New Auxiliaries for Copper-Catalyzed Asymmetric Michael Reactions: Generation of Quaternary Stereocenters at Room Temperature

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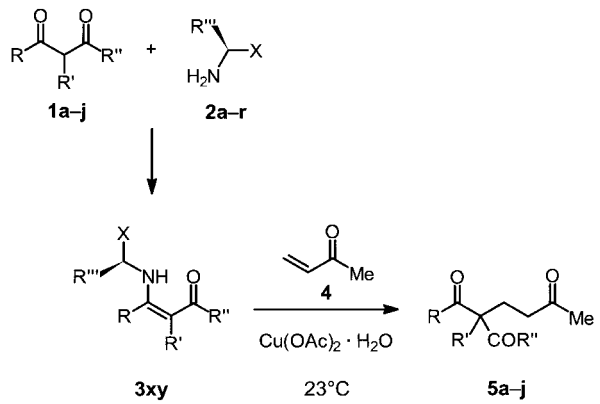
Abstract: Dialkyl amides of L-valine, L-isoleucine, and L-*tert*-leucine (**2**) are excellent chiral auxiliaries for the construction of quaternary stereocenters at ambient temperature. Enaminoesters **3**, prepared from these auxiliaries **2** and Michael donors **1**, undergo a copper-catalyzed asymmetric Michael reaction with methyl vinyl ketone (MVK, **4**) to afford products **5** in 70–90% yield and 90–99% *ee* (enantiomeric excess). The exclusion of moisture or oxygen is not necessary. The auxiliaries **2** are readily available by standard procedures. After workup they can be recovered almost quantitatively.

Keywords: amino acids · asymmetric catalysis · chiral auxiliaries · copper · Michael additions

Introduction

The Michael addition is a common and valuable C–C bond-forming reaction[1] that has been known for over 100 years.[2] To achieve enantioselective Michael reactions, a number of chiral auxiliaries has been utilized since then. Recent examples were reported by Enders et al.,[3] d'Angelo et al.,[4] and Koga et al.[5] Pioneering work on the asymmetric catalysis of the Michael reaction has been performed by Wynberg et al.,[6] who applied cinchona alkaloids as chiral Brönstedt-basic catalysts. Brunner and Hammer,[7] Desimoni et al.,[8] Ito et al.,[9] and Pfaltz et al.[10] have investigated chiral metal complexes in the asymmetric catalysis of the Michael reaction. In 1995, Shibasaki et al. introduced their hetero-bimetallic catalysts, which currently define the state-of-the art in this field.[11]

Since 1996 our group has been searching for a catalyst for asymmetric Michael reactions following a combinatorial strategy.[12] We have screened a large number of catalytically active species generated in situ by a combination of various chiral ligands[13] with different metal salts. Recently, we were able to obtain 91% *ee* in the conversion of a cyclic β-keto ester (**1d**) and methyl vinyl ketone (**4**) from a combination of $Ni(OAc)_2 \cdot 4H_2O$ with optically active 1,2-diaminocyclohexane.[14] Importantly, this formation of a quaternary stereocenter[15] was achieved at ambient temperature. This is a significant improvement compared to established methods: For example, Shibasaki's lanthanum sodium binaphtholate (LSB) catalyst converts **1d** and **4** with 93% *ee* at $-50\,^{\circ}C$.[16] Koga et al. were able to obtain 90% *ee* at $-100\,^{\circ}C$ for the same product (**5d**; Scheme 1).[17] However, the yield of **5d** was always approximately equal to the amount of the diaminocyclohexane applied. Hence, we had to face the fact that our ligand was actually serving as an auxiliary. We learned from these initial experiments and



Scheme 1. Copper-catalyzed asymmetric Michael reactions of enaminoesters **3xy** with MVK (**4**). Letter **x** refers to the Michael donor **1a–j**, letter **y** to the auxiliary **2a–r** used in the synthesis of **3xy**. For yields and enantioselectivities see Table 1 and Table 2. For R, R′, R″ in **1a–j** see Scheme 2, for R‴ and X in **2a–r** see Scheme 3. R, R′, R″ in **5a–j** correspond to **1a–j** in Scheme 2.

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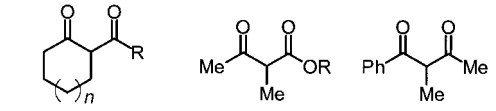
0947-6539/01/0705-1014 $ 17.50+.50/0

designed a new lead structure of chiral auxiliaries for asymmetric Michael reactions: a primary amine with an adjacent donor function which can coordinate to a metal center. We screened a number of chiral auxiliaries together with fourteen metal salts and three Michael donors (**1a**, **1d**, **1f**) following again a combinatorial strategy. As the most important result, selectivities >90% *ee* were obtained by using $Cu(OAc)_2 \cdot H_2O$ as the metal catalyst.[18] No other metal compounds, not even $CuCl_2$, $CuCl_2 \cdot 2H_2O$, or $Cu(OTf)_2$ gave enantioselectivities that exceeded the results obtained with $Cu(OAc)_2 \cdot H_2O$.

In a preceeding communication[18] we only reported on three cyclic β-keto esters as Michael donors. Herein work on cyclic as well as acyclic β-keto esters and β-diketones is compiled and the number of chiral auxiliaries was enlarged. Moreover, all selectivities and yields have been optimized and procedures scaled-up. We are currently focusing on the application of copper acetate as the catalyst.

Results and Discussion

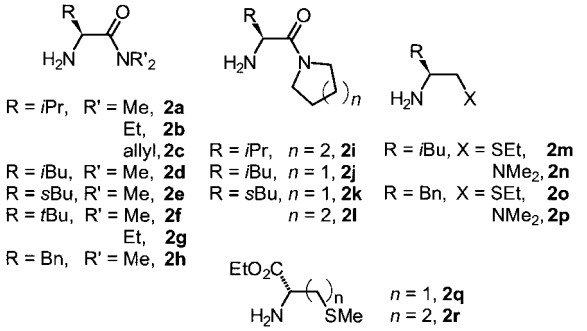
Synthesis of enaminoesters: The lead structure for a suitable chiral auxiliary was a primary amine with an additional donor group. This donor function should not exhibit strong nucleophilicity with respect to conjugate addition to a Michael acceptor. Nevertheless, it should show great affinity in the coordination to a copper(II) center. Consequently, we decided to focus on primary amines (**2**, Scheme 3) with an adjacent



Scheme 2. List of Michael donors **1a–j**.

tertiary amide (**2a–l**), tertiary amine (**2n**, **2p**), or a thioether function (**2m**, **2o**, **2q–r**). Since optically active α-amino acids are readily available from the chiral pool, we prepared the auxiliaries from L-valine (**2a–c**, **2i**), L-leucine (**2d**, **2j**, **2m–n**), L-isoleucine (**2e**, **2k–l**), L-*tert*-leucine (**2f–g**), L-phenylalanine (**2h**, **2o–p**), L-cysteine (**2q**), and L-methionine (**2r**). The synthesis of these auxiliaries is described below. Cyclic and acyclic β-keto esters as well as cyclic and acyclic β-diketones were employed as Michael donor molecules (**1**, Scheme 2).

Compounds **1** and **2** were then allowed to react to give a set of enaminoesters **3xy** (Scheme 1). The first letter **x** indicates the donor **1x**, the second letter **y** the auxiliary **2y**. The reaction was carried out with a catalytic amount of concentrated hydrochloric acid and molecular sieves in toluene at different temperatures (23–80 °C, see the Experimental Section for details). Yields of up to 95% were obtained for optimized



Scheme 3. List of auxiliaries **2a–r**: primary amines with an additional thioether, tertiary amine or amide donor function.

reaction conditions. Without optimization, the yields ranged from 40–95%. Enaminoesters **3xy** hydrolyzed on SiO_2, therefore, purification had to be performed on basic alumina. All compounds **3xy** were found as the enamine tautomers exclusively, the respective imine species were not detectable by ^{1}HNMR spectroscopy. The enamine moiety is always stabilized by H bonding to the adjacent carbonyl group ($\delta_{NH} \approx 9$). The constitution of **3cb**, **3cg**, and **3cl** was established by 2D NMR experiments (HMQC and HMBC) to be an 1-acetyl-2-amino-cyclohexene. Hence, the amine was regioselectively converted with the endocyclic carbonyl group. In the case of **3jb** the same experiments proved that the amine had reacted with the more electrophilic and sterically less hindered acetyl moiety. Not all the possible 10×18 combinations of **3xy** were prepared, but a selection of 33 compounds.

Copper-catalyzed Michael reactions: In primary screening experiments, enaminoesters **3dx** derived from only one donor (**1d**) and auxiliaries **2a–r** were converted with MVK (**4**) and a varying amount of $Cu(OAc)_2 \cdot H_2O$ (2.5–20 mol%). Without any copper salt, the conversions were below 5% within 16 h. Acetone was employed as the solvent, which had been found to be optimal in earlier experiments.[18] After the mixture had been stirred overnight at ambient temperature and protic hydrolysis, the metal was removed by filtration through SiO_2. A sample of the filtrate was submitted to *ee* analysis of the product (**5d**) by GC on a chiral column. A selection of the results is given in Table 1. Amino acid amides **2a–l** were suitable auxiliaries for the transformation of **1d** to **5d** with <40% *ee*. Auxiliaries **2m–r** resulted in enantiomeric ratios below 40% *ee*. Therefore, compounds **2m–r** were not considered in further experiments. At this stage of the primary screening process, the yields of the product **5d** were not determined. It turned out that the auxiliary **2b** was optimal. Hence, conversion of **3db** with MVK (**4**) was scaled up, to yield ≈2 g of the product **5d** with 98% *ee* and 90% yield. The amount of $Cu(OAc)_2 \cdot H_2O$ applied here was 5 mol%. Importantly, after workup the auxiliary **2b** was recovered by extraction from the aqueous layer in almost quantitative yield. This material could be directly resubmitted to enamine formation without any purification.

In further screening experiments, only auxiliaries **2a–l** were investigated in combination with different Michael donors **1**. This time yields of the respective Michael products

Table 1. Enantioselectivities obtained in copper-catalyzed reactions of MVK (**4**) with enaminoesters **3dx** derived from β-ketoester **1d**. In all cases the product was (*R*)-**5d**.[a]

Starting material	$Cu(OAc)_2 \cdot H_2O$ [mol%]	*ee* [%]	Starting material	$Cu(OAc)_2 \cdot H_2O$ [mol%]	*ee* [%]
3da	0	65	**3dg**	2.5	93
	2.5	83		5	93
	5	84		10	95
	10	85	**3dh**	5	56
	20	85	**3di**	0	55
3db	0	57		2.5	95
	2.5	**98**		5	96
	5	98		10	98
	10	98		20	92
	20	98	**3dj**	0	53
3dc	0	55		10	73
	2.5	95		20	75
	5	95	**3dk**	0	76
	10	94		2.5	93
	20	92		5	97
3dd	20	45		10	90
3de	0	70		20	93
	2.5	91			
	5	92			
	10	92			
	20	91			
3df	0	85			
	2.5	97			
	5	96			
	10	97			
	20	**99**			

[a] Reaction conditions: acetone, 12–16 h, 23 °C. Yields were not determined.

Table 2. Yields, enantioselectivities, and absolute configurations obtained in copper-catalyzed reactions of MVK (**4**) with enaminoesters **3xy**.[a]

Product	Starting material	$Cu(OAc)_2 \cdot H_2O$ [mol%]	Yield [%]	*ee* [%]	Configuration
5a	**3ab**	5	42	93	*R*
		10	52	94	*R*
	3af	**5**	**40**	**≥98**	*R*
		10	42	≥98	*R*
		20	42	≥98	*R*
	3al	5	34	≥98	*R*
		10	31	≥98	*R*
5b	**3bb**	**5**	**40**	**96**	*R*
		10	41	96	*R*
5c	**3cb**	10	70	77	[b]
	3cg	**10**	**79**	**95**	[b]
	3cl	5	70	86	[b]
		10	78	93	[b]
5e	**3eb**	5	80	86	*R*
5f	**3ff**	5	75	72	[b]
		10	74	74	[b]
	3fg	5	68	77	[b]
		10	66	79	[b]
	3fi	5	80	87	[b]
		10	**76**	**90**	[b]
5g	**3gb**	5	54	80	[c]
5h	**3hb**	5	60	92	*R*
		10	74	93	*R*
	3hg	5	74	95	*R*
		10	**74**	**96**	*R*
5i	**3ib**	5	65	74	*R*
		10	69	74	*R*
5j	**3jb**	5	4–8	[d]	[d]

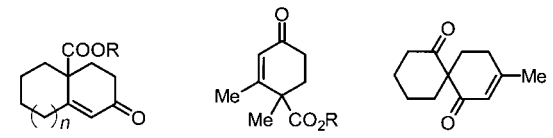
[a] Reaction conditions: acetone, 12–16 h, 23 °C. [b] Unknown. [c] Unknown, but equal to **5f**. [d] Not determined.

were determined. Again, all experiments were performed in acetone and at ambient temperature. Selected results are compiled in Table 2. In general, the use of amides derived from L-valine, L-isoleucine, and L-*tert*-leucine resulted in excellent enantioselectivities. All these amino acids have a α-branching in the alkyl sidechain in common. Interestingly, the amide-nitrogen substitution seemed not to have a significant influence on the stereoselectivity. This effect provides an insight into mechanistic details and will be discussed in detail later on.

Five-membered ring esters **5a** and **5b** were obtained with 96–98% *ee*. The yields were, however, moderate (41–42%). Six-membered ring products **5c**, **5d**, and **5e** were formed in good yields (80–90%), while the optical purity was excellent only in the cases of the diketone **5c** (95% *ee*) and the ethyl ester **5d** (98% *ee*). Seven-membered ring methyl ester **5f** and the acyclic ester **5h** were isolated in good yields (74–76%) and acceptable, respectively excellent, selectivities (90% and 96% *ee*). Again, isobutyl congeners **5g** and **5i** were obtained with lower yield and *ee*. Finally, acyclic diketone **1j** could not be converted under our standard conditions to give product **5j** in acceptable quantities (4–8% yield). Therefore, the optical purity of this material was not determined.

Analysis of enantiomeric ratios: All enantiomeric ratios of compounds **5a–i** were determined by GC on a chiral column. Prior to the analysis of optically active materials, suitable elution conditions were elaborated by the application of racemates of the Michael products **5a–i** or derivatives **6a–f** (Scheme 4). Compounds **5a–i** were, however, not polar enough to give baseline resolu-

0947-6539/01/0705-1016 $ 17.50+.50/0 *Chem. Eur. J.* **2001**, *7*, No. 5



R = Et, n = 1, **6a**
R = Me, n = 2, **6b**
R = *i*Bu, n = 2, **6c**

R = Et, **6d**
R = *i*Bu, **6e**

6f

Scheme 4. List of derivatives **6a–f** for GC analysis derived from **5a–i** by intramolecular aldol condensation.

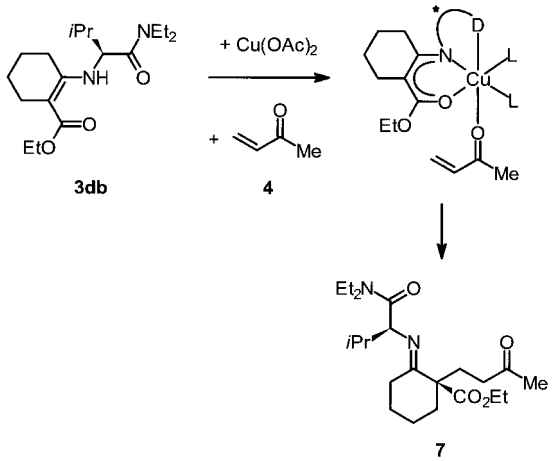
tion of the enantiomers with a temperature gradient. With isotherm elution, only product **5a** was resolved sufficiently and ratios up to 98% *ee* were determined. Compound **5d**, which was chosen for the primary screening, could be analyzed with isotherm elution only up to 90% *ee*, since the absolute error was approximately ±2-3% *ee*. Values exceeding 90% *ee* were determined after aldol cyclization of **5d** to derivative **6a**. The latter was polar enough to give very good baseline resolution up to ratios of 99% *ee* even with a temperature gradient.

As already mentioned, products **5c–i** gave no or only very poor resolution of the enantiomers on our column. However, the preparation of more polar derivatives **6a–f** by intramolecular aldol condensation of **5c–i** turned out to be a generally applicable method for the analysis of these products (compound **5c** was converted to **6f**, **5d** to **6a**, **5f** to **6b**, **5g** to **6c**, **5h** to **6d**, and **5i** to **6e**; for preparative details, see Experimental Section). All derivatives **6a–f** were analyzed with a temperature gradient, except **6c**. The latter had to be transesterified to **6b** before analysis. Isobutyl esters **5b** and **5e** were also transesterified to the corresponding ethyl esters **5a** and **5d**, which were then analyzed by GC.

Absolute configurations: The absolute configurations of **5a**, **5d**, and **5h** were determined by comparison of the optical rotations with literature values. Compounds (−)-**5a**[19] and (+)-**5d**[6b] were reported to have *R* configuration, and (−)-**5h** to have *S* configuration.[20] The absolute configurations of isobutyl esters **5b**, **5e**, and **5i** were related to the corresponding ethyl esters by transesterifications. For compound **5i** this was not carried out directly, but after cyclization to **6e** followed by transesterification to **6d**. In contrast to an earlier statement,[14] compound (−)-**5b** has decidedly *R* configuration. For compounds (+)-**5c**, (+)-**5f** and (+)-**5g**, the absolute configurations are still unknown. By transesterification of **6c**, derived from (+)-**5g**, to **6b** it was shown, that (+)-**5f** and (+)-**5g** possess the same absolute configuration. The use of auxiliaries derived from natural L-amino acids leads exclusively to products with *R* configuration, as shown in Table 1 and Table 2.

Mechanistic considerations: In the classic base-catalyzed Michael reaction, the β-dicarbonyl donor **1** is deprotonated prior to the reaction with the electrophile to give a planar intermediate dionato anion. The negative charge is delocalized over the nucleophilic carbon center and the two carbonyl oxygen atoms. At least for Ni-, Co-, Cu-, and Fe-catalyzed processes, the intermediate dionato anion coordinates to the metal center as a chelating ligand.[21] Dionato–metal complexes of this sort are not nucleophilic enough to be alkylated at the central carbon atom by a Michael acceptor. Commonly, the acceptor, for example **4**, needs further activation by coordination of the carbonyl moiety to a Lewis acid. The metal center of the dionato complex can act as this Lewis acid to form a metal template that maintains the donor and acceptor in close proximity and activating both by coordination.

We propose a template reaction of such a kind for the copper-catalyzed conversion of enamino esters **3xy** with MVK (**4**) (Scheme 5). The acetate counterion of the Cu^{II}



Scheme 5. Mechanistic proposal for the copper-catalyzed asymmetric Michael reaction of enaminoesters **3xy**. Compound **7** was isolated.

cation deprotonates the acidified ($\delta_{NH} \approx 9$) enamino proton to give an aza-diketonate, which coordinates to the copper center as a chelating ligand. The choice of the counterion seems to be crucial for the enantioselectivity of the reaction. $Cu(OTf)_2$, $CuCl_2$, or $CuCl_2 \cdot 2H_2O$, which do not have sufficient Brönstedt basicity, all give lower *ee* values than $Cu(OAc)_2 \cdot H_2O$.

After coordination of the aza-diketonate to the copper center, the additional donor function D, being a carboxylic amide, leads to diastereofacial differentiation of the *Si* and *Re* faces of the Michael donor. Another chelate ring is formed which makes the enaminoester anion a tridentate ligand bound on one face of the octahedral coordination polyhedron. Coordination of D from the upper *Si* face (Scheme 5) results in a pseudoequatorial arrangement of the alkyl residue on the amino acid (R in Scheme 1) in the five-membered chelate ring. Coordination from the lower *Re* face would place the alkyl group into a pseudoaxial conformation, which is evidently disfavored due to diaxial strain with one of the other ligands (L, which is presumably water or solvent). Interestingly, this strain seems to be distinct with alkyl residues that contain α-branching, namely *i*Pr, *s*Bu, and *t*Bu. This hypothesis is strongly supported by the fact that selectivities >90% *ee* are observed with auxiliaries derived from L-valine, L-isoleucine, and L-*tert*-leucine only.

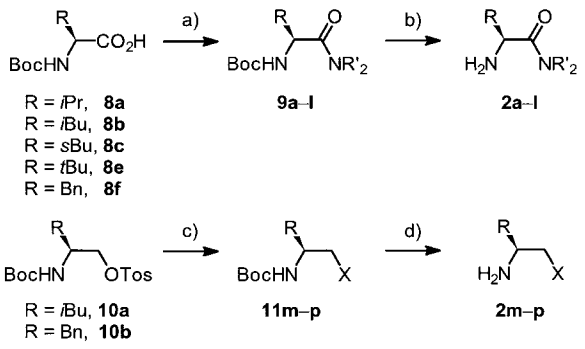
Without activation by a Lewis acid, the conversion of MVK (**4**) with the enamines **3xy** is very slow at ambient temper-

ature.[22] Consequently, the acceptor needs to be activated by coordination to the Lewis-acidic copper center. With the additional donor function D coordinating from the *Si* face of the aza-dionate, the MVK (**4**) must coordinate at the opposite *Re* face. After activation, **4** reacts from this *Re* face with the aza-dionate to result exclusively in products **5a–i** with *R* configuration. After the conjugate addition, π-electron density cannot be delocalized over the quaternary carbon center. Therefore, a copper–chelate complex no longer exhibits particular thermodynamic stability. The enolate moiety of the former MVK (**4**) deprotonates the next equivalent of the enaminoester **3xy**. The primary product is an imine, which is hydrolyzed to the product **5** upon aqueous protic workup. This imine **7** was isolated in one case (Scheme 5).

In addition to the correct choice of the central metal, the counterion, and the stereogenic alkyl group in the auxiliary (α-branching is required), the additional donor function D is an important parameter. Only carboxylic amides result in high selectivities. The use of thioethers or tertiary amines has not been successful. We presume that the carbonyl oxygen is the coordinating donor atom rather than the amide nitrogen atom, since yields and selectivities are nearly independent of the nitrogen substituents. We are presently seeking a structural proof of the tridentate coordination of enaminoesters **3xy** to copper(II) centers.

Although the role of Cu^{II} in activating the substrate is evident from the yields, one aspect remains puzzling and cannot be explained by the mechanistic interpretation discussed above: the chiral auxiliary can also exert lower, but still considerable, stereocontrol without the presence of copper. In this case the mechanistic proposal from d'Angelo et al.[4] might be applicable.

Synthesis of auxiliaries: Amino acid amides **2a–l**, most of which have already been reported in the literature, are accessible on a large scale by standard transformations from common starting materials (Scheme 6). The amino function



Scheme 6. Synthesis of chiral auxiliaries. For yields see the Experimental Section. Reagents and conditions: a) DCC, HNR'_2, CH_2Cl_2, 23 °C; b) TFA, CH_2Cl_2, 23 °C; c) for **11m** and **11o**: NaSEt, DMF, 23 °C; for **11n** and **11p**: $HNMe_2$, pyridine, 0 → 23 °C; d) TFA, CH_2Cl_2, 23 °C. Letters **a–p** in **9a–l** and **11m–p** correspond to compounds **2a–p**.

had to be protected prior to amide formation. We have chosen the *tert*-butyl carbamate. Different protocols for *N*-Boc protections of amino acids are found in the literature. Our favorable procedure to prepare **8a–f** was the conversion of the respective amino acid with one equivalent of Boc_2O and one equivalent of Na_2CO_3 in MeOH/H_2O (1:1; 16 h, 23 °C) without 4-dimethylaminopyridine (DMAP). After removal of the solvents and acidification with citric acid, the mixtures were extracted with CH_2Cl_2 to furnish the protected amino acids **8a–f**. Residual *tert*-butyl alcohol was removed in high vacuum (5 h). The yields were nearly quantitative in all cases. The crude products could be submitted to amide formation without further purification. Compounds **8a–f** were activated with DCC and converted with the respective secondary amine to give the amides **9a–l** in 50–95% yield. We never applied catalytic amounts of DMAP in order to avoid epimerization. After deprotection with trifluoroacetic acid (TFA), compounds **2a–l** were obtained by Kugelrohr distillation as generally pure materials. Handling and storage required exclusion of moisture and air, since the amines are all very hygroscopic and sensitive to CO_2.

Compounds **2m–p** were prepared from N-protected and O-activated L-leucinol and L-phenylalaninol (**10a** and **10b**). Nucleophilic substitution with NaSEt and $HNMe_2$/pyridine proceeded with 82–94% yield (**11m–p**). Deprotection with TFA followed by Kugelrohr distillation yielded amines **2m–p**, which are hygroscopic and sensitive to CO_2.

Future work: Herein we have reported on the highly enantioselective construction of quaternary stereocenters at room temperature by copper-catalyzed Michael reactions. The chiral information provided by L-valine, L-isoleucine, and L-*tert*-leucine dialkylamides was used stoichiometrically. As mentioned above, the auxiliaries are readily accessible. Moreover they can be almost quantitatively recovered from the reaction mixtures. Despite these facts, the final aim has to be to use them catalytically. To close a catalytic cycle from the reactions shown in Scheme 5, the in situ formation of enamines **3xy** and the in situ hydrolysis of imines, such as **7**, has to be performed. Both reactions, however, are presently catalyzed by Brönstedt acids, which is not compatible with the catalysis of the Michael reaction. Therefore, a careful control of Brönstedt basicity is crucial for the success of the latter, as outlined in the mechanistic considerations. Consequently, the key to the catalysis is to be found in conditions for enamine formation and imine hydrolysis, which do not affect the Michael reaction. We are currently working on the solution to this problem.

Experimental Section

General: Column chromatography was accomplished on Merck silica gel (Type 60, 0.063–0.200 mm) or ICN alumina (Al_2O_3 90, activity II–III) with *tert*-butyl methyl ether (MTB) and hexanes (PE) as solvents. ^{1}HNMR spectra were recorded on Bruker DRX500 (500 MHz), AM400 (400 MHz), and AC200 (200 MHz) spectrometers. ^{13}CNMR spectra were recorded on Bruker DRX500 (125 MHz) and AC200 (50 MHz) spectrometers, assignments were made with DEPT experiments. The constitutions of compounds **3cb**, **3cg**, **3cl**, and **3jb** were additionally confirmed by HMQC and HMBC experiments. MS spectra were obtained with a Varian MAT711 and MAT955Q (high resolution). IR spectra were recorded on a Nicolet Magna IR750. Elemental analyses were obtained with an Analytik Jena Vario EL. Melting points were measured with a Leica Galen III and are uncorrected. Chiral GC analysis was performed with a Packard 437A

0947-6539/01/0705-1018 $ 17.50+.50/0 *Chem. Eur. J.* **2001**, *7*, No. 5

with FI detection, a Shimadzu C-R6a integrator, and a Macherey–Nagel column FS-LIPODEX E (25 m, 0.25 mm) with nitrogen carrier gas. $HNMe_2$ was purchased from Fluka and cooled below 0 °C before use. Starting materials **1a**, **1c**, **1d**, and **1f** were commercially available and used as purchased. Compounds **1b**,[23] **1e**, **1g**,[24] **1h–i**,[25] **2q**·HCl,[26] **2r**·HCl,[27] **8a–f**,[28] and **10a**,[29] **10b**[30] were prepared according to literature protocols. Synthesis of **1j**[31] and **5i,j**[32] followed adapted literature procedures. The racemates of **5a,b**, **5d,e**, **5h**,[33] **5c**,[14] **5e**, **5g**[24] and derivatives **6a,b**,[14] **6d**,[20] **6f**[14] have been reported earlier. Spectral data of the following compounds were in accordance with the literature: **2a**,[34] **2b**,[35] **2d**,[36] **2e**,[37] **2h**,[38] **2i**,[39] **2j**,[40] **2k**,[41] **2l**,[37] **2p**,[42] **9a**,[36] **9d**,[36] **9e**,[37] **9h**,[43] **9i**,[44] **9j**,[45] **9l**,[37] **11o**.[46] Experimental details on the synthesis and characterization of the following compounds are given in the Supporting Information: **2a,b**, **d,e**, **h–l**, **p**, **9a**, **d,e**, **h,j**, **l** and **11o**.

2-Methyl-1-phenylbutane-1,3-dione (1j): Iodomethane (1.65 mL, 3.76 g, 26.5 mmol) was added to a mixture of benzoylacetone (2.15 g, 13.3 mmol), nBu$_4$NF·3H$_2$O (4.18 g, 13.3 mmol), and CH_2Cl_2 (5 mL). After stirring overnight at ambient temperature, the mixture was transferred onto a SiO_2 column and eluted with MTB/PE (1:5, $R_f = 0.39$) to yield the product **1j** (1.73 g, 9.82 mmol, 74 %) as a colorless oil. ^{1}HNMR (200 MHz, $CDCl_3$) shows a mixture of keto and enol tautomers (ratio ≈9:1), keto isomer: $\delta =$ 1.42 (d, $J = 7.2$ Hz, 3H), 2.23 (s, 3H), 4.47 (q, $J = 7.0$ Hz, 1H), 7.43–7.60 (m, 3H), 7.94–7.99 (m, 2H); enol tautomer: $\delta = 1.93$ (s, 3H), 2.26 (s, 3H), 7.43–7.60 (m, 5H), 16.5 (s, 1H); ^{13}CNMR (50 MHz, $CDCl_3$): $\delta = 13.51$ (CH_3), 27.85 (CH_3), 56.61 (CH), 128.57 (2CH), 128.79 (2CH), 133.60 (CH), 135.83 (C), 197.26 (C=O), 204. 94 (C=O); IR (ATR): $\tilde{\nu} = 1716$, 1673, 691 cm^{-1}; MS (EI, 70 eV): m/z (%): 175 (14) $[M-H]^+$, 133 (100), 105 (80), 77 (90); HR-MS: $C_{11}H_{12}O_2$ (176.22): calcd: 175.0756; found: 175.0759 $[M-H]^+$.

General procedure 1 (GP1) for the synthesis of auxiliaries 2a–p: To a solution of the respective *N*-Boc-protected compound **9a–l** and **11m–p** in CH_2Cl_2 was added trifluoroacetic acid (≈2.3 equiv) and the reaction mixture was stirred for 14–24 h at 23 °C. All volatile materials were removed in vacuo. The residue was dissolved in water and treated with KOH (10 % aqueous solution) at 0 °C. The resulting mixture was extracted with CH_2Cl_2 and the combined organic layers were dried over $MgSO_4$. After filtration and evaporation of the solvent, the crude product was purified by Kugelrohr distillation (1 mbar). The amines **2a–p** are very hygroscopic and sensitive to CO_2 and were therefore stored under nitrogen. Details for compounds **2a,b**, **d,e**, **h–l**, and **p** are given in the Supporting Information.

L-Valine diallylamide (2c): Deprotection of **9c** (6.000 g, 20.24 mmol) yielded **2c** after Kugelrohr distillation (125 °C, oven temperature) as a colorless oil (2.786 g, 14.05 mmol, 70 %). $[\alpha]_D^{23} = +7.0$ ($c = 5.7$ in $CHCl_3$); ^{1}HNMR (200 MHz, $CDCl_3$): $\delta = 0.93$ (d, $J = 6.8$ Hz, 3H), 0.95 (d, $J =$ 6.7 Hz, 3H), 1.77 (br s, 2H), 1.76–1.96 (m, 1H), 3.34 (d, $J = 5.9$ Hz, 1H), 3.68–4.07 (m, 3H), 4.18–4.32 (m, 1H), 5.15–5.26 (m, 4H), 5.66–5.89 (m, 2H); ^{13}CNMR (50 MHz, $CDCl_3$): $\delta = 16.97$ (CH_3), 20.15 (CH_3), 32.23 (CH), 47.96 (CH_2), 48.81 (CH_2), 56.67 (CH), 116.89 (CH_2), 117.27 (CH_2), 133.16 (2CH), 175.39 (C=O); IR (ATR): $\tilde{\nu} = 1641$ cm^{-1}; MS (EI, 70 eV): m/z (%): 197 (23) $[M+H]^+$, 98 (18), 72 (100); HR-MS: $C_{11}H_{20}N_2O$ (196.29): calcd: 197.1654; found: 197.1651 $[M+H]^+$.

L-*tert*-Leucine dimethylamide (2f): Deprotection of **9f** (4.450 g, 17.22 mmol) yielded **2f** after Kugelrohr distillation (120 °C, oven temperature) as a colorless solid (2.611 g, 16.50 mmol, 96 %). M.p. 34–35 °C; $[\alpha]_D^{23} = +107$ ($c = 6.4$ in $CHCl_3$); ^{1}HNMR (200 MHz, $CDCl_3$): $\delta = 0.95$ (s, 9H), 1.55 (s, 2H), 2.94 (s, 3H), 3.06 (s, 3H), 3.51 (s, 1H); ^{13}CNMR (50 MHz, $CDCl_3$): $\delta = 26.26$ (3CH_3), 35.32 (C), 35.55 (CH_3), 38.04 (CH_3), 57.63 (CH), 174.62 (C=O); IR (ATR): $\tilde{\nu} = 1636$ cm^{-1}; MS (EI, 70 eV): m/z (%): 159 (63) $[M+H]^+$, 86 (100), 72 (18); HR-MS: $C_8H_{18}N_2O$: calcd: 158.1419; found: 158.1420 $[M]^+$; elemental analysis calcd (%) for $C_8H_{18}N_2O$ (158.24): C 60.72, H 11.47, N 17.70; found: C 60.64, H 11.69, N 17.46.

L-*tert*-Leucine diethylamide (2g): Deprotection of **9g** (4.950 g, 17.28 mmol) yielded **2g** after Kugelrohr distillation (120 °C, oven temperature) as a colorless oil (2.730 g, 14.65 mmol, 85 %). $[\alpha]_D^{23} = +89.9$ ($c = 5.75$ in $CHCl_3$); ^{1}HNMR (200 MHz, $CDCl_3$): $\delta = 0.98$ (s, 9H), 1.12 (t, $J = 7.0$ Hz, 3H), 1.18 (t, $J = 7.0$ Hz, 3H), 1.54 (br s, 2H), 2.98–3.29 (m, 2H), 3.38 (s, 1H), 3.49–3.80 (m, 2H); ^{13}CNMR (50 MHz, $CDCl_3$): $\delta = 12.99$ (CH_3), 14.73 (CH_3), 26.41 (3CH_3), 35.13 (C), 40.35 (CH_2), 42.39 (CH_2), 57.75 (CH), 173.80 (C=O); IR (ATR): $\tilde{\nu} = 1633$ cm^{-1}; MS (EI, 70 eV): m/z (%): 187 (3) $[M+H]^+$, 129 (13), 101 (14), 86 (100), 74 (26), 72 (43), 69 (36), 56 (16); HR-MS: $C_{10}H_{22}N_2O$ (186.30): calcd: 187.1810; found: 187.1814 $[M+H]^+$.

(*S*)-2-Amino-1-(ethylsulfanyl)-4-methylpentane (2m): Deprotection of **11m** (840 mg, 3.21 mmol) yielded **2m** after Kugelrohr distillation (90 °C, oven temperature) as a colorless oil (403 mg, 2.50 mmol, 78 %). $[\alpha]_D^{23} = +41$ ($c = 7.9$ in $CHCl_3$); ^{1}HNMR (400 MHz, $CDCl_3$): $\delta = 0.90$ (d, $J = 6.7$ Hz, 3H), 0.92 (d, $J = 6.7$ Hz, 3H), 1.23–1.29 (m, 2H), 1.26 (t, $J = 7.6$ Hz, 3H), 1.59 (s, 2H), 1.69–1.80 (m, 1H), 2.34 (dd, $J = 13.0$, 8.6 Hz, 1H), 2.54 (q, $J =$ 7.5 Hz, 2H), 2.68 (dd, $J = 13.1$, 3.9 Hz, 1H), 2.90–2.97 (m, 1H); ^{13}CNMR (50 MHz, $CDCl_3$): $\delta = 14.94$ (CH_3), 22.06 (CH_3), 23.34 (CH_3), 24.98 (CH), 26.41 (CH_2), 41.04 (CH_2), 46.54 (CH_2), 48.27 (CH); IR (ATR): $\tilde{\nu} = 2955$, 2927, 2913, 2869, 1366 cm^{-1}; MS (EI, 70 eV): m/z (%): 161 (1) $[M]^+$, 104 (13), 86 (100), 75 (7); HR-MS: $C_8H_{19}NS$ (161.31): calcd: 161.1238; found: 161.1237.

(*S*)-2-Amino-1-(dimethylamino)-4-methylpentane (2n): Deprotection of **11n** (803 mg, 3.29 mmol) yielded **2n** after Kugelrohr distillation (95 °C, oven temperature) as a colorless oil (394 mg, 2.73 mmol, 83 %). $[\alpha]_D^{23} =$ +37.0 ($c = 9.60$ in $CHCl_3$); ^{1}HNMR (400 MHz, $CDCl_3$): $\delta = 0.89$ (d, $J =$ 7.0 Hz, 3H), 0.91 (d, $J = 6.9$ Hz, 3H), 1.11–1.24 (m, 2H), 1.69–1.80 (m, 1H), 2.06 (dd, $J = 12.0$, 3.8 Hz, 1H), 2.12–2.19 (m, 1H), 2.15 (br s, 2H), 2.22 (s, 6H), 2.90–2.98 (m, 1H); ^{13}CNMR (50 MHz, $CDCl_3$): $\delta = 22.01$ (CH_3), 23.49 (CH_3), 24.63 (CH), 44.91 (CH_2), 45.81 (2CH_3), 46.19 (CH), 67.17 (CH_2); IR (ATR): $\tilde{\nu} = 2958$, 1745, 1684, 1202, 1177, 1132 cm^{-1}; MS (EI, 70 eV): m/z (%): 144 (3) $[M]^+$, 86 (50), 70 (6), 59 (88), 58 (100); HR-MS: $C_8H_{20}N_2$ (144.26): calcd: 144.1626; found: 144.1619.

(*S*)-2-Amino-1-(ethylsulfanyl)-3-phenylpropane (2o): Deprotection of **11o** (450 mg, 1.52 mmol) yielded **2o** as a colorless oil (294 mg, 1.51 mmol, 99 %), which could be used without further purification. $[\alpha]_D^{23} = +32.0$ ($c =$ 5.0 in $CHCl_3$); ^{1}HNMR (400 MHz, $CDCl_3$): $\delta = 1.24$ (t, $J = 7.3$ Hz, 3H), 1.16 (br s, 2H), 2.44 (dd, $J = 13.2$, 8.3 Hz, 1H), 2.55 (q, $J = 7.3$ Hz, 2H), 2.61 (dd, $J = 13.3$, 8.1 Hz, 1H), 2.72 (dd, $J = 13.0$, 4.2 Hz, 1H), 2.84 (dd, $J = 13.3$, 5.2 Hz, 1H), 3.12–3.19 (m, 1H), 7.19–7.24 (m, 3H), 7.28–7.34 (m, 2H); ^{13}CNMR (50 MHz, $CDCl_3$): $\delta = 14.89$ (CH_3), 26.45 (CH_2), 39.67 (CH_2), 43.51 (CH_2), 52.03 (CH), 126.40 (CH), 128.51 (2CH), 129.24 (2CH), 138.85 (C); IR (ATR): $\tilde{\nu} = 2924$, 1453, 746, 700 cm^{-1}; MS (EI, 70 eV): m/z (%): 196 (3) $[M+H]^+$, 179 (18), 120 (100), 104 (31), 91 (23), 77 (6), 75 (16); HR-MS: $C_{11}H_{17}NS$ (195.33): calcd: 196.1160; found: 196.1162.

General procedure 2 (GP2) for the synthesis of enamines 3xy: A mixture of β-dicarbonyl compound **1x**, auxiliary **2y**, and molecular sieves (4 Å) under nitrogen in toluene was treated with a catalytic amount of concentrated HCl (1 drop). After stirring for 12–14 h at 60–65 °C (unless otherwise stated), the reaction mixture was filtered and the residue washed with CH_2Cl_2. All volatile materials were removed in vacuo and the residue was chromatographed on Al_2O_3 90 (activity II–III, eluent: MTB/PE) to yield the title compound.

***N*-(2-Ethoxycarbonyl-1-cyclopentenyl)-L-valine diethylamide (3ab)**: Oxoester **1a** (453 mg, 2.90 mmol), auxiliary **2b** (500 mg, 2.90 mmol), and molecular sieves (2.5 g) in toluene (5 mL) were converted according to GP2 to yield **3ab** after chromatography (MTB/PE = 2:1, $R_f = 0.45$) as a colorless solid (691 mg, 2.23 mmol, 77 %). M.p. 52–56 °C; $[\alpha]_D^{23} = +95$ ($c =$ 5.2 in $CHCl_3$); ^{1}HNMR (400 MHz, $CDCl_3$): $\delta = 0.97$ (d, $J = 6.9$ Hz, 3H), 0.97 (d, $J = 6.8$ Hz, 3H), 1.11 (t, $J = 7.1$ Hz, 3H), 1.20 (t, $J = 7.1$ Hz, 3H), 1.27 (t, $J = 7.1$ Hz, 3H), 1.77–1.84 (m, 2H), 1.97–2.05 (m, 1H), 2.38–2.47 (m, 1H), 2.49–2.58 (m, 3H), 3.09–3.18 (m, 1H), 3.20–3.29 (m, 1H), 3.37–3.44 (m, 1H), 3.58–3.67 (m, 1H), 3.93 (dd, $J = 9.9$, 6.0 Hz, 1H), 4.10–4.22 (m, 2H), 7.72 (br s, 1H); ^{13}CNMR (50 MHz, $CDCl_3$): $\delta = 12.90$ (CH_3), 14.66 (CH_3), 14.73 (CH_3), 17.53 (CH_3), 19.81 (CH_3), 20.91 (CH_2), 29.30 (CH_2), 32.66 (CH), 32.79 (CH_2), 40.19 (CH_2), 41.54 (CH_2), 58.55 (CH_2), 59.98 (CH), 94.29 (C), 161.81 (C), 167.86 (C=O), 170.60 (C=O); IR (ATR): $\tilde{\nu} =$ 1661, 1598, 1262 cm^{-1}; MS (EI, 70 eV): m/z (%): 310 (7) $[M]^+$, 265 (7), 210 (65), 164 (100), 116 (10), 100 (15), 72 (25); HR-MS: $C_{17}H_{30}N_2O_3$: calcd: 310.2256; found: 310.2251; elemental analysis calcd (%) for $C_{17}H_{30}N_2O_3$ (310.42): C 65.77, H 9.74, N 9.02; found: C 65.88, H 9.60, N 9.23.

***N*-(2-Ethoxycarbonyl-1-cyclopentenyl)-L-*tert*-leucine dimethylamide (3af)**: Oxoester **1a** (296 mg, 1.90 mmol), auxiliary **2f** (300 mg, 1.90 mmol), and molecular sieves (1.5 g) in toluene (5 mL) were converted according to GP2 to yield **3af** after chromatography (MTB/PE = 2:1, $R_f = 0.18$) as a colorless solid (260 mg, 0.877 mmol, 46 %). M.p. 59–60 °C; $[\alpha]_D^{23} = +160$ ($c = 5.4$ in $CHCl_3$); ^{1}HNMR (400 MHz, $CDCl_3$): $\delta = 1.03$ (s, 9H), 1.28 (t, $J = 7.1$ Hz, 3H), 1.77–1.85 (m, 2H), 2.39 (pent, $J = 7.8$ Hz, 1H), 2.49–2.59

(m, 3H), 2.97 (s, 3H), 3.09 (s, 3H), 4.06 (d, $J = 10.3$ Hz, 1H), 4.10–4.23 (m, 2H), 7.85 (brs, 1H); ^{13}CNMR (50 MHz, $CDCl_3$): $\delta = 14.71$ (CH_3), 20.79 (CH_2), 26.42 (3CH_3), 29.35 (CH_2), 32.73 (CH_2), 35.68 (CH_3), 36.07 (C), 37.97 (CH_3), 58.62 (CH_2), 60.47 (CH), 94.35 (C), 161.31 (C), 167.81 (C=O), 171.41 (C=O); IR (ATR): $\tilde{\nu} = 1659$, 1598, 1264, 1098 cm^{-1}; MS (EI, 70 eV): m/z (%): 296 (13) $[M]^+$, 251 (7), 239 (13), 224 (64), 193 (30), 178 (100), 165 (24), 130 (15), 122 (8), 101 (13), 86 (54), 72 (25), 69 (20); HR-MS: $C_{16}H_{28}N_2O_3$: calcd: 296.2100; found: 296.2103; elemental analysis calcd (%) for $C_{16}H_{28}N_2O_3$ (296.38): C 64.83, H 9.45, N 9.02; found: C 64.44, H 9.63, N 9.38.

***N*-(2-Ethoxycarbonyl-1-cyclopentenyl)-L-isoleucine piperidide (3al)**: Oxoester **1a** (520 mg, 3.33 mmol), auxiliary **2l** (600 mg, 3.03 mmol), and molecular sieves (2.5 g) in toluene (7 mL) were converted according to GP2 to yield **3al** after chromatography (MTB/PE = 2:1, $R_f = 0.56$) as a colorless solid (802 mg, 2.38 mmol, 79%). M.p. 69–70 °C; $[\alpha]_D^{23} = +173$ ($c = 8.5$ in $CHCl_3$); ^{1}HNMR (400 MHz, $CDCl_3$): $\delta = 0.89$ (t, $J = 7.3$ Hz, 3H), 0.95 (d, $J = 6.7$ Hz, 3H), 1.10–1.20 (m, 1H), 1.27 (t, $J = 7.1$ Hz, 3H), 1.50–1.85 (m, 10H), 2.35–2.45 (m, 1H), 2.46–2.55 (m, 3H), 3.38–3.47 (m, 2H), 3.56–3.62 (m, 2H), 4.04 (dd, $J = 9.7$, 6.6 Hz, 1H), 4.12–2.20 (m, 2H), 7.72 (brs, 1H); ^{13}CNMR (50 MHz, $CDCl_3$): $\delta = 11.49$ (CH_3), 14.70 (CH_3), 16.03 (CH_3), 20.78 (CH_2), 24.26 (CH_2), 24.48 (CH_2), 25.58 (CH_2), 26.60 (CH_2), 29.24 (CH_2), 32.60 (CH_2), 38.67 (CH), 43.17 (CH_2), 46.62 (CH_2), 58.53 (CH_2), 59.42 (CH), 94.33 (C), 162.13 (C), 167.98 (C=O), 170.13 (C=O); IR (ATR): $\tilde{\nu} = 1639$, 1601, 1564, 1442, 1258 cm^{-1}; MS (EI, 70 eV): m/z (%): 336 (3) $[M]^+$, 224 (38), 178 (100), 150 (8), 122 (13), 94 (8), 69 (15); HR-MS: $C_{19}H_{32}N_2O_3$: calcd: 336.2413; found: 336.2419; elemental analysis calcd (%) for $C_{19}H_{32}N_2O_3$ (336.47): C 65.77, H 9.74, N 9.02; found: C 65.88, H 9.60, N 9.23.

***N*-(2-Isobutoxycarbonyl-1-cyclopentenyl)-L-valine diethylamide (3bb)**: Oxoester **1b** (570 mg, 3.09 mmol), auxiliary **2b** (533 mg, 3.09 mmol) and molecular sieves (3 g) in toluene (5 mL) were converted according to GP2 for 24 h at 80 °C to yield **3bb** after chromatography (MTB/PE = 1:1, $R_f = 0.45$) as a colorless solid (668 mg, 1.97 mmol, 64%). M.p. 45–47 °C; $[\alpha]_D^{23} = +94.8$ ($c = 12.3$ in $CHCl_3$); ^{1}HNMR (400 MHz, $CDCl_3$): $\delta = 0.94$ (d, $J = 6.7$ Hz, 6H), 0.97 (d, $J = 6.8$ Hz, 3H), 0.98 (d, $J = 6.7$ Hz, 3H), 1.11 (t, $J = 7.0$ Hz, 3H), 1.20 (t, $J = 7.1$ Hz, 3H), 1.81 (pent, $J = 7.6$ Hz, 2H), 1.90–2.06 (m, 2H), 2.43 (pent, $J = 7.8$ Hz, 1H), 2.49–2.59 (m, 3H), 3.11–3.20 (m, 1H), 3.21–3.30 (m, 1H), 3.37–3.46 (m, 1H), 3.57–3.66 (m, 1H), 3.83–3.95 (m, 3H), 7.70 (brs, 1H); ^{13}CNMR (50 MHz, $CDCl_3$): $\delta = 12.90$ (CH_3), 14.66 (CH_3), 17.63 (CH_3), 19.24 (CH_3), 19.27 (CH_3), 19.80 (CH_3), 20.86 (CH_2), 27.93 (CH), 29.29 (CH_2), 32.68 (CH), 32.80 (CH_2), 40.18 (CH_2), 41.54 (CH_2), 60.06 (CH), 68.97 (CH_2), 94.36 (C), 161.71 (C), 167.94 (C=O), 170.62 (C=O); IR (ATR): $\tilde{\nu} = 1662$, 1598, 1261 cm^{-1}; MS (EI, 70 eV): m/z (%): 338 (13) $[M]^+$, 265 (14), 238 (100), 221 (9), 186 (7), 182 (9), 164 (100), 136 (7), 122 (7), 100 (8), 91 (11), 72 (9), 69 (10); HR-MS: $C_{19}H_{34}N_2O_3$: calcd: 338.2569; found: 338.2570; elemental analysis calcd (%) for $C_{19}H_{34}N_2O_3$ (338.49): C 67.42, H 10.12, N 8.28; found: C 67.42, H 10.01, N 8.38.

***N*-(2-Acetyl-1-cyclohexenyl)-L-valine diethylamide (3cb)**: Diketone **1c** (688 mg, 4.91 mmol), auxiliary **2b** (650 mg, 3.77 mmol), and molecular sieves (2 g) in toluene (4 mL) were converted according to GP2 at 23 °C to yield **3cb** after chromatography (MTB/PE = 3:1, $R_f = 0.24$) as a colorless resin (504 mg, 1.71 mmol, 45%). $[\alpha]_D^{23} = +201$ ($c = 2.8$ in $CHCl_3$); ^{1}HNMR (500 MHz, $CDCl_3$): $\delta = 1.00$ (d, $J = 6.8$ Hz, 3H), 1.03 (d, $J = 6.8$ Hz, 3H), 1.10 (t, $J = 7.0$ Hz, 3H), 1.16 (t, $J = 7.0$ Hz, 3H), 1.55–1.67 (m, 4H), 2.03–2.17 (m, 2H), 2.08 (s, 3H), 2.28–2.36 (m, 3H), 3.17–3.25 (m, 1H), 3.29–3.43 (m, 2H), 3.46–3.54 (m, 1H), 4.11 (dd, $J = 8.3$, 6.5 Hz, 1H), 11.79 (br d, $J = 7.8$ Hz); ^{13}CNMR (125 MHz, $CDCl_3$): $\delta = 12.76$ (CH_3), 14.41 (CH_3), 18.13 (CH_3), 19.95 (CH_3), 21.88 (CH_2), 22.94 (CH_2), 26.09 (CH_2), 26.67 (CH_2), 27.72 (CH_3), 31.92 (CH), 40.26 (CH_2), 41.39 (CH_2), 59.49 (CH), 101.05 (C), 159.82 (C), 170.27 (C=O), 196.69 (C=O); IR (ATR): $\tilde{\nu} = 1643$, 1602, 1564, 1260 cm^{-1}; MS (EI, 70 eV): m/z (%): 294 (15) $[M]^+$, 251 (5), 208 (7), 194 (100), 176 (8), 166 (6), 150 (23), 136 (8), 125 (6), 114 (5), 100 (10), 84 (23), 72 (68); HR-MS: $C_{17}H_{30}N_2O_2$: calcd: 294.2307; found: 294.2309.

***N*-(2-Acetyl-1-cyclohexenyl)-L-*tert*-leucine diethylamide (3cg)**: Diketone **1c** (361 mg, 2.58 mmol), auxiliary **2g** (480 mg, 2.58 mmol), and molecular sieves (3 g) in toluene (4 mL) were converted according to GP2 at 23 °C to yield **3cg** after chromatography (MTB/PE = 3:1, $R_f = 0.25$) as a colorless solid (206 mg, 0.668 mmol, 23%). M.p. 86–87 °C; $[\alpha]_D^{23} = +97$ ($c = 5.6$ in $CHCl_3$); ^{1}HNMR (500 MHz, $CDCl_3$): $\delta = 1.05$ (s, 9H), 1.11 (t, $J = 7.1$ Hz, 3H), 1.18 (t, $J = 7.1$ Hz, 3H), 1.56–1.65 (m, 4H), 2.08 (s, 3H), 2.13–2.21 (m, 1H), 2.31–2.39 (m, 3H), 3.06–3.14 (m, 1H), 3.30–3.37 (m, 1H), 3.51–3.58 (m, 1H), 3.64–3.71 (m, 1H), 4.25 (d, $J = 9.4$ Hz, 1H), 11.99 (br d, $J = 9.4$ Hz, 1H); ^{13}CNMR (125 MHz, $CDCl_3$): $\delta = 12.71$ (CH_3), 14.38 (CH_3), 21.95 (CH_2), 22.99 (CH_2), 26.13 (CH_2), 26.64 (CH_2), 26.95 (3CH_3), 27.75 (CH_3), 36.12 (C), 39.75 (CH_2), 42.06 (CH_2), 59.01 (CH), 100.76 (C), 158.78 (C), 169.58 (C=O), 196.53 (C=O); IR (ATR): $\tilde{\nu} = 1640$, 1602, 1564, 1263 cm^{-1}; MS (EI, 70 eV): m/z (%): 308 (6) $[M]^+$, 251 (12), 208 (100), 150 (23), 95 (5), 81 (7), 69 (10); HR-MS: $C_{18}H_{32}N_2O_2$: calcd: 308.2464; found: 308.2466; elemental analysis calcd (%) for $C_{18}H_{32}N_2O_2$ (308.46): C 70.09, H 10.46, N 9.08; found: C 69.62, H 10.04, N 9.01.

***N*-(2-Acetyl-1-cyclohexenyl)-L-isoleucine piperidide (3cl)**: Diketone **1c** (763 mg, 5.45 mmol), auxiliary **2l** (900 mg, 4.54 mmol), and molecular sieves (3 g) in toluene (6 mL) were converted according to GP2 at 45 °C to yield **3cl** after chromatography (MTB/PE = 3:1, $R_f = 0.31$) as a colorless solid (1.13 g, 3.52 mmol, 77%). M.p. 77–78 °C; $[\alpha]_D^{23} = +335$ ($c = 6.6$ in $CHCl_3$); ^{1}HNMR (500 MHz, $CDCl_3$): $\delta = 0.89$ (t, $J = 7.4$ Hz, 3H), 0.98 (d, $J = 6.8$ Hz, 3H), 1.20–1.31 (m, 1H), 1.49–1.73 (m, 11H), 1.76–1.86 (m, 1H), 2.08 (s, 3H), 2.12–2.20 (m, 1H), 2.27–2.35 (m, 3H), 3.43–3.52 (m, 2H), 3.52–3.60 (m, 2H), 4.20 (t, $J = 7.7$ Hz, 1H), 11.82 (br d, $J = 8.0$ Hz, 1H); ^{13}CNMR (50 MHz, $CDCl_3$): $\delta = 11.38$ (CH_3), 16.10 (CH_3), 21.88 (CH_2), 22.91 (CH_2), 24.50 (CH_2), 24.88 (CH_2), 25.74 (CH_2), 26.06 (CH_2), 26.53 (CH_2), 26.59 (CH_2), 27.67 (CH_3), 38.05 (CH), 43.41 (CH_2), 46.52 (CH_2), 59.13 (CH), 101.07 (C), 160.05 (C), 169.75 (C=O), 196.69 (C=O); IR (ATR): $\tilde{\nu} = 1639$, 1601, 1564, 1442, 1259 cm^{-1}; MS (EI, 70 eV): m/z (%): 320 (5) $[M]^+$, 238 (6), 208 (100), 190 (6), 150 (11), 136 (8), 112 (19), 84 (8), 69 (21); HR-MS: $C_{19}H_{32}N_2O_2$ (320.48): calcd: 320.2464; found: 320.2467.

***N*-(2-Ethoxycarbonyl-1-cyclohexenyl)-L-valine dimethylamide (3da)**: Diketone **1d** (2.360 g, 13.87 mmol), auxiliary **2a** (2.000 g, 13.87 mmol), and molecular sieves (6 g) in toluene (10 mL) were converted according to GP2 to yield **3da** after chromatography (MTB/PE = 3:1, $R_f = 0.30$) as a colorless solid (3.470 g, 11.71 mmol, 84%). M.p. 56 °C; $[\alpha]_D^{23} = +104$ ($c = 10.9$ in $CHCl_3$); ^{1}HNMR (400 MHz, $CDCl_3$): $\delta = 0.98$ (d, $J = 6.8$ Hz, 3H), 1.02 (d, $J = 6.8$ Hz, 3H), 1.24 (t, $J = 7.1$ Hz, 3H), 1.45–1.66 (m, 4H), 1.98–2.10 (m, 2H), 2.18–2.31 (m, 3H), 2.96 (s, 3H), 3.07 (s, 3H), 4.07–4.18 (m, 3H), 9.27 (br d, $J = 9.0$ Hz, 1H); ^{13}CNMR (50 MHz, $CDCl_3$): $\delta = 14.60$ (CH_3), 18.31 (CH_3), 19.67 (CH_3), 22.34 (CH_2), 22.53 (CH_2), 23.91 (CH_2), 26.73 (CH_2), 31.96 (CH), 35.96 (CH_3), 36.95 (CH_3), 58.02 (CH), 58.70 (CH_2), 91.43 (C), 157.23 (C), 170.53 (C=O), 172.19 (C=O); IR (ATR): $\tilde{\nu} = 1647$, 1593, 1231 cm^{-1}; MS (EI, 70 eV): m/z (%): 296 (16) $[M]^+$, 251 (6), 224 (86), 207 (7), 178 (100), 150 (7), 81 (8), 72 (8); HR-MS: $C_{16}H_{28}N_2O_3$: calcd: 296.2100; found: 296.2101; elemental analysis calcd (%) for $C_{16}H_{28}N_2O_3$ (296.41): C 64.83, H 9.52, N 9.45; found: C 64.86, H 9.61, N 9.55.

***N*-(2-Ethoxycarbonyl-1-cyclohexenyl)-L-valine diethylamide (3db)**: Oxoester **1d** (3.082 g, 18.11 mmol), auxiliary **2b** (2.600 g, 15.09 mmol), and molecular sieves (8 g) in toluene (15 mL) were converted according to GP2 to yield **3db** after chromatography (MTB/PE = 1:1, $R_f = 0.43$) as a colorless solid (4.478 g, 13.80 mmol, 91%). M.p. 58 °C; $[\alpha]_D^{23} = +112$ ($c = 5.9$ in $CHCl_3$); ^{1}HNMR (400 MHz, $CDCl_3$): $\delta = 0.99$ (d, $J = 6.8$ Hz, 3H), 1.01 (d, $J = 6.7$ Hz, 3H), 1.10 (t, $J = 7.1$ Hz, 3H), 1.18 (t, $J = 7.1$ Hz, 3H), 1.25 (t, $J = 7.1$ Hz, 3H), 1.47–1.65 (m, 4H), 1.98–2.14 (m, 2H), 2.20–2.32 (m, 3H), 3.13–3.22 (m, 1H), 3.26–3.35 (m, 1H), 3.37–3.47 (m, 1H), 3.52–3.61 (m, 1H), 4.09 (dd, $J = 9.0$, 2.8 Hz, 1H), 4.10–4.18 (m, 2H), 9.30 (br d, $J = 9.0$ Hz, 1H); ^{13}CNMR (50 MHz, $CDCl_3$): $\delta = 12.80$ (CH_3), 14.52 (CH_3), 14.62 (CH_3), 18.03 (CH_3), 19.92 (CH_3), 22.33 (CH_2), 22.60 (CH_2), 23.94 (CH_2), 26.85 (CH_2), 32.34 (CH), 40.18 (CH_2), 41.40 (CH_2), 58.25 (CH), 58.69 (CH_2), 91.20 (C), 157.38 (C), 170.52 (C=O), 170.94 (C=O); IR (ATR): $\tilde{\nu} = 1648$, 1593, 1232 cm^{-1}; MS (EI, 70 eV): m/z (%): 324 (4) $[M]^+$, 224 (73), 178 (100), 129 (6), 111 (7), 100 (8), 72 (88); HR-MS: $C_{18}H_{32}N_2O_3$: calcd: 324.2413; found: 324.2417; elemental analysis calcd (%) for $C_{18}H_{32}N_2O_3$ (324.46): C 66.63, H 9.94, N 8.63; found: C 66.58, H 10.17, N 8.64.

***N*-(2-Ethoxycarbonyl-1-cyclohexenyl)-L-valine diallylamide (3dc)**: Oxoester **1d** (1.327 g, 7.795 mmol), auxiliary **2c** (1.530 g, 7.795 mmol), and molecular sieves (4.5 g) in toluene (8 mL) were converted according to GP2 to yield **3dc** after chromatography (MTB/PE = 3:1, $R_f = 0.69$) as a colorless solid (928 mg, 2.66 mmol, 34%). M.p. 45–46 °C; $[\alpha]_D^{23} = +90.8$ ($c = 10.2$ in $CHCl_3$); ^{1}HNMR (400 MHz, $CDCl_3$): $\delta = 0.99$ (d, $J = 6.7$ Hz, 3H), 1.01 (d, $J = 6.8$ Hz, 3H), 1.25 (t, $J = 7.1$ Hz, 3H), 1.46–1.63 (m, 4H), 2.00–2.13 (m, 2H), 2.16–2.29 (m, 3H), 3.70 (dd, $J = 14.9$, 6.5 Hz, 1H), 3.86 (dd, $J = 17.3$, 5.0 Hz, 1H), 4.01 (dd, $J = 17.4$, 4.6 Hz, 1H), 4.09–4.21 (m, 3H), 4.28 (dd, $J = 14.7$, 5.4 Hz, 1H), 5.08–5.25 (m, 4H), 5.69–5.81 (m, 2H), 9.33 (br d, $J = 9.4$ Hz, 1H); ^{13}CNMR (50 MHz, $CDCl_3$): $\delta = 14.63$ (CH_3), 17.68 (CH_3), 20.01 (CH_3), 22.31 (CH_2), 22.62 (CH_2), 23.97 (CH_2), 26.90

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(CH_2), 32.31 (CH), 47.96 (CH_2), 48.76 (CH_2), 57.90 (CH), 58.74 (CH_2), 91.45 (C), 117.39 (CH_2), 117.60 (CH_2), 133.01 (CH), 133.08 (CH), 157.28 (C), 170.52 (C=O), 171.86 (C=O); IR (ATR): $\tilde{\nu}$ = 1650, 1593, 1232 cm^{-1}; MS (EI, 70 eV): *m/z* (%): 348 (10) $[M]^+$, 303 (6), 238 (6), 224 (92), 178 (100), 150 (6), 136 (6), 124 (5), 108 (5), 96 (5), 81 (16), 72 (12); HR-MS: $C_{20}H_{32}N_2O_3$: calcd: 348.2413; found: 348.2413; elemental analysis calcd (%) for $C_{20}H_{32}N_2O_3$ (348.49): C 68.93, H 9.26, N 8.04; found: C 68.92, H 9.51, N 8.04.

***N*-(2-Ethoxycarbonyl-1-cyclohexenyl)-L-leucine dimethylamide (3dd)**: Oxoester **1d** (1.076 g, 6.320 mmol), auxiliary **2d** (1.000 g, 6.320 mmol), and molecular sieves (2.5 g) in toluene (7 mL) were converted according to GP2 to yield **3dd** after chromatography (MTB/PE = 1:1, R_f = 0.24) as a colorless solid (1.324 g, 4.266 mmol, 68%). M.p. 87–89 °C; $[\alpha]_D^{23}$ = +127 (*c* = 4.6 in $CHCl_3$); ^{1}HNMR (400 MHz, $CDCl_3$): δ = 0.93 (d, *J* = 6.7 Hz, 3H), 0.95 (d, *J* = 6.8 Hz, 3H), 1.25 (t, *J* = 7.1 Hz, 3H), 1.45 (ddd, *J* = 13.7, 9.3, 4.2 Hz, 1H), 1.50–1.58 (m, 2H), 1.59–1.69 (m, 3H), 1.81–1.89 (m, 1H), 2.01–2.09 (m, 1H), 2.19–2.32 (m, 3H), 2.95 (s, 3H), 3.07 (s, 3H), 4.09–4.16 (m, 2H), 4.37 (ddd, *J* = 9.7, 8.7, 4.2 Hz, 1H), 9.09 (br d, *J* = 8.5 Hz, 1H); ^{13}CNMR (50 MHz, $CDCl_3$): δ = 14.60 (CH_3), 21.59 (CH_3), 22.32 (CH_2), 22.48 (CH_2), 23.32 (CH_3), 23.85 (CH_2), 24.65 (CH), 26.53 (CH_2), 36.17 (CH_3), 36.64 (CH_3), 42.19 (CH_2), 51.46 (CH), 58.73 (CH_2), 91.93 (C), 157.32 (C), 170.55 (C=O), 172.95 (C=O); IR (ATR): $\tilde{\nu}$ = 1651, 1597, 1230 cm^{-1}; MS (EI, 70 eV): *m/z* (%): 310 (8) $[M]^+$, 265 (5), 252 (8), 238 (87), 192 (100), 150 (9), 122 (5), 81 (11), 72 (17); HR-MS: $C_{17}H_{30}N_2O_3$ (310.44): calcd: 310.2256; found: 310.2255.

***N*-(2-Ethoxycarbonyl-1-cyclohexenyl)-L-isoleucine dimethylamide (3de)**: Oxoester **1d** (538 mg, 3.16 mmol), auxiliary **2e** (500 mg, 3.16 mmol), and molecular sieves (2 g) in toluene (6 mL) were converted according to GP2 to yield **3de** after chromatography (MTB, R_f = 0.49) as a colorless oil (701 mg, 2.26 mmol, 71%). $[\alpha]_D^{23}$ = +124 (*c* = 5.9 in $CHCl_3$); ^{1}HNMR (400 MHz, $CDCl_3$): δ = 0.90 (t, *J* = 7.5 Hz, 3H), 0.96 (d, *J* = 6.8 Hz, 3H), 1.15–1.26 (m, 1H), 1.25 (t, *J* = 7.1 Hz, 3H), 1.48–1.58 (m, 2H), 1.58–1.66 (m, 2H), 1.70 (ddd, *J* = 13.4, 7.4, 3.1 Hz, 1H), 1.74–1.84 (m, 1H), 2.03–2.11 (m, 1H), 2.20–2.31 (m, 3H), 2.97 (s, 3H), 3.08 (s, 3H), 4.09–4.15 (m, 2H), 4.17 (dd, *J* = 9.2, 7.1 Hz, 1H), 9.25 (br d, *J* = 9.1 Hz, 1H); ^{13}CNMR (50 MHz, $CDCl_3$): δ = 11.41 (CH_3), 14.61 (CH_3), 15.83 (CH_3), 22.36 (CH_2), 22.54 (CH_2), 23.91 (CH_2), 24.71 (CH_2), 26.73 (CH_2), 36.05 (CH_3), 36.99 (CH_3), 38.49 (CH), 57.55 (CH), 58.73 (CH_2), 91.42 (C), 157.34 (C), 170.57 (C=O), 172.35 (C=O); IR (ATR): $\tilde{\nu}$ = 1648, 1593, 1231 cm^{-1}; MS (EI, 70 eV): *m/z* (%): 310 (8) $[M]^+$, 252 (7), 238 (86), 207 (6), 192 (100), 179 (6), 111 (7), 101 (9), 86 (50), 81 (9), 72 (23), 69 (15); HR-MS: $C_{17}H_{30}N_2O_3$: calcd: 310.2256; found: 310.2254; elemental analysis calcd (%) for $C_{17}H_{30}N_2O_3$ (310.44): C 65.77, H 9.74, N 9.02; found: C 65.70, H 9.66, N 9.12.

***N*-(2-Ethoxycarbonyl-1-cyclohexenyl)-L-*tert*-leucine dimethylamide (3df)**: Oxoester **1d** (1.291 g, 7.583 mmol), auxiliary **2f** (1.200 g, 7.583 mmol), and molecular sieves (3 g) in toluene (8 mL) were converted according to GP2 to yield **3df** after chromatography (MTB, R_f = 0.50) as a colorless solid (1.457 g, 4.693 mmol, 62%). M.p. 104 °C; $[\alpha]_D^{23}$ = +194 (*c* = 5.8 in $CHCl_3$); ^{1}HNMR (400 MHz, $CDCl_3$): δ = 1.05 (s, 9H), 1.25 (t, *J* = 7.1 Hz, 3H), 1.48–1.58 (m, 2H), 1.58–1.67 (m, 2H), 1.99–2.08 (m, 1H), 2.23–2.34 (m, 3H), 2.97 (s, 3H), 3.11 (s, 3H), 4.10–4.19 (m, 2H), 4.24 (d, *J* = 9.9 Hz, 1H), 9.45 (br d, *J* = 9.8 Hz, 1H); ^{13}CNMR (50 MHz, $CDCl_3$): δ = 14.61 (CH_3), 22.43 (CH_2), 22.55 (CH_2), 23.97 (CH_2), 26.66 (3CH_3), 26.76 (CH_2), 35.74 (CH_3), 35.96 (C), 37.90 (CH_3), 57.75 (CH), 58.72 (CH_2), 91.27 (C), 156.47 (C), 170.41 (C=O), 171.67 (C=O); IR (ATR): $\tilde{\nu}$ = 1647, 1635, 1591, 1253, 1239, 1094, 1058 cm^{-1}; MS (EI, 70 eV): *m/z* (%): 310 (10) $[M]^+$, 253 (18), 238 (88), 207 (29), 192 (100), 179 (21), 136 (11), 111 (14), 101 (17), 86 (60), 72 (28), 69 (21); HR-MS: $C_{17}H_{30}N_2O_3$: calcd: 310.2256; found: 310.2249; elemental analysis calcd (%) for $C_{17}H_{30}N_2O_3$ (310.44): C 65.77, H 9.74, N 9.02; found: C 65.94, H 9.76, N 9.16.

***N*-(2-Ethoxycarbonyl-1-cyclohexenyl)-L-*tert*-leucine diethylamide (3dg)**: Oxoester **1d** (749 mg, 4.40 mmol), auxiliary **2g** (820 mg, 4.40 mmol), and molecular sieves (2.5 g) in toluene (6 mL) were converted according to GP2 to yield **3dg** after chromatography (MTB/PE = 2:1, R_f = 0.56) as a colorless solid (1.26 g, 3.72 mmol, 84%). M.p. 72–73 °C; $[\alpha]_D^{23}$ = +126 (*c* = 5.40 in $CHCl_3$); ^{1}HNMR (400 MHz, $CDCl_3$): δ = 1.04 (s, 9H), 1.11 (t, *J* = 7.1 Hz, 3H), 1.19 (t, *J* = 7.1 Hz, 3H), 1.25 (t, *J* = 7.1 Hz, 3H), 1.48–1.59 (m, 2H), 1.59–1.66 (m, 2H), 2.06–2.15 (m, 1H), 2.24–2.36 (m, 3H), 3.01–3.10 (m, 1H), 3.25–3.34 (m, 1H), 3.53–3.63 (m, 1H), 3.69–3.78 (m, 1H), 4.09–4.21 (m, 2H), 4.21 (d, *J* = 10.0 Hz, 1H), 9.47 (br d, *J* = 9.9 Hz, 1H); ^{13}CNMR (50 MHz, $CDCl_3$): δ = 12.73 (CH_3), 14.48 (CH_3), 14.65 (CH_3), 22.40 (CH_2), 22.69 (CH_2), 24.04 (CH_2), 26.82 (CH_2), 26.88 (3CH_3), 36.34 (C), 39.69 (CH_2), 42.06 (CH_2), 57.96 (CH), 58.73 (CH_2), 90.96 (C), 156.47 (C), 170.26 (C=O), 170.35 (C=O); IR (ATR): $\tilde{\nu}$ = 1649, 1590, 1237, 1222, 1097 cm^{-1}; MS (EI, 70 eV): *m/z* (%): 338 (7) $[M]^+$, 293 (6), 281 (13), 238 (100), 207 (13), 192 (83), 136 (8), 130 (14), 100 (13), 86 (21), 69 (13); HR-MS: $C_{19}H_{34}N_2O_3$: calcd: 338.2569; found: 338.2569; elemental analysis calcd (%) for $C_{19}H_{34}N_2O_3$ (338.49): C 67.42, H 10.12, N 8.28; found: C 67.35, H 10.26, N 8.26.

***N*-(2-Ethoxycarbonyl-1-cyclohexenyl)-L-phenylalanine dimethylamide (3dh)**: Oxoester **1d** (651 mg, 3.82 mmol), auxiliary **2h** (735 mg, 3.82 mmol), and molecular sieves (2 g) in toluene (5 mL) were converted according to GP2 to yield **3dh** after chromatography (MTB/PE = 1:1, R_f = 0.13) as a colorless wax (1.15 g, 3.33 mmol, 87%). Crystallization from PE gave colorless needles. M.p. 102 °C; $[\alpha]_D^{23}$ = −25 (*c* = 6.9 in $CHCl_3$); ^{1}HNMR (400 MHz, $CDCl_3$): δ = 1.27 (t, *J* = 7.1 Hz, 3H), 1.43–1.59 (m, 4H), 1.93–2.06 (m, 2H), 2.20–2.26 (m, 2H), 2.67 (s, 3H), 2.89 (s, 3H), 2.94 (dd, *J* = 13.2, 7.0 Hz, 1H), 3.04 (dd, *J* = 13.2, 7.3 Hz, 1H), 4.15 (q, *J* = 7.1 Hz, 2H), 4.52 (dt, *J* = 8.8, 7.2 Hz, 1H), 7.19–7.31 (m, 5H), 9.38 (br d, *J* = 9.1 Hz, 1H); ^{13}CNMR (50 MHz, $CDCl_3$): δ = 14.61 (CH_3), 22.25 (CH_2), 22.56 (CH_2), 23.86 (CH_2), 26.41 (CH_2), 35.81 (CH_3), 36.51 (CH_3), 41.37 (CH_2), 53.79 (CH), 58.79 (CH_2), 92.04 (C), 126.85 (CH), 128.43 (2CH), 129.39 (2CH), 137.16 (C), 156.26 (C), 170.36 (C=O), 171.71 (C=O); IR (ATR): $\tilde{\nu}$ = 1648, 1585, 1229, 1175, 1094, 1061 cm^{-1}; MS (EI, 70 eV): *m/z* (%): 344 (16) $[M]^+$, 299 (6), 272 (49), 253 (28), 226 (90), 207 (20), 198 (16), 179 (24), 131 (9), 120 (100), 103 (27), 101 (34), 91 (62), 77 (23), 73 (58), 65 (12); HR-MS: $C_{20}H_{28}N_2O_3$: calcd: 344.2100; found: 344.2101; elemental analysis calcd (%) for $C_{20}H_{28}N_2O_3$ (344.45): C 69.74, H 8.19, N 8.13; found: C 69.44, H 7.84, N 8.15.

***N*-(2-Ethoxycarbonyl-1-cyclohexenyl)-L-valine piperidide (3di)**: Oxoester **1d** (924 mg, 5.43 mmol), auxiliary **2i** (1.00 g, 5.43 mmol), and molecular sieves (2.5 g) in toluene (6 mL) were converted according to GP2 to yield **3di** after chromatography (MTB/PE = 4:1, R_f = 0.41) as a colorless solid (1.64 g, 4.88 mmol, 90%). M.p. 88 °C; $[\alpha]_D^{23}$ = +169 (*c* = 7.0 in $CHCl_3$); ^{1}HNMR (400 MHz, $CDCl_3$): δ = 1.00 (d, *J* = 6.7 Hz, 3H), 1.03 (d, *J* = 6.7 Hz, 3H), 1.25 (t, *J* = 7.0 Hz, 3H), 1.46–1.68 (m, 10H), 1.96–2.15 (m, 1H), 2.05–2.13 (m, 1H), 2.19–2.32 (m, 3H), 3.42–3.52 (m, 2H), 3.52–3.61 (m, 2H), 4.09–4.18 (m, 3H), 9.29 (br d, *J* = 8.8 Hz, 1H); ^{13}CNMR (50 MHz, $CDCl_3$): δ = 14.63 (CH_3), 18.40 (CH_3), 19.90 (CH_3), 22.36 (CH_2), 22.59 (CH_2), 23.92 (CH_2), 24.55 (CH_2), 25.72 (CH_2), 26.65 (CH_2), 26.76 (CH_2), 31.95 (CH), 43.27 (CH_2), 46.54 (CH_2), 58.42 (CH), 58.72 (CH_2), 91.33 (C), 157.52 (C), 170.39 (C=O), 170.60 (C=O); IR (ATR): $\tilde{\nu}$ = 1647, 1593, 1230 cm^{-1}; MS (EI, 70 eV): *m/z* (%): 336 (3) $[M]^+$, 224 (59), 178 (61), 141 (9), 111 (14), 91 (21), 84 (22), 72 (100); HR-MS: $C_{19}H_{32}N_2O_3$: calcd: 336.2413; found: 336.2411; elemental analysis calcd (%) for $C_{19}H_{32}N_2O_3$ (336.47): C 67.82, H 9.59, N 8.33; found: C 67.78, H 9.53, N 8.52.

***N*-(2-Ethoxycarbonyl-1-cyclohexenyl)-L-leucine pyrrolidide (3dj)**: Oxoester **1d** (924 mg, 5.43 mmol), auxiliary **2j** (1.00 g, 5.43 mmol), and molecular sieves (2.5 g) in toluene (8 mL) were converted according to GP2 to yield **3dj** after chromatography (MTB/PE = 1:1, R_f = 0.23) as a colorless solid (1.59 g, 6.24 mmol, 87%). M.p. 83–84 °C; $[\alpha]_D^{23}$ = +125 (*c* = 4.4 in $CHCl_3$); ^{1}HNMR (400 MHz, $CDCl_3$): δ = 0.92 (d, *J* = 6.6 Hz, 3H), 0.95 (d, *J* = 6.6 Hz, 3H), 1.25 (t, *J* = 7.0 Hz, 3H), 1.41–1.72 (m, 6H), 1.78–1.87 (m, 3H), 1.93–2.00 (m, 2H), 2.02–2.11 (m, 1H), 2.17–2.30 (m, 3H), 3.38–3.55 (m, 4H), 4.08–4.15 (m, 2H), 4.15–4.21 (m, 1H), 9.09 (br d, *J* = 9.0 Hz, 1H); ^{13}CNMR (50 MHz, $CDCl_3$): δ = 14.58 (CH_3), 21.62 (CH_3), 22.31 (CH_2), 22.49 (CH_2), 23.24 (CH_3), 23.80 (2CH_2), 24.62 (CH), 26.44 (CH_2), 26.56 (CH_2), 42.00 (CH_2), 45.79 (CH_2), 46.36 (CH_2), 53.48 (CH), 58.72 (CH_2), 91.61 (C), 157.46 (C), 170.56 (C=O), 171.52 (C=O); IR (ATR): $\tilde{\nu}$ = 1649, 1596, 1231 cm^{-1}; MS (EI, 70 eV): *m/z* (%): 336 (5) $[M]^+$, 238 (28), 192 (67), 186 (34), 130 (64), 101 (17), 86 (100), 81 (18), 72 (34), 69 (28); HR-MS: $C_{19}H_{32}N_2O_3$: calcd: 336.2413; found: 336.2422; elemental analysis calcd (%) for $C_{19}H_{32}N_2O_3$ (336.47): C 67.82, H 9.59, N 8.33; found: C 67.27, H 9.69, N 8.65.

***N*-(2-Ethoxycarbonyl-1-cyclohexenyl)-L-isoleucine pyrrolidide (3dk)**: Oxoester **1d** (1.107 g, 6.501 mmol), auxiliary **2k** (1.198 g, 6.501 mmol), and molecular sieves (2.5 g) in toluene (8 mL) were converted according to GP2 to yield **3dk** after chromatography (MTB/PE = 4:1, R_f = 0.31) as a colorless solid (1.126 g, 3.347 mmol, 51%). M.p. 70 °C; $[\alpha]_D^{23}$ = +188 (*c* = 4.6 in $CHCl_3$); ^{1}HNMR (400 MHz, $CDCl_3$): δ = 0.90 (t, *J* = 7.4 Hz, 3H), 0.96 (d, *J* = 6.8 Hz, 3H), 1.15–1.24 (m, 1H), 1.25 (t, *J* = 7.1 Hz, 3H), 1.47–1.58 (m, 2H), 1.58–1.67 (m, 2H), 1.72 (ddd, *J* = 10.7, 7.6, 3.2 Hz, 1H), 1.79–1.87

(m, 3H), 1.91–1.99 (m, 2H), 2.09 (dt, $J = 16.5$, 7.0 Hz, 1H), 2.21–2.32 (m, 3H), 3.43–3.58 (m, 4H), 3.97 (dd, $J = 9.0$, 7.5 Hz, 1H), 4.10–4.16 (m, 2H), 9.25 (br d, $J = 9.0$ Hz, 1H); ^{13}CNMR (50 MHz, $CDCl_3$): $\delta = 11.32$ (CH_3), 14.57 (CH_3), 15.75 (CH_3), 22.33 (CH_2), 22.52 (CH_2), 23.79 (CH_2), 23.88 (CH_2), 24.86 (CH_2), 26.39 (CH_2), 26.78 (CH_2), 38.23 (CH), 46.06 (CH_2), 46.19 (CH_2), 58.67 (CH_2), 59.70 (CH), 91.10 (C), 157.41 (C), 170.53 (C=O), 170.81 (C=O); IR (ATR): $\tilde{\nu} = 1647$, 1592, 1231 cm^{-1}; MS (EI, 70 eV): *m/z* (%): 336 (3) $[M]^+$, 238 (57), 205 (5), 192 (100), 164 (5), 136 (6), 98 (8), 81 (20), 69 (13); HR-MS: $C_{19}H_{32}N_2O_3$: calcd: 336.2413; found: 336.2419; elemental analysis calcd (%) for $C_{19}H_{32}N_2O_3$ (336.47): C 67.82, H 9.59, N 8.33; found: C 67.86, H 9.57, N 8.47.

(*S*)-Ethyl 2-[1-(ethylsulfanyl)methyl-3-methylbutylamino]-1-cyclohexenecarboxylate (3dm): Oxoester **1d** (514 mg, 3.02 mmol), auxiliary **2m** (487 mg, 3.02 mmol), and molecular sieves (1.5 g) in toluene (7 mL) were converted according to GP2 at 23 °C to yield **3dm** as a yellowish resin (943 mg, 3.01 mmol, 100%), which was used without further purification. $[\alpha]_D^{23} = +135$ ($c = 6.4$ in $CHCl_3$); ^{1}HNMR (400 MHz, $CDCl_3$): $\delta = 0.89$ (d, $J = 6.5$ Hz, 3H), 0.92 (d, $J = 6.6$ Hz, 3H), 1.24 (t, $J = 7.3$ Hz, 3H), 1.26 (t, $J = 7.2$ Hz, 3H), 1.37–1.46 (m, 1H), 1.47–1.52 (m, 1H), 1.52–1.61 (m, 3H), 1.63–1.77 (m, 3H), 2.24–2.33 (m, 2H), 2.37–2.46 (m, 1H), 2.50–2.65 (m, 4H), 3.56–3.67 (m, 1H), 4.11 (q, $J = 7.1$ Hz, 2H), 8.94 (br d, $J = 9.0$ Hz, 1H); ^{13}CNMR (50 MHz, $CDCl_3$): $\delta = 14.65$ (CH_3), 14.89 (CH_3), 22.07 (CH_3), 22.43 (CH_2), 22.76 (CH_2), 23.30 (CH_3), 23.91 (CH_2), 24.84 (CH), 26.68 (CH_2), 27.21 (CH_2), 39.42 (CH_2), 44.80 (CH_2), 50.38 (CH), 58.61 (CH_2), 89.84 (C), 158.54 (C), 170.89 (C=O); IR (ATR): $\tilde{\nu} = 1647$, 1597, 1227 cm^{-1}; MS (EI, 70 eV): *m/z* (%): 313 (6) $[M]^+$, 268 (5), 238 (72), 192 (100), 186 (13), 150 (5), 130 (18), 111 (7), 101 (5), 86 (51), 75 (9), 57 (27); HR-MS: $C_{17}H_{31}NO_2S$ (313.50): calcd: 313.2076; found: 313.2077.

(*S*)-Ethyl 2-[1-(dimethylamino)methyl-3-methylbutylamino]-1-cyclohexenecarboxylate (3dn): Oxoester **1d** (354 mg, 2.08 mmol), auxiliary **2n** (300 mg, 2.08 mmol), and molecular sieves (0.5 g) in toluene (4 mL) were converted according to GP2 at 23 °C to yield **3dn** as a yellowish resin (531 mg, 1.79 mmol, 86%), which was used without further purification. $[\alpha]_D^{23} = +4.8$ ($c = 5.6$ in $CHCl_3$); ^{1}HNMR (400 MHz, $CDCl_3$): $\delta = 0.87$ (d, $J = 6.6$ Hz, 3H), 0.91 (d, $J = 6.6$ Hz, 3H), 1.25 (t, $J = 7.0$ Hz, 3H), 1.27–1.32 (m, 2H), 1.48–1.56 (m, 3H), 1.62–1.68 (m, 2H), 2.18–2.36 (m, 6H), 2.36 (s, 6H), 3.50–3.60 (m, 1H), 4.10 (q, $J = 7.1$ Hz, 2H), 8.85 (br d, $J = 10.0$ Hz, 1H); ^{13}CNMR (50 MHz, $CDCl_3$): $\delta = 14.63$ (CH_3), 22.04 (CH_3), 22.42 (CH_2), 22.74 (CH_2), 23.37 (CH_3), 23.86 (CH_2), 24.62 (CH), 26.47 (CH_2), 43.86 (CH_2), 46.07 (2 CH_3), 48.39 (CH), 58.49 (CH_2), 66.30 (CH_2), 89.31 (C), 158.94 (C), 170.88 (C=O); IR (ATR): $\tilde{\nu} = 1647$, 1597, 1229 cm^{-1}; MS (EI, 70 eV): *m/z* (%): 296 (7) $[M]^+$, 238 (88), 192 (100), 178 (8), 150 (8), 111 (9), 81 (8), 58 (59); HR-MS: $C_{17}H_{32}N_2O_2$ (296.45): calcd: 296.2464; found: 296.2466.

(*S*)-Ethyl 2-[1-benzyl-2-(ethylsulfanyl)ethylamino]-1-cyclohexenecarboxylate (3do): Oxoester **1d** (209 mg, 1.23 mmol), auxiliary **2o** (240 mg, 1.23 mmol), and molecular sieves (0.5 g) in toluene (4 mL) were converted according to GP2 at 23 °C to yield **3do** (359 mg, 1.03 mmol, 84%) as a yellowish resin, which was used without further purification. $[\alpha]_D^{23} = -99$ ($c = 6.0$ in $CHCl_3$); ^{1}HNMR (400 MHz, $CDCl_3$): $\delta = 1.23$ (t, $J = 7.3$ Hz, 3H), 1.27 (t, $J = 7.1$ Hz, 3H), 1.36–1.55 (m, 4H), 1.78–1.87 (m, 1H), 2.17–2.25 (m, 3H), 2.51–2.58 (m, 2H), 2.64 (d, $J = 6.2$ Hz, 2H), 2.73 (dd, $J = 13.5$, 7.8 Hz, 1H), 2.95 (dd, $J = 13.5$, 5.5 Hz, 1H), 3.72–3.82 (m, 1H), 4.13 (q, $J = 7.0$ Hz, 2H), 7.15–7.33 (m, 5H), 9.12 (br d, $J = 10.0$ Hz, 1H); ^{13}CNMR (50 MHz, $CDCl_3$): $\delta = 14.64$ (CH_3), 14.86 (CH_3), 22.27 (CH_2), 22.62 (CH_2), 23.88 (CH_2), 26.49 (CH_2), 27.16 (CH_2), 37.96 (CH_2), 42.53 (CH_2), 54.23 (CH), 58.67 (CH_2), 90.19 (C), 126.42 (CH), 128.35 (2 CH), 129.44 (2 CH), 138.34 (C), 158.37 (C), 170.83 (C=O); IR (ATR): $\tilde{\nu} = 1645$, 1595, 1244, 1222, 1176 cm^{-1}; MS (EI, 70 eV): *m/z* (%): 347 (25) $[M]^+$, 302 (10), 286 (8), 272 (96), 256 (59), 226 (100), 210 (44), 198 (10), 179 (8), 120 (33), 117 (11), 91 (25), 75 (13); HR-MS: $C_{20}H_{29}NO_2S$ (347.52): calcd: 347.1919; found: 347.1919.

(*S*)-Ethyl 2-[1-benzyl-2-(dimethylamino)ethylamino]-1-cyclohexenecarboxylate (3dp): Oxoester **1d** (209 mg, 1.23 mmol), auxiliary **2p** (219 mg, 1.23 mmol), and molecular sieves (0.5 g) in toluene (4 mL) were converted according to GP2 at 23 °C to yield **3dp** (345 mg, 1.04 mmol, 85%) as a yellowish resin, which was used without further purification. $[\alpha]_D^{23} = -220$ ($c = 4.3$ in $CHCl_3$); ^{1}HNMR (400 MHz, $CDCl_3$): $\delta = 1.26$ (t, $J = 7.1$ Hz, 3H), 1.37–1.51 (m, 3H), 1.63–1.81 (m, 1H), 2.08–2.40 (m, 6H), 2.26 (s, 6H), 2.61 (dd, $J = 13.5$, 8.1 Hz, 1H), 2.93 (dd, $J = 13.5$, 4.5 Hz, 1H), 3.64–3.82 (m, 1H), 4.11 (q, $J = 7.2$ Hz, 2H), 7.12–7.32 (m, 5H), 9.01 (br d, $J = 10.0$ Hz, 1H); ^{13}CNMR (50 MHz, $CDCl_3$): $\delta = 14.59$ (CH_3), 22.18 (CH_2), 22.54 (CH_2), 23.80 (CH_2), 26.27 (CH_2), 41.67 (CH_2), 45.94 (2 CH_3), 52.09 (CH), 58.49 (CH_2), 64.75 (CH_2), 89.72 (C), 126.17 (CH), 128.15 (2 CH), 129.50 (2 CH), 138.55 (C), 158.81 (C), 170.76 (C=O) cm^{-1}; MS (EI, 70 eV): *m/z* (%): 330 (5) $[M]^+$, 272 (58), 226 (88), 198 (6), 111 (11), 91 (17), 83 (8), 58 (100); HR-MS: $C_{20}H_{30}N_2O_2$ (330.47): calcd: 330.2307; found: 330.2307.

***N*-(2-Ethoxycarbonyl-1-cyclohexenyl)-(*S*)-methyl-L-cysteine ethylester (3dq)**: To a suspension of (*S*)-methyl-L-cysteine ethyl ester hydrochloride (**2q**·HCl) (350 mg, 1.75 mmol) and oxoester **1d** (298 mg, 1.75 mmol) in toluene (5 mL) were added NEt_3 (177 mg, 1.75 mmol) and molecular sieves (1.5 g). The mixture was stirred for 14 h at 23 °C. After filtration all volatile materials were removed in vacuo to yield **3dq** as a colorless viscous oil (464 mg, 1.47 mmol, 84%), which was used without further purification. $[\alpha]_D^{23} = +0.56$ ($c = 5.4$ in $CHCl_3$); ^{1}HNMR (400 MHz, $CDCl_3$): $\delta = 1.26$ (t, $J = 7.2$ Hz, 3H), 1.28 (t, $J = 7.1$ Hz, 3H), 1.51–1.60 (m, 2H), 1.60–1.69 (m, 2H), 2.16 (s, 3H), 2.19–2.33 (m, 4H), 2.83–2.94 (m, 2H), 4.13 (q, $J = 7.1$ Hz, 2H), 4.21 (q, $J = 7.1$ Hz, 2H), 4.25–4.31 (m, 1H), 9.30 (br d, $J = 9.7$ Hz, 1H); ^{13}CNMR (50 MHz, $CDCl_3$): $\delta = 14.16$ (CH_3), 14.55 (CH_3), 16.51 (CH_3), 22.20 (CH_2), 22.47 (CH_2), 23.86 (CH_2), 26.45 (CH_2), 37.69 (CH_2), 55.36 (CH), 58.93 (CH_2), 61.48 (CH_2), 93.01 (C), 156.74 (C), 170.62 (C=O), 171.54 (C=O); IR (ATR): $\tilde{\nu} = 1741$, 1652, 1598, 1231, 1175, 1062 cm^{-1}; MS (EI, 70 eV): *m/z* (%): 315 (29) $[M]^+$, 270 (11), 254 (75), 242 (15), 208 (100), 196 (28), 180 (15), 170 (6), 152 (13), 147 (7), 61 (7); HR-MS: $C_{15}H_{25}NO_4S$ (315.43): calcd: 315.1504; found: 315.1511.

***N*-(2-Ethoxycarbonyl-1-cyclohexenyl)-L-methionine ethylester (3dr)**: According to the procedure given above for compound **3dq**, L-methionine ethyl ester hydrochloride (**2r**·HCl) (600 mg, 2.81 mmol) and oxoester **1d** (478 mg, 2.81 mmol) were converted in toluene (7 mL) in the presence of NEt_3 (284 mg, 2.81 mmol) and molecular sieves (1.5 g) to yield **3dr** as a yellowish viscous oil (781 mg, 2.37 mmol, 84%), which was used without further purification. $[\alpha]_D^{23} = -8.6$ ($c = 4.9$ in $CHCl_3$); ^{1}HNMR (400 MHz, $CDCl_3$): $\delta = 1.26$ (t, $J = 7.1$ Hz, 6H), 1.50–1.68 (m, 4H), 1.72–1.86 (m, 2H), 1.93–2.04 (m, 1H), 2.09 (s, 3H), 2.14–2.32 (m, 3H), 2.57–2.65 (m, 2H), 4.12 (q, $J = 7.1$ Hz, 2H), 4.16–4.22 (m, 2H), 4.27–4.34 (m, 1H), 9.10 (br d, $J = 9.4$ Hz, 1H); ^{13}CNMR (125 MHz, $CDCl_3$): $\delta = 12.28$ (CH_3), 14.65 (CH_3), 15.32 (CH_3), 22.28 (CH_2), 22.58 (CH_2), 23.91 (CH_2), 26.50 (CH_2), 30.31 (CH_2), 32.49 (CH_2), 53.60 (CH), 58.96 (CH_2), 61.35 (CH_2), 92.70 (C), 157.86 (C), 170.85 (C=O), 172.90 (C=O); IR (ATR): $\tilde{\nu} = 1739$, 1650, 1601, 1235, 1172, 1097 cm^{-1}; MS (EI, 70 eV): *m/z* (%): 329 (38) $[M]^+$, 284 (13), 256 (53), 210 (83), 208 (37), 177 (8), 168 (14), 162 (46), 111 (35), 104 (28), 83 (36), 69 (30), 61 (92), 55 (100); HR-MS: $C_{16}H_{27}NO_4S$ (329.46): calcd: 329.1661; found: 329.1661.

***N*-(2-Isobutoxycarbonyl-1-cyclohexenyl)-L-valine diethylamide (3eb)**: Oxoester **1e** (806 mg, 4.06 mmol), auxiliary **2b** (700 mg, 4.06 mmol), and molecular sieves (2 g) in toluene (6 mL) were converted according to GP2 to yield **3eb** after chromatography (MTB/PE = 1:1, $R_f = 0.43$) as a colorless solid (623 mg, 1.77 mmol, 43%). M.p. 94–96 °C; $[\alpha]_D^{23} = +135$ ($c = 5.2$ in $CHCl_3$); ^{1}HNMR (400 MHz, $CDCl_3$): $\delta = 0.93$ (d, $J = 6.7$ Hz, 6H), 0.99 (d, $J = 6.8$ Hz, 3H), 1.02 (d, $J = 6.8$ Hz, 3H), 1.10 (t, $J = 7.1$ Hz, 3H), 1.18 (t, $J = 7.1$ Hz, 3H), 1.49–1.66 (m, 4H), 1.88–1.98 (m, 1H), 1.98–2.06 (m, 1H), 2.06–2.14 (m, 1H), 2.23–2.34 (m, 3H), 3.14–3.23 (m, 1H), 3.27–3.36 (m, 1H), 3.36–3.45 (m, 1H), 3.51–3.60 (m, 1H), 3.82 (dd, $J = 10.6$, 6.6 Hz, 1H), 3.87 (dd, $J = 10.6$, 6.7 Hz, 1H), 4.09 (dd, $J = 9.1$, 5.1 Hz, 1H), 9.32 (br d, $J = 9.0$ Hz, 1H); ^{13}CNMR (50 MHz, $CDCl_3$): $\delta = 12.81$ (CH_3), 14.52 (CH_3), 18.06 (CH_3), 19.28 (2 CH_3), 19.97 (CH_3), 22.34 (CH_2), 22.62 (CH_2), 23.88 (CH_2), 26.83 (CH_2), 27.88 (CH), 32.29 (CH), 40.18 (CH_2), 41.39 (CH_2), 58.39 (CH), 69.12 (CH_2), 91.31 (C), 157.48 (C), 170.60 (C=O), 170.95 (C=O); IR (ATR): $\tilde{\nu} = 1649$, 1591, 1231 cm^{-1}; MS (EI, 70 eV): *m/z* (%): 352 (5) $[M]^+$, 279 (5), 252 (86), 196 (6), 178 (100), 91 (6), 81 (8), 69 (8); HR-MS: $C_{20}H_{36}N_2O_3$: calcd: 352.2726; found: 352.2726; elemental analysis calcd (%) for $C_{20}H_{36}N_2O_3$ (352.52): C 68.14, H 10.29, N 7.95; found: C 67.91, H 9.81, N 8.07.

***N*-(2-Methoxycarbonyl-1-cycloheptenyl)-L-*tert*-leucine dimethylamide (3ff)**: Oxoester **1f** (538 mg, 3.16 mmol), auxiliary **2f** (500 mg, 3.16 mmol), and molecular sieves (2 g) in toluene (5 mL) were converted according to GP2 to yield **3ff** after chromatography (MTB/PE = 1:3, $R_f = 0.31$) as a colorless solid (214 mg, 0.689 mmol, 22%). M.p. 89 °C; $[\alpha]_D^{23} = +220$ ($c = 3.9$ in $CHCl_3$); ^{1}HNMR (400 MHz, $CDCl_3$): $\delta = 1.06$ (s, 9H), 1.36–1.77 (m, 6H), 2.33–2.44 (m, 3H), 2.57 (ddd, $J = 15.3$, 8.5, 1.8 Hz, 1H), 2.97 (s, 3H), 3.11 (s, 3H), 3.67 (s, 3H), 4.31 (d, $J = 9.2$ Hz, 1H), 9.78 (br d, $J = 8.8$ Hz, 1H); ^{13}CNMR (50 MHz, $CDCl_3$): $\delta = 24.91$ (CH_2), 26.00 (CH_2), 26.75

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(3 CH_3), 28.12 (CH_2), 29.01 (CH_2), 31.71 (CH_2), 35.87 (CH_3), 39.91 (CH), 37.84 (CH_3), 50.55 (CH_3), 59.41 (CH), 95.50 (C), 164.98 (C), 160.72 (C=O), 171.44 (C=O); IR (ATR): $\tilde{\nu}$ = 1636, 1580, 1276, 1261, 1206, 1096, 1085 cm^{-1}; MS (EI, 70 eV): *m*/*z* (%): 310 (26) $[M]^+$, 279 (8), 253 (38), 238 (85), 221 (73), 206 (100), 193 (38), 150 (20), 120 (10), 95 (42), 93 (23), 91 (26), 81 (21), 72 (72), 69 (38); HR-MS: $C_{17}H_{30}N_2O_3$: calcd: 310.2256; found: 310.2253; elemental analysis calcd (%) for $C_{17}H_{30}N_2O_3$ (310.44): C 65.77, H 9.74, N 9.02; found: C 65.41, H 10.07, N 9.08.

***N*-(2-Methoxycarbonyl-1-cycloheptenyl)-L-*tert*-leucine diethylamide (3 fg)**: Oxoester **1 f** (503 mg, 2.95 mmol), auxiliary **2 g** (550 mg, 2.95 mmol), and molecular sieves (2 g) in toluene (5 mL) were converted according to GP2 to yield **3 fg** after chromatography (MTB/PE = 2:1, R_f = 0.45) as a colorless solid (252 mg, 0.744 mmol, 25 %). M.p. 97 °C; $[\alpha]_D^{23}$ = +120 (*c* = 5.8 in $CHCl_3$); ^{1}HNMR (200 MHz, $CDCl_3$): δ = 1.03 (s, 9 H), 1.11 (t, *J* = 7.1 Hz, 3 H), 1.17 (t, *J* = 7.1 Hz, 3 H), 1.30–1.78 (m, 6 H), 2.36 (ddd, *J* = 15.3, 9.2, 1.9 Hz, 1 H), 2.40–2.48 (m, 2 H), 2.58 (ddd, *J* = 15.3, 8.0, 2.0 Hz, 1 H), 2.93–3.11 (m, 1 H), 3.15–3.34 (m, 1 H), 3.50–3.86 (m, 2 H), 3.67 (s, 3 H), 4.26 (d, *J* = 9.6 Hz, 1 H), 9.86 (br d, *J* = 9.0 Hz, 1 H); ^{13}CNMR (50 MHz, $CDCl_3$): δ = 12.82 (CH_3), 14.42 (CH_3), 25.52 (CH_2), 26.17 (CH_2), 26.82 (3 CH_3), 28.17 (CH_2), 28.71 (CH_2), 31.79 (CH_2), 36.32 (C), 40.05 (CH_2), 42.16 (CH_2), 50.50 (CH_3), 59.19 (CH), 95.01 (C), 164.81 (C), 170.06 (C=O), 170.51 (C=O); IR (ATR): $\tilde{\nu}$ = 1642, 1585, 1253 cm^{-1}; MS (EI, 70 eV): *m*/*z* (%): 338 (9) $[M]^+$, 281 (11), 249 (21), 238 (100), 221 (8), 206 (87); HR-MS: $C_{19}H_{34}N_2O_3$: calcd: 338.2569; found: 338.2569; elemental analysis calcd (%) for $C_{19}H_{34}N_2O_3$ (338.49): C 67.42, H 10.12, N 8.28; found: C 67.38, H 10.03, N 8.38.

***N*-(2-Methoxycarbonyl-1-cycloheptenyl)-L-valine piperidide (3 fi)**: Oxoester **1 f** (508 mg, 2.99 mmol), auxiliary **2 i** (550 mg, 2.99 mmol), and molecular sieves (2 g) in toluene (5 mL) were converted according to GP2 to yield **3 fi** after chromatography (MTB/PE = 2:1, R_f = 0.36) as a colorless solid (328 mg, 0.975 mmol, 33 %). M.p. 72–73 °C; $[\alpha]_D^{23}$ = +252 (*c* = 6.6 in $CHCl_3$); ^{1}HNMR (400 MHz, $CDCl_3$): δ = 1.00 (d, *J* = 6.7 Hz, 3 H), 1.04 (d, *J* = 6.7 Hz, 3 H), 1.35–1.74 (m, 12 H), 2.01–2.10 (m, 1 H), 2.35–2.43 (m, 3 H), 2.53 (ddd, *J* = 15.3, 8.5, 1.8 Hz, 1 H), 3.42–3.55 (m, 3 H), 3.56–3.65 (m, 1 H), 3.66 (s, 3 H), 4.18 (t, *J* = 7.6 Hz, 1 H), 9.64 (br d, *J* = 7.9 Hz, 1 H); ^{13}CNMR (50 MHz, $CDCl_3$): δ = 18.71 (CH_3), 19.83 (CH_3), 24.53 (CH_2), 25.12 (CH_2), 25.67 (CH_2), 25.96 (CH_2), 26.60 (CH_2), 28.18 (CH_2), 29.17 (CH_2), 31.78 (CH_2), 31.88 (CH), 43.34 (CH_2), 46.48 (CH_2), 50.48 (CH_3), 60.14 (CH), 95.37 (C), 165.87 (C), 170.21 (C=O), 170.80 (C=O); IR (ATR): $\tilde{\nu}$ = 1640, 1591, 1438, 1251, 1205 cm^{-1}; MS (EI, 70 eV): *m*/*z* (%): 336 (9) $[M]^+$, 256 (5), 224 (92), 192 (100), 164 (5), 137 (6), 129 (23), 101 (8), 95 (14), 86 (67), 81 (18), 69 (45); HR-MS: $C_{19}H_{32}N_2O_3$: calcd: 336.2413; found: 336.2420; elemental analysis calcd (%) for $C_{19}H_{32}N_2O_3$ (336.47): C 67.82, H 9.59, N 8.33; found: C 67.85, H 9.48, N 8.50.

***N*-(2-Isobutoxycarbonyl-1-cycloheptenyl)-L-valine diethylamide (3 gb)**: Oxoester **1 g** (863 mg, 4.06 mmol), auxiliary **2 b** (500 mg, 2.90 mmol), and molecular sieves (2.5 g) in toluene (6 mL) were converted according to GP2 to yield **3 gb** after chromatography (MTB/PE = 1:2, R_f = 0.43) as a colorless solid (410 mg, 1.12 mmol, 39 %). M.p. 103–104 °C; $[\alpha]_D^{23}$ = +140 (*c* = 10.0 in $CHCl_3$); ^{1}HNMR (400 MHz, $CDCl_3$): δ = 0.93 (d, *J* = 6.6 Hz, 6 H), 0.99 (d, *J* = 6.8 Hz, 3 H), 1.02 (d, *J* = 6.8 Hz, 3 H), 1.11 (t, *J* = 7.1 Hz, 3 H), 1.17 (t, *J* = 7.1 Hz, 3 H), 1.36–1.75 (m, 6 H), 1.85–2.00 (m, 1 H), 2.01–2.10 (m, 1 H), 2.38–2.45 (m, 3 H), 2.57 (ddd, *J* = 15.1, 8.5, 1.7 Hz, 1 H), 3.16–3.25 (m, 1 H), 3.27–3.37 (m, 1 H), 3.37–3.47 (m, 1 H), 3.48–3.57 (m, 1 H), 3.83 (dd, *J* = 10.6, 6.7 Hz, 1 H), 3.87 (dd, *J* = 10.6, 6.6 Hz, 1 H), 4.11 (dd, *J* = 8.2, 6.8 Hz, 1 H), 9.64 (br d, *J* = 8.3 Hz, 1 H); ^{13}CNMR (50 MHz, $CDCl_3$): δ = 12.83 (CH_3), 14.42 (CH_3), 18.46 (CH_3), 19.28 (2 CH_3), 19.82 (CH_3), 25.22 (CH_2), 26.03 (CH_2), 27.90 (CH), 28.11 (CH_2), 29.06 (CH_2), 31.78 (CH_2), 32.30 (CH), 40.36 (CH_2), 41.42 (CH_2), 60.11 (CH), 69.13 (CH_2), 95.62 (C), 165.21 (C), 170.44 (C=O), 170.83 (C=O); IR (ATR): $\tilde{\nu}$ = 1635, 1581, 1251 cm^{-1}; MS (EI, 70 eV): *m*/*z* (%): 366 (8) $[M]^+$, 293 (5), 266 (97), 252 (9), 210 (8), 192 (100), 178 (11), 165 (8), 150 (13), 138 (7), 95 (15), 81 (13), 69 (17); HR-MS: $C_{21}H_{38}N_2O_3$ (366.54): calcd: 366.2882; found: 366.2881.

***N*-(2-Ethoxycarbonyl-1-methyl-1-propenyl)-L-valine diethylamide (3 hb)**: Oxoester **1 h** (502 mg, 3.48 mmol), auxiliary **2 b** (600 mg, 3.48 mmol), and molecular sieves (2.5 g) in toluene (5 mL) were converted according to GP2 to yield **3 hb** after chromatography (MTB/PE = 1:1, R_f = 0.35) as a colorless resin (444 mg, 1.49 mmol, 43 %). $[\alpha]_D^{23}$ = +167 (*c* = 5.40 in $CHCl_3$); ^{1}HNMR (400 MHz, $CDCl_3$): δ = 1.00 (d, *J* = 6.9 Hz, 3 H), 1.02 (d, *J* = 7.0 Hz, 3 H), 1.11 (t, *J* = 7.0 Hz, 3 H), 1.19 (t, *J* = 7.1 Hz, 3 H), 1.26 (t, *J* = 7.2 Hz, 3 H), 1.78 (s, 3 H), 3.19 (s, 3 H), 2.00–2.10 (m, 1 H), 3.15–3.24 (m, 1 H), 3.26–3.36 (m, 1 H), 3.38–3.47 (m, 1 H), 3.51–3.61 (m, 1 H), 4.10 (dd, *J* = 8.8, 6.3 Hz, 1 H), 4.10–4.17 (m, 2 H), 9.59 (br d, *J* = 8.9 Hz, 1 H); ^{13}CNMR (50 MHz, $CDCl_3$): δ = 12.83 (CH_3), 12.95 (CH_3), 14.52 (CH_3), 14.65 (CH_3), 15.84 (CH_3), 18.10 (CH_3), 19.89 (CH_3), 32.34 (CH), 40.26 (CH_2), 41.45 (CH_2), 58.78 (CH_2), 59.78 (CH), 88.37 (C), 157.34 (C), 170.74 (C=O), 170.83 (C=O); IR (ATR): $\tilde{\nu}$ = 1646, 1590, 1247, 1105 cm^{-1}; MS (EI, 70 eV): *m*/*z* (%): 299 (1) $[M+H]^+$, 209 (7), 198 (19), 181 (5), 152 (100), 124 (8), 110 (6), 96 (6), 70 (7); HR-MS: $C_{16}H_{30}N_2O_3$ (298.43): calcd: 298.2256; found: 298.2255.

***N*-(2-Ethoxycarbonyl-1-methyl-1-propenyl)-L-*tert*-leucine diethylamide (3 hg)**: Oxoester **1 h** (542 mg, 3.76 mmol), auxiliary **2 g** (700 mg, 3.76 mmol), and molecular sieves (2.5 g) in toluene (5 mL) were converted according to GP2 to yield **3 hg** after chromatography (MTB/PE = 2:1, R_f = 0.56) as a colorless solid (717 mg, 2.29 mmol, 61 %). M.p. 81 °C; $[\alpha]_D^{23}$ = +136 (*c* = 5.7 in $CHCl_3$); ^{1}HNMR (400 MHz, $CDCl_3$): δ = 1.03 (s, 9 H), 1.11 (t, *J* = 7.0 Hz, 3 H), 1.19 (t, *J* = 7.1 Hz, 3 H), 1.26 (t, *J* = 7.2 Hz, 3 H), 1.78 (s, 3 H), 1.92 (s, 3 H) 3.00–3.09 (m, 1 H), 3.22–3.32 (m, 1 H), 3.54–3.64 (m, 1 H), 3.69–3.79 (m, 1 H), 4.10–4.19 (m, 2 H), 4.21 (d, *J* = 9.8 Hz, 1 H), 9.75 (d, *J* = 9.7 Hz, 1 H); ^{13}CNMR (50 MHz, $CDCl_3$): δ = 12.78 (CH_3), 13.07 (CH_3), 14.51 (CH_3), 14.66 (CH_3), 15.73 (CH_3), 26.82 (3 CH_3), 36.41 (C), 39.87 (CH_2), 42.12 (CH_2), 58.80 (CH_2), 59.45 (CH), 88.13 (C), 156.35 (C), 170.13 (C=O), 170.50 (C=O); IR (ATR): $\tilde{\nu}$ = 1635, 1580, 1250, 1096 cm^{-1}; MS (EI, 70 eV): *m*/*z* (%): 312 (8) $[M]^+$, 267 (9), 255 (22), 212 (100), 209 (43), 181 (9), 166 (91), 110 (7), 100 (16), 86 (10), 72 (15); HR-MS: $C_{17}H_{32}N_2O_3$: calcd: 312.2413; found: 312.2420; elemental analysis calcd (%) for $C_{17}H_{32}N_2O_3$ (312.45): C 65.35, H 10.32, N 8.97; found: C 65.32, H 10.49, N 8.96.

***N*-(2-Isobutoxycarbonyl-1-methyl-1-propenyl)-L-valine diethylamide (3 ib)**: Oxoester **1 i** (720 mg, 4.18 mmol), auxiliary **2 b** (600 mg, 3.48 mmol), and molecular sieves (2.5 g) in toluene (5 mL) were converted according to GP2 to yield **3 ib** after chromatography (MTB/PE = 1:1, R_f = 0.43) as a colorless solid (702 mg, 2.15 mmol, 62 %). M.p. 39 °C; $[\alpha]_D^{23}$ = +123 (*c* = 6.1 in $CHCl_3$); ^{1}HNMR (500 MHz, $CDCl_3$): δ = 0.92 (d, *J* = 6.7 Hz, 6 H), 0.99 (d, *J* = 6.9 Hz, 3 H), 1.01 (d, *J* = 6.9 Hz, 3 H), 1.10 (t, *J* = 7.1 Hz, 3 H), 1.17 (t, *J* = 7.1 Hz, 3 H), 1.78 (s, 3 H), 1.89 (s, 3 H), 1.87–1.96 (m, 1 H), 2.01–2.08 (m, 1 H), 3.14–3.23 (m, 1 H), 3.26–3.35 (m, 1 H), 3.37–3.46 (m, 1 H), 3.50–3.58 (m, 1 H), 3.83 (dd, *J* = 10.5, 6.6 Hz, 1 H), 3.86 (dd, *J* = 10.6, 6.7 Hz, 1 H), 4.08 (dd, *J* = 8.7, 6.4 Hz, 1 H), 9.60 (br d, *J* = 8.5 Hz, 1 H); ^{13}CNMR (125 MHz, $CDCl_3$): δ = 12.80 (CH_3), 12.82 (CH_3), 14.48 (CH_3), 15.77 (CH_3), 18.07 (CH_3), 19.26 (2 CH_3), 19.88 (CH_3), 27.87 (CH), 32.25 (CH), 40.23 (CH_2), 41.40 (CH_2), 59.82 (CH), 69.19 (CH_2), 88.43 (C), 157.37 (C), 170.79 (C=O), 170.80 (C=O); IR (ATR): $\tilde{\nu}$ = 1645, 1591, 1244, 1106, 1088 cm^{-1}; MS (EI, 70 eV): *m*/*z* (%): 326 (9) $[M]^+$, 253 (11), 226 (100), 209 (6), 170 (19), 152 (88), 100 (8), 72 (9); HR-MS: $C_{18}H_{34}N_2O_3$: calcd: 326.2569; found: 326.2630; elemental analysis calcd (%) for $C_{18}H_{34}N_2O_3$ (326.50): C 66.22, H 10.50, N 8.58; found: C 66.00, H 10.21, N 8.72.

***N*-(1,2-Dimethyl-3-oxo-3-phenyl-1-propenyl)-L-valine diethylamide (3 jb)**: Diketone **1 j** (640 mg, 3.63 mmol), auxiliary **2 b** (626 mg, 3.63 mmol), and molecular sieves (2.5 g) in toluene (5 mL) were converted according to GP2 to yield **3 jb** after chromatography (MTB/PE = 1:1, R_f = 0.11) as a colorless solid (550 mg, 1.66 mmol, 50 %). M.p. 128–129 °C; $[\alpha]_D^{23}$ = +257 (*c* = 6.3 in $CHCl_3$); ^{1}HNMR (500 MHz, $CDCl_3$): δ = 1.05 (d, *J* = 6.8 Hz, 3 H), 1.09 (d, *J* = 6.8 Hz, 3 H), 1.12 (t, *J* = 7.0 Hz, 3 H), 1.19 (t, *J* = 7.0 Hz, 3 H), 1.81 (s, 3 H), 1.99 (s, 3 H), 2.12–2.19 (m, 1 H), 3.21–3.28 (m, 1 H), 3.34–3.46 (m, 2 H), 3.48–3.56 (m, 1 H), 4.23 (t, *J* = 7.2 Hz, 1 H), 7.27–7.34 (m, 3 H), 7.38–7.42 (m, 2 H), 12.74 (br d, *J* = 7.3 Hz, 1 H); ^{13}CNMR (125 MHz, $CDCl_3$): δ = 12.76 (CH_3), 14.37 (CH_3), 16.25 (CH_3), 16.57 (CH_3), 18.16 (CH_3), 19.92 (CH_3), 31.81 (CH), 40.36 (CH_2), 41.47 (CH_2), 61.21 (CH), 98.24 (C), 127.10 (2 CH), 127.61 (2 CH), 128.30 (CH), 143.14 (C), 163.66 (C), 169.78 (C=O), 193.34 (C=O); IR (ATR): $\tilde{\nu}$ = 1644, 1590, 1576, 1546, 1227, 1003 cm^{-1}; MS (EI, 70 eV): *m*/*z* (%): 330 (3) $[M]^+$, 230 (100), 186 (6), 105 (95), 100 (7), 77 (16), 72 (9); HR-MS: $C_{20}H_{30}N_2O_2$ (330.47): calcd: 330.2307; found: 330.2306.

***rac*-Isobutyl 2-acetyl-2-methyl-5-oxohexanoate (5 i)**: MVK (**4**, 0.50 mg, 0.70 mmol) was added to a mixture of donor **1 i** (60 mg, 0.35 mmol) and $FeCl_3 \cdot 6H_2O$ (7.1 mg, 0.026 mmol) in CH_2Cl_2 (1 mL). After the mixture had been stirred for 12 h at 23 °C, all volatile materials were removed in vacuo and the residue was chromatographed on SiO_2 (MTB/PE = 1:4, R_f = 0.12) to afford **5 i** as a colorless oil (71 mg, 0.29 mmol, 84 %). ^{1}HNMR (200 MHz, $CDCl_3$): δ = 0.92 (d, *J* = 6.7 Hz, 6 H), 1.34 (s, 3 H), 2.83–2.25 (m, 3 H), 2.13 (s, 3 H), 2.16 (s, 3 H), 2.39 (dd, *J* = 6.3, 2.2 Hz, 1 H), 2.44 (dd, *J* = 6.6, 3.5 Hz,

1H), 4.27–4.33 (m, 2H); ^{13}CNMR (125 MHz, $CDCl_3$): $\delta = 18.96$ ($2CH_3$), 19.26 (CH_3), 26.18 (CH_3), 27.59 (CH_3), 28.37 (CH_2), 29.87 (CH), 38.56 (CH_2), 58.70 (C), 71.51 (CH_2), 172.63 (C=O), 205.26 (C=O), 207.25 (C=O); IR (ATR): $\tilde{\nu} = 1712\ cm^{-1}$; MS (EI, 70 eV): m/z (%): 242 (1) $[M]^+$, 200 (44), 143 (8), 126 (29), 116 (8), 98 (100), 87 (22), 69 (11), 57 (27); HR-MS: $C_{13}H_{22}O_4$ (242.32): calcd: 242.1518; found: 242.1521.

***rac*-2-Acetyl-2-methyl-1-phenylhexane-1,5-dione (5j)**: MVK (**4**, 590 mg, 8.43 mmol) was added to a mixture of donor **1j** (928 mg, 5.72 mmol) and $FeCl_3 \cdot 6H_2O$ (71 mg, 0.26 mmol) in CH_2Cl_2 (2 mL). After stirring for 12 h at 23 °C, all volatile materials were removed in vacuo and the residue was chromatographed on SiO_2 (MTB/PE = 1:1, $R_f = 0.24$) to afford **5j** as a colorless solid (800 mg, 3.44 mmol, 60%). M.p. 71 °C; ^{1}HNMR (200 MHz, $CDCl_3$): $\delta = 1.41$ (s, 3H), 2.08 (s, 3H), 2.09 (s, 3H), 2.14–2.42 (m, 4H), 7.36–7.56 (m, 3H), 7.72–7.78 (m, 2H); ^{13}CNMR (50 MHz, $CDCl_3$): $\delta =$ 19.70 (CH_3), 26.80 (CH_3), 28.64 (CH_2), 29.61 (CH_3), 37.67 (CH_2), 63.40 (C), 128.44 (2CH), 128.47 (2CH), 132.87 (CH), 135.17 (C), 198.57 (C=O), 206.89 (C=O), 207.60 (C=O); IR (ATR): $\tilde{\nu} = 1712$, $1671\ cm^{-1}$; MS (EI, 70 eV): m/z (%): 204 (6) $[M+H-COMe]^+$, 147 (16), 105 (100); elemental analysis calcd (%) for $C_{15}H_{18}O_3$ (246.31): C 73.15, H 7.37; found: C 72.84, H 7.01.

General procedure 3 (GP3) for the asymmetric synthesis of Michael products 5: Enaminoester **3** and $Cu(OAc)_2 \cdot H_2O$ were stirred in acetone (1 mL per 0.2–0.3 mmol **3**) at 23 °C for 1 h. MVK (**4**) (2 equiv) was added and the mixture was stirred for a further 12–14 h at 23 °C. All volatile materials were removed in vacuo and the residue was treated with 1N HCl. The mixture was stirred vigorously for 2–3 h at 0 °C and subsequently extracted with MTB. After washing (saturated aqueous $NaHCO_3$) and drying ($MgSO_4$) of the combined extracts, the solvent was evaporated and the residue chromatographed on SiO_2. The *ee* values were determined by GC on a chiral column.

(*R*)-Ethyl 2-oxo-1-(3-oxobutyl)cyclopentanecarboxylate [(*R*)-5a]: According to GP3, enamine **3af** (55 mg, 0.19 mmol) and $Cu(OAc)_2 \cdot H_2O$ (1.9 mg, 0.0093 mmol) were converted to give (*R*)-**5a** (17 mg, 0.076 mmol, 40%) as a colorless oil (MTB/PE = 1:2, $R_f = 0.13$). $[\alpha]_D^{23} = -6.3$ ($c = 6.2$ in $CHCl_3$, 98% *ee* material); chiral GC: isotherm elution at 115 °C, $t(S) =$ 32.9 min, $t(R) = 34.7$ min.

(*R*)-Isobutyl 2-oxo-1-(3-oxobutyl)cyclopentanecarboxylate [(*R*)-5b]: According to GP3, enamine **3bb** (90 mg, 0.27 mmol) and $Cu(OAc)_2 \cdot H_2O$ (2.6 mg, 0.013 mmol) were converted to give (*R*)-**5b** (27 mg, 0.11 mmol, 40%) as a colorless oil (MTB/PE = 1:4, $R_f = 0.19$). $[\alpha]_D^{23} = -5.0$ ($c = 6.4$ in $CHCl_3$, 96% *ee* material); enantiomeric excess and configuration of (*R*)-**5b** were determined after transesterification to (*R*)-**5a**.

(+)-2-Acetyl-2-(3-oxobutyl)cyclohexanone (5c): According to GP3, enamine **3cg** (80 mg, 0.26 mmol) and $Cu(OAc)_2 \cdot H_2O$ (5.2 mg, 0.026 mmol) were converted to give (+)-**5c** (43 mg, 0.20 mmol, 79%) as a colorless oil (MTB/PE = 1:1, $R_f = 0.19$). $[\alpha]_D^{23} = +161$ ($c = 13.0$ in $CHCl_3$, 95% *ee* material); the enantiomeric excess of (+)-**5c** was determined after derivatization to **6f**.

(*R*)-Ethyl 2-oxo-1-(3-oxobutyl)cyclohexanecarboxylate [(*R*)-5d]: According to GP3, (*R*)-**5d** was obtained as a colorless oil (MTB/PE = 1:2, $R_f =$ 0.19). $[\alpha]_D^{23} = +94$ ($c = 4.3$ in $CHCl_3$, 99% *ee* material); chiral GC: isotherm elution at 115 °C, $t(S) = 114.2$ min, $t(R) = 120.8$ min; the enantiomeric excess of (*R*)-**5d** was also checked after conversion to **6a** according to GP4.

(*R*)-Isobutyl 2-oxo-1-(3-oxobutyl)cyclohexanecarboxylate [(*R*)-5e]: According to GP3, enamine **3eb** (80 mg, 0.23 mmol) and $Cu(OAc)_2 \cdot H_2O$ (2.3 mg, 0.011 mmol) were converted to give (*R*)-**5e** (49 mg, 0.18 mmol, 80%) as a colorless oil (MTB/PE = 1:4, $R_f = 0.15$). $[\alpha]_D^{23} = +81$ ($c = 5.4$ in $CHCl_3$, 86% *ee* material); enantiomeric excess and configuration of (*R*)-**5e** were determined after transesterification to (*R*)-**5d**.

(+)-Methyl 2-oxo-1-(3-oxobutyl)cycloheptanecarboxylate (5f): According to GP3, enamine **3fi** (70 mg, 0.21 mmol) and $Cu(OAc)_2 \cdot H_2O$ (4.2 mg, 0.021 mmol) were converted to give (+)-**5f** (38 mg, 0.16 mmol, 76%) as a colorless oil (MTB/PE = 1:2, $R_f = 0.19$). $[\alpha]_D^{23} = +29$ ($c = 7.5$ in $CHCl_3$, 90% *ee* material); the enantiomeric excess of (+)-**5f** was determined after derivatization to **6b** according to GP4.

(+)-Isobutyl 2-oxo-1-(3-oxobutyl)cycloheptanecarboxylate (5g): According to GP3, enamine **3gb** (90 mg, 0.25 mmol) and $Cu(OAc)_2 \cdot H_2O$ (2.5 mg, 0.012 mmol) were converted to give (+)-**5g** (38 mg, 0.13 mmol, 54%) as a colorless oil (MTB/PE = 1:4, $R_f = 0.14$). $[\alpha]_D^{23} = +26$ ($c = 6.5$ in $CHCl_3$, 80% *ee* material); the enantiomeric excess of (+)-**5g** was determined after transesterification to **5f** and derivatization to **6b** according to GP4.

(*R*)-Ethyl 2-acetyl-2-methyl-5-oxohexanoate [(*R*)-5h]: According to GP3, enamine **3hg** (100 mg, 0.320 mmol) and $Cu(OAc)_2 \cdot H_2O$ (6.4 mg, 0.032 mmol) were converted to give (*R*)-**5h** (51 mg, 0.24 mmol, 74%) as a colorless oil (MTB/PE = 1:2, $R_f = 0.14$). $[\alpha]_D^{23} = +9.02$ ($c = 13.3$ in $CHCl_3$, 96% *ee* material), Ref. [17] $[\alpha]_D^{22} = +8.38$ ($c = 12.9$ in $CHCl_3$, 87% *ee* material), Ref. [20] $[\alpha]_D^{22} = -8.32$ [$c = 13.0$ in $CHCl_3$, 86% *ee* material, (*S*)-**5h**]; the enantiomeric excess of (*R*)-**5h** was determined after conversion into **6d** according to GP4. ^{1}HNMR (400 MHz, $CDCl_3$): $\delta = 1.26$ (t, $J =$ 7.1 Hz, 3H), 1.33 (s, 3H), 2.02 (ddd, $J = 15.8, 9.8, 6.1$ Hz, 1H), 2.09–2.18 (m, 1H), 2.13 (s, 3H), 2.15 (s, 3H), 2.38–2.44 (m, 2H), 4.15–4.22 (m, 2H); $C_{11}H_{18}O_4$ (214.26).

(*R*)-Isobutyl 2-acetyl-2-methyl-5-oxohexanoate [(*R*)-5i]: According to GP3, enamine **3ib** (100 mg, 0.306 mmol) and $Cu(OAc)_2 \cdot H_2O$ (3.0 mg, 0.015 mmol) were converted to give (*R*)-**5i** (48 mg, 0.20 mmol, 65%) as a colorless oil (MTB/PE = 1:4, $R_f = 0.12$). $[\alpha]_D^{23} = +4.8$ ($c = 6.1$ in $CHCl_3$, 74% *ee* material). The enantiomeric excess of (*R*)-**5i** was determined after conversion into **6e** according to GP4, the configuration established after transesterification of **6e** into **6d**.

Upscaling procedure: synthesis of (*R*)-5d from 3db: $Cu(OAc)_2 \cdot H_2O$ (83.1 mg, 0.416 mmol) was added to a solution of enamine **3db** (2.700 g, 8.322 mmol) in acetone (25 mL). The mixture was stirred at ambient temperature until all solids had been dissolved (45 min). MVK (**4**, 1.39 mL, 16.6 mmol) was added and the mixture was stirred for additional 22 h at ambient temperature. (*R*)-**5d** was isolated according to GP3 (MTB/PE = 1:2, $R_f = 0.19$) as a colorless oil (1.801 g, 7.495 mmol, 90%) with 98% *ee* (determined after transformation to **6a**). The auxiliary **2b** was recovered from the combined aqueous layers: after addition of KOH (aqueous solution, 5%) at 0 °C (pH 12–13), extraction with CH_2Cl_2, drying of the combined organic layers with $MgSO_4$, and filtration, evaporation of the solvent gave **2b** (1.376 g, 7.989 mmol, 96%), which was pure by ^{1}H and ^{13}CNMR spectroscopy. The auxiliary could be reused directly without loss of selectivity.

Transesterification of 5b to 5a and 5e to 5d: To a solution of isobutyl ester **5b** or **5e** (0.080–0.15 mmol) in absolute EtOH ($\approx 0.1\ mol\,L^{-1}$) was added $Ti(OEt)_4$ (2 equiv). The mixture was stirred for 6 h at 80 °C in a tightly closed reaction flask, and subsequently poured into 1N HCl. After extraction with MTB, the combined organic layers were washed with saturated $NaHCO_3$ solution and dried over $MgSO_4$ followed by filtration. The solvent was evaporated and the residue was directly analyzed by chiral GC without purification. The conversions achieved with this method were between 15–50%. Moreover, a number of unspecified decomposition products were formed.

Transesterification of 6c to 6b and 6e to 6d: To a solution of isobutyl ester **6c** or **6e** (0.080–0.15 mmol) in absolute MeOH (for **6c**) or EtOH (for **6e**) ($\approx 0.1\ mol\,L^{-1}$), were added 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) (0.5 equiv) and LiBr (5 equiv). The mixture was stirred for 72 h at 50 °C in a tightly closed reaction flask. The workup procedure was carried out as given above for the transesterification of compounds **5b** and **5e**. The conversions achieved with this method were between 50% and 70%; no byproducts were detected.

General procedure 4 (GP4) for the synthesis of derivatives 6a–e: A solution of the respective Michael product **5** in MTB ($\approx 0.15\ mmol\,mL^{-1}$) was treated with pyrrolidine (0.85 equiv) and acetic acid (0.85 equiv). The reaction mixture was stirred for 14 h at 23 °C, the solvent was evaporated and the residue was chromatographed on SiO_2 to give compounds **6a–e**.

Ethyl bicyclo[4.4.0]dec-1-en-3-one-6-carboxylate (6a): According to GP4, compound **5d** (100 mg, 0.416 mmol) was converted to **6a** (colorless oil, 49 mg, 0.22 mmol, 53%, MTB/PE = 1:4, $R_f = 0.14$). $[\alpha]_D^{23} = +258$ [$c = 5.70$ in $CHCl_3$, 99% *ee* material, (*R*)-**6a**]; chiral GC: gradient elution from 115 °C to 160 °C with 0.5 K min^{-1}, $t(S) = 58.9$ min, $t(R) = 62.7$ min.

Methyl bicyclo[5.4.0]undec-7-en-9-one-1-carboxylate (6b): According to GP4, compound **5f** (38 mg, 0.16 mmol) was converted to **6b** (colorless oil, 18 mg, 0.081 mmol, 51%, MTB/PE = 1:4, $R_f = 0.12$). Chiral GC: gradient elution from 115 °C to 160 °C with 0.33 K min^{-1}, $t_1 = 94.5$ min, $t_2 = 98.0$ min.

Isobutyl bicyclo[5.4.0]undec-7-en-9-one-1-carboxylate (6c): According to GP4, compound **5g** (85 mg, 0.30 mmol) was converted to **6c** (yellowish oil, 40 mg, 0.15 mmol, 50%, MTB/PE = 1:4, $R_f = 0.20$). ^{1}HNMR (200 MHz, $CDCl_3$): $\delta = 0.90$ (d, $J = 6.7$ Hz, 6H), 1.18–1.42 (m, 3H), 1.70–2.16 (m,

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7H), 2.20–2.58 (m, 5H), 3.89 (d, $J = 6.4$ Hz, 2H), 5.98 (s, 1H); ^{13}CNMR (50 MHz, $CDCl_3$): $\delta = 18.88$ (2 CH_3), 23.71 (CH_2), 27.60 (CH), 30.26 (CH_2), 30.76 (CH_2), 33.15 (CH_2), 34.82 (CH_2), 35.79 (CH_2), 37.14 (CH_2), 51.03 (C), 71.22 (CH_2), 129.32 (CH), 167.22 (C), 173.95 (C=O), 198.82 (C=O); IR (ATR): $\tilde{\nu} = 1722$, 1672 cm^{-1}; MS (EI, 70 eV): *m/z* (%): 264 (46) $[M]^+$, 212 (10), 208 (29), 184 (8), 180 (37), 163 (100), 152 (31), 135 (18), 121 (21), 107 (11), 91 (26), 79 (21), 77 (19), 67 (15), 57 (42); HR-MS: $C_{16}H_{24}O_3$ (264.36): calcd: 264.1725; found: 264.1727.

(*R*)-Ethyl 1,6-dimethyl-3-oxocyclohexene-6-carboxylate (6d): According to GP4, compound **5h** (169 mg, 0.789 mmol) was converted to **6d** (colorless oil, 136 mg, 0.693 mmol, 89%, MTB/PE = 1:2, $R_f = 0.24$). $[\alpha]_D^{23} = +129$ [$c = 10.2$ in $CHCl_3$, 96% *ee* material, (*R*)-**6d**], Ref. [20] $[\alpha]_D^{23} = -106.5$ [$c = 11.5$ in $CHCl_3$, 86% *ee* material, (*S*)-**6d**]; chiral GC: gradient elution from 85 °C to 115 °C with 0.4 K min^{-1}, $t(S) = 84.7$ min, $t(R) = 87.5$ min.

(*R*)-Isobutyl 1,6-dimethyl-3-oxocyclohexene-6-carboxylate (6e): According to GP4, compound **5i** (30 mg, 0.13 mmol) was converted to **6e** (colorless oil, 26 mg, 0.12 mmol, 93%, MTB/PE = 1:4, $R_f = 0.16$). Chiral GC: isotherm elution at 95 °C for 30 min, then gradient elution from 95 °C to 110 °C with 0.25 K min^{-1}, $t(S) = 125.4$ min, $t(R) = 130.5$ min. ^{1}HNMR (200 MHz, $CDCl_3$): $\delta = 0.92$ (d, $J = 6.8$ Hz, 6H), 1.44 (s, 3H), 1.84–2.04 (m, 2H), 1.97 (d, $J = 1.3$ Hz, 3H), 2.35–2.57 (m, 3H), 3.86–3.97 (m, 2H), 5.92 (q, $J = 1.1$ Hz, 1H); ^{13}CNMR (50 MHz, $CDCl_3$): $\delta = 19.03$ (2 CH_3), 21.10 (CH_3), 22.45 (CH_3), 27.71 (CH), 34.30 (CH_2), 34.40 (CH_2), 47.38 (C), 71.50 (CH_2), 128.12 (CH), 161.44 (C), 174.06 (C=O), 198.27 (C=O); IR (ATR): $\tilde{\nu} = 1727$, 1677, 1254, 1176 cm^{-1}; MS (EI, 70 eV): *m/z* (%): 224 (21) $[M]^+$, 196 (6), 140 (22), 123 (74), 112 (26), 109 (35), 95 (43), 79 (15), 67 (24), 57 (100); HR-MS: $C_{13}H_{20}O_3$ (224.30): calcd: 224.1421; found: 224.1421.

4-Methylspiro[5.5]undec-3-en-2,7-dione (6f): Compound **5c** was treated with the threefold volume of conc. H_2SO_4. The mixture was stirred for 14 h at 23 °C, ice was added and the resulting mixture extracted with MTB. The combined organic layers were washed with $NaHCO_3$ (saturated aqueous solution) and dried over $MgSO_4$ followed by filtration. After evaporation of the solvent, the residue containing **6f** was directly analyzed by chiral GC without further purification. Chiral GC: gradient elution from 100 °C to 140 °C with 0.25 K min^{-1}, $t_1 = 97.5$ min, $t_2 = 115.1$ min.

***N*-[2-Ethoxycarbonyl-2-(3-oxobutyl)cyclohexylidene]-L-valine diethylamide (7)**: $Cu(OAc)_2 \cdot H_2O$ (3.4 mg, 0.017 mmol) was added to a solution of enamine **3db** (110 mg, 0.339 mmol) in acetone (1.5 mL). The mixture was stirred at 23 °C until the metal salt was completely dissolved (30 min) then MVK (60 µL, 0.7 mmol) was added. After 14 h, all volatile materials were removed in vacuo and the residue was chromatographed on alumina 90 (II–III) (MTB/PE = 1:1, $R_f = 0.26$) to yield **7** as a colorless oil (92 mg, 0.23 mmol, 69%). $[\alpha]_D^{23} = +30.8$ ($c = 6.00$ in $CHCl_3$); ^{1}HNMR (500 MHz, C_6D_6): $\delta = 0.99$ (t, $J = 7.0$ Hz, 3H), 1.05 (t, $J = 7.1$ Hz, 3H), 1.10 (d, $J = 6.6$ Hz, 3H), 1.12 (t, $J = 7.0$ Hz, 3H), 1.22 (d, $J = 6.7$ Hz, 3H), 1.29–1.41 (m, 2H), 1.50–1.65 (m, 3H), 1.89 (s, 3H), 2.00–2.08 (m, 1H), 2.20 (ddd, $J = 13.8$, 10.6, 5.3 Hz, 1H), 2.41–2.54 (m, 3H), 2.58 (ddd, $J = 14.4$, 10.0, 4.7 Hz, 1H), 2.71 (ddd, $J = 16.8$, 10.6, 4.7 Hz, 1H), 2.83 (dt, $J = 13.9$, 4.3 Hz, 1H), 3.28–3.36 (m, 3H), 3.49–3.57 (m, 1H), 4.04–4.09 (m, 2H), 4.26 (d, $J = 9.0$ Hz, 1H); ^{13}CNMR (125 MHz, $CDCl_3$): $\delta = 12.64$ (CH_3), 14.06 (CH_3), 14.40 (CH_3), 19.54 (CH_3), 19.61 (CH_3), 22.76 (CH_2), 26.79 (CH_2), 28.31 (CH_2), 29.60 (CH_2), 29.83 (CH_3), 31.81 (CH), 36.32 (CH_2), 39.27 (CH_2), 39.80 (CH_2), 40.71 (CH_2), 56.71 (C), 60.66 (CH_2), 71.79 (CH), 170.93 (C), 171.92 (C), 173.97 (C), 208.64 (C=O); IR (ATR): $\tilde{\nu} = 1718$, 1631, 1219 cm^{-1}; MS (EI, 70 eV): *m/z* (%): 394 (2) $[M]^+$, 351 (5), 324 (5), 294 (72), 224 (39), 220 (9), 194 (14), 178 (38), 170 (30), 151 (28), 142 (29), 124 (22), 100 (25), 95 (17), 81 (25), 72 (100); HR-MS: $C_{22}H_{38}N_2O_4$: calcd: 394.2832; found: 394.2827; elemental analysis calcd (%) for $C_{22}H_{38}N_2O_4$ (394.55): C 66.97, H 9.71, N 7.10; found: C 66.19, H 9.63, N 6.87.

General procedure 5 (GP5) for the synthesis of *N*-Boc-protected amino acid amides 9a–l: To a solution of *N*-Boc-protected amino acid **8a–f** in CH_2Cl_2 was added dicyclohexylcarbodiimide (DCC) in small portions at 0 °C, followed by addition of the respective amine dissolved in CH_2Cl_2. The mixture was stirred overnight at 23 °C, filtered through SiO_2 (eluent: MTB), and all volatile materials were removed in vacuo. The residue was chromatographed on SiO_2 (eluent: MTB/PE) to give the title compounds **9a–l**. Details for **9a**, **d**, **e**, **h–j**, and **l** are given in the Supporting Information.

***N*-(*tert*-Butyloxycarbonyl)-L-valine diethylamide (9b)**: *N*-Boc-L-valine (**8a**) (13.00 g, 59.84 mmol) and DCC (14.20 g, 68.82 mmol) in CH_2Cl_2 (40 mL) were converted according to GP5 with $HNEt_2$ (6.128 g, 83.78 mmol) in CH_2Cl_2 (10 mL) to yield **9b** after chromatography (MTB/PE = 1:2, $R_f = 0.25$) as a colorless viscous oil (10.46 g, 38.40 mmol, 64%). $[\alpha]_D^{23} = -6.0$ ($c = 5.3$ in $CHCl_3$); ^{1}HNMR (200 MHz, $CDCl_3$): $\delta = 0.91$ (d, $J = 6.6$ Hz, 3H), 0.94 (d, $J = 6.6$ Hz, 3H), 1.11 (t, $J = 7.1$ Hz, 3H), 1.22 (t, $J = 7.1$ Hz, 3H), 1.42 (s, 9H), 1.96–2.06 (m, 1H), 3.08–3.24 (m, 1H), 3.27–3.52 (m, 2H), 3.52–3.70 (m, 1H), 4.36 (dd, $J = 9.4$, 6.6 Hz, 1H), 5.25 (br d, $J = 9.4$ Hz, 1H); ^{13}CNMR (50 MHz, $CDCl_3$): $\delta = 12.93$ (CH_3), 14.57 (CH_3), 17.48 (CH_3), 19.56 (CH_3), 28.32 (3 CH_3), 32.08 (CH), 40.18 (CH_2), 41.98 (CH_2), 54.94 (CH), 79.29 (C), 155.73 (C=O), 171.41 (C=O); IR (ATR): $\tilde{\nu} = 1706$, 1637, 1174 cm^{-1}; MS (EI, 70 eV): *m/z* (%): 272 (4) $[M]^+$, 199 (32), 172 (61), 129 (13), 116 (83), 100 (78), 72 (100), 57 (91); HR-MS: $C_{14}H_{28}N_2O_3$: calcd: 272.2100; found: 272.2103; elemental analysis calcd (%) for $C_{14}H_{28}N_2O_3$ (272.39): C 61.73, H 10.36, N 10.28; found: C 61.54, H 10.02, N 10.29.

***N*-(*tert*-Butyloxycarbonyl)-L-valine diallylamide (9c)**: *N*-Boc-L-valine (**8a**) (4.400 g, 20.25 mmol) and DCC (4.806 g, 23.29 mmol) in CH_2Cl_2 (20 mL) were converted according to GP5 with diallylamine (2.361 g, 24.30 mmol) in CH_2Cl_2 (5 mL) to yield **9c** after chromatography (MTB/PE = 1:4, $R_f = 0.21$) as a colorless viscous oil (5.582 g, 18.83 mmol, 93%). $[\alpha]_D^{23} = -3.21$ ($c = 13.4$ in $CHCl_3$); ^{1}HNMR (400 MHz, $CDCl_3$): $\delta = 0.90$ (d, $J = 6.9$ Hz, 3H), 0.94 (d, $J = 6.8$ Hz, 3H), 1.42 (s, 9H), 1.92–2.01 (m, 1H), 3.87 (dd, $J = 15.2$, 5.9 Hz, 1H), 3.95 (dd, $J = 16.7$, 4.8 Hz, 1H), 3.99 (dd, $J = 14.5$, 5.7 Hz, 1H), 4.09 (dd, $J = 15.3$, 5.5 Hz, 1H), 4.39 (dd, $J = 9.4$, 6.3 Hz, 1H), 5.09–5.24 (m, 5H), 5.68–5.84 (m, 2H); ^{13}CNMR (50 MHz, $CDCl_3$): $\delta = 17.10$ (CH_3), 19.53 (CH_3), 28.09 (3 CH_3), 31.47 (CH), 47.37 (CH_2), 49.56 (CH_2), 54.94 (CH), 79.06 (C), 117.12 (CH_2), 117.40 (CH_2), 132.57 (CH), 132.68 (CH), 155.48 (C=O), 171.99 (C=O); IR (ATR): $\tilde{\nu} = 1707$, 1638, 1172 cm^{-1}; MS (EI, 70 eV): *m/z* (%): 296 (16) $[M]^+$, 240 (8), 223 (74), 197 (6), 180 (6), 172 (81), 153 (12), 124 (55), 116 (100), 96 (25), 81 (12), 72 (73), 57 (98); HR-MS: $C_{16}H_{28}N_2O_3$ (296.41): calcd: 296.2100; found: 296.2103.

***N*-(*tert*-Butyloxycarbonyl)-L-*tert*-leucine dimethylamide (9f)**: *N*-Boc-L-*tert*-leucine (**8e**) (6.000 g, 25.94 mmol) and DCC (6.155 g, 29.83 mmol) in CH_2Cl_2 (35 mL) were converted according to GP5 with $HNMe_2$ (4.4 mL, 65 mmol) in CH_2Cl_2 (10 mL) to yield **9f** after chromatography (MTB/PE = 1:1, $R_f = 0.26$) as a colorless solid (4.612 g, 17.85 mmol, 69%). M.p. 38 °C; $[\alpha]_D^{23} = +34$ ($c = 4.9$ in $CHCl_3$); ^{1}HNMR (200 MHz, $CDCl_3$): $\delta = 0.97$ (s, 9H), 1.42 (s, 9H), 2.96 (s, 3H), 3.13 (s, 3H), 4.52 (d, $J = 9.7$ Hz, 1H), 5.33 (br d, $J = 9.7$ Hz, 1H); ^{13}CNMR (50 MHz, $CDCl_3$): $\delta = 25.92$ (3 CH_3), 27.88 (3 CH_3), 34.98 (CH_3), 35.26 (C), 37.81 (CH_3), 55.31 (CH), 78.67 (C), 155.18 (C=O), 171.34 (C=O); IR (ATR): $\tilde{\nu} = 1713$, 1642, 1494, 1366, 1172 cm^{-1}; MS (EI, 70 eV): *m/z* (%): 258 (2) $[M]^+$, 186 (58), 146 (52), 130 (87), 128 (5), 101 (14), 86 (100), 72 (62), 57 (99); HR-MS: $C_{13}H_{26}N_2O_3$: calcd: 258.1943; found: 258.1938; elemental analysis calcd (%) for $C_{13}H_{26}N_2O_3$ (258.36): C 60.44, H 10.14, N 10.84; found: C 59.64, H 9.96, N 10.80.

***N*-(*tert*-Butyloxycarbonyl)-L-*tert*-leucine diethylamide (9g)**: *N*-Boc-L-*tert*-leucine (**8e**) (6.500 g, 28.10 mmol) and DCC (6.668 g, 32.32 mmol) in CH_2Cl_2 (40 mL) were converted according to GP5 with $HNEt_2$ (3.289 g, 44.97 mmol) in CH_2Cl_2 (10 mL) to yield **9g** after chromatography (MTB/PE = 1:2, $R_f = 0.33$) as a colorless solid (5.081 g, 17.74 mmol, 63%). M.p. 55 °C; $[\alpha]_D^{23} = -12$ ($c = 5.9$ in $CHCl_3$); ^{1}HNMR (200 MHz, $CDCl_3$): $\delta = 0.98$ (s, 9H), 1.12 (t, $J = 7.2$ Hz, 3H), 1.21 (t, $J = 7.2$ Hz, 3H), 1.42 (s, 9H), 2.91–3.10 (m, 1H), 3.14–3.33 (m, 1H), 3.55–3.86 (m, 2H), 4.45 (d, $J = 9.9$ Hz, 1H), 5.29 (br d, $J = 9.7$ Hz, 1H); ^{13}CNMR (50 MHz, $CDCl_3$): $\delta = 12.96$ (CH_3), 14.47 (CH_3), 26.44 (3 CH_3), 28.31 (3 CH_3), 35.71 (C), 40.19 (CH_2), 42.77 (CH_2), 55.77 (CH), 79.30 (C), 155.59 (C=O), 170.95 (C=O); IR (ATR): $\tilde{\nu} = 1715$, 1638, 1497, 1365, 1173 cm^{-1}; MS (EI, 70 eV): *m/z* (%): 286 (2) $[M]^+$, 213 (12), 186 (28), 174 (15), 130 (66), 100 (33), 86 (100), 72 (19), 57 (78); HR-MS: $C_{15}H_{30}N_2O_3$: calcd: 286.2256; found: 286.2252; elemental analysis calcd (%) for $C_{15}H_{30}N_2O_3$ (286.41): C 62.90, H 10.56, N 9.78; found: C 62.73, H 10.53, N 9.92.

***N*-(*tert*-Butyloxycarbonyl)-L-isoleucine pyrrolidide (9k)**: *N*-Boc-L-isoleucine (**8c**) (5.220 g, 22.57 mmol) and DCC (5.122 g, 24.83 mmol) in CH_2Cl_2 (30 mL) were converted according to GP5 with pyrrolidine (2.087 g, 29.34 mmol) in CH_2Cl_2 (10 mL) to yield **9k** after chromatography (MTB/PE = 1:2, $R_f = 0.07$) as a colorless solid (4.481 g, 15.76 mmol, 70%). M.p. 51 °C; $[\alpha]_D^{23} = -1.3$ ($c = 6.05$ in $CHCl_3$); ^{1}HNMR (200 MHz, $CDCl_3$): $\delta = 0.88$ (t, $J = 7.2$ Hz, 3H), 0.92 (d, $J = 6.7$ Hz, 3H), 0.99–1.20 (m, 1H), 1.42 (s, 9H), 1.49–1.77 (m, 2H), 1.79–2.03 (m, 4H), 3.34–3.60 (m, 3H), 3.61–3.77

(m, 1H), 4.26 (dd, $J = 9.4$, 7.1 Hz, 1H), 5.21 (br d, $J = 9.7$ Hz, 1H); ^{13}CNMR (50 MHz, $CDCl_3$): $\delta = 11.28$ (CH_3), 15.58 (CH_3), 24.19 (CH_2), 26.01 (CH_2), 26.89 (CH_2), 28.35 (3CH_3), 37.99 (CH), 45.74 (CH_2), 46.71 (CH_2), 56.37 (CH), 79.32 (C), 155.76 (C=O), 170.91 (C=O); IR (ATR): $\tilde{\nu} = 1706$, 1637, 1437, 1171 cm^{-1}; MS (EI, 70 eV): m/z (%): 284 (2) $[M]^+$, 228 (12), 224 (14), 211 (8), 186 (28), 143 (14), 130 (100), 98 (25), 86 (58), 74 (16), 70 (45), 57 (63); HR-MS: $C_{15}H_{28}N_2O_3$: calcd: 284.2100; found: 286.2101; elemental analysis calcd (%) for $C_{15}H_{28}N_2O_3$ (284.40): C 63.35, H 9.92, N 9.85; found: C 62.96, H 10.11, N 10.37.

***tert*-Butyl (*S*)-*N*-[1-(ethylsulfanylmethyl)-3-methylbutyl]carbamate (11m)**: To a solution of tosylate **10a** (1.400 g, 3.769 mmol) in DMF (5 mL) under nitrogen was added dropwise NaSEt (80%, 566 mg, 5.38 mmol) in DMF (6 mL). The mixture was stirred for 16 h at 23 °C. Water was added and the resulting solution was extracted with MTB. The combined organic layers were washed with H_2O (twice) and brine, dried with $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by chromatography on SiO_2 (MTB/PE = 1:15, $R_f = 0.14$) to afford **11m** as a colorless oil (608 mg, 2.33 mmol, 86%). $[\alpha]_D^{23} = +23$ ($c = 5.5$ in $CHCl_3$); ^{1}HNMR (200 MHz, $CDCl_3$): $\delta = 0.92$ (d, $J = 6.4$ Hz, 6H), 1.25 (t, $J = 7.3$ Hz, 3H), 1.30–1.46 (m, 2H), 1.44 (s, 9H), 1.58–1.74 (m, 1H), 2.56 (q, $J = 7.3$ Hz, 2H), 2.63–2.69 (m, 2H), 3.61–4.06 (br m, 1H), 4.52 (br s, 1H); ^{13}CNMR (50 MHz, $CDCl_3$): $\delta = 14.92$ (CH_3), 22.12 (CH_3), 23.10 (CH_3), 24.91 (CH), 26.92 (CH_2), 28.41 (3CH_3), 37.67 (CH_2), 43.15 (CH_2), 48.20 (CH), 79.14 (C), 155.41 (C=O); IR (ATR): $\tilde{\nu} = 2959$, 1696, 1366, 1170 cm^{-1}; MS (EI, 70 eV): m/z (%): 261 (3) $[M]^+$, 186 (18), 144 (8), 130 (42), 101 (8), 86 (63), 75 (13), 57 (100); HR-MS: $C_{13}H_{27}NO_2S$: calcd: 261.1763; found: 261.1765; elemental analysis calcd (%) for $C_{13}H_{27}NO_2S$ (261.43): C 59.73, H 10.41, N 5.36; found: C 59.75, H 10.57, N 5.50.

***tert*-Butyl (*S*)-*N*-[1-(dimethylaminomethyl)-3-methylbutyl]carbamate (11n)**: To a solution of **10a** (500 mg, 1.35 mmol) in pyridine (1.5 mL) was added $HNMe_2$ (0.64 mL, 9.4 mmol) in one portion at 0 °C. The mixture was stirred for 16 h at 23 °C. KOH was added (10% in water, 20 mL) and the mixture was extracted with CH_2Cl_2. The combined organic layers were dried with $MgSO_4$, filtered, and all volatile materials were removed in vacuo. The residue was chromatographed on SiO_2 (MTB/MeOH = 4:1, $R_f = 0.2$–0.4) to afford **11n** as a colorless solid (310 mg, 1.27 mmol, 94%). M.p. 98–99 °C; $[\alpha]_D^{23} = -8.7$ ($c = 3.9$ in $CHCl_3$); ^{1}HNMR (400 MHz, $CDCl_3$): $\delta = 0.88$ (d, $J = 6.6$ Hz, 6H), 1.27–1.41 (m, 2H), 1.44 (s, 9H), 1.64–1.72 (m, 1H), 2.16–2.34 (m, 2H), 2.24 (s, 6H), 3.50–3.93 (br m, 1H), 4.49 (br s, 1H); ^{13}CNMR (50 MHz, $CDCl_3$): $\delta = 22.24$ (CH_3), 23.16 (CH_3), 24.73 (CH), 28.39 (3CH_3), 43.25 (CH_2), 45.77 (2CH_3), 47.09 (CH), 64.13 (CH_2), 79.00 (C), 155.77 (C=O); IR (ATR): $\tilde{\nu} = 1699$, 1528, 1174, 1164 cm^{-1}; MS (EI, 70 eV): m/z (%): 244 (12) $[M]^+$, 171 (49), 130 (6), 105 (5), 101 (5), 86 (21), 84(11), 72 (7), 59 (69), 58 (100), 57 (100); HR-MS: $C_{13}H_{28}N_2O_2$: calcd: 244.2151; found: 244.2149; elemental analysis calcd (%) for $C_{13}H_{28}N_2O_2$ (244.38): C 63.89, H 11.55, N 11.46; found: C 63.81, H 11.78, N 11.47.

***tert*-Butyl (*S*)-*N*-[1-(ethylsulfanylmethyl)-2-phenylethyl]carbamate (11o)**: see Supporting Information.

***tert*-Butyl (*S*)-*N*-[1-benzyl-2-(dimethylamino)ethyl]carbamate (11p)**: According to the procedure given above for compound **11n**, tosylate **10b** (500 mg, 1.23 mmol) was converted with $HNMe_2$ (0.59 mL, 8.63 mmol) in pyridine (2 mL) for 60 h to afford **11p** after chromatography on SiO_2 (MTB/MeOH = 8:1, $R_f = 0.10$–0.25) as a colorless solid (283 mg, 1.02 mmol, 82%). M.p. 68–70 °C; $[\alpha]_D^{23} = +33$ ($c = 4.7$ in $CHCl_3$); ^{1}HNMR (400 MHz, $CDCl_3$): $\delta = 1.42$ (s, 9H), 2.15 (dd, $J = 13.9$, 7.6 Hz, 1H), 2.21 (s, 6H), 2.23–2.30 (m, 1H), 2.82 (dd, $J = 13.5$, 6.5 Hz, 1H), 2.87–2.97 (m, 1H), 3.56–4.02 (br m, 1H), 4.70 (br s, 1H), 7.16–7.24 (m, 3H), 7.25–7.32 (m, 2H); ^{13}CNMR (125 MHz, $CDCl_3$): $\delta = 28.38$ (3CH_3), 38.96 (CH_2), 45.50 (2CH_3), 49.43 (CH), 61.79 (CH_2), 79.14 (C), 126.23 (CH), 128.24 (2CH), 129.67 (2CH), 137.93 (C), 155.71 (C=O); IR (ATR): $\tilde{\nu} = 1709$, 1496, 1365, 1248, 1172, 701 cm^{-1}; MS (EI, 70 eV): m/z (%): 278 (5) $[M]^+$, 205 (11), 161 (5), 120 (5), 91 (11), 58 (100); HR-MS: $C_{16}H_{26}N_2O_2$: calcd: 278.1994; found: 278.1989; elemental analysis calcd (%) for $C_{16}H_{26}N_2O_2$ (278.39): C 69.03, H 9.41, N 10.06; found: C 68.53, H 9.44, N 10.20.

Acknowledgements

We are grateful to the Fonds der Chemischen Industrie and the Deutsche Forschungsgemeinschaft for generous support. We also thank the Degussa–Hüls AG for gifts of amino acids.

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Received: August 7, 2000 [F2655]