 4.38 (CH_2), 4.88, 5.15 (CH_2), 9.05, 9.14 (CH), 26.78, 27.01 (*t*Bu), 28.36 (*t*Bu), 34.93, 35.30 (CH_2), 37.16, 37.34 (CH), 38.45, 38.60 (C), 39.63, 40.73 (CH_2), 52.07 (Me), 73.30, 74.20 (CH), 79.60, 79.91 (C), 155.20, 155.68 (C), 161.89, 162.83 (C). − EI-MS; *m/z* (%): 325.2 (0.1) $[M + 1]^+$, 267.1 (10), 211.1 (100), 167.1 (28), 57.1 (10). − $C_{18}H_{32}N_2O_3$ (324.46): calcd. 66.63 C, 9.94 H, 8.63 N; found C 66.52, H 9.71, N 8.64.

tert*-Butyl *rac*-(2*S*,5*R*)-2-*tert*-Butyl-4-methoxy-5-(3-methoxybenzyl)-5,6-dihydro-2*H*-pyrimidine-1-carboxylate (*rac*-17):** The alkylation of *rac*-**7** (3.0 g, 11.1 mmol) with *m*-methoxybenzyl iodide[37] (5.51 g, 22.2 mmol) was performed according to *GP4*. Purification of the crude product by FC (pentane/Et_2O, 9:1) gave *rac*-**17** (4.25 g, 98%) as a colorless oil. − IR ($CHCl_3$): $\tilde{\nu}$ = 2976 m, 1687 s, 1602 m, 1456 w, 1409 m, 1366 m, 1336 m, 1265 m, 1159 s, 1136 m, 1086 w, 1045 m, 963 w, 873 m. − ^{1}H NMR ($CDCl_3$, 400 MHz) 2 conformers: δ = 0.98 (s, 9 H, *t*Bu), 1.45, 1.52 (s, 9 H, *t*Bu), 2.29−2.54 [m, 2 H, H-C(1′)], 2.79−2.91 [m, 1 H, H-C(5)], 2.91, 3.08 [ABX***, $J_{AB}(1)$ = 13.7, $J_{AX}(1)$ = 4.3, $J_{AB}(2)$ = 14.1, $J_{AX}(2)$ = 3.8, 1 H, H-C(6)], 3.65, 3.69 (s, 3 H, MeO), 3.80, 3.83 (s, 3 H, MeO), 4.03, 4.26 [***ABX***, $J_{AB}(2)$ = 14.1, $J_{BX}(2)$ = 0, $J_{AB}(1)$ = 13.7, $J_{BX}(1)$ = 0, 1 H, H-C(6)], 5.30, 5.48 [s, 1 H, H-C(2)], 6.75−6.95 (m, 3 arom. H), 7.22 (dd, *J* = 8.0, 7.7, arom. H). − ^{13}C NMR ($CDCl_3$, 100 MHz) 2 conformers: δ = 26.90, 27.05 (*t*Bu), 28.35, 28.39 (*t*Bu), 35.92, 36.10 (CH_2), 38.05, 39.33 (CH), 38.27, 39.85 (CH_2), 38.63, 38.72 (C), 52.25 (Me), 55.20 (Me), 73.17, 74.27 (CH), 79.87, 80.02 (C), 111.26, 112.36 (CH), 114.85, 115.11 (CH), 121.47, 121.75 (CH), 129.24, 129.31 (CH), 140.98, 141.06 (C), 154.99, 155.57 (C), 159.61, 159.75 (C), 161.16, 162.10 (C). − EI-MS; *m/z* (%): 391.3 (0.1) $[M + 1]^+$, 333.2 (19), 277.1 (43), 233.1 (100), 121.0 (18), 85.9 (31), 84.0 (51), 49.0 (17). − $C_{22}H_{34}N_2O_4$ (390.52): calcd. C 67.66, H 8.78, N 7.17; found C 67.77, H 8.66, N 7.05.

***tert*-Butyl *rac*-(2*S*,5*R*)-2-*tert*-Butyl-4-methoxy-5-oxiranylmethyl-5,6-dihydro-2*H*-pyrimidine-1-carboxylate (*rac*-18):** The alkylation of *rac*-**7** (3.0 g, 11.1 mmol) with epibromohydrin (2.76 mL, 33.3 mmol) was performed according to *GP4*. Purification of the crude product (mixture of 2 diastereoisomers in a ratio 3:1) by FC (pentane/Et_2O, 15:5) gave the major diastereoisomer *rac*-**18** (1.71 g, 47%) as a colorless oil. − IR ($CHCl_3$): $\tilde{\nu}$ = 2977 m, 1690 s, 1480 w, 1458 w, 1408 m, 1366 m, 1336 m, 1281 m, 1144 m, 1089 w, 1018 w, 964 w, 871 m. − ^{1}H NMR ($CDCl_3$, 400 MHz) 2 conformers: δ = 0.98 (s, 9 H, *t*Bu), 1.47 (s, 9 H, *t*Bu), 1.50−1.74 (m, 2 H), 2.33−2.45 (m, 1 H), 2.53−2.59 (m, 1 H), 2.79−2.83 (m, 1 H), 3.05−3.21 (m, 2 H), 3.64, 3.66 (s, 3 H, MeO), 4.17, 4.37 [d, *J*(1) = 14.1, *J*(2) = 13.9, 1 H, H-C(6)], 5.23, 5.37 [s, 1 H, H-C(2)]. − ^{13}C NMR ($CDCl_3$, 100 MHz) 2 conformers: δ = 26.79, 27.00 (*t*Bu), 28.34, 28.43 (*t*Bu), 32.74, 33.10 (CH_2), 34.30, 34.34 (CH), 38.42, 38.51 (C), 39.16, 40.57 (CH_2), 47.33, 47.88 (CH_2), 49.86, 50.21 (CH), 52.28 (Me), 73.37, 74.28 (CH), 79.88, 80.21 (C), 154.91, 155.74 (C), 161.06, 161.93 (C). − EI-MS; *m/z* (%): 327.2 (4.5) $[M + 1]^+$, 269.1 (29), 213.0 (97), 169.1 (100), 57.1 (40). − $C_{17}H_{30}N_2O_4$ (326.44): calcd. C 62.55, H 9.26, N 8.58; found C 62.33, H 9.02, N 8.60.

tert*-Butyl *rac*-(1′*R*,2*S*,5*R*)-2-*tert*-Butyl-5-cyclohex-2-enyl-4-methoxy-5,6-dihydro-2*H*-pyrimidine-1-carboxylate (*rac*-19):** The alkylation of *rac*-**7** (4.06 g, 15.0 mmol) with 3-bromocyclohexene[38] (12.1 g, 75 mmol) was performed according to *GP4*. Purification of the crude product by FC (pentane/Et_2O, 4:1) gave *rac*-**19** (3.41 g, 65%, the minor diastereoisomer could not be separated, *dr* = 8:1) as a colorless oil. − IR ($CHCl_3$): $\tilde{\nu}$ = 2977 s, 1686 s, 1459 w, 1407 m, 1366 m, 1327 w, 1162 s, 1076 w, 1030 w, 995 w, 946 m, 860 w. − ^{1}H NMR ($CDCl_3$, 400 MHz) 2 conformers: δ = 0.97 (s, 9 H, *t*Bu), 1.24−2.38 (*m*, 8 H, 3 $H_{2\ C,}$ H-C(1′), H-C(5)], 1.45, 1.46 (s, 9 H, *t*Bu), 2.96, 3.05 [ABX***, J_{AB} = 13.9, J_{AX} = 4.6, 1 H, H-C(6)], 3.67, 3.68 (s, MeO), 4.19, 4.41 [***ABX***, J_{AB} = 13.9, J_{BX} = 0, 1 H, H-C(6)], 5.25, 5.37 [s, 1 H, H-C(2)], 5.42−5.45 (m, 1 H, HC=), 5.75−5.81 (m, 1 H, HC=). − ^{13}C NMR ($CDCl_3$, 100 MHz) 2 conformers: δ = 21.61, 21.84 (CH_2), 25.08, 25.16 (CH_2), 26.65 (CH_2), 26.76, 26.93 (*t*Bu), 28.33, 28.39 (*t*Bu), 36.09, 36.65 (CH), 38.59, 39.61 (CH_2), 38.89, 38.91 (C), 41.06, 41.08 (CH), 52.00 (Me), 73.08, 74.04 (CH), 79.52, 79.95 (C), 128.60, 129.10 (CH), 129.21, 129.53 (CH), 154.66, 155.25 (C), 160.59, 161.58 (C). − EI-MS; *m/z* (%): 293.1 (6.1) $[M - 57]^+$, 237.0 (36), 87.9 (11), 85.9 (67), 83.9 (100), 51.0 (14), 49.0 (46). − $C_{20}H_{34}N_2O_3$ (350.50): calcd. C 68.54, H 9.78, N 7.99; found C 68.36, H 9.91, N 7.88.

Introduction of a Second Substituent in 5-Postion (20)

***tert*-Butyl *rac*-(2*S*,5*R*)-5-Allyl-2-*tert*-butyl-4-methoxy-5-methyl-5,6-dihydro-2*H*-pyrimidine-1-carboxylate (*rac*-20):** Dihydropyrimidine *rac*-**11** (1.96 g, 6.9 mmol) was dissolved in THF (20 mL). After cooling to −78°C, *t*BuLi (6.9 mmol) and 1 h later allyl bromide (1.17 mL, 13.8 mmol) were added. After 4 h at −78°C the reaction mixture was warmed up to room temp. within 1 h and satd. NH_4Cl solution (75 mL) was added. The aqueous layer was extracted three times with Et_2O (100 mL), and the combined organic layers washed with satd. NaCl solution (100 mL) and dried with anhydrous $MgSO_4$. The solvent was removed by rotary evaporation. Purification of the crude product by FC (pentane/Et_2O, 19:1) gave *rac*-**20** (1.63 g, 73%) as a colorless oil. − IR ($CHCl_3$): $\tilde{\nu}$ = 2977 s, 1686 s, 1461 w, 1411 m, 1366 m, 1326 w, 1282 m, 1152 s, 1091 w, 978 w, 917 m, 873 w. − ^{1}H NMR ($CDCl_3$, 400 MHz) 2 conformers: δ = 0.97 (s, 9 H, *t*Bu), 0.98, 1.02 (s, 3 H, Me), 1.47 (s, 9 H, *t*Bu), 2.08−2.20 (m, 2 allylic H), 2.76, 2.85 [d, *J*(1) = 13.7, *J*(2) = 13.9, 1 H, H-C(6)], 3.61, 3.63 (s, MeO), 3.92, 4.14 [d, *J*(2) = 13.9, *J*(1) = 13.7, 1 H, H-C(6)], 5.01−5.08 (m, 2 H, H_2C=), 5.25, 5.39 [s, 1 H, H-C(2)], 5.71−5.82 (1 H, HC=). − ^{13}C NMR ($CDCl_3$, 100 MHz) 2 conformers: δ = 19.97, 20.34 (Me), 26.86, 27.05 (*t*Bu), 28.38 (*t*Bu), 37.89, 38.17 (C), 38.41, 38.51 (C), 40.56, 41.41 (CH_2), 46.44, 47.42 (CH_2), 52.17 (Me), 73.82, 74.78 (CH), 79.65, 79.94 (C), 118.00, 118.04 (CH_2), 133.56, 133.67 (CH), 154.11, 155.11 (C), 163.34, 164.07 (C). − EI-MS; *m/z* (%): 325.3 (0.01) $[M + 1]^+$, 267.2 (10), 211.1 (100), 167.1 (34), 125.1 (15), 86.0 (48), 84.0 (78), 57.1 (26), 51.0 (30), 49.0 (90), 47.0 (14), 41.1 (15). − $C_{18}H_{32}N_2O_3$ (360.50): calcd. C 66.63, H 9.94, N 8.63; found C 66.71, H 9.86, N 8.87.

Alkylation of the *Z*- and *Alloc*-Protected Pyrimidines (21−31)

Benzyl *rac*-(2*R*,5*S*,6*S*)-2-*tert*-Butyl-4-methoxy-5,6-dimethyl-5,6-dihydro-2*H*-pyrimidine-1-carboxylate (*rac*-21): The alkylation of *rac*-**8a** (8.00 g, 25.1 mmol) with MeI (4.7 mL, 75.4 mmol) was performed according to *GP5*. Purification of the crude product by FC (pentane/Et_2O, 9:1) gave *rac*-**21** (6.51 g, 78%) as a colorless oil. − IR ($CHCl_3$): $\tilde{\nu}$ = 2973 m, 1693 s, 1462 w, 1380 w, 1334 m, 1178 w, 1107 w, 1067 m, 1027 w, 901 w, 838 w. − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.98 (s, 9 H, *t*Bu), 1.02 (br, 3 H, Me), 1.22 (d, *J* = 6.5,

3 H, Me), 2.06−2.21 [br, 1 H, H-C(5)], 3.65 (s, 3 H, MeO), 4.19−4.39 [br, 1 H, H-C(6)], 5.00−5.28 (br, 2 benzylic H), 5.47 [s, 1 H, H-C(2)], 7.28−7.37 (m, 5 arom. H). − ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 16.23 (Me), 22.53 (Me), 27.22 (*t*Bu), 36.50 (CH), 38.07 (C), 51.44 (CH), 52.28 (Me), 67.23 (CH_2), 75.46 (CH), 127.98 (CH), 128.05 (CH), 128.44 (CH), 136.67 (C), 157.21 (C), 162.20 (C). − EI-MS; *m/z* (%): 333.3 (0.2) $[M + 1]^+$, 275.2 (20), 231.2 (30), 91.1 (100). − $C_{19}H_{28}N_2O_3$ (332.44): calcd. C 68.65, H 8.49, N 8.43; found C 68.75, H 8.27, N 8.28.

Benzyl (2*R*,5*S*,6*S*)-2-*tert*-Butyl-4-methoxy-5,6-dimethyl-5,6-dihydro-2*H*-pyrimidine-1-carboxylate (21): The alkylation of (2*R*,6*S*)-**8** (3.20 g, 10.1 mmol) with MeI (2.5 mL, 40.0 mmol) was performed according to *GP5*. Purification of the crude product by FC (pentane/Et_2O, 9:1) gave **21** (2.83 g, 85%) as a colorless oil. − $[\alpha]_D$ = −34.7 (*c* = 1.25, $CHCl_3$). − IR ($CHCl_3$): $\tilde{\nu}$ = 2975 m, 1693 s, 1462 w, 1380 w, 1333 m, 1178 w, 1109 w, 1069 m, 1027 w, 901 w, 838 w. − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.98 (s, 9 H, *t*Bu), 1.02 (br, 3 H, Me), 1.22 (d, *J* = 6.5, 3 H, Me), 2.06−2.21 [m, 1 H, H-C(5)], 3.65 (s, 3 H, MeO), 4.19−4.39 [m, 1 H, H-C(6)], 5.00−5.28 (br, 2benzylic H), 5.47 [s, 1 H, H-C(2)], 7.28−7.37 (m, 5 arom. H). − ^{1}H NMR ([D_6]DMSO, 300 MHz, 90°C): δ = 0.92 (s, 9 H, *t*Bu), 0.93 (d, *J* = 6.8, 3 H, Me), 1.14 (d, *J* = 7.1, 3 H, Me), 2.15 [qd, J_q = 6.8, J_d = 3.1, 1 H, H-C(5)], 3.92 (s, 3 H, MeO), 4.22 [qd, J_q = 7.1, J_d = 3.1, 1 H, H-C(6)], 5.10 (s, 2 benzylic H), 5.34 [s, 1 H, H-C(2)], 7.28−7.35 (m, 5 arom. H). − ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 16.25 (Me), 22.60 (Me), 27.25 (*t*Bu), 36.52 (CH), 38.10 (C), 51.49 (CH), 52.30 (Me), 67.26 (CH_2), 75.48 (CH), 128.01 (CH), 128.08 (CH), 128.46 (CH), 136.67 (C), 157.24 (C), 162.20 (C). − EI-MS; *m/z* (%): 333.2 (0.28) $[M + 1]^+$, 275.1 (87), 231.1 (100), 91.1 (95). − $C_{19}H_{28}N_2O_3$ (332.44): calcd. C 68.65, H 8.49, N 8.43; found C 68.79, H 8.38, N 8.59.

Benzyl *rac*-(2*R*,5*S*,6*S*)-5-Benzyl-2-*tert*-butyl-4-methoxy-6-methyl-5,6-dihydro-2*H*-pyrimidine-1-carboxylate (*rac*-22): The alkylation of *rac*-**8a** (0.50 g, 1.6 mmol) with benzyl bromide (0.75 mL, 6.3 mmol) was performed according to *GP5*. Purification of the crude product by FC (pentane/Et_2O, 9:1) gave *rac*-**22** (0.26 g, 40%) as a white solid, m.p. 56.5−57.5°C. − IR ($CHCl_3$): $\tilde{\nu}$ = 2957 m, 1694 s, 1455 w, 1391 m, 1366 m, 1335 w, 1302 m, 1139 w, 1102 w, 1066 m, 1001 m, 914 w. − ^{1}H NMR ($CDCl_3$, 400 MHz) 2 conformers: δ = 0.96, 1.00 (s, 9 H, *t*Bu), 1.09 (d, *J* = 7.1, 3 H, Me), 2.28 [br, 1 H, H-C(5)], 2.44 [br, 1 H, H-C(1′)], 2.75 [br, 1 H, H-C(1′)], 3.66 (s, 1 H, MeO), 4.42, 4.60 [br, 1 H, H-C(6)], 5.04−5.29 (m, 2 benzylic H), 5.37, 5.53 [s, 1 H, H-C(2)], 6.99−7.38 (m, 10 arom. H). − ^{1}H NMR ([D_6]DMSO, 300 MHz, 90°C): δ = 0.92 (s, 9 H, *t*Bu), 1.05 (d, *J* = 7.2, 3 H, Me), 2.33−2.38 [m, 1 H, H-C(5)], 2.47 [***A**BX*, J_{AB} = 13.7, J_{AX} = 8.7, 1 H, H-C(1′)], 2.66 [***A**BX*, J_{AB} = 13.7, J_{BX} = 5.3, 1 H, H-C(1′)], 3.58 (s, 3 H, MeO), 4.38−4.44 [m, 1 H, H-C(6)], 5.01 (***C**D*, *J* = 12.5, 1 benzylic H), 5.13 (*C**D***, *J* = 12.5, 1 benzylic H), 5.34 [s, 1 H, H-C(2)], 7.03−7.36 [m, 10 arom. H). − ^{13}C NMR ($CDCl_3$, 100 MHz) 2 conformers: δ = 23.54 (Me), 27.61, 27.79 (*t*Bu), 37.17, 37.53 (CH_2), 38.21, 38.66 (C), 44.31, 44.87 (CH), 47.66 (CH), 52.61 (Me), 67.58, 67.73 (CH_2), 75.32, 75.56 (CH), 126.77 (CH), 128.41 (CH), 128.78 (CH), 128.86 (CH), 129.24 (CH), 129.62 (CH), 137.01 (C), 139.19 (C), 157.54 (C), 160.73, 161.19 (C). − EI-MS; *m/z* (%): 409.3 (1.0) $[M + 1]^+$, 351.2 (100), 307.2 (82), 91.0 (6). − $C_{25}H_{32}N_2O_3$ (408.54): calcd. C 73.50, H 7.89, N 6.86; found C 73.71, H 8.01, N 6.74.

Benzyl (2*R*,5*S*,6*S*)-5-Benzyl-2-*tert*-butyl-4-methoxy-6-methyl-5,6-dihydro-2*H*-pyrimidine-1-carboxylate (22): The alkylation of (2*R*,6*S*)-**8** (3.20 g, 10.1 mmol) with benzyl bromide (2.40 mL, 20.1 mmol) was performed according to *GP5*. Purification of the crude product by FC (pentane/Et_2O, 9:1) gave **22** (3.00 g, 73%) as a white solid, m.p. 41−43°C. − $[\alpha]_D$ = −43.2 (*c* = 1.03, $CHCl_3$). − IR ($CHCl_3$): $\tilde{\nu}$ = 2957 m, 1693 s, 1455 w, 1391 m, 1366 m, 1335 w, 1302 m, 1102 w, 1001 m. − ^{1}H NMR ($CDCl_3$, 400 MHz) 2 conformers: δ = 0.99, 1.04 (s, 9 H, *t*Bu), 1.13 (d, *J* = 7.1, 3 H, Me), 2.31 [br, 1 H, H-C(5)], 2.47 [br, 1 H, H-C(1′)], 2.78 [br, 1 H, H-C(1′)], 3.69 (s, 3 H, MeO), 4.45, 4.63 [br, 1 H, H-C(6)], 5.07−5.32 (m, 2 benzylic H), 5.41, 5.56 [s, 1 H, H-C(2)], 7.02−7.41 (m, 10 arom. H). − ^{1}H NMR ([D_6]DMSO, 300 MHz, 90°C): δ = 0.92 (s, 9 H, *t*Bu), 1.03 (d, *J* = 7.2, 3 H, Me), 2.33−2.38 [m, 1 H, H-C(5)], 2.47 [***A**BX*, J_{AB} = 13.4, J_{AX} = 8.7, 1 H, H-C(1′)], 2.67 [***A**BX*, J_{AB} = 13.4, J_{BX} = 5.0, 1 H, H-C(1′)], 3.57 (s, 3 H, MeO), 4.35−4.41 [m, 1 H, H-C(6)], 5.01 (***C**D*, *J* = 12.5, 1 benzylic H), 5.13 (*C**D***, *J* = 12.5, 1 benzylic H), 5.34 [s, 1 H, H-C(2)], 7.02−7.36 (m, 10 arom. H). − ^{13}C NMR ($CDCl_3$, 100 MHz) 2 conformers: δ = 23.17 (Me), 27.22, 27.40 (*t*Bu), 36.77, 37.14 (CH_2), 37.82, 38.26 (C), 43.92, 44.47 (CH), 47.26 (CH), 52.23 (Me), 67.19 (CH_2), 74.92, 75.17 (CH), 126.38 (CH), 128.03 (CH), 128.39 (CH), 128.47 (CH), 128.85 (CH), 129.23 (CH), 136.61 (C), 138.79 (C), 157.15 (C), 160.35, 160.80 (C). − EI-MS; *m/z* (%): 409.2 (0.2) $[M + 1]^+$, 351.1 (42), 307.1 (45), 91.0 (100). − $C_{25}H_{32}N_2O_3$ (408.54): calcd. C 73.50, H 7.89, N 6.86; found C 73.46, H 7.61, N 6.89.

Benzyl *rac*-(2*R*,5*S*,6*S*)-5-*tert*-Butoxycarbonylmethyl-2-*tert*-butyl-4-methoxy-6-methyl-5,6-dihydro-2*H*-pyrimidine-1-carboxylate (*rac*-23): The alkylation of *rac*-**8a** (8.85 g, 27.8 mmol) with *tert*-butyl bromoacetate (6.2 mL, 41.7 mmol) was performed according to *GP5*. Purification of the crude product by FC (pentane/Et_2O, 4:1) gave *rac*-**23** (9.94 g, 83%) as a colorless oil. − IR ($CHCl_3$): $\tilde{\nu}$ = 2980 m, 1698 s, 1446 w, 1438 w, 1393 w, 1369 w, 1302 m, 1153 m, 1085 w, 1047 m, 1045 w, 1003 m, 960 w, 910 w, 846 w. − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.98 (s, 9 H, *t*Bu), 1.27 (d, *J* = 6.8, 3 H, Me), 1.40 (s, 9 H, *t*Bu), 2.26−2.35 [m, 2 H, H-C(1′)], 2.52 [br, 1 H, H-C(5)], 3.64 (s, 3 H, MeO), 4.43−4.45 [m, 1 H, H-C(6)], 5.07 (***A**B*, *J* = 12.4, 1 benzylic H), 5.21 (*A**B***, *J* = 12.4, 1 benzylic H), 5.49 [s, 1 H, H-C(2)], 7.27−7.35 (m, 5 arom. H). − ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 22.62 (Me), 27.25 (*t*Bu), 28.00 (*t*Bu), 36.26 (CH_2), 38.09 (CH), 49.20 (CH), 52.36 (Me), 67.34 (CH_2), 75.59 (CH), 80.90 (C), 127.98 (CH), 128.48 (CH), 136.61 (C), 156.82 (C), 159.80 (C), 170.44 (C). − EI-MS; *m/z* (%): 433.3 (1.9) $[M + 1]^+$, 375.2 (88), 359.2 (19), 319.2 (39), 275.2 (100), 91.0 (10). − $C_{24}H_{36}N_2O_5$ (432.56): calcd. C 66.64, H 8.39, N 6.48; found C 66.52, H 8.14, N 6.38.

Benzyl *rac*-(2*R*,5*S*,6*S*)-5-Allyl-2-*tert*-butyl-4-methoxy-6-methyl-5,6-dihydro-2*H*-pyrimidine-1-carboxylate (*rac*-24): The alkylation of *rac*-**8a** (3.20 g, 10.1 mmol) with allyl bromide (2.55 mL, 30.2 mmol) was performed according to *GP5*. Purification of the crude product by FC (pentane/Et_2O, 9:1) gave *rac*-**24** (2.35 g, 65%) as a colorless oil. − IR (film): $\tilde{\nu}$ = 2978 m, 1702 s, 1439 w, 1385 w, 1336 w, 1200 w, 1190 m, 1098 w, 1001 m, 917 w, 775 w, 698 m. − ^{1}H NMR ($CDCl_3$, 400 MHz) 2 conformers: δ = 0.98 (s, 9 H, *t*Bu), 1.18 (d, *J* = 6.3, 3 H, Me), 2.12 [br, 3 H, H-C(5), 2 allylic H), 3.66 (s, 3 H, MeO), 4.48, 4.61 [br, 1 H, H-C(6)], 4.88, 4.97, 5.13, 5.24, 5.40, 5.45, 5.65 [br, 6 H, 2 benzylic H, H_2C=, HC=, H-C(2)], 7.27−7.38 (m, 5 arom. H). − ^{1}H NMR ([D_6]DMSO, 300 MHz, 90°C): δ = 0.92 (s, 9 H, *t*Bu), 1.11 (d, *J* = 7.2, 3 H, Me), 1.96−2.16 [m, 3 H, H-C(5), 2 allylic H], 3.60 (s, 3 H, MeO), 4.42 [q, *J* = 7.2, 1 H, H-C(6)], 4.87−4.94 (m, 2 H, H_2C=), 5.04 (***A**B*, *J* = 12.5, 1 benzylic H), 5.13 (*A**B***, *J* = 12.5, 1 benzylic H), 5.31 [s, 1 H, H-C(2)], 5.55−5.67 (m, 1 H, HC=), 7.29−7.35 (m, 5 arom. H). − ^{13}C NMR ($CDCl_3$, 100 MHz) 2 conformers: δ = 23.01 (Me), 27.24 (*t*Bu), 35.26 (CH_2), 38.17 (C), 42.00 (CH), 47.88 (CH), 52.19 (Me), 67.16 (CH_2), 75.20 (CH), 117.19 (CH_2), 128.02 (CH), 128.12 (CH), 128.46 (CH), 135.03 (CH), 136.55, 136.80 (C), 157.14 (C), 160.40, 161.00 (C). − EI-MS; *m/z* (%): 359.2 (1.6) $[M + 1]^+$, 301.2 (92),

257.2 (99), 91.0 (100). − $C_{21}H_{30}N_2O_3$ (358.48): calcd. C 70.36, H 8.43, N 7.81; found C 70.35, H 8.52, N 7.72.

Benzyl *rac*-(2*R*,5*S*,6*S*)-2-*tert*-Butyl-5-ethyl-4-methoxy-6-methyl-5,6-dihydro-2*H*-pyrimidine-1-carboxylate (*rac*-25): The alkylation of *rac*-**8a** (3.20 g, 10.1 mmol) with EtI (2.43 mL, 30.2 mmol) was performed according to *GP5*. Purification of the crude product by FC (pentane/Et_2O, 9:1) gave *rac*-**25** (2.82 g, 81%) as a colorless oil. − IR (film): $\tilde{\nu}$ = 2959 m, 1700 s, 1458 w, 1385 m, 1297 m, 1212 m, 1104 w, 1046 w, 1000 m, 899 w, 776 w, 698 m. − ^{1}H NMR ($CDCl_3$, 400 MHz) 2 conformers: δ = 0.80, 0.90, 0.97, 1.17, 1.37 [br, 17 H, *t*Bu, 2 Me, 2 H-C(1′)], 1.87, 1.94 [br, 1 H, H-C(5)], 3.66 (s, 3 H, MeO), 4.49, 4.66 [br, 1 H, H-C(6)], 5.08, 5.22, 5.40 (*br*, 3 H, 2 benzylic H, H-C(2)], 7.27−7.38 (m, 5 arom. H). − ^{1}H NMR ([D_6]DMSO, 300 MHz, 90°C): δ = 0.77 (t, *J* = 7.5, 3 H, Me), 0.92 (s, 9 H, *t*Bu), 1.11 (d, *J* = 7.2, 3 H, Me), 1.21−1.34 [m, 2 H, H-C(1′)], 1.93−1.97 [m, *J* = 4.7, 1 H, H-C(5)], 3.60 (s, 3 H, MeO), 4.63−4.46 [q, 1 H, H-C(6)], 5.10 (s, 2 benzylic H), 5.29 [s, 1 H, H-C(2)], 7.26−7.35 (m, 5 arom. H). − ^{13}C NMR ($CDCl_3$, 100 MHz) 2 conformers: δ = 11.87 (Me), 22.98 (Me), 24.03 (CH_2), 27.22 (*t*Bu), 38.10 (C), 43.97 (CH), 48.12 (CH), 52.09 (Me), 67.18 (CH_2), 74.94, 75.18 (CH), 128.03 (CH), 128.17 (CH), 128.45 (CH), 137.35, 137.80 (C), 157.25, 157.60 (C), 161.29, 161.90 (C). − EI-MS; *m/z* (%): 347.3 (0.9) [M + 1]$^+$, 289.2 (76), 245.2 (100). − $C_{20}H_{30}N_2O_3$ (346.47): calcd. C 69.33, H 8.73, N 8.09; found C 69.15, H 8.48, N 7.96.

Benzyl *rac*-(2*R*,5*S*,6*S*)-2-*tert*-Butyl-4-methoxy-6-methyl-5-(methylethyl)-5,6-dihydro-2*H*-pyrimidine-1-carboxylate (*rac*-26): The alkylation of *rac*-**8a** (3.50 g, 11.0 mmol) with isoproyl iodide (3.3 mL, 33.0 mmol) was performed according to *GP5*. Purification of the crude product by FC (pentane/Et_2O, 9:1) gave *rac*-**26** (0.35 g, 9%) as a colorless oil. − IR (film): $\tilde{\nu}$ = 2956 s, 1682 s, 1463 m, 1392 m, 1325 m, 1191 m, 1095 w, 1001 w, 906 w, 878 w, 775 w, 698 m. − ^{1}H NMR ($CDCl_3$, 400 MHz) 2 conformers: δ = 0.74−0.81 (m, 6 H, 2 Me), 0.95, 0.99 (s, 9 H, *t*Bu), 1.14, 1.18 (d, *J* = 7.1, 3 H, Me), 1.51−1.79 [m, 2 H, H-C(5), H-C(1′)], 3.66 (s, 3 H, MeO), 4.57−4.63, 4.75−4.80 [m, 1 H, H-C(6)], 5.02, 5.10 (***AB***, J_{AB}(1) = 12.3, J_{AB}(2) = 12.2, 1 benzylic H), 5.20, 5.29 (*A**B***, J_{AB}(2) = 12.2, J_{AB}(1) = 12.3, 1 benzylic H), 5.32, 5.37 [s, 1 H, H-C(2)], 7.27−7.38 (m, 5 arom. H). − ^{13}C NMR ($CDCl_3$, 100 MHz) 2 conformers: δ = 20.52, 20.64 (Me), 20.69 (Me), 23.61, 23.67 (Me), 27.18, 27.36 (*t*Bu), 29.36, 29.78 (CH), 37.88, 38.30 (C), 46.58, 46.80 (CH), 49.05, 49.26 (CH), 51.82, 51.91 (Me), 67.17, 67.28 (CH_2), 74.79, 75.14 (CH), 128.00, 128.08 (CH), 128.15, 128.33 (CH), 128.42, 128.48 (CH), 136.45, 136.74 (C), 157.08, 157.38 (C), 160.65, 161.16 (C). − EI-MS; *m/z* (%): 361.2 (0.3) [M + 1]$^+$, 303.1 (61), 259.1 (75), 91.0 (100), 48.9 (11). − $C_{21}H_{32}N_2O_3$ (360.50): calcd. C 69.97, H 8.95, N 7.77; found C 69.99, H 8.76, N 7.99.

Benzyl *rac*-(1′*R*,2*R*,5*S*,6*S*)- and *rac*-(1′*S*,2*R*,5*S*,6*S*)-2-*tert*-Butyl-4-methoxy-6-methyl-5-(1-phenylethyl)-5,6-dihydro-2*H*-pyrimidine-1-Δcarboxylate (*rac*-27a and *rac*-27b): The alkylation of *rac*-**8a** (3.20 g, 10.1 mmol) with (3.3 mL, 33.0 mmol) was performed according to *GP5*. Purification of the crude product and separation of the diastereoisomers in a ratio of 1.3:1 by FC (pentane/Et_2O,, 9:1) gave *rac*-**27a** (1.31 g, 31%) and *rac*-**27b** (0.94 g, 22%) as colorless oils.

rac-**27a**: IR ($CHCl_3$): $\tilde{\nu}$ = 2979 m, 1695 s, 1454 w, 1392 w, 1363 w, 1325 m, 1302 m, 1177 w, 1098 w, 1068 w, 998 m. − ^{1}H NMR ($CDCl_3$, 400 MHz) 2 conformers: δ = 0.92, 0.99 (s, 9 H, *t*Bu), 1.03−1.22 (m, 6 H, 2 Me), 2.11, 2.19 (*d*, *J* = 6.9, 6.3, 1 H, H-C(5)], 2.81−2.92 [m, 1 H, H-C(1′)], 3.40, 3.45 (s, 3 H, MeO), 4.56, 4.78 [q, *J* = 7.0, 7.1, H-C(6)], 5.03, 5.10 (***AB***, *J* = 12.3, 12.2, 1 benzylic H), 5.24−5.46 [m, 1 benzylic H, H-C(2)], 7.02−7.42 (m, 10 arom. H). − ^{13}C NMR ($CDCl_3$, 100 MHz) 2 conformers: δ = 16.75, 17.56 (Me), 23.78, 23.94 (Me), 27.22, 27.40 (*t*Bu), 37.80, 38.27 (C), 40.52, 41.35 (CH), 46.03, 46.45 (CH), 49.27, 49.36 (CH), 51.81, 51.90 (Me), 67.24 (CH_2), 74.88, 75.27 (CH), 126.35, 127.48, 127.60, 128.02, 128.13, 128.17, 128.43, 128.54 (6 CH), 136.44, 136.69 (C), 143.52, 143.61 (C), 156.69, 157.07 (C), 159.39, 159.92 (C). − EI-MS; *m/z* (%): 423.4 (0.1) [M + 1]$^+$, 365.2 (100), 321.2 (69), 105.1 (16), 91.1 (80), 84.0 (13), 49.1 (11). − $C_{26}H_{34}N_2O_3$ (422.57): calcd. C 73.90, H 8.11, N 6.63; found C 74.05, H 8.20, N 6.60.

rac-**27b**: IR ($CHCl_3$): $\tilde{\nu}$ = 2978 m, 1694 s, 1455 w, 1392 w, 1365 w, 1327 m, 1303 m, 1178 w, 1101 w, 999 m. − ^{1}H NMR ($CDCl_3$, 400 MHz) 2 conformers: δ = 0.93, 0.98 (s, 9 H, *t*Bu), 1.04, 1.06 (d, *J* = 7.1, 3 H, Me), 1.16, 1.19 (d, *J* = 7.1, 3 H, Me), 2.24, 2.31 [d, *J* = 8.8, 10.4, 1 H, H-C(5)], 2.57−2.65 [m, 1 H, H-C(1′)], 3.73, 3.75 (s, 1 H, MeO), 4.26, 4.45 [q, *J* = 6.9, 7.1, 1 H, H-C(6)], 4.78, 4.99 (***AB***, *J* = 12.5, 12.3, 1 benzylic H), 5.20, 5.25 (*A**B***, *J* = 12.3, 12.5, 1 benzylic H), 5.25, 5.46 [s, 1 H, H-C(2)], 7.02−7.41 (m, 10 arom. H). − ^{13}C NMR ($CDCl_3$, 100 MHz) 2 conformers: δ = 20.32, 21.73 (Me), 22.95, 23.35 (Me), 27.04, 27.31 (*t*Bu), 38.02, 38.64 (C), 40.86, 41.05 (CH), 47.02, 48.11 (CH), 48.80, 49.31 (CH), 51.96 (Me), 66.83, 67.15 (CH_2), 74.63, 74.86 (CH), 126.48, 126.55, 127.05, 127.45, 127.74, 127.79, 128.03, 128.25, 128.31, 128.43, 128.66 (6 CH), 136.56 (C), 144.33, 145.09 (C), 157.12, 157.53 (C), 160.51, 160.67 (C). − EI-MS; *m/z* (%): 407.2 (1.4, [M-15]$^+$), 365.2 (100), 321.2 (81), 105.1 (19), 91.1 (94), 84.0 (26). − $C_{26}H_{34}N_2O_3$ (422.57): calcd. C 73.90, H 8.11, N 6.63; found C 73.94, H 8.01, N 6.61.

Benzyl (2*R*,5*S*,6*S*)-2-*tert*-Butyl-4-methoxy-6-methyl-5-(1-phenylethyl)-5,6-dihydro-2*H*-pyrimidine-1-carboxylate (27): The alkylation of (2*R*,6*S*)-**8** (2.00 g, 6.3 mmol) with (1-bromoethyl)benzene (1.80 mL, 13.2 mmol) was performed according to *GP5*. Purification of the crude product and separation of the diastereoisomers by FC (pentane/Et_2O, 9:1) gave **27a** (0.69 g, 26%) and **27b** (0.57 g, 21%) as colorless oils with the same analytical datas as *rac*-**27a** and *rac*-**27b**. (1′*R*,2*R*,5*S*,6*S*)-**27a**: $[\alpha]_D$ = −112.5 (*c* = 1.10, $CHCl_3$). (1′*S*,2*R*,5*S*,6*S*)-**27b**: $[\alpha]_D$ = −50.1 (*c* = 1.14, $CHCl_3$). The assignment of the configuration in 1′-position was made by measurement of the optical rotation of the unreacted (1-bromoethyl)benzene (for the optical rotation of the enantiopure compound see ref.[39]).

Benzyl *rac*-(1′*S*,2*R*,5*S*,6*S*)-2-*tert*-Butyl-5-cyclohex-2-enyl-4-methoxy-6-methyl-5,6-dihydro-2*H*-pyrimidine-1-carboxylate (*rac*-28): The alkylation of *rac*-**8a** (4.02 g, 12.8 mmol) with 3-bromocyclohexene[38] (10.3 g, 64.0 mmol) was performed according to *GP5*. Purification of the crude product by FC (pentane/Et_2O, 9:1) gave *rac*-**28** (4.29 g, 84%, the minor diastereoisomer could not be separated, *dr* = 8:1) as a colorless oil. − IR ($CHCl_3$): $\tilde{\nu}$ = 2944 s, 1694 s, 1438 w, 1393 m, 1364 m, 1302 m, 1178 m, 1082 w, 1002 w, 965 w, 879 m. − ^{1}H NMR ($CDCl_3$, 400 MHz) 2 conformers: δ = 0.73−2.13 (*m*, 8 H), 0.91, 0.93 (s, 9 H, *t*Bu), 1.09 (d, *J* = 7.1, 3 H, Me), 3.60 (s, MeO), 4.44−4.56 [m, 1 H, H-C(6)], 4.96−5.76 [m, 5 H, H-C(2), 2 benzylic H, 2 HC=], 7.21−7.51 (m, 5 arom. H). − ^{1}H NMR ([D_6]DMSO, 500 MHz, 139°C): δ = 0.90−2.23 (m, 7 H), 0.97 (s, 9 H, *t*Bu), 1.15 (d, *J* = 7.0, 3 H, Me), 2.02 (d, *J* = 6.5, 1 H, H-C(5)], 3.65 (s, 3 H, MeO), 4.51−4.58 [m, 1 H, H-C(6)], 5.08 (***AB***, *J* = 12.4, benzylic H), 5.16 (*A**B***, *J* = 12.4, benzylic H), 5.34, 5.38, 5.70, 5.72 [br, H-C(2), 2 HC=), 7.19−7.36 (m, 5 arom. H). − ^{13}C NMR ([D_6]DMSO, 125 MHz, 139°C): δ = 20.52 (CH_2), 22.71 (Me), 23.80 (CH_2), 25.18(CH_2), 26.44 (*t*Bu), 36.56 (CH), 37.03 (C), 45.51 (CH), 45.64 (CH), 50.74 (Me), 65.94 (CH_2), 74.22 (CH), 127.05 (CH), 127.11 (CH), 127.57 (CH), 128.05 (CH), 128.12 (CH), 136.18 (C), 155.58 (C), 159.26 (C). − EI-MS; *m/z* (%): 399.3 (0.1) [M + 1]$^+$, 341.2 (52), 297.3 (36), 91.0 (100), 84.0 (39), 49.0

(45). − $C_{24}H_{34}N_2O_3$ (362.47): calcd. C 72.33, H 8.60, N 7.03; found C 72.33, H 8.41, N 6.86.

Allyl *rac*-(2*R*,5*S*,6*S*)-2-*tert*-Butyl-4-methoxy-5,6-dimethyl-5,6-dihydro-2*H*-pyrimidine-1-carboxylate (*rac*-29): The alkylation of *rac*-**9** (0.50 g, 1.9 mmol) with MeI (0.46 mL, 7.5 mmol) was performed according to *GP5*. Purification of the crude product by FC (pentane/Et_2O, 17:3) gave *rac*-**29** (0.22 g, 42%) as colorless oil. − IR (film): $\tilde{\nu}$ = 2972 s, 1702 s, 1461 m, 1375 m, 1217 m, 1108 w, 1069 w, 994 w, 932 w, 840 w, 776 w. − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.99 (s, 9 H, *t*Bu), 1.08 (d, *J* = 7.1, 3 H, Me), 1.23 (d, *J* = 6.9, 3 H, Me), 2.12−2.18 [m, 1 H, H-C(5)], 3.66 (s, 3 H, MeO), 4.29 [br, 1 H, H-C(6)], 4.61 (br, 2 allylic H), 5.19−5.34 (m, 2 H, H_2C=), 5.45 [s, 1 H, H-C(2)], 5.89−5.99 (m, 1 H, HC=). − ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 16.32 (Me), 22.51 (Me), 27.26 (*t*Bu), 36.54 (CH), 38.10 (C), 51.46 (CH), 52.32 (Me), 66.13 (CH_2), 75.45 (CH), 117.53 (CH_2), 132.99 (CH), 157.13 (C), 162.30 (C). − EI-MS; *m/z* (%): 283.2 (1.0) $[M + 1]^+$, 225.2 (100). − $C_{15}H_{26}N_2O_3$ (282.38): calcd. C 63.80, H 9.28, N 9.92; found C 63.86, H 9.10, N 9.80.

Propenyl *rac*-(2*R*,5*S*,6*S*)-2-*tert*-Butyl-4-methoxy-5,6-dimethyl-5,6-dihydro-2*H*-pyrimidine-1-carboxylate (*rac*-30): The alkylation of *rac*-**9** (1.00 g, 3.7 mmol) with MeI (0.46 mL, 7.5 mmol) was performed according to *GP5*, but a second equiv.equiv. BuLi was added before the addition of MeI. Purification of the crude product by FC (pentane/Et_2O, 17:3) gave *rac*-**30** (0.43 g, 41%) as colorless oil. − IR ($CHCl_3$): $\tilde{\nu}$ = 2975 m, 1715 s, 1462 w, 1363 m, 1330 m, 1217 m, 1191 w, 1072 w, 1028 w, 899 w, 842 w, 773 w, 734 w. − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.02 (s, 9 H, *t*Bu), 1.11 (d, *J* = 7.1, 3 H, Me), 1.28 (d, *J* = 6.9, 3 H, Me), 1.68 (d, *J* = 6.4, 3 H, allylic Me), 2.16−2.22 [m, 1 H, H-C(5)], 3.68 (s, 3 H, MeO), 4.30 [br, 1 H, H-C(6)], 4.75−4.86 (m, 1 H, HC=), 5.51 [s, 1 H, H-C(2)], 6.98 [br, 1 H, HC(O)=]. − ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 10.02 (Me), 14.10 (Me), 22.17 (Me), 27.25 (*t*Bu), 36.51 (CH), 38.10; 51.81 (CH), 52.41 (Me), 75.60 (CH), 105.96 (CH), 135.88 (CH), 154.57 (C), 162.69 (C). − EI-MS; *m/z* (%): 283.3 (0.53) $[M + 1]^+$, 267.2 (3), 239.2 (6), 225.2 (100), 141.2 (7), 101.1 (4). − $C_{15}H_{26}N_2O_3$ (282.38): calcd. C 63.80, H 9.28, N 9.92; found C 63.78, H 9.12, N 9.74.

Benzyl (2*R*,5*S*,6*S*)-5-Benzyl-2-*tert*-butyl-6-isobutyl-4-methoxy-5,6-dihydro-2*H*-pyrimidine-1-carboxylate (31): The alkylation of (2*R*,6*S*)-**10** (2.00 g, 5.6 mmol) with benzyl bromide (1.98 mL, 16.6 mmol) was performed according to *GP5*. Purification of the crude product by FC (pentane/Et_2O, 9:1) gave **31** (1.95 g, 78%) as a colorless oil. − $[\alpha]_D$ = −27.6° (*c* = 1.05, $CHCl_3$). − IR ($CHCl_3$): $\tilde{\nu}$ = 2956 s, 2870 w, 1685 s, 1496 w, 1454 w, 1438 w, 1391 m, 1367 m, 1301 m, 1178 w, 1086 w, 1029 w, 964 m. − ^{1}H NMR ($CDCl_3$, 400 MHz) 2 conformers: δ = 0.58, 0.67 (d, *J* = 6.2, 6.0, 3 H, Me), 0.73, 0.86 (d, *J* = 6.2, 5.9, 3 H, Me), 0.96, 1.00 (s, 9 H, *t*Bu), 1.03−1.09 [m, 1 H, H-C(2″)], 1.24−1.37 [m, 2 H, H-C(1″)], 2.26−2.30 [m, 1 H, H-C(5)], 2.35−2.42 [m, 1 H, H-C(1′)], 2.71−2.80 3.66 (s, 3 H, MeO), 4.26−4.29, 4.52−4.55 [m, 1 H, H-C(6)], 5.04, 5.08 (***AB***, *J* = 12.2, 1 benzylic H), 5.18, 5.32 (***AB***, *J* = 12.2, 1 benzylic H), 5.39, 5.53 [s, 1 H, H-C(2)], 6.99−7.39 (m, 10 arom. H). − ^{13}C NMR ($CDCl_3$, 100 MHz) 2 conformers: δ = 21.80 (Me), 22.63, 22.74 (Me), 24.97, 25.29 (CH), 27.10, 27.28 (*t*Bu), 36.91, 37.29 (CH_2), 37.76, 38.20 (C), 42.62, 43.11 (CH), 45.33 (CH_2), 49.84 (CH), 52.18 (Me), 67.32, 67.44 (CH_2), 74.87, 75.16 (CH), 126.36, 128.05, 128.326, 128.35, 128.39, 128.47, 128.87, 129.27 (6 CH), 136.36, 136.52 (C), 138.79 (C), 157.55, 157.69 (C), 160.32, 160.78 (C). − EI-MS; *m/z* (%): 483.2 (0.4) $[M + 33]^+$, 393.1 (43), 349.1 (47), 91.0 (100), 85.9 (27), 83.9 (44), 49.0 (44). − $C_{28}H_{38}N_2O_3$ (450.62): calcd. C 74.63, H 8.50, N 6.22; found C 74.73, H 8.35, N 6.13.

Aldol Additions (32−38)

Benzyl *rac*-(1′*R*,2*R*,5*R*,6*S*)- and *rac*-(1′*S*,2*R*,5*R*,6*S*)-2-*tert*-Butyl-5-(1-hydroxy-ethyl)-4-methoxy-6-methyl-5,6-dihydro-2*H*-pyrimidine-1-carboxylate (*rac*-32a and *rac*-32b): The aldol addition of *rac*-**8a** (4.00 g, 12.6 mmol) to acetaldehyde (1.42 mL, 25.1 mmol) according to *GP6* gave after purification of the crude product and separation of the diasteroisomers (*dr* = 3:1) by FC (pentane/Et_2O, 1:1) *rac*-**32a** (2.38 g, 52%) as a white solid and *rac*-**32b** (0.74 g, 16%) as colorless oil.

rac-**32a**: M.p. 84−86°C. − IR ($CHCl_3$): $\tilde{\nu}$ = 3455 s, 2976 s, 1698 s, 1391 m, 1327 m, 1212 m, 1105 w, 1009 w, 912 m, 776 w, 698 m. − ^{1}H NMR ($CDCl_3$, 400 MHz) 2 conformers: δ = 0.98 (s, 9 H, *t*Bu), 1.17 (br, 3 H, Me), 1.21 (d, *J* = 6.7, 3 H, Me), 1.63, 1.83, 2.06, 2.10 [br, 2 H, H-C(5), HO), 3.70 (s, 3 H, MeO), 3.76, 3.82 [br, 1 H, H-C(1′)], 4.65, 4.83, 5.07, 5.22, 5.39, 5.44 [br, 4 H, H-C(6), 2 benzylic H, H-C(2)], 7.28−7.36 (m, 5 arom. H). − ^{1}H NMR ([D_6]DMSO, 300 MHz, 90°C): δ = 0.86 (d, *J* = 6.2, 3 H, Me), 0.91 (s, 9 H, *t*Bu), 1.11 (d, *J* = 6.8, 3 H, Me), 2.11 [d, *J* = 4.7, 1 H, H-C(5)], 3.60 (s, 3 H, MeO), 3.78−3.89 [m, 1 H, H-C(1′)], 4.46 (br, 1 H, HO), 4.63−4.73 [m, 1 H, H-C(6)], 5.04 (***AB***, *J* = 12.6, 1 benzylic H), 5.14 (***AB***, *J* = 12.6, 1 benzylic H), 5.31 [s, 1 H, H-C(2)], 7.28−7.35 (m, 5 arom. H). − ^{13}C NMR ($CDCl_3$, 100 MHz) 2 conformers: δ = 21.24, 21.52 (Me), 23.70, 23.86 (Me), 27.26, 27.35 (*t*Bu), 37.73, 38.10 (C), 46.15 (CH), 49.04 (CH), 52.34 (Me), 67.25, 67.46 (CH_2), 68.40, 68.73 (CH), 75.22, 75.42 (CH), 128.12 (CH), 128.27 (CH), 128.49 (CH), 136.32, 136.75 (C), 156.61, 157.34 (C), 158.25, 158.84 (C). − EI-MS; *m/z* (%): 363.3 (1.2) $[M + 1]^+$, 305.2 (52), 261.2 (38), 217.2 (14), 100.1 (28), 91.0 (100). − $C_{20}H_{30}N_2O_4$ (362.47): calcd. C 66.27, H 8.34, N 7.73; found C 66.35, H 8.08, N 7.66.

rac-**32b**: IR (film): $\tilde{\nu}$ = 3554 s, 2976 s, 1695 s, 1456 w, 1391 m, 1325 m, 1188 m, 1101 w, 1002 w, 913 m, 777 w, 698 m. − ^{1}H NMR ($CDCl_3$, 400 MHz) 2 conformers: δ = 0.98 (s, 9 H, *t*Bu), 1.05, 1.16 (br, 3 H, Me), 1.18 (d, *J* = 7.1, 3 H, Me), 1.58, 2.01, 2.05, 5.06, 2.88 [br, 2 H, H-C(5), HO], 3.38, 3.49 [br, 1 H, H-C(1′)], 3.68 (s, 3 H, MeO), 4.70, 4.76, 4.92, 5.08, 5.11, 5.24, 5.27, 5.41 [br, 4 H, H-C(6), 2 benzylic H, H-C(2)], 7.27−7.37 (m, 5 arom. H). − ^{1}H NMR ([D_6]DMSO, 300 MHz, 90°C): δ = 0.91 (s, 9 H, *t*Bu), 1.04 (d, *J* = 6.2, 3 H, Me), 1.08 (d, *J* = 7.2, 3 H, Me), 1.91 [d, *J* = 7.2, 1 H, H-C(5)], 3.43−3.54 [m, 1 H, H-C(1′)], 3.61 (s, 3 H, MeO), 4.42 (br, 1 H, HO), 4.87−4.90 [m, 1 H, H-C(6)], 5.01 (***AB***, *J* = 12.6, 1 benzylic H), 5.13 (***AB***, *J* = 12.6, 1 benzylic H), 5.26 [s, 1 H, H-C(2)], 7.28−7.39 (m, 5 arom. H). − ^{13}C NMR ($CDCl_3$, 100 MHz) 2 conformers: δ = 20.71, 21.32 (Me), 22.24, 22.93 (Me), 27.14, 27.49 (*t*Bu), 37.52, 38.13 (C), 45.29, 45.86 (CH), 50.11, 51.08 (CH), 52.24 (Me), 66.41, 66.95 (CH), 67.29, 68.01 (CH_2), 75.51, 75.84 (CH), 128.28 (CH), 128.35 (CH), 128.57 (CH), 136.08, 136.76 (C), 157.06 (C), 158.47, 159.59 (C). − EI-MS; *m/z* (%): 363.2 (0.4) $[M + 1]^+$, 305.1 (52), 261.1 (53), 217.1 (27), 153.1 (16), 91.0 (100), 84.0 (40), 49.0 (17). − $C_{20}H_{30}N_2O_4$ (362.47): calcd. C 66.27, H 8.34, N 7.73; found C 66.37, H 8.23, N 7.76.

Benzyl *rac*-(1′*R*,2*R*,5*R*,6*S*)- and *rac*-(1′*S*,2*R*,5*R*,6*S*)-2-*tert*-Butyl-4-methoxy-6-methyl-5-(1-hydroxy-2-methylpropyl)-5,6-dihydro-2*H*-pyrimidine-1-carboxylate (*rac*-33a and *rac*-33b): The aldol addition of *rac*-**8a** (3.20 g, 10.1 mmol) to isobutyraldehyde (2.75 mL, 30.2 mmol) according to *GP6* gave after purification of the crude product and separation of the diasteroisomers (*dr* = 4:1) by FC (pentane/Et_2O, 3:1) *rac*-**33a** (2.05 g, 52%) and *rac*-**33b** (0.83 g, 21%) as white solids.

rac-**33a**: M.p. 60−62°C. − IR ($CHCl_3$): $\tilde{\nu}$ = 3595 w, 2959 m, 1697 s, 1458 w, 1389 m, 1328 m, 1178 w, 1101 w, 1036 w, 998 m, 925 w. − ^{1}H NMR ($CDCl_3$, 400 MHz) 2 conformers: δ = 0.84 (br, 6 H,

2 Me), 0.98 (s, 9 H, *t*Bu), 1.18 (d, *J* = 7.0, 3 H, Me), 1.44, 1.62, 1.68, 1.85 [br, 2 H, HO, H-C(2′)], 2.20 [br, 1 H, H-C(5)], 3.13, 3.25 [br, H-C(1′)], 3.71 (s, 3 H, MeO), 4.55, 4.78, 5.04, 5.26, 5.38 [br, 4 H, H-C(6), 2 benzylic H, H-C(2)], 7.28−7.38 (m, 5 arom. H). − ^{1}H NMR ([D$_6$]DMSO, 300 MHz, 90°C): δ = 0.74 (d, *J* = 6.8, 3 H, Me), 0.78 (d, *J* = 6.9, 3 H, Me), 0.92 (s, 9 H, *t*Bu), 1.09 (d, *J* = 7.1, 3 H, Me), 1.59−1.66 [m, 1 H, H-(2′)], 2.16 [d, *J* = 5.6, 1 H, H-C(5)], 3.12−3.18 [m, 1 H, H-C(1′)], 3.60 (s, 3 H, MeO), 4.16 (br, 1 H, HO), 4.52−4.55 [m, 1 H, H-C(6)], 5.03 (***A****B*, *J* = 12.5, 1 benzylic H), 5.12 (*A****B***, *J* = 12.5, 1 benzylic H), 5.29 [s, 1 H, H-C(2)], 7.28−7.35 (m, 5 arom. H). − ^{13}C NMR (CDCl$_3$, 100 MHz) 2 conformers: δ = 16.28 (Me), 19.67 (Me), 23.28 (Me), 27.31 (*t*Bu), 31.23 (CH), 38.09 (C), 45.16, 45.52 (CH), 47.88 (CH), 52.27 (Me), 67.35 (CH$_2$), 75.27, 75.66 (CH), 77.60 (CH), 128.14 (CH), 128.50 (CH), 136.22, 136.89 (C), 156.73, 157.67 (C), 158.29, 159.12 (C). − EI-MS; *m/z* (%): 391.3 (0.3) [M + 1]$^+$, 333.2 (76), 289.2 (18), 261.1 (86), 217.1 (100), 153.1 (18), 91.0 (78). − $C_{22}H_{34}N_2O_4$ (390.52): calcd. C 67.66, H 8.78, N 7.17; found C 67.72, H 8.57, N 7.11.

rac-**33b**: M.p. 102−104°C. − IR (CHCl$_3$): ṽ = 3585 w, 2964 m, 1692 s, 1462 w, 1393 m, 1326 m, 1303 w, 1178 w, 1097 w, 1067 w, 999 m, 925 w. − ^{1}H NMR (CDCl$_3$, 400 MHz) 2 conformers: δ = 0.75−0.97 (m, 6 H, 2 Me), 0.99 (s, 9 H, *t*Bu), 1.15 (br, 3 H, Me), 1.50, 1.65, 2.09, 2.22, 2.24, 2.46, 2.51 [br, 3 H, HO, H-C(5), H-C(2′)], 2.98 [br, 1 H, H-C(1′)], 3.66 (s, 3 H, MeO), 4.85−5.51 [br, 4 H, H-C(6), 2 benzylic H, H-C(2)], 7.28−7.44 (m, 5 arom. H). − ^{1}H NMR ([D$_6$]DMSO, 300 MHz, 90°C): δ = 0.80 (d, *J* = 6.9, 3 H, Me), 0.85 (d, *J* = 6.5, 3 H, Me), 0.91 (s, 9 H, *t*Bu), 1.08 (d, *J* = 7.2, 3 H, Me), 1.51−1.58 [m, 1 H, H-(2′)], 2.08 [d, *J* = 6.2, 1 H, H-C(5)], 3.08−3.14 [m, H-C(1′)], 3.61 (s, 3 H, MeO), 4.30 (br, 1 H, HO), 4.83−4.91 [m, 1 H, H-C(6)], 5.01 (***A****B*, *J* = 12.9, 1 benzylic H), 5.14 (*A****B***, *J* = 12.9, 1 benzylic H), 5.26 [s, 1 H, H-C(2)], 7.27−7.38 (m, 5 arom. H). − ^{13}C NMR (CDCl$_3$, 100 MHz) 2 conformers: δ = 15.20 (Me), 20.39, 20.63 (Me), 22.31, 22.72 (Me), 27.15, 27.49 (*t*Bu), 30.43 (CH), 37.22, 38.13 (C), 45.13, 45.62 (CH), 46.73, 47.13 (CH), 52.18 (Me), 67.08, 67.74 (CH$_2$), 74.11, 74.28 (CH), 75.35, 75.75 (CH), 128.29 (CH), 128.56 (CH), 128.71 (CH), 136.33, 136.98 (C), 157.32, 158.62 (C), 158.85, 159.94 (C). − EI-MS; *m/z* (%): 391.3 (0.1) [M + 1]$^+$, 333.2 (55), 289.2 (19), 261.1 (66), 217.1 (82), 153.0 (12), 100.0 (13), 91.0 (100). − $C_{22}H_{34}N_2O_4$ (390.52): calcd. C 67.66, H 8.78, N 7.17; found C 67.69, H 8.64, N 7.37.

Benzyl *rac*-(1′*S*,2*R*,5*R*,6*S*)-2-*tert*-Butyl-5-(1-hydroxy-2,2-dimethylpropyl)-4-methoxy-6-methyl-5,6-dihydro-2*H*-pyrimidine-1-carboxylate (*rac*-34): The aldol addition of *rac*-**8a** (2.89 g, 9.1 mmol) to pivalaldehyde (4.0 mL, 36.3 mmol) according to *GP5* gave after purification of the crude product (*dr* = 96:4) by FC (pentane/Et$_2$O,, 7:3) and recrystallization (pentane) *rac*-**34** (2.20 g, 60%) as a white solid, m.p. 98−99°C. − IR (CHCl$_3$): ṽ = 3587 w, 2960 m, 1697 s, 1462 w, 1391 m, 1324 m, 1178 w, 1101 w, 1069 m, 1004 m, 914 w. − ^{1}H NMR (CDCl$_3$, 400 MHz) 2 conformers: δ = 0.79, 0.91 (s, 9 H, *t*Bu), 0.97, 1.01 (s, 9 H, *t*Bu), 1.14 (br, 3 H, Me), 1.40−1.48 (br, 1 H, HO), 2.25, 2.31 [br, 1 H, H-C(5)], 2.98, 3.14 [br, H-C(1′)], 3.68 (s, 3 H, MeO), 4.44, 4.72 [br, 1 H, H-C(6)], 4.97−5.07 (m, 1 benzylic H), 5.27−5.45 [m, 1 benzylic H, H-C(2)], 7.28−7.40 (m, 5 arom. H). − ^{1}H NMR ([D$_6$]DMSO, 300 MHz, 90°C): δ = 0.79 (s, 9 H, *t*Bu), 0.93 (s, 9 H, *t*Bu), 1.05 (d, *J* = 7.2, 3 H, Me), 2.24 [d, *J* = 4.7, 1 H, H-C(5)], 3.01 [br, 1 H, H-C(1′)], 3.58 (s, 3 H, MeO), 4.08 (d, *J* = 6.2, 1 H, HO), 4.42 [br, 1 H, H-C(6)], 5.07 (***A****B*, *J* = 12.5, 1 benzylic H), 5.14 (*A****B***, *J* = 12.5, 1 benzylic H), 5.30 [s, H-C(2)], 7.28−7.37 (m, 5 arom. H). − ^{13}C NMR (CDCl$_3$, 100 MHz) 2 conformers: δ = 22.46, 22.66 (Me), 25.41 (*t*Bu), 27.29, 27.46 (*t*Bu), 36.12 (C), 37.69, 38.12 (C), 44.45, 44.75 (CH), 50.14 (CH), 52.08 (Me), 67.18, 67.38 (CH$_2$), 75.15, 75.54 (CH), 79.51 (CH), 128.20 (CH), 128.46 (CH), 128.59 (CH), 136.40, 136.60 (C), 157.00, 158.22 (C), 158.24, 158.80 (C). − EI-MS; *m/z* (%): 405.3 (2.1) [M + 1]$^+$, 347.2 (100), 303.3 (10), 261.1 (6), 217.1 (8), 91.1 (5). − $C_{23}H_{36}N_2O_4$ (404.55): calcd. C 68.29, H 8.97, N 6.92; found C 68.12, H 8.74, N 6.90.

Benzyl (1′*S*,2*R*,5*R*,6*S*)-2-*tert*-Butyl-5-(1-hydroxy-2,2-dimethylpropyl)-methoxy-6-methyl-5,6-dihydro-2*H*-pyrimidine-1-carboxylate (34): The aldol addition of (2*R*,6*S*)-**8** (3.00 g, 9.4 mmol) to pivalaldehyde (3.1 mL, 28.3 mmol) according to *GP6* gave after purification of the crude product (*dr* = 96:4) by FC (pentane/Et$_2$O, 7:3) and recrystallization (pentane) **34** (2.44 g, 64%) as a white solid, m.p. 74−76°C. − $[\alpha]_D$ = −126.2 (*c* = 1.07, CHCl$_3$). − IR (CHCl$_3$): ṽ = 3589 w, 2960 m, 1697 s, 1463 w, 1391 m, 1324 s, 1178 w, 1102 w, 1004 m, 914 w. − ^{1}H NMR (CDCl$_3$, 400 MHz) 2 conformers: δ = 0.79, 0.91 (s, 9 H, *t*Bu), 0.97, 1.01 (s,9 H, *t*Bu), 1.14 (br, 3 H, Me), 1.40−1.48 (br, 1 H, HO), 2.25, 2.31 [br, 1 H, H-C(5)], 2.97, 3.14 [br, 1 H, H-C(1′)], 3.68 (s, 3 H, MeO), 4.44, 4.72 [br, 1 H, H-C(6)], 4.97−5.08 (m, 1 benzylic H), 5.27−5.43 [m, 2 H, 1 benzylic H, H-C(2)], 7.30−7.40 (m, 5 arom. H). − ^{1}H NMR ([D$_6$]DMSO, 300 MHz, 90°C): δ = 0.79 (s, 9 H, *t*Bu), 0.93 (s, 9 H, *t*Bu), 1.05 (d, *J* = 7.2, 3 H, Me), 2.24 [d, *J* = 4.4, 1 H, H-C(5)], 3.01 [br, 1 H, H-C(1′)], 3.57 (s, 3 H, MeO), 4.14 (d, *J* = 6.2, 1 H, HO), 4.41 [br, 1 H, H-C(6)], 5.02 (***A****B*, *J* = 12.3, 1 benzylic H), 5.14 (*A****B***, *J* = 12.3, 1 benzylic H), 5.29 [s, 1 H, H-C(2)], 7.27−7.36 (m, 5 arom. H). − ^{13}C NMR (CDCl$_3$, 100 MHz) 2 conformers: δ = 22.46, 22.66 (Me), 25.39 (*t*Bu), 27.28, 27.47 (*t*Bu), 36.07 (C), 37.68, 38.12 (C), 44.44, 44.74 (CH), 50.15 (CH), 52.09 (Me), 67.18, 67.38 (CH$_2$), 75.14, 75.54 (CH), 79.51 (CH), 128.06, 128.20 (CH), 128.47 (CH), 128.60 (CH), 136.47, 136.75 (C), 157.01, 158.10 (C), 158.23, 158.71 (C). − EI-MS; *m/z* (%): 404.3 (0.02, M$^+$), 347.2 (24), 261.1 (13), 217.2 (19), 153.1 (12), 100.1 (13), 91.1 (81), 86.0 (60), 84.0 (95), 51.0 (32), 49.0 (100), 46.9 (15). − $C_{23}H_{36}N_2O_4$ (404.55): calcd. C 68.29, H 8.97, N 6.92; found C 68.49, H 8.97, N 6.90.

Benzyl *rac*-(1′*R*,2*R*,5*R*,6*S*)- and *rac*-(1′*S*,2*R*,5*R*,6*S*)-2-*tert*-Butyl-5-(hydroxyphenylmethyl)-4-methoxy-6-methyl-5,6-dihydro-2*H*-pyrimidine-1-carboxylate (*rac*-35a and *rac*-35b): The aldol addition of *rac*-**8a** (4.00 g, 12.6 mmol) to benzaldehyde (3.8 mL, 37.7 mmol) according to *GP6* gave after purification of the crude product and separation of the diasteroisomers (*dr* = 1.3:1) by FC (pentane/Et$_2$O, 6:4) *rac*-**35a** (2.73 g, 51%) as a colorless oil and *rac*-**35b** (2.42 g, 45%) as a white solid.

35a: M.p. 110−111°C. − IR (CHCl$_3$): ṽ = 3598 w, 2958 m, 1694 s, 1455 w, 1392 m, 1324 m, 1178 w, 1099 w, 1069 m, 1001 m, 912 w. − ^{1}H NMR (CDCl$_3$, 400 MHz) 2 conformers: δ = 0.98 (br, 9 H, *t*Bu), 1.11 (br, 3 H, Me), 1.82, 2.28, 2.36, 2.78 [br, 2 H, HO, H-C(5)], 3.43 (s, 3 H, MeO), 4.48, 4.52 [br, 1 H, H-C(6)], 4.88, 5.01, 5.07, 5.10, 5.25, 5.29, 5.32, 5.42, 5.51 [br, 4 H, 2 benzylic H, H-C(1′), H-C(2)], 7.17−7.40 (m, 10 arom. H). − ^{13}C NMR (CDCl$_3$, 100 MHz) 2 conformers: δ = 22.83, 23.18 (Me), 27.15, 27.45 (*t*Bu), 37.64, 38.19 (C), 45.16, 45.33 (CH), 50.21, 50.76 (CH), 52.01 (Me), 67.19, 67.71 (CH$_2$), 73.26, 73.60 (CH), 75.46 (CH), 125.91, 126.12 (CH), 127.71 (CH), 128.16 (CH), 128.20 (CH), 128.28 (CH), 128.51 (CH), 136.20, 136.95 (C), 141.33, 141.73 (C), 157.23, 157.82 (C), 157.90, 158.75 (C). − EI-MS; *m/z* (%): 425.3 (0.1) [M + 1]$^+$, 261.2 (52), 217.2 (69), 168.2 (19), 153.2 (100), 105.1 (25), 91.1 (70). − $C_{25}H_{32}N_2O_4$ (424.54): calcd. C 70.73, H 7.60, N 6.60; found C 70.64, H 7.68, N 6.59.

rac-**35b**: IR (CHCl$_3$): ṽ = 3596 w, 2957 m, 1694 s, 1455 w, 1392 m, 1326 m, 1304 w, 1177 w, 1071 w, 1002 m, 913 w, 648 w. − ^{1}H NMR (CDCl$_3$, 400 MHz) 2 conformers: δ = 0.95, 0.99 (br, 9 H, *t*Bu), 1.13 (d, *J* = 7.0, 3 H, Me), 2.41−2.50 [m, 2 H, HO, H-C(5)], 3.79

(s, 3 H, MeO), 4.39, 4.64 [br, 2 H, H-C(6), H-C(1′)], 4.96−5.21 (m, 2 benzylic H), 5.26, 5.44 [s, 1 H, H-C(2)], 7.25−7.40 (m, 10 arom. H). − ^{13}C NMR ($CDCl_3$, 100 MHz) 2 conformers: δ = 23.56 (Me), 27.14, 27.35 (*t*Bu), 37.82, 38.36 (C), 45.40, 46.00 (CH), 49.19, 49.69 (CH), 52.50 (Me), 66.98, 67.26 (CH_2), 74.31, 74.51 (CH), 74.87, 75.11 (CH), 126.49 (CH), 127.89 (CH), 127.98 (CH), 128.23 (CH), 128.43 (CH), 128.52 (CH), 136.35, 136.61 (C), 141.31 (C), 156.50, 156.81 (C), 158.10 (C). − EI-MS; *m/z* (%): 425.3 (0.4) $[M + 1]^+$, 367.2 (39), 261.2 (84), 217.1 (99), 168.1 (23), 153.0 (100), 105.0 (16), 91.0 (56). − $C_{25}H_{32}N_2O_4$ (424.54): calcd. C 70.73, H 7.60, N 6.60; found C 70.68, H 7.80, N 6.54.

Benzyl *rac*-(1′*S*,2*R*,5*R*,6*S*)-2-*tert*-Butyl-5-(furan-2-yl-hydroxymethyl)-4-methoxy-6-methyl-5,6-dihydro-2*H*-pyrimidine-1-carboxylate (*rac*-36): The aldol addition of *rac*-**8a** (1.0 g, 3.1 mmol) to 2-furaldehyde (0.78 mL, 9.4 mmol) according to *GP6* gave after purification of the crude product and separation of the diasteroisomers (*dr* = 3:1) by FC (pentane/Et_2O, 6:4) and recrystallization (hexane/Et_2O) *rac*-**36** (0.85 g, 65%) as a white solid, m.p. 110−112°C. − IR ($CHCl_3$): ṽ = 3592 w, 2956 m, 1694 s, 1438 w, 1392 m, 1326 m, 1303 m, 1178 m, 1150 w, 1070 w, 1003 m, 918 w, 884 w. − ^{1}H NMR ($CDCl_3$, 400 MHz) 2 conformers: δ = 0.98 (*br*, 9 H, *t*Bu), 1.11 (d, *J* = 7.1, 3 H, Me), 2.51, 2.61, 2.63 [br, 2 H, HO, H-C(5)], 3.73 (s, 3 H, MeO), 4.46, 4.65 [br, 2 H, H-C(6), H-C(1′)], 5.01, 5.04, 5.11, 5.14, 5.17 (br, 2 benzylic H), 5.35, 5.47 [br, 1 H, H-C(2)], 6.04, 6.16, 6.22 (br, 2 furanyl. H), 7.24−7.41 (m, 6 arom. H). − ^{1}H NMR ([D_6]DMSO, 300 MHz, 90°C): δ = 0.88 (s, 9 H, *t*Bu), 1.13 (d, *J* = 7.2, 3 H, Me), 2.45−2.50 [m, *J* = 4.7, 1 H, H-C(5)], 3.60 (s, 3 H, MeO), 4.56−4.64 [m, 1 H, H-C(6)], 4.71 [dd, *J* = 5.6, 5.3, 1 H, H-C(1′)], 4.91 (***A****B*, *J* = 12.6, 1 benzylic H), 5.06 (*A****B***, *J* = 12.6, 1 benzylic H), 5.18 [s, 1 H, H-C(2)], 5.39 (br, 1 H, HO), 6.08 (d, *J* = 3.2, 1 furanyl. H), 6.24 (dd, *J* = 3.2, 1.9, 1 furanyl. H), 7.28−7.37 (m, 6 arom. H). − ^{13}C NMR ($CDCl_3$, 100 MHz) 2 conformers: δ = 23.43 (Me), 27.16, 27.34 (*t*Bu), 37.78, 38.24 (C), 45.88, 46.15 (CH), 46.86, 47.09 (CH), 52..55 (Me), 67.11, 67.36 (CH_2), 67.93, 68.21 (CH), 75.17 (CH), 107.66 (CH), 110.25 (CH), 128.01 (CH), 128.45 (CH), 136.33, 136.63 (C), 142.32, 142.50 (CH), 153.61 (C), 156.68, 157.03 (C), 157.64, 157.80 (C). − EI-MS; *m/z* (%): 415.2 (1.0) $[M + 1]^+$, 357.1 (49), 261.1 (70), 168.2 (19), 217.1 (72), 100.1 (25), 91.1 (100). − $C_{23}H_{30}N_2O_5$ (414.50): calcd. C 66.65, H 7.29, N 6.76; found C 66.70, H 7.17, N 6.77.

***tert*-Butyl *rac*-(1′*R*,2*S*,5*S*)- and *rac*-(1′*S*,2*S*,5*S*)-2-*tert*-Butyl-5-(1-hydroxy-2,2-dimethylpropyl)-4-methoxy-5,6-dihydro-2*H*-pyrimidine-1-carboxylate (*rac*-37a and *rac*-37b):** The aldol addition of *rac*-**7** (2.72 g, 9.9 mmol) to pivalaldehyde (3.3 mL, 29.7 mmol) according to *GP6* gave after purification of the crude product and separation of the diasteroisomers (*dr* = 92:8) by FC (pentane/Et_2O, 4:1) and recrystallization (pentane/Et_2O) *rac*-**37a** (2.76 g, 78%) and *rac*-**37** (0.19 g, 5%) as white solids.

rac-**37a**: M.p. 98−99°C. − IR ($CHCl_3$): ṽ = 3480 w, 2962 s, 1690 s, 1480 w, 1407 w, 1366 m, 1324 m, 1160 s, 1084 w, 1012 m, 944 m, 863 w. − ^{1}H NMR ($CDCl_3$, 400 MHz) 2 conformers: δ = 0.96 (s, 9 H, *t*Bu), 0.97 (s, 9 H, *t*Bu), 1.48, 1.49 (s, 9 H, *t*Bu), 1.73, 1.83 [d, *J*(1) = 9.5, *J*(2) = 9.4, 1 H, HO], 2.43−2.49 [m, 1 H, H-C(5)], 3.03, 3.14 (*dd*, *J*(1) = 13.7, 3.7, *J*(2) = 14.0, 3.6, 1 H, H-C(6)], 3.29−3.33 [m, 1 H, H-C(1′)], 3.68, 3.69 (s, 3 H, MeO), 4.01, 4.29 [d, *J*(2) = 14.0, *J*(1) = 13.7, 1 H, H-C(6)], 5.27, 5.39 [s, 1 H, H-C(2)]. − ^{13}C NMR ($CDCl_3$, 100 MHz) 2 conformers: δ = 25.46 (*t*Bu), 26.75, 26.96 (*t*Bu), 28.28, 28.49 (*t*Bu), 36.27, 36.36 (C), 38.62, 38.66 (C), 39.06, 39.15 (CH), 41.59, 42.52 (CH_2), 52.15, 52.20 (Me), 73.25, 74.19 (CH), 77.24, 78.16 (CH), 79.87, 80.28 (C);154.70, 156.13 (C), 159.13, 159.86 (C). − EI-MS; *m/z* (%): 357.3 (0.2) $[M + 1]^+$, 243.2 (35), 157.1 (70), 113.1 (56), 86.0 (70), 84.0 (100), 57.1 (48), 50.1 (22), 49.0 (66), 41.0 (15). − $C_{19}H_{36}N_2O_4$ (356.50): calcd. C 64.01, H 10.18, N 7.86; found C 64.09, H 10.31, N 7.83.

rac-**37b**: M.p. 105−107°C. − IR ($CHCl_3$): ṽ = 3472 w, 2964 s, 1692 s, 1652 m, 1479 w, 1394 w, 1367 m, 1306 m, 1165 w, 1054 w, 1002 m, 945 w, 860 w. − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.97 (s, 9 H, *t*Bu), 0.98 (s, 9 H, *t*Bu), 1.48 (s, 9 H, *t*Bu), 2.41−2.43 [m, 1 H, H-C(5)], 3.03 [dd, *J* = 14.5, 4.9, 1 H, H-C(6)], 3.13 (d, *J* = 10.1, 1 H, HO), 3.27 [dd, *J* = 10.1, 4.0, H-C(1′)], 3.65 (s, 3 H, MeO), 4.43 [d, *J* = 14.5, 1 H, H-C(6)], 5.20 [s, 1 H, H-C(2)]. − ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 26.54 (*t*Bu), 26.97 (*t*Bu), 28.38 (*t*Bu), 35.92 (C), 38.12 (CH), 38.29 (CH_2), 38.31 (C), 52.15 (Me), 74.72 (CH), 78.29 (CH), 80.98 (C);157.13 (C), 161.14 (C). − EI-MS; *m/z* (%): 357.3 (12.5) $[M + 1]^+$, 299.2 (44), 243.1 (100), 199.1 (58), 157.0 (43), 113.0 (52). − $C_{19}H_{36}N_2O_4$ (356.50): calcd. C 64.01, H 10.18, N 7.86; found C 63.95, H 10.23, N 7.83.

Allyl *rac*-(1′*S*,2*R*,5*R*,6*S*)-2-*tert*-Butyl-5-(1-hydroxy-2,2-dimethylpropyl)-4-methoxy-6-methyl-5,6-dihydro-2*H*-pyrimidine-1-carboxylate (*rac*-38): The aldol addition of *rac*-**9** (0.70 g, 2.6 mmol) to pivalaldehyde (1.15 mL, 10.4 mmol) according to *GP6* gave after purification of the crude product and separation of the diasteroisomers (*dr* = 96:4) by FC (pentane/Et_2O, 4:1) and recrystallization (pentane/Et_2O) *rac*-**38** (0.40 g, 43%) as a white solid, m.p. 133.5−135.0°C. − IR ($CHCl_3$): ṽ = 3548 w, 2960 m, 1696 s, 1463 w, 1366 m, 1323 m, 1178 w, 1101 w, 1004 w, 936 w. − ^{1}H NMR ($CDCl_3$, 400 MHz) 2 conformers: δ = 0.94 (s, 9 H, *t*Bu), 1.00 (s, 9 H, *t*Bu), 1.11 (d, *J* = 7.1, 3 H, Me), 1.56, 1.72 (br, 1 H, HO), 2.31 [br, 1 H, H-C(5)], 3.12, 3.18 [br, H-C(1′)], 3.70 (s, 3 H, MeO), 4.48, 4.57, 4.66 [br, 3 H, 2 allylic H, H-C(6)], 5.21−5.36 (m, 2 H, H_2C=), 5.38, 5.41 [s, 1 H, H-C(2)], 5.91−6.00 (m, 1 H, HC=). − ^{13}C NMR ($CDCl_3$, 100 MHz) 2 conformers: δ = 22.53 (Me), 25.48 (*t*Bu), 27.27, 27.47 (*t*Bu), 36.22 (C), 37.71, 38.04 (C), 44.76 (CH), 49.84 (CH), 52.12 (Me), 66.18, 66.40 (CH_2), 75.06, 75.40 (CH), 79.04, 79.40 (CH), 117.88, 118.22 (CH_2), 132.69, 133.00 (CH), 156.85, 157.89 (C), 158.38, 158.62 (C). − EI-MS; *m/z* (%): 355.3 (5.8) $[M + 1]^+$, 297.2 (77), 211.1 (100), 167.1 (9), 153.1 (33), 100.1 (9). − $C_{19}H_{34}N_2O_4$ (354.49): calcd. C 64.38, H 9.67, N 7.90; found C 64.50, H 9.56, N 7.89.

Mannich and Michael Additions (39−42)

Benzyl *rac*-(2*R*,5*R*,6*S*)-2-*tert*-Butyl-4-methoxy-6-methyl-5-[phenyl-(trifluoro-methanesulfonylamino)methyl]-5,6-dihydro-2*H*-pyrimidine1-carboxylate (*rac*-39): The addition of *rac*-**8a** (1.00 g, 3.1 mmol) to *N*-benzylidene-*C,C,C*-trifluoromethanesulfonamide[40] (1.49 g, 6.3 mmol) according to *GP6* gave after purification of the crude product (mixture of several diastereoisomers) by FC (pentane/Et_2O, 3:1) and recrystallization (pentane/Et_2O) *rac*-**39** (0.21 g, 12%, single diastereoisomer) as a white solid, m.p. 159−160°C. − IR ($CHCl_3$): ṽ = 3364 m, 2957 m, 1706 s, 1438 w, 1383 m, 1323 m, 1146 w, 1059 w, 1004 m, 923 w. − ^{1}H NMR ($CDCl_3$, 400 MHz) 2 conformers: δ = 0.95, 0.99 (br, 9 H, *t*Bu), 1.10 (br, 3 H, Me), 2.50, 2.52 [br, 1 H, H-C(5)], 3.78 (s, 3 H, MeO), 4.24, 4.36, 4.60 [br, 2 H, H-C(6), H-C(1′)], 5.04, 5.07, 5.24, 5.27, 5.32, 5.58, 5.79, 6.22 [br, 4 H, 2 benzylic H, NH, H-C(2)], 7.08−7.37 (m, 10 arom. H). − ^{1}H NMR ([D_6]DMSO, 300 MHz, 90°C): δ = 0.89 (s, 9 H, *t*Bu), 1.02 (d, *J* = 7.2, 3 H, 3 H, Me), 2.64 [d, *J* = 9.3, 1 H, H-C(5)], 3.71 (s, 9 H, MeO), 4.49, 4.24, 4.27 [m, 2 H, H-C(6), H-C(1′)], 4.82 (***A****B*, *J* = 12.5, 1 benzylic H), 5.16 (*A****B***, *J* = 12.5, 1 benzylic H), 5.27 [s, 1 H, H-C(2)], 7.17−7.35 (m, 10 arom. H). − ^{13}C NMR ($CDCl_3$, 100 MHz) 2 conformers: δ = 23.22 (Me), 27.36 (*t*Bu), 37.78, 38.42 (C), 45.18, 45.98 (CH), 48.17, 49.12 (CH), 52.78 (Me), 59.21 (CH), 67.36, 67.66 (CH_2), 75.06 (CH), 119.34 (CF_3, *J* = 321.2), 126.97 (CH), 128.05 (CH), 128.15 (CH), 128.55 (CH), 128.82 (CH), 136.14 (C), 138.20, 138.59 (C), 156.45 (C), 157.21 (C).

− EI-MS; *m/z* (%): 556.3 (0.1) [M + 1]$^+$, 498.2 (52), 454.2 (54), 217.2 (40), 91.1 (100). − $C_{26}H_{32}F_3N_3O_5S$ (555.62): calcd. C 56.21, H 5.80, N 7.56; found C 56.32, H 5.76, N 7.49.

Benzyl *rac*-(2*R*,5*R*,6*S*)-5-(Allyloxycarbonylaminophenylmethyl)-2-*tert*-butyl-4-methoxy-6-methyl-5,6-dihydro-2*H*-pyrimidine-1-carboxylate (*rac*-40 and 1′-*epi*-*rac*-40): The addition of *rac*-**8a** (1.00 g, 3.1 mmol) to allyl benzylidenecarbamate[41] (1.43 g, 7.5 mmol) according to *GP6* gave after purification of the crude product and separation of the diastereoisomers (*dr* = 1.3:1) by FC (pentane/Et_2O, 3:2) and recrystallization (pentane/Et_2O) *rac*-**40** (0.97 g, 38%) and 1′-*epi*-*rac*-**40** (0.83 g, 33%) as white solids.

rac-**40**: M.p. 107−108.5°C. − IR ($CHCl_3$): ṽ = 3434 w, 2957 m, 1705 s, 1499 m, 1392 w, 1334 m, 1303 m, 1094 m, 1040 m, 1009 m, 936 w. − ^{1}H NMR ($CDCl_3$, 400 MHz) 2 conformers: δ = 0.88, 0.93 (s, 9 H, *t*Bu), 1.17 (d, *J* = 6.4, 3 H, Me), 2.48 [br, 1 H, H-C(5)], 3.64 (s, 3 H, MeO), 4.43−5.87 [m, 10 H, H-C(5), 2 allylic H, H_2C=, 2 benzylic H, H-C(1′), H-C(2), HC=], 6.99 (br, 1 H, HN), 7.10−7.34 (m, 10 arom. H). − ^{13}C NMR ($CDCl_3$, 100 MHz) 2 conformers: δ = 24.14 (Me), 27.20, 27.43 (*t*Bu), 37.52, 38.16 (C), 45.75 (CH), 46.50 (CH), 52.56 (Me), 56.79 (CH), 65.72 (CH_2), 67.20, 67.57(CH_2), 75.16 (CH), 117.82 (CH_2), 126.69 (CH), 127.67 (CH), 128.04 (CH), 128.51 (CH), 132.83 (CH), 135.99, 136.62 (C), 138.92 (C);155.20 (C), 156.66 (C), 156.71, 157.20 (C). − EI-MS; *m/z* (%): 508.2 (0.2) [M + 1]$^+$, 392.1 (51), 348. 2 (56), 261.1 (34), 132.0 (26), 91.0 (100), 84.0 (36), 49.0 (36). − $C_{29}H_{37}N_3O_5$ (507.63): calcd. C 68.62, H 7.35, N 8.28; found C 68.48, H 7.33, N 8.15.

1′-*epi*-*rac*-**40**: M.p. 125−126°C. − IR ($CHCl_3$): ṽ = 3433 w, 2958 m, 1716 s, 1508 m, 1394 m, 1002 m, 928 w. − ^{1}H NMR ($CDCl_3$, 400 MHz) 2 conformers: δ = 0.92, 0.98 (s, 9 H, *t*Bu), 1.09 (d, *J* = 7.0, 3 H, Me), 2.48 [br, 1 H, H-C(5)], 3.74 (s, 3 H, MeO), 4.29−5.55 [m, 10 H, H-C(6), 2 allylic H, H_2C=, 2 benzylic H, H-C(1′), H-C(2), NH], 5.86 (br, 1 H, HC=), 7.16−7.40 (m, 10 arom. H). − ^{1}H NMR ([D$_6$]DMSO, 300 MHz, 90°C): δ = 0.88 (s, 9 H, *t*Bu), 1.01 (d, *J* = 6.8, 3 H, Me), 2.58 [d, *J* = 9.0, 1 H, H-C(5)], 3.64 (s, 3 H, MeO), 4.23 [br, 1 H, H-C(6)], 4.40−5.24 [m, 8 H, 2 allylic H, H_2C=, 2 benzylic H, H-C(1′), H-C(2)], 5.78−5.89 (m, 1 H, HC=), 7.17−7.29 (m, 10 arom. H), 7.48 (br, 1 H, HN). − ^{13}C NMR ($CDCl_3$, 100 MHz) 2 conformers: δ = 23.27 (Me), 27.18, 27.36 (*t*Bu), 37.88, 38.47 (C), 45.64, 46.45 (CH), 47.31, 47.90 (CH), 52.52 (Me), 55.81 (CH), 65.61 (CH_2), 67.16, 67.52 (CH_2), 74.90, 75.13 (CH), 117.68 (CH_2), 127.62 (CH), 127.83 (CH), 127.99 (CH), 128.19 (CH), 128.46 (CH), 128.61 (CH), 132.84 (CH), 136.48 (C), 140.05, 140.43 (C), 155.07 (C), 156.97 (C), 157.74 (C). − EI-MS; *m/z* (%): 507.3 (0.1, M$^+$), 392.1 (100), 348. 1 (73), 261.1 (35), 132.0 (18), 91.0 (68), 44.0 (29), 36.0 (18), 28.0 (20), 18.0 (20). − $C_{29}H_{37}N_3O_5$ (507.63): calcd. C 68.62, H 7.35, N 8.28; found C 68.57, H 7.35, N 8.29.

Benzyl *rac*-(1′*S*,2*R*,5*R*,6*S*)-2-*tert*-Butyl-5-[2-(2,6-di-*tert*-butyl-4-methoxyphenoxycarbonyl)-1-methylethyl]-4-methoxy-6-methyl-5,6-dihydro-2*H*-pyrimidine-1-carboxylate (*rac*-41): After the reaction (6 h) of 2,6-di-*tert*-butyl-4-methoxy-phenyl but-2-encarboxylate[26] (1.08 g, 3.5 mmol) with *rac*-**8a** (1.69 g, 5.3 mmol) according to *GP7*, purification of the crude product (*dr* > 95:5) by FC (pentane/Et_2O, 4:1) and recrystallization (MeOH) gave *rac*-**41** (1.79 g, 81%) as a white solid, m.p. 105−106°C. − IR ($CHCl_3$): ṽ = 2970 s, 1754 s, 1697 s, 1589 m, 1457 w, 1365 w, 1302 m, 1140 m, 1103 m, 1063 w, 1005 w. − ^{1}H NMR ($CDCl_3$, 400 MHz) 2 conformers: δ = 0.85−1.26 [m, 7 H, 2 Me, H-C(1′)], 0.96, 1.01 (s, 9 H, *t*Bu), 1.29, 1.31 (s, 18 H, 2 *t*Bu), 2.15−2.74 [m, 3 H, H-C(5), 2 H-C(2′)], 3.68, 3.69 (s, 3 H, MeO), 3.78 (s, 3 H, MeO), 4.61, 4.80 [br, 1 H, H-C(6)], 5.05, 5.14 (***A****B*, *J* = 12.3, 12.0, 1 benzylic H), 5.17, 5.26 (*A****B***, *J* = 12.0, 12.3, 1 benzylic H), 5.35, 5.41 [s, 1 H, H-C(2)], 6.64−6.99 (m, 2 arom. H), 7.02−7.41 (m, 5 arom. H). − ^{1}H NMR ([D$_6$]DMSO, 300 MHz, 90°C): δ = 0.83 (d, *J* = 6.5, 3 H, Me), 0.93 (s, 9 H, *t*Bu), 1.13 (d, *J* = 7.2, 3 H, Me), 1.22, 1.24 [s, 19 H, 2 *t*Bu, H-C-(1′)], 2.08−2.67 [m, 3 H, H-C(5), 2 H-C(2′)], 3.64 (s, 3 H, MeO), 3.73 (s, 3 H, MeO), 4.62 [br, 1 H, H-C(6)], 5.06 (***A****B*, *J* = 12.4, 1 benzylic H), 5.14 (*A****B***, *J* = 12.4, 1 benzylic H), 5.26 [s, 1 H, H-C(2)], 6.79 (s, 2 arom. H), 7.26−7.34 (m, 5 arom. H). − ^{13}C NMR ($CDCl_3$, 100 MHz) 2 conformers: δ = 17.18, 17.62 (Me), 23.96 (Me), 27.24, 27.40 (*t*Bu), 30.56, 30.80 (CH), 31.36, 31.41 (*t*Bu), 35.52 (C), 37.85, 38.29 (C), 39.87, 40.10 (CH_2), 45.33, 45.68 (CH), 46.02, 46.09 (CH), 52.09, 52.18 (Me), 55.26 (Me), 67.32, 67.43 (CH_2), 74.90, 75.27 (CH), 111.67 (CH), 128.02, 128.14, 128.32, 128.45, 128.58 (3 CH), 136.30, 136.59 (C), 141.48 (C), 143.39, 143.48 (C), 156.25 (C), 156.45, 157.05 (C), 159.72, 160.10 (C), 172.38, 172.64 (C). − FAB-MS; *m/z* (%): 623.2 (68) [M + 1]$^+$, 565.1 (94), 521.2 (100), 515.2 (11), 446.2 (20), 531.1 (13), 387.1 (37), 343.1 (16), 90.8 (45). − $C_{37}H_{54}N_2O_6$ (622.84): calcd. C 71.35, H 8.74, N 4.50; found C 71.26, H 8.77, N 4.55.

Benzyl (1′*S*,2*R*,5*R*,6*S*)-2-*tert*-Butyl-5-[2-(2,6-di-*tert*-butyl-4-methoxyphenoxycarbonyl)-1-methylethyl]-4-methoxy-6-methyl-5,6-dihydro-2*H*-pyrimidine-1-carboxylate (41): After the reaction (6 h) of 2,6-di-*tert*-butyl-4-methoxyphenyl but-2-encarboxylate[26] (2.39 g, 7.9 mmol) with (2*R*,6*S*)-**8** (2.5 g, 7.9 mmol) according to *GP7*, purification of the crude product (*dr* > 95:5) by FC (pentane/Et_2O, 4:1) gave **41** (2.35 g, 48%) as a colorless foam, with the same analytical datas as *rac*-**41**. − $[\alpha]_D$ = −49.5 (*c* = 0.95, $CHCl_3$).

Benzyl (2*R*,5*R*,6*S*)-2-*tert*-Butyl-5-[2-(2,6-di-*tert*-butyl-4-methoxyphenoxycarbonyl)-1-phenylethyl]-4-methoxy-6-methyl-5,6-dihydro-2*H*-pyrimidine-1-carboxylate (42): After the reaction (48 h) of 2,6-di-*tert*-butyl-4-methoxyphenyl 3-phenylacrylate[42] (2.56 g, 5.3 mmol) with (2*R*,6*S*)-**8** (2.5 g, 7.9 mmol) according to *GP7*, purification of the crude product (*dr* > 95:5) by FC (pentane/Et_2O, 4:1) gave **42** (1.09 g, 30%) as a colorless foam. − $[\alpha]_D$ = −82.3 (*c* = 1.17, $CHCl_3$). − IR ($CHCl_3$): ṽ = 3008 w, 2960 m, 1756 s, 1697 s, 1589 m, 1414 w, 1366 w, 1329 m, 1301 m, 1178 w, 1135 m, 1103 m, 1064 w, 999 w. − ^{1}H NMR ($CDCl_3$, 400 MHz) 2 conformers: δ = 0.89−1.25 (m, 3 H, 3 *t*Bu, Me), 2.54, 2.63 (d, *J* = 8.9, 10.8, 1 H), 2.96−329 (m, 3 H), 3.74, 3.75 (s, 3 H, MeO), 3.76, 3.78 (s, 3 H, MeO), 4.31, 4.51 [q, *J* = 7.0, 7.1, 1 H, H-C(6)], 4.62, 4.99 (***A****B*, *J* = 12.5, 12.3, 1 benzylic H), 5.13−5.19 (m, 1 benzylic H), 5.16, 5.49 [s, 1 H, H-C(2)], 6.73−6.80 (m, 2 arom. H), 7.06−7.35 (m, 5 arom. H). − ^{1}H NMR ([D$_6$]DMSO, 300 MHz, 90°C): δ = 0.83 (d, *J* = 6.5, 3 H, Me), 0.93 (s, 9 H, *t*Bu), 1.13 (d, *J* = 7.2, 3 H, Me), 1.22, 1.24 [s, 19 H, 2 *t*Bu, H-C-(1′)], 2.08−2.67 [m, 3 H, H-C(5), 2 H-C(2′)], 3.64 (s, 3 H, MeO), 3.73 (s, 3 H, MeO), 4.62 [br, 1 H, H-C(6)], 5.06 (***A****B*, *J* = 12.4, 1 benzylic H), 5.14 (*A****B***, *J* = 12.4, 1 H, benzylic H), 5.26 [s, 1 H, H-C(2)], 6.79 (s, 2 arom. H), 7.26−7.34 (m, 5 arom. H). − ^{13}C NMR ($CDCl_3$, 100 MHz) 2 conformers: δ = 23.16, 23.58 (Me), 27.09, 27.33 (*t*Bu), 30.96, 31.01 (*t*Bu), 31.24, 21.32 (*t*Bu), 35.17 (C), 35.43 (C), 37.98, 38.67 (C), 39.95, 40.98 (CH_2), 41.74, 41.93 (CH), 46.22, 46.56 (CH), 47.24, 47.37 (CH), 52.09 (Me), 55.22 (Me), 66.72, 67.30 (CH_2), 74.54, 74.77 (CH), 111.58, 111.62 (CH), 127.06, 127.63, 127.70, 127.96, 128.24, 128.33, 128.44, 128.51, 128.60 (8 CH), 136.22, 136.56 (C), 140.81, 141.48 (C), 141.23 (C), 143.29 (C), 143.47, 143.58 (C), 156.16 (C), 156.92, 157.06 (C), 159.50, 159.86 (C), 171.54, 172.07 (C). − FAB-MS; *m/z* (%): 685.5 (72) [M + 1]$^+$, 627.4 (100), 583.4 (47), 508.4 (18), 405.3 (27), 90.9 (59). − $C_{42}H_{56}N_2O_6$ (684.91): calcd. C 73.65, H 8.24, N 4.09; found C 73.69, H 8.38, N 4.25.

Deprotection and Hydrolysis of the Pyrimidine Derivatives (43−58)

Methyl (*R*)-3-*tert*-Butoxycarbonylamino-2-methylpropionate (43): The Boc group of compound **11** (1.09 g, 3.8 mmol) was removed with TMS-OTf (4.2 mL, 23.0 mmol) in CH_2Cl_2 (20 mL) according to *GP8*. Subsequent hydrolysis of the ring, performed in 0.1 N TFA/H_2O (77 mL), and protection of the free amino acid methyl ester with Boc_2O (0.84 g, 3.8 mmol) provided after purification by FC (pentane/Et_2O, 7:3) **43** (0.10 g, 12%) as a colorless oil. − $[\alpha]_D$ = −26.0 (*c* = 1.33, $CHCl_3$). − IR ($CHCl_3$): $\tilde{\nu}$ = 3455 m, 3008 m, 2980 m, 1712 s, 1507 s, 1457 m, 1437 w, 1368 m, 1168 m, 1053 w, 992 w, 928 w, 860 w. − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.17 (d, *J* = 7.2, 3 H, Me), 1.43 (s, 9 H, *t*Bu), 2.64−2.72 [m, 1 H, H-C(2)], 3.21−3.36 [m, 2 H, H-C(3)], 3.70 (s, 3 H, MeO), 4.95 (br, 1 H, HN). − ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 14.73 (Me), 28.39 (*t*Bu), 40.01 (CH), 42.99 (CH_2), 51.84 (Me), 79.34 (C), 155.95(C), 175.85 (C). − EI-MS; *m/z* (%): 218.2 (1.1) $[M + 1]^+$, 161.1 (26), 144.1 (28), 130.1 (39), 112.0 (32), 88.0 (36), 57.1 (100), 41.0 (22). − $C_{10}H_{19}NO_4$ (217.26): calcd. C 55.28, H 8.81, N 6.45; found C 55.16, H 8.70, N 6.39.

Methyl (*R*)-2-Benzyl-3-*tert*-butoxycarbonylaminopropionate (44): The Boc group of compound **12** (1.88 g, 6.4 mmol) was removed with TMS-OTf (7.0 mL, 38.4 mmol) in CH_2Cl_2 (30 mL) according to *GP8*. Subsequent hydrolysis of the ring, performed in 0.1 N TFA/H_2O (192 mL), and protection of the free amino acid methyl ester with Boc_2O (2.10 g, 9.6 mmol) provided after purification by FC (pentane/Et_2O, 7:3) **44** (0.77 g, 41%) as a colorless oil. − $[\alpha]_D$ = +0.9 (*c* = 1.11, $CHCl_3$). − IR ($CHCl_3$): $\tilde{\nu}$ = 3456 m, 3008 m, 2981 m, 1711 s, 1506 s, 1454 m, 1368 m, 1168 m, 1049 m, 929 w. − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.42 (s, 9 H, *t*Bu), 2.69−2.98 [m, 3 H, H-C(2), 2 H-C(1′)], 3.23−3.39 [m, 2 H, H-C(3)], 3.64 (s, 3 H, MeO), 4.85 (br, 1 H, HN), 7.14−7.29 (m, 5 arom. H). − ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 28.36 (*t*Bu), 35.90 (CH_2), 41.55 (CH_2), 47.39 (CH), 51.80 (Me), 79.42 (C), 126.61 (CH), 128.54 (CH), 128.85 (CH), 138.29 (C), 155.80 (C), 177.67 (C). − EI-MS; *m/z* (%): 294.3 (0.3) $[M + 1]^+$, 237.2 (99), 193.1 (26), 190.1 (100), 188.1 (26), 177.1 (50), 176.1 (44), 163.1 (56), 145.1 (29), 131.1 (53), 117.1 (58), 91.0 (78), 57.1(33). − $C_{16}H_{23}NO_4$ (293.36): calcd. C 65.51, H 7.90, N 4.77; found C 65.44, H 8.04, N 4.63.

Methyl 2-(*tert*-Butoxycarbonylaminomethyl)pent-4-enoate (*rac*-45): The Boc group of compound *rac*-**13** (1.81 g, 5.8 mmol) was removed with TMS-OTf (6.3 mL, 35.0 mmol) in CH_2Cl_2 (30 mL) according to *GP8*. Subsequent hydrolysis of the ring, performed in 0.1 N TFA/H_2O (175 mL), and protection of the free amino acid methyl ester with Boc_2O (1.78 g, 8.2 mmol) provided after purification by FC (pentane/Et_2O, 4:1) *rac*-**45** (0.88 g, 62%) as a colorless oil. − IR ($CHCl_3$): $\tilde{\nu}$ = 3455 m, 3007 m, 2981 m, 1712 s, 1506 s, 1441 m, 1368 m, 1168 m, 1078 w, 993 w, 923 m, 860 w. − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.43 (s, 9 H, *t*Bu), 2.23−2.31 [m, 1 H, H-C(3)], 2.35−2.43 [m, 1 H, H-C(3)], 2.67−2.74 [m, 1 H, H-C(2)], 3.22−3.29 [m, 1 H, H-C(1′)], 3.36−3.42 [m, 1 H, H-C(1′)], 3.70 (s, 3 H, MeO), 4.90 (br, 1 H, HN), 5.03−5.11 (m, 2 H, H_2C=), 5.70−5.80 (m, 1 H, HC=). − ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 28.38 (*t*Bu), 33.99 (CH_2), 41.24 (CH_2), 45.28 (CH), 51.80 (Me), 79.40 (C), 117.49 (CH_2), 134.50 (CH), 155.84(C), 174.76 (C). − EI-MS; *m/z* (%): 244.2 (1.7) $[M + 1]^+$, 187.1 (56), 170.1 (56), 156.1 (54), 143.1 (52), 114.1 (41), 59.0 (22), 57.1 (100), 41.0 (22). − $C_{12}H_{21}NO_4$ (243.30): calcd. C 59.24, H 8.70, N 5.76; found C 59.14, H 8.71, N 5.67.

Methyl 2-(*tert*-Butoxycarbonylaminomethyl)pent-4-ynoate (*rac*-46): The Boc group of compound *rac*-**14** (2.59 g, 8.4 mmol) was removed with TMS-OTf (9.1 mL, 50.3 mmol) in CH_2Cl_2 (30 mL) according to *GP8*. Subsequent hydrolysis of the ring, performed in 0.1 N TFA/H_2O (240 mL), and protection of the free amino acid methyl ester with Boc_2O (2.38 g, 10.9 mmol) provided after purification by FC (pentane/Et_2O, 2:1) *rac*-**46** (0.83 g, 41%) as a colorless oil. − IR ($CHCl_3$): $\tilde{\nu}$ = 3456 m, 3308 m, 2980 m, 1712 s, 1504 s, 1439 m, 1368 m, 1168 m, 975 w, 858 w, 650 m. − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.44 (s, 9 H, *t*Bu), 2.03 (t, *J* = 2.7, 1 H, H-C≡), 2.53 [dd, *J* = 6.1, 2.7, 2 H, H-C(3)], 2.78−2.84 [m, 1 H, H-C(2)], 3.39−3.53 [m, 2 H, H-C(1′)], 3.73 (s, 3 H, MeO), 4.93 (br, 1 H, HN). − ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 18.97 (CH_2), 28.36 (*t*Bu), 40.90 (CH_2), 44.16 (CH), 52.14 (Me), 70.67 (C), 79.54 (C), 80.30 (CH), 155.81 (C), 173.34 (C). − EI-MS; *m/z* (%): 242.1 (0.2) $[M + 1]^+$, 168.1 (28), 154.1 (20), 141.1 (25), 82.1 (42), 57.1 (100). − $C_{12}H_{19}NO_4$ (241.29): calcd. C 59.73, H 7.94, N 5.81; found C 59.79, H 7.84, N 5.73.

Methyl 3-*tert*-Butoxycarbonylamino-2-(trimethylsilylmethyl)propionate (*rac*-47): The Boc group of compound *rac*-**15** (0.92 g, 2.6 mmol) was removed with TMS-OTf (2.8 mL, 15.5 mmol) in CH_2Cl_2 (20 mL) according to *GP8*. Subsequent hydrolysis of the ring, performed in 0.1 N TFA/H_2O (77 mL), and protection of the free amino acid methyl ester with Boc_2O (0.73 g, 3.4 mmol) provided after purification by FC (pentane/Et_2O, 4:1) *rac*-**47** (0.68 g, 91%) as a colorless oil. − IR ($CHCl_3$): $\tilde{\nu}$ = 3455 m, 2954 m, 1708 s, 1507 s, 1468 m, 1407 m, 1368 m, 1071 w, 841 s. − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.15 (s, 9 H, Me_3Si), 0.79 [***ABX***, J_{AB} = 14.7, J_{AX} = 5.9, 1 H, H-C(1′)], 1.03 [***ABX***, J_{AB} = 14.7, J_{BX} = 9.0, 1 H, H-C(1′)], 1.56 (s, 9 H, *t*Bu), 2.77−2.84 [m, 1 H, H-C(2)], 3.27−3.34 [m, 1 H, H-C(3)], 3.43−3.49 [m, 1 H, H-C(3)], 3.81 (s, 3 H, MeO), 5.00 (br, 1 H, HN). − ^{13}C NMR ($CDCl_3$, 100 MHz): δ = −1.26 (Me_3Si), 17.45 (CH_2), 28.40 (*t*Bu), 41.71 (CH), 44.66 (CH_2), 51.72 (Me), 79.28 (C), 155.82 (C), 176.26 (C). − EI-MS; *m/z* (%): 290.1 (0.3) $[M + 1]^+$, 218.1 (51), 200.1 (38), 160.1 (100), 159.1 (64), 157.1 (59), 145.1 (29), 89.0 (56), 73.1 (61), 57.1 (49). − $C_{13}H_{27}NO_4Si$ (289.45): calcd. C 53.95, H 9.40, N 8.84; found C 53.85, H 9.31, N 4.87.

Methyl 3-*tert*-Butoxycarbonylamino-2-(cyclopropylmethyl)propionate (*rac*-48): The Boc group of compound *rac*-**16** (1.58 g, 4.9 mmol) was removed with TMS-OTf (5.3 mL, 29.2 mmol) in CH_2Cl_2 (30 mL) according to *GP8*. Subsequent hydrolysis of the ring, performed in 0.1 N TFA/H_2O (146 mL), and protection of the free amino acid methyl ester with Boc_2O (1.28 g, 5.8 mmol) provided after purification by FC (pentane/Et_2O, 4:1) *rac*-**48** (0.66 g, 53%) as a colorless oil. − IR ($CHCl_3$): $\tilde{\nu}$ = 3455 m, 3007 m, 2952 m, 1711 s, 1506 s, 1446 m, 1392 w, 1368 m, 1168 s, 1020 w, 861 m. − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.01−0.08 (m, 2 H, H_2C), 0.41−0.51 (m, 2 H, H_2C), 0.66−0.76 [m, 1 H, H-C(2′)], 1.43 (s, 9 H, *t*Bu), 1.47−1.51 [m, 2 H, H-C(1′)], 2.70−2.77 [m, 1 H, H-C(2)], 3.27−3.34 [m, 1 H, H-C(3)], 3.40−3.46 [m, 1 H, H-C(3)], 3.71 (s, 3 H, MeO), 4.90 (br, 1 H, HN). − ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 4.47 (CH_2), 4.69 (CH_2), 8.64 (CH), 28.39 (*t*Bu), 34.87 (CH_2), 41.51 (CH_2), 46.13 (CH), 51.73 (Me), 79.34 (C), 155.89 (C), 175.51 (C). − EI-MS; *m/z* (%): 258.2 (1.3) $[M + 1]^+$, 202.1 (25), 184.1 (29), 172.0 (35), 128.0 (100), 125.0 (25), 57.0 (67). − $C_{13}H_{23}NO_4$ (257.33): calcd. C 60.68, H 9.01, N 5.44; found C 60.68, H 8.93, N 5.44.

Methyl 3-*tert*-Butoxycarbonylamino-2-(3-methoxybenzyl)propionate (*rac*-49): The Boc group of compound *rac*-**17** (3.80 g, 9.7 mmol) was removed with TMS-OTf (10.6 mL, 58.4 mmol) in CH_2Cl_2 (40 mL) according to *GP8*. Subsequent hydrolysis of the ring, performed in 0.1 N TFA/H_2O (297 mL), and protection of the free amino acid methyl ester with Boc_2O (2.55 g, 11.7 mmol) provided after purification by FC (pentane/Et_2O, 11:9) *rac*-**49** (2.42 g, 77%) as a colorless oil. − IR ($CHCl_3$): $\tilde{\nu}$ = 3455 m, 3007 m, 1712 s, 1602

m, 1505 s, 1437 m, 1368 m, 1263 m, 1167 m, 1052 m, 967 w, 858 w. – ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.42 (s, 9 H, *t*Bu), 2.75–2.82 [m, 1 H, H-C(2)], 2.88–2.96 [m, 2 H, H-C(1′)], 3.23–3.30 [m, 1 H, H-C(3)], 3.33–3.41 [m, 1 H, H-C(3)], 3.66 (s, 3 H, MeO), 3.78 (s, 3 H, MeO), 4.85 (br, 1 H, HN), 6.69–6.78 (m, 3 arom. H), 7.19 (dd, *J* = 7.9, 7.8, arom. H). – ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 28.36 (*t*Bu), 35.90 (CH_2), 41.52 (CH_2), 47.28 (CH), 51.83 (Me), 55.15 (Me), 79.41 (C), 112.08 (CH), 114.54 (CH), 121.19 (CH), 129.52 (CH), 139.86 (C), 155.79 (C), 159.72 (C), 174.65 (C). – EI-MS; *m/z* (%): 323.2 (5.8, M^+), 268.1 (29), 267.1 (78), 207.1 (33), 193.1 (39), 161.1 (40), 147.1 (28), 146.1 (41), 122.1 (100), 121.1 (32), 57.1 (63). – $C_{17}H_{25}NO_5$ (323.39): calcd. C 63.14, H 7.79, N 4.33; found C 63.24, H 7.65, N 4.41.

Methyl *rac*-(1′*R*,2R)-3-*tert*-Butoxycarbonylamino-2-cyclohex-2-enpropionate (*rac*-50): The Boc group of compound *rac*-**19** (2.77 g, 7.9 mmol) was removed with TMS-OTf (8.6 mL, 47.4 mmol) in CH_2Cl_2 (30 mL) according to *GP9*. Subsequent hydrolysis of the ring, performed in 0.1 N TFA/H_2O (240 mL), and protection of the free amino acid methyl ester with *Z*-chloride (1.70 mL, 11.9 mmol) and NEt_3 (2.2 mL, 15.8 mmol) provided after purification by FC (pentane/Et_2O, 7:3) *rac*-**50** (1.00 g, 40%) as a colorless oil. – IR ($CHCl_3$): ṽ = 3451 m, 3008 m, 2937 m, 1721 s, 1513 s, 1438 m, 1140 w, 1088 w, 977 m. – ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.24–1.96 (m, 6 H, 3 H_2C), 2.55–2.66 [m, 2 H, H-C(2), H-C(1′)], 3.35 [***ABX***, J_{AB} = 13.8, J_{AX} = 5.5, 1 H, H-C(3)], 3.50 [***ABX***, J_{AB} = 13.8, J_{BX} = 3.7, 1 H, H-C(3)], 3.69 (s, 3 H, MeO), 5.07 (***CD***, *J* = 12.3, 1 benzylic H), 5.10 (*C**D***, *J* = 12.3, 1 benzylic H), 5.12 (br, 1 H, HN), 5.48–5.51 (m, 1 H, HC=), 5.76–5.79 (m, 1 H, HC=), 7.28–7.37 (m, 5 arom. H). – ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 21.64 (CH_2), 24.90 (CH_2), 25.74 (CH_2), 36.03 (CH), 39.59 (CH_2), 50.21 (CH), 51.76 (Me), 66.73 (CH_2), 128.13 (CH), 128.17 (CH), 128.53 (CH), 129.40 (CH), 136.53 (C), 156.30 (C), 174.64 (C). – EI-MS; *m/z* (%): 317.2 (0.4, M^+), 194.1 (20), 153.1 (68), 108.1 (23), 107.1 (24), 91.1 (100), 81.1 (24), 79.1 (31). – $C_{18}H_{23}NO_4$ (317.4): calcd. C 68.12, H 7.30, N 4.41; found C 68.08, H 7.29, N 4.47.

Methyl (2*S*,3*S*)-3-*tert*-Butoxycarbonylamino-2-methylbutyrate (51): The Z group of compound **21** (2.08 g, 6.3 mmol) was removed according to *GP9*. Subsequent hydrolysis of the ring, performed in 0.1 N TFA/H_2O (190 mL), and protection of the free amino acid methyl ester with Boc_2O (2.05 g, 9.4 mmol) provided after purification by FC (pentane/Et_2O, 7:3) *rac*-**51** (2.42 g, 77%) as a white solid. The analytical data correlated with those in the literature[43].

Methyl *rac*-(2*S*,3*S*)-3-*tert*-Butoxycarbonylamino-2-ethylbutyrate (*rac*-52): The Z group of compound *rac*-**25** (2.76 g, 8.0 mmol) was removed according to *GP9*. Subsequent hydrolysis of the ring, performed in 0.1 N TFA/H_2O (240 mL), and protection of the free amino acid methyl ester with Boc_2O (2.61 g, 11.9 mmol) provided after purification by FC (pentane/Et_2O, 4:1) *rac*-**52** (1.41 g, 72%) as a colorless oil. – IR ($CHCl_3$): ṽ = 3430 m, 3007 w, 2975 m, 2877 w, 1704 s, 1503 s, 1458 m, 1368 m, 1168 s, 1096 m, 1016 w, 995 w, 877 *w*. – ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.93 (t, *J* = 7.4, 3 H, Me), 1.13 (d, *J* = 6.8, 3 H, Me), 1.44 (s, 9 H, *t*Bu), 1.53–1.76 [m, 2 H, H-C(1′)], 2.37–2.42 [m, 1 H, H-C(2)], 3.70 (s, 3 H, MeO), 3.88–3.94 [m, 1 H, H-C(3)], 5.23 (d, *J* = 8.3, 1 H, HN). – ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 12.04 (Me), 20.07 (Me), 22.96 (CH_2), 28.42 (*t*Bu), 46.76 (CH), 51.49 (Me), 52.10 (CH), 79.03 (C);155.56 (C), 175.55 (C). – EI-MS; *m/z* (%): 246.1 (6.8) [M + 1]$^+$, 190.1 (45), 172.1 (34), 158.1 (47), 144.1 (100), 140.1 (29), 130.1 (22), 102.1 (54), 88.0 (45), 57.1 (68), 44.0 (25). – $C_{12}H_{23}NO_4$ (245.32): calcd. C 58.75, H 9.45, N 5.71; found C 58.54, H 9.31, N 5.67.

Methyl *rac*-(2*S*,3*S*)-3-*tert*-Butoxycarbonylamino-2-(1-methylethyl)-butyrate (*rac*-53): The Z group of compound *rac*-**26** (0.35 g, 1.0 mmol) was removed according to *GP9*. Subsequent hydrolysis of the ring, performed in 0.1 N TFA/H_2O (30 mL), and protection of the free amino acid methyl ester with Boc_2O (0.31 g, 1.4 mmol) provided after purification by FC (pentane/Et_2O, 17:3) *rac*-**53** (0.09 g, 35%) as a colorless oil. – IR ($CHCl_3$): ṽ = 3427 m, 2971 m, 2874 m, 1703 s, 1503 s, 1448 w, 1367 m, 1165 s, 1098 w, 1022 w, 877 *w*. – ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.89 (d, *J* = 6.6, 3 H, Me), 0.98 (d, *J* = 6.6, 3 H, Me), 1.10 (d, *J* = 6.7, 3 H, Me), 1.43 (s, 9 H, *t*Bu), 1.91–2.02 [m, 1 H, H-C(1′)], 2.12 [dd, *J* = 10.1, 4.0, 1 H, H-C(2)], 3.71 (s, 3 H, MeO), 3.94–4.07 [m, 1 H, H-C(3)], 5.45 (d, *J* = 9.3, 1 H, HN). – ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 20.35 (Me), 20.66 (Me), 21.10 (Me), 28.30 (CH), 28.43 (*t*Bu), 44.72 (CH), 51.30 (Me), 57.46 (CH), 78.96 (C);155.49 (C), 175.81 (C). – EI-MS; *m/z* (%): 260.2 (3.8) [M + 1]$^+$, 204.1 (22), 197.1 (27), 186.1 (34), 172.1 (40), 154.1 (29), 144.1 (100), 101.1 (40), 88.0 (26), 57.1 (49). – $C_{13}H_{25}NO_4$ (259.34): calcd. C 60.21, H 9.72, N 5.40; found C 60.03, H 9.64, N 5.45.

Methyl *rac*-(2*S*,3*S*)-2-Benzyl-3-*tert*-butoxycarbonylaminobutyrate (*rac*-54): The Z group of compound *rac*-**22** (1.72 g, 4.2 mmol) was removed according to *GP9*. Subsequent hydrolysis of the ring, performed in 0.1 N TFA/H_2O (126 mL), and protection of the free amino acid methyl ester with Boc_2O (1.37 g, 6.3 mmol) provided after purification by FC (pentane/Et_2O, 17:3) *rac*-**54** (0.96 g, 74%) as a white solid, m.p. 48–50°C. – IR ($CHCl_3$): ṽ = 3430 m, 3007 w, 2980 m, 1706 s, 1500 s, 1455 m, 1368 m, 1091 m, 856 w. – ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.14 (d, *J* = 6.8, 3 H, Me), 1.46 (s, 9 H, *t*Bu), 2.76–2.81 [m, 1 H, H-C(2)], 2.85 [***ABX***, J_{AB} = 13.4, J_{AX} = 6.3, 1 benzylic H), 2.97 [***ABX***, J_{AB} = 13.4, J_{BX} = 8.7, 1 benzylic H), 3.60 (s, 3 H, MeO), 3.90–3.95 [m, 1 H, H-C(3)], 5.32 (d, *J* = 8.9, 1 H, HN), 7.15–7.29 (m, 5 arom. H). – ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 19.99 (Me), 28.43 (*t*Bu), 35.78(CH_2), 46.88 (CH), 51.67 (Me), 52.35 (CH), 79.19 (C), 126.52 (CH), 128.50 (CH), 128.87 (CH), 138.81 (C), 155.45 (C), 174.82 (C). – EI-MS; *m/z* (%): 307.2 (0.5, M^+), 163.0 (27), 131.0 (100), 104.0 (22), 91.0 (93), 70.0 (23), 59.0 (46), 57.0 (49), 44.0 (70). – $C_{17}H_{25}NO_4$ (307.39): calcd. C 66.43, H 8.20, N 4.56; found C 66.50, H 8.19, N 4.56.

Methyl (2*S*,3*S*)-2-Benzyl-3-*tert*-butoxycarbonylaminobutyrate (54): The Z group of compound **22** (2.79 g, 6.8 mmol) was removed according to *GP9*. Subsequent hydrolysis of the ring, performed in 0.1 N TFA/H_2O (205 mL), and protection of the free amino acid methyl ester with Boc_2O (2.23 g, 10.2 mmol) provided after purification by FC (pentane/Et_2O, 4:1) **54** (1.18 g, 86%) as a white solid, with the same analytical datas as *rac*-**54** and m.p. 69–70°C. – $[\alpha]_D$ = −60.4 (*c* = 1.09, $CHCl_3$).

tert*-Butyl *rac*-(3*S*,4*S*)-4-Benzyloxycarbonylamino-3-methyloxycarbonylpentanoate (*rac*-55):** The Z group of compound *rac*-**23** (5.31 g, 17.8 mmol) was removed according to *GP9*. Subsequent hydrolysis of the ring, performed in 0.1 N TFA/H_2O (530 mL), and protection of the free amino acid methyl ester with *Z*-chloride (2.5 mL, 17.8 mmol) and NEt_3 (2.5 mL, 17.8 mmol) provided after purification by FC (pentane/EtOAc 4:1) *rac*-**55** (3.06 g, 47%) as a colorless oil. – IR ($CHCl_3$): ṽ = 3344 m, 2978 m, 1732 s, 1530 m, 1368 w, 1236 m, 1153 m, 1058 w, 949 w, 850 w, 741 w, 698 m. – ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.18 (d, *J* = 6.8, 3 H, Me), 1.42 (s, 9 H, *t*Bu), 2.45 [ABX***, J_{AB} = 16.6, J_{AX} = 5.4, 1 H, H-C(2)], 2.68 [***ABX***, J_{AB} = 16.6, J_{BX} = 9.4, 1 H, H-C(2)], 2.96–3.01 [m, 1 H, H-C(3)], 3.70 (s, 3 H, MeO), 3.99–4.07 [m, H-C(4)], 5.07 (***CD***, *J* = 12.2, 1 benzylic H), 5.11 (*C**D***, *J* = 12.2, benzylic H), 5.25 (d, *J* = 8.9, HN), 7.28–7.38 (m, 5 arom. H). – ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 19.58 (Me), 28.00 (*t*Bu), 35.32 (CH_2), 46.05 (CH), 47.74 (CH), 51.89 (Me), 66.71 (CH_2), 81.12 (C), 128.11 (CH), 128.52

(CH), 136.51 (C), 155.81 (C), 170.66 (C), 173.87 (C). − EI-MS; *m/z* (%): 365.2 (0.5) $[M + 1]^+$, 202.1 (18), 184.1 (38), 141.1 (33), 132.0 (24), 114. (19), 108.1 (49), 91.1 (100), 79.1 (29), 57.1 (72). − $C_{19}H_{27}NO_6$ (365.43): calcd. C 62.45, H 7.45, N 3.83; found C 62.42, H 7.53, N 3.87.

Methyl *rac*-(1′*S*,2*S*,3*S*)-3-*tert*-Butoxycarbonylamino-2-(1-phenylethyl)butyrate (*rac*-56): The Z group of compound *rac*-**27b** (0.84 g, 2.0 mmol) was removed according to *GP9*. Subsequent hydrolysis of the ring, performed in 0.1 N TFA/H_2O (60 mL), and protection of the free amino acid methyl ester with Boc_2O (0.65 g, 3.0 mmol) provided after purification by FC (pentane/Et_2O, 4:1) *rac*-**56** (0.21 g, 33%) as a colorless oil. − IR ($CHCl_3$): $\tilde{\nu}$ = 3626 w, 3428 w, 3008 m, 2973 m, 1710 s, 1499 s, 1436 w, 1367 m, 1167 m, 1050 w, 1020 w, 928 *w*. − ^{1}H NMR ($CDCl_3$, 400 MHz) 2 conformers: δ = 0.98 (d, *J* = 6.7, 3 H, Me), 1.22 (d, *J* = 7.0, 3 H, Me), 1.29, 1.44 (s, 9 H, *t*Bu), 2.56−2.64 [m, 1 H, H-C(2)], 3.07−3.15 [m, 1 H, H-C(1′)], 3.27−3.43 [m, 1 H, H-C(3)], 3.78 (s, 3 H, MeO), 5.33, 5.50 (d, *J* = 8.0, 9.2, 1 H, HN), 7.13−7.30 (m, 5 arom. H). − ^{13}C NMR ($CDCl_3$, 100 MHz) 2 conformers: δ = 20.42, 20.72 (Me), 20.53, 20.56 (Me), 28.17, 28.44 (*t*Bu), 39.67 (CH), 45.19, 46.19 (CH), 51.63 (Me), 56.94, 57.08 (CH), 78.75 (C), 126.67, 126.96 (CH), 127.35 (CH), 128.65 (CH), 143.36 (C), 154.83 (C), 175.47 (C). − EI-MS; *m/z* (%): 321.2 (2.3, M^+), 265.1 (100), 248.1 (23), 234.1 (23), 177.1 (28), 163.1 (36), 145.1 (46), 144.1 (85), 131.1 (23), 105.1 (50), 57.1 (22). − $C_{18}H_{27}NO_4$ (321.42): calcd. C 67.26, H 8.47, N 4.36; found C 67.11, H 8.44, N 4.34.

Methyl (2*S*,3*S*)-2-Benzyl-3-*tert*-butoxycarbonylamino-5-methylhexanoate (57): The Z group of compound **31** (1.84 g, 4.1 mmol) was removed according to *GP9*. Subsequent hydrolysis of the ring, performed in 0.1 N TFA/H_2O (60 mL), and protection of the free amino acid methyl ester with Boc_2O (1.07 g, 4.9 mmol) provided after purification by FC (pentane/Et_2O, 4:1) **57** (0.35 g, 25%) as a white solid, m.p. 66.5−67.5°C. − $[\alpha]_D$ = −62.1 (*c* = 1.24, $CHCl_3$). − IR ($CHCl_3$): $\tilde{\nu}$ = 3429 m, 2958 m, 1706 s, 1504 s, 1455 w, 1436 w, 1367 m, 1166 s, 1115 w, 1046 w, 1023 w. − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.85 (d, *J* = 6.7, 3 H, Me), 0.89 (d, *J* = 6.5, 3 H, Me), 1.16−1.23 [m, 1 H, H-C(4)], 1.26−1.35 [m, 1 H, H-C(4)], 1.47 (s, 9 H, *t*Bu), 1.60−1.69 [m, 1 H, H-C(5)], 2.78−2.88 (*m*, 3 H, H-C(2), H-C(1′)], 2.97 (*dd*, *J* = 13.3, 8.9, 1 H, H-C(1′)], 3.58 (s, 3 H, MeO), 3.88−3.96 [m, 1 H, H-C(3)], 4.85 (d, *J* = 9.9, 1 H, HN), 7.16−7.29 (m, 5 arom. H). − ^{13}C NMR ($CDCl_3$, 400 MHz): δ = 22.27 (Me), 22.83 (Me), 24.88 (CH), 28.43 (*t*Bu), 35.91 (CH_2), 43.66 (CH_2), 49.40 (CH), 51.44 (Me), 51.48 (CH), 79.05 (C), 126.47 (CH), 128.47 (CH), 128.86 (CH), 138.97 (C), 155.78 (C), 174.96 (C). − EI-MS; *m/z* (%): 349.3 (0.1, M^+), 130.1 (20), 91.1 (59), 86.1 (100), 57.1 (25). − $C_{20}H_{31}NO_4$ (349.47): calcd. C 68.74, H 8.94, N 4.01; found C 68.78, H 8.81, N 3.97.

Methyl 2-(*tert*-Butoxycarbonylaminomethyl)-2-methylpent-4-enoate (*rac*-58): A solution of **20** (1.46 g, 4.5 mmol) in CH_2Cl_2/TFA (10 mL/5 mL) was stirred at room temp. for 4 h. The solvent was removed by rotary evaporation and 2 N TFA/H_2O (18 mL) was added. After 4 d at 0°C the mixture was set to pH > 10 with a 10%-NH_3 solution, saturated with NaCl and the aqueous layer was extracted three times with CH_2Cl_2. The combined organic layers were dried with anhydrous Na_2SO_4. The solvent was partionally removed by rotary evaporation, and Boc_2O (1.01 g, 4.6 mmol) was added and the reaction mixture was stirred at room temp. for 12 h. The reaction mixture was washed with satd. $NaHCO_3$ solution and dried with anhydrous $MgSO_4$. The solvent was removed by rotary evaporation. Purification of the crude product by FC (pentane/Et_2O, 4:1) gave rac-**58** (0. 98 g, 85%) as a colorless oil. − IR ($CHCl_3$): $\tilde{\nu}$ = 3454 m, 2981 m, 1712 s, 1508 s, 1461 w, 1368 m, 1168 m, 994 w, 924 w, 856 w. − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.17 (s, 3 H, Me), 1.43 (s, 9 H, *t*Bu), 2.28 [***A****BX*, J_{AB} = 13.8, J_{AX} = 7.4, 1 H, H-C(3)], [***A****BX*, J_{AB} = 13.8, J_{BX} = 7.5, 1 H, H-C(3)], 3.24 (***C****DY*, J_{CD} = 13.9, J_{CY} = 7.2, 1 H, H-C(1′)], 3.32 (C***D***Y, J_{CD} = 13.9, J_{CY} = 6.1, 1 H, H-C(1′)], 4.91−5.07 (*m*, 2 H, H_2C=), 5.09 (*s*, 1 H, HN), 5.67−5.78 (m, 1 H, HC=). − ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 20.23 (Me), 28.38 (*t*Bu), 41.16 (CH_2), 46.65 (CH_2), 47.23 (C), 51.94 (Me), 79.23 (C), 118.65 (CH_2), 133.09 (CH), 156.09 (C), 176.62 (C). − ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 258.2 (0.2) $[M + 1]^+$, 201.1 (34), 184.1 (25), 170.1 (27), 157.1 (19), 128.1 (100), 57.1 (40). − $C_{13}H_{23}NO_4$ (257.33): calcd. C 60.68, H 9.01, N 5.44; found C 60.64, H 9.00, N 5.48.

Hydrolysis of the Aldol Adducts 59−61

***rac*-(1′*R*,2*R*,3*S*)-3-(*tert*-Butoxycarbonylamino)-2-(1-hydroxyethyl)-butyric Acid (*rac*-59):** The aldol adduct *rac*-**32a** (1.63 g, 4.5 mmol) was hydrolyzed with 4 N HCl (30 mL) to the corresponding amino acid and protected with Boc_2O (1.96 g, 9.0 mmol) and NaOH (0.22 g, 5.4 mmol) according to *GP10*. Purification by recrystallization (hexane/AcOEt) gave *rac*-**59** (0.12 g, 11%) as a white solid, m.p. 134−136°C. − IR (KBr): $\tilde{\nu}$ = 3512 w, 3328 s, 2981 s, 1682 s, 1530 m, 1453 m, 1368 m, 1285 m, 1252 m, 1180 m, 1098 m, 1025 m, 904 w, 857 w, 759 w, 673 w. − ^{1}H NMR ($CDCl_3$, 400 MHz) 2 conformers: δ = 1.26 (d, *J* = 6.4, 3 H, Me), 1.33 (d, *J* = 6.2, 3 H, Me), 1.44 (s, 9 H, *t*Bu), 2.35, 2.48 [br, 1 H, H-C(2)], 3.92−4.15 [m, 2 H, H-C(3), H-C(1′)], 5.28, 5.60 [d, *J*(1) = 8.7, *J*(2) = 9.1, 1 H, HN], 6.07 (br, 1 H, HO), 7.05 (br, 1 H, HO_2C). − ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 20.18, 20.59 (Me), 21.47 (Me), 28.37 (*t*Bu), 45.81, 46.30 (CH), 57.59, 57.79 (CH), 66.65, 67.69 (CH), 79.94, 81.36 (C), 155.89, 156.94 (C), 176.39, 177.65 (C). − ESI-MS; *m/z* (%): 246.0 (100, $[M-1]^+$. − $C_{11}H_{21}NO_5$ (247.29): calcd. C 53.43, H 8.56, N 5.66; found C 53.48, H 8.37, N 5.64.

***rac*-(1′*S*,2*R*,3*S*)-2-(1-*tert*-Butoxycarbonylaminoethyl)-3-hydroxy-4,4-dimethylpentanoic Acid (*rac*-60):** The aldol adduct *rac*-**34** (4.67 g, 11.5 mmol) was hydrolyzed with 4 N HCl to the corresponding amino acid and protected with Boc_2O (1.09 g, 5.0 mmol) and NaOH (0.20 g, 5.0 mmol) according to *GP10*. Purification by recrystallization (hexane/AcOEt) gave *rac*-**60** (0.83 g, 25%) as a white solid, m.p. 155.0−156.5°C. − IR (KBr): $\tilde{\nu}$ = 3425 s, 3392 s, 1683 s, 1522 m, 1457 w, 1366 m, 1276 m, 1180 m, 1092 m, 994 w, 949 w, 850 w, 784 w, 701 w, 615 w. − ^{1}H NMR ($CDCl_3$, 400 MHz) 2 conformers: δ = 0.96 (s, 9 H, *t*Bu), 1.36 (d, *J* = 6.8, 3 H, Me), 1.44 (s, 9 H, *t*Bu), 2.72, 2.87 [br, 1 H, H-C(2)], 3.34, 3.59 [br, 1 H, H-C(3)], 3.96 [br, 1 H, H-C(1′)], 4.95 (d, *J* = 6.9, 1 H, HN), 6.29 (br, 1 H, HO). − ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 20.98 (Me), 26.23 (*t*Bu), 28.30 (*t*Bu), 35.65 (C), 50.33 (CH), 50.53 (CH), 80.29 (CH), 80.87 (C), 156.93 (C), 174.40 (C). − FAB-MS; *m/z* (%): 312.2 (100) $[M + Na]^+$, 290.2 (36) $[M + 1]^+$, 234.2 (70), 190.2 (78), 154.1 (30), 137.1 (32). − $C_{14}H_{27}NO_5$ (289.37): calcd. C 58.11, H 9.40, N 4.84; found C 58.22, H 9.24, N 5.04.

Methyl *rac*-(1′*R*,2*R*,3*S*)-3-(*tert*-Butoxycarbonylamino)-2-(hydroxyphenylmethyl)butyrate (*rac*-61): The aldol adduct *rac*-**35b** (1.26 g, 3.0 mmol) was hydrolyzed with 4 N HCl to the corresponding amino acid and protected with Boc_2O (1.96 g, 9.0 mmol) and NaOH (0.22 g, 5.4 mmol) according to *GP10* and converted to the methyl carboxylate with CH_2N_2. Purification by FC (pentane/Et_2O, 3:2) gave *rac*-**61** (0.35 g, 38%) as a white solid, m.p. 87.0−88.5°C. − IR ($CHCl_3$): $\tilde{\nu}$ = 3437 m, 2975 m, 2877 w, 1719 s, 1682 s, 1509 s, 1455 m, 1436 w, 1369 m, 1162 m, 1091 m, 1044 w, 893 w, 852 *w*. − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.19 (d, *J* = 7.0, 3 H, Me), 1.50 (s, 9 H, *t*Bu), 2.75 [dd, *J* = 10.0, 3.2, 1 H, H-C(2)], 3.37 (s, 3 H, MeO), 4.37 [qdd, *J* = 7.0, 4.0, 3.2, 1 H, H-C(3)], 4.69 [dd, *J* = 10.0, 4.0, 1 H, H-C(1′)], 4.85 (d, *J* = 4.0, 1 H, HO), 5.23 (d, *J* = 10.2, 1 H,

Table 1. Crystal data of *rac*-**4b**, **6b**, *rac*-**32a**, *rac*-**34**, *rac*-**35a**, *rac*-**36**, *rac*-**37a**, *rac*-**38**, *rac*-**41**, *rac*-**62**, and *rac*-**63**

	rac-**4b**	**6b**	*rac*-**32a**	*rac*-**34**	*rac*-**35a**	*rac*-**36**	*rac*-**37a**	*rac*-**38**	*rac*-**41**	*rac*-**62**	*rac*-**63**
Formula	$C_{17}H_{24}N_2O_3$	$C_{20}H_{30}N_2O_3$	$C_{20}H_{30}N_2O_4$	$C_{23}H_{36}N_2O_4$	$C_{25}H_{32}N_2O_4$	$C_{23}H_{30}N_2O_5$	$C_{19}H_{36}N_2O_4$	$C_{19}H_{34}N_2O_4$	$C_{37}H_{54}N_2O_6$	$C_{21}H_{32}N_2O_5$	$C_{23}H_{32}N_2O_4$
M_r	304.39	346.47	362.47	404.55	424.54	414.50	356.50	354.49	622.84	392.49	400.52
T	293	203(2)	293	293	293	293	203 (2)	293	200(2)	180(2)	180(2)
Crystal system	monoclinic	ortho-rhombic	monoclinic	triclinic	triclinic	monoclinic	monoclinic	triclinic	monoclinic	ortho-rhombic	monoclinic
Space group	*C*2/c	*P*212121	*P*21/**c**	*P*-1	*P*-1	*C*2/*c*	*P*21/*c*	*P*-1	*I*2/*c*	*Pnaa*	*P*21/*c*
a [Å]	23.30(4)	7.916(1)	12.132(10)	12.494(1)	9.804(2)	27.531(3)	11.105(2)	9.025(3)	27.121(6)	9.104(6)	11.326(3)
b [Å]	6.535(9)	11.495(3)	10.158(8)	13.566(3)	15.738(2)	8.664(1)	12.751(3)	10.702(2)	9.410(9)	10.799(2)	10.292(4)
c [Å]	22.72(4)	21.738(3)	33.633(11)	14.913(3)	16.029(2)	20.156(2)	14.995(4)	11.991(3)	30.581(9)	22.540(7)	19.201(9)
α [°]	90	90	90	85.52(2)	87.96(2)	90	90	82.59(2)	90	90	90
β [°]	102.31(13)	90	98.43(4)	79.97(1)	77.64(2)	112.753(8)	94.77(2)	70.86(2)	111.09(4)	90	105.70(3)
γ [°]	90	90	90	72.40(2)	83.32(2)	90	90	74.19(2)	90	90	90
V [Å^3]	3381(10)	1978.1(6)	4100(5)	2371.9(8)	2399.4(6)	4433.5(8)	2115.9(8)	1051.7(5)	7282(7)	2216(2)	2154.7(14)
Z	8	4	8	4	4	8	4	2	8	4	4
D_x (g·cm^{-3})	1.196	1.163	1.174	1.133	1.175	1.242	1.119	1.119	1.136	1.176	1.235
F [000]	1312	752	1568	880	912	1776	784	388	2704	848	864
Unique reflect.	1230	3268	7195	7490	7974	3842	3639	1962	6398	1970	3833
of which $I > 3\sigma$	1230 (2σ)	3065	3425	5506	5887	3140	3325	1962 (2σ)	4542	886	2966
Final R (%)	9.05	6.84	10.68	5.38	6.81	4.20	5.52	5.14	4.61	17.00	6.02

[a] Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-102575 (**6b**), -102576 (*rac*-**32a**), -102577 (*rac*-**34**), -102578 (*rac*-**35a**), -102579 (*rac*-**36**), -102580 (*rac*-**37a**), -102581 (*rac*-**38**), -102582 (*rac*-**41**), -102583 (*rac*-**4b**), -102584 (*rac*-**62**), -102585 (*rac*-**63**). Copies of the data can be obtained free of charge on application to The Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: (int. Code) +44(1223)336-033, E-mail: deposit@chemcrys.cam.ac.uk, World Wide Web: http://www.ccdc.cam.ac.uk].

HN), 7.23−7.32 (m, 5 arom. H). − ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 19.49 (Me), 28.35 (*t*Bu), 44.42 (CH), 51.21 (Me), 60.29 (CH), 72.70 (CH), 80.51 (C);126.38 (CH), 127.87 (CH), 128.30 (CH), 141.19 (C), 157.32 (C), 172.64 (C). − EI-MS; *m/z* (%): 324.2 (0.3) [M + 1]$^+$, 217.1 (20), 179.1 (27), 163.1 (37), 162.1 (37), 161.1 (100), 131.1 (35), 117.1 (41), 105.0 (55), 101.1 (28), 77.0 (32), 57.1 (33). − $C_{17}H_{25}NO_5$ (323.39): calcd. C 63.14, H 7.79, N 4.33; found C 63.13, H 7.78, N 4.30.

Derivatizations for Resolution of the Relative Configuration of *rac*-19 and *rac*-28

Methyl *rac*-(1′*R*,1′′′′*R*,2*R*,2′′′*R*)-2-Cyclohex-2-enyl-3-[3-(2-cyclohex-2-enyl-2-methoxycarbonylethyl)ureido]propionate (*rac*-62): During the conversion of compound *rac*-**19** to *rac*-**50** a second product was formed and isolated. Purification by FC (AcOEt) and recrystallization (Et_2O,/pentane) gave *rac*-**62** (0.40 g, 26%), a white solid, as a mixture of two diastereoisomers (*dr* ≈ 4:1), m.p. 89−90°C. − IR ($CHCl_3$): ṽ = 3450 m, 3002 w, 2940 m, 2862 w, 1721 s, 1669 s, 1534 s, 1437 m, 1357 w, 1175 w, 962 w. − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.31−1.42 (m, 2 H), 1.44−1.57 (m, 2 H), 1.66−1.78 (m, 4 H), 1.93−2.00 (m, 4 H), 2.49−2.57 (m, 2 H), 2.58−2.65 (m, 2 H), 3.22−3.36 (m, 2 H, H-CN), 3.45−3.56 (m, 2 H, H-CN), 3.70 (s, 6 H, MeO), 4.76 (t, *J* = 6.0, 2 H, HN), 5.47−5.53 (m, 2 H, H-C=), 5.74−5.80 (m, 2 H, H-C=). − ^{13}C NMR ($CDCl_3$, 400 MHz): δ = 21.65 (CH_2), 24.94 (CH_2), 25.84 (CH_2), 36.02 (CH), 38.98 (CH_2), 50.47 (CH), 51.69 (Me), 128.33 (CH), 129.24 (CH), 157.67 (C), 175.25 (C). − EI-MS; *m/z* (%): 392.2 (100) [M + 1]$^+$, 361.2 (29), 184.2 (33), 80.8 (27). − $C_{21}H_{32}N_2O_5$ (392.49): calcd. C 64.26, H 8.22, N 7.14; found C 64.15, H 8.16, N 7.09.

Benzyl (2*R*,4*S*,4a*S*,4b*R*,8*S*,8a*R*)-2-*tert*-Butyl-8-hydroxy-4-methyl-4,4a,4b,5,6,7,8,8a-octahydro-2*H*-benzo[4,5]furo[2,3-*d*]pyrimidine-3-carboxylate[44] **(*rac*-63):** **N**-methylmorpholine *N*-oxide monohydrate (0.046 g, 0.3 mmol) and OsO_4 (several mg) were added under Ar atmosphere to a solution of *rac*-**19** (0.12 g, 0.3 mmol) in H_2O (6 mL) and acetone (3 mL). After 12 h at room temp. sodium hydrosulfite (0.1 g in 30 mL H_2O) was added to the black suspension. The slurry was stirred for 10 min, filtered through a pad of Celite on a sintered-glass funnel and wash with acetone. Then 12 N H_2SO_4 (1 mL) was added and the acetone was removed by a rotary evaporator. The aqueous layer was satd. with NaCl and extracted 5 times with AcOEt. The combined organic extracts were and dried with anhydrous Na_2SO_4. Purification by FC (AcOEt) and recrystallization (Et_2O) gave rac-**63** (40 mg, 42%) as a white solid, m.p. 186.0−186.5°C. − IR ($CHCl_3$): ṽ = 3308*br*, 2948 m, 1721 s, 1687 s, 1448 w, 1392 m, 1301 s, 1177 w, 1117 w, 1080 m, 1002 m, 902 w. − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.98 (s, 9 H, *t*Bu), 1.27 (qd, *J* = 12.4, 4.0, 1 H), 1.44 (d, *J* = 6.3, 3 H, Me), 1.47−1.77 (m, 3 H), 1.94−2.11 (m, 3 H), 2.27 (qd, *J* = 11.6, 2.9, 1 H), 3.18 (br, 1 H, HO), 3.70 (dd, *J* = 10.8, 2.3, 1 H), 4.06 [br, 1 H, H-C(4)], 4.35 [br, 1 H, H-C(OH)], 5.10 (***AB***, *J* = 12.3, 1 benzylic H), 5.18 (*A**B***, *J* = 12.3, 1 benzylic H), 5.64 [s, H-C(2)], 7.29−7.39 (m, 5 arom. H). − ^{13}C NMR ($CDCl_3$, 400 MHz): δ = 19.90 (CH_2), 23.58 (Me), 26.99 (*t*Bu), 28.18 (CH_2), 30.30 (CH_2), 38.70 (CH), 43.39 (CH), 43.92 (CH), 53.11 (CH), 64.51 (CH), 67.56 (CH_2), 77.54 (CH), 85.07 (CH), 128.04 (CH), 128.11 (CH), 128.51 (CH), 136.50 (C), 156.16 (C), 168.01 (C). − FAB-MS; *m/z* (%): 401.2 (100) [M + 1]$^+$, 343.1 (47), 299.1(18), 154.1 (32), 136.0 (28), 90.8 (99). − $C_{23}H_{32}N_2O_4$ (400.52): calcd. C 68.97, H 8.05, N 6.99; found C 68.87, H 8.14, N 6.93.

X-ray Crystal Structure Analyses: The data for the compounds **6b**, *rac*-**32a**, *rac*-**34**, *rac*-**35a**, *rac*-**36**, *rac*-**37a**, *rac*-**41**, *rac*-**62** and *rac*-**63** were collected on an Enraf-Nonius CAD-4 diffractometer with a graphite monochromator. Datareduction was done with MolEN.[45] For compound *rac*-**4b** a Syntex P21 diffractometer was used and *rac*-**38** was measured on a Picker 4-circle diffractometer (Stoe upgrade). For experimental details see Table 1. Structures were solved with SHELXS-86[46] and refined by full matrix least-squares with SHELXL-92.[47]

6b: The structure shows disorder on the methylene carbon of the benzyl ester. Two positions with fixed occupancy of 0.5 have been refined. The intermolecular H-bond between the amide N and the carboxylic O of the amide group forms a chain along the *a* axis of

the unit cell (N−H···O (−1/2 + *x*, 1/2 − *y*, − *z*): 2.16Å, N···O: 2.88 Å).

rac-**32a**: Due to the poor crystal quality with wide peaks and the relatively long *c* axis (33.6 Å) some problems with reflexion overlapping during data collection could not be avoided (see the unusually high *R* value of 10%). The two symmetrically independent molecules in the crystal structure form a chain connected by H bonds between the hydroxy group and the carbonyl O atom of the benzyl ester along the diagonal of the *a*/*b* plane [$O_{(mol1)}(H)\cdots O_{(2)}$=C (−1 + *x*,*y*,*z*): 2.81 &ARING;, $O_{(2)}(H)\cdots O_{(1)}$=C (*x*, −1 + *y*,*z*): 2.78 Å]. A remarkable feature is the almost perfect overlap of the two molecules by a *a*/2,*b*/2,0 translation with only the benzyl substituent adopting a different conformation (Figure 7).

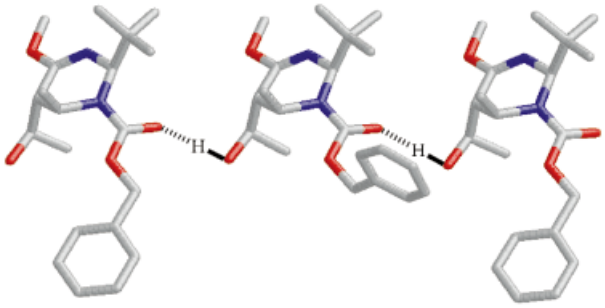


Figure 7. Section of the crystal packing pattern of compound *rac*-**32a**

rac-**34**: The asymmetric unit contains two symmetrically independent molecules. Both form dimers by H-bonding between the OH and the carbonyl group through inversion centres. Molecule 1: O(H)···O=C (1 − *x*, 1 − *y*, 2 − *z*): 2.728 Å, 2: O(H)···O=C (−*x*, 2 − *y*, 1 − *z*: 2.841 Å. The disordered methoxy carbon atom and one of the *tert*-butyl methyl groups have been refined on two positions with fixed occupancy of 0.5.

rac-**35a**: The same H-bonding pattern as in *rac*-**34** is observed Molecule 1: O(H)···O=C (1 − *x*, 1 − *y*, 2 − *z*): 2.790 Å, 2: O(H)···O=C (−*x*, 2 − *y*, 1 − *z*): 2.756 Å.

rac-**36**: The H-bond between the hydroxy group and the carbonyl-O of the benzyl ester form a chain along the *b* axis (O(H)···O=C (1.5 − *x*, 0.5 + *y*, 1.5 − *z*): 2.803 Å).

rac-**37a**:Two molecules form a dimer through an inversion centre with H bonds between the hydroxy group and the carbonyl oxygen (O(H)···O=C (2 − *x*, −*y*, 2 − *z*): 2.796 Å).

rac-**62**: The structure is heavily disordered. Attempts to refine in spacegroups with lower symmetry failed.

rac-**63**: The H bond between the hydroxy group and the carbonyl O atom form a chain along the *b* axis (O(H)···O=C (2 − *x*, 0.5 + *y*, 0.5 − *z*): 2.827 Å).

Acknowledgments

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[19] With $Et_3O{\cdot}BF_4$ the corresponding 4-ethoxy analog of **8a** was formed but not further studied in deprotonations. The compound is characterized in the experimental section.

[20] For unknown reasons the lithiation of the *trans* isomer **8b** failed completely!

[21] Double alkylations leading to the analogs of **20** with 5-methyl-5-propargyl and the epimer of **20**, were also carried out, but the products (conversion *ca.* 50 and 80%) could not be separated from starting material. For Li enaminate formation, *t*BuLi had

to be used; therefore reactions with Alloc- and Z-protected analogs were impossible, i.e. not compatible with the allyl and benzyl groups!

[22] This analysis was complicated by the presence of rotamers, so that NMR spectra with single sharp signals could only be obtained at high temperature (*ca.* 90°C for Z-protected derivatives), the Boc-protected products showed two rotamers with sharp signals at room temperature and coalescence behavior at *ca.* 90°C.

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