DOI: 10.1002/ejoc.200600654

The Proline-Catalyzed Asymmetric Amination of Branched Aldehydes

Thomas Baumann,[a] Henning Vogt,[b] and Stefan Bräse*[a]

Keywords: Amination / Amino acids / Organocatalysis / Aldehydes / Asymmetric synthesis

An efficient access to configurationally stable α,α-disubstituted α-amino aldehydes, oxazolidinones, and α-amino acids has been presented. Starting from simple and easily available racemic aldehydes, the α-aminated products were obtained using azodicarboxylates as the nitrogen source in up to 86 % *ee* and moderate to excellent yield. These products could further be converted both into the corresponding α-amino alcohols and, depending on the residue of the azodicarboxylates and the reaction conditions, into the oxazolidinones. On the other hand, oxidation towards the carboxylic acid and cleavage of the hydrazide bond under mild conditions revealed the free α-alkylated phenylglycine derivative.

Introduction

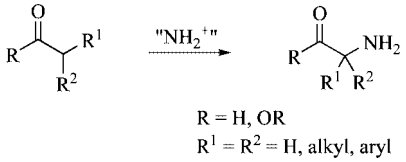
The stereocontrolled synthesis of nonracemic α,α-disubstituted amino acids, aldehydes, and alcohols with simple experimental procedures is still an interesting challenge in organic chemistry. These non-natural amino acid derivatives play an important role not only as replacements for their proteogenic counterparts, but furthermore, possess interesting structural features and exhibit pronounced biological activities. Due to the tetrasubstituted asymmetric carbon atom, incorporation of these compounds into peptides results in increased proteolytic stability and conformational restrictions; hence their use as enzyme inhibitors for the investigation of enzymatic mechanisms.[1,2] In addition, some α-alkylated phenylglycine derivatives have proven to be selective group I/group II metabotropic glutamate receptor antagonists.[3] The substance class can often be found in nature either in free form, or as constituents of biologically active compounds that are known as enzyme inhibitors, ion channel blockers, and antibiotics.

Along these same lines, another representative of this class, L-isovaline, has been found in moderate enantiomeric excess on meteorites – possibly giving insight into the very beginning of life.[4] Non-proteogenic α-amino acids are also expected to play key roles in improving the conformational properties and activity of peptides. In particular α-amino acids carrying an additional substituent at the α-position are sterically constrained within their free rotation or conformational flexibility of their side chains. When incorporated into peptides, they form well-defined folded conformations and induce secondary structures such as β-bends and α-or 3_{10}-helices.[5] Since some of the major drawbacks in the application of peptides as pharmaceuticals deal with their conformational flexibility, α,α-disubstituted amino acid residues can be used to minimize the nonselective interactions with different receptors. In addition, their modified properties such as increased lipophilicity and higher resistance towards enzymatic hydrolysis result in better bioavailability.[6]

Due to these reasons, the development of stereoselective transformations of readily available starting materials to α,α-disubstituted amino acids by simple experimental procedures has become a rapidly growing area in synthetic organic chemistry. Several methods for the preparation of functionalized enantiomerically pure compounds with structural diversity have been devized over the years. These include the diastereoselective alkylation of chiral, nonracemic oxazaborolidinone enolates,[7] as well as asymmetric phase-transfer catalysis reactions.[8] For example, the reaction of chiral auxiliary derivatized pre-formed enolates and enol ethers with azodicarboxylates furnishes α-amino acids in good to excellent stereoselectivities.[9] One major drawback of most of these methods is the tedious pre-formation of highly reactive imine or enolate equivalents, which usually require many steps and careful optimization. Moreover, the synthesis of complex α,α-disubstituted α-amino acids by auxiliary controlled methods is restricted due to the limited chiral pool.[10,11] Auxiliary-controlled and catalytic Strecker synthesis[12] employing chiral amines have also been successfully used in synthesizing chiral α-monosubstituted α-amino acids from aldehydes,[13] and, some specific α,α-disubstituted α-amino acids from ketones.[14] However, reactive and mostly unstable imine intermediates have to be generated and reacted with nucleophiles in a well-defined manner. Considering these complications and limitations, the direct enantioselective addition of a nitrogen source to

[a] Institut für Organische Chemie, Universität Karlsruhe (TH), Fritz-Haber-Weg 6, 76131 Karlsruhe, Germany
Fax: +49-721-608-8581
[b] Institut für Organische Chemie, Universität Bonn, Gerhard-Domagk-Str. 1, 53121 Bonn, Germany
Supporting information for this article is available on the WWW under http://www.eurjoc.org or from the author.

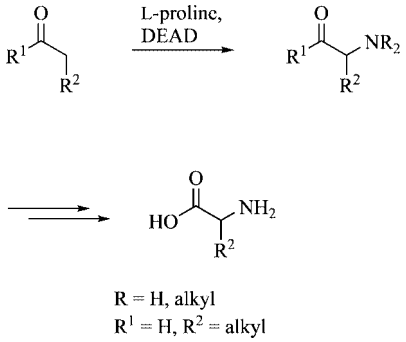
a disubstituted carbon center, represents a highly economical and simple approach for the synthesis of a stereogenic carbon atom attached to a nitrogen atom (Scheme 1).



Scheme 1. Electrophilic addition of a nitrogen source to carbonyl compounds.

Recently, two different catalytic, asymmetric variants have been developed: the C–C and the C–N bond-forming reactions. The catalytic enantioselective C–C bond-forming reaction involves the addition of carbon nucleophiles to imines by a Mannich[15] reaction.

The direct, catalytic asymmetric α-amination[16] of unmodified carbonyl compounds with azodicarboxylates as a nitrogen source represents one of the simplest procedures for the construction of a chiral carbon center bound to a nitrogen atom (Scheme 2). These types of enamine catalysis using proline and praline derivatives as organocatalysts have been expanded to a variety of catalytic asymmetric reactions; among them the stereoselective α-amination is best used for the construction of secondary and tertiary amines. Examples have been reported by List and Jorgensen, who synthesized amino carbonyl compounds and the corresponding alcohols by enantioselective proline-catalyzed amination of various achiral linear aldehydes and ketones.[17] These reactions give easy access to many classes of optically active molecules such as α-amino aldehydes, α-amino alcohols and α-amino acids with high structural diversity.



Scheme 2. L-Proline-catalyzed asymmetric α-amination of aldehydes and ketones with azodicarboxylates.

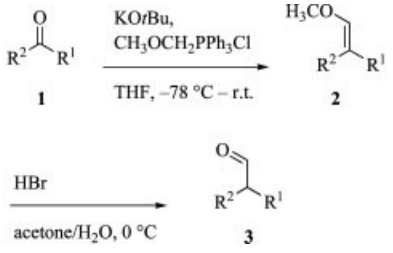
In an ongoing project towards the synthesis of biologically active peptides, the potential of the easy-to-handle procedures using organocatalysis reactions was clearly shown. Therefore, we decided to investigate the asymmetric direct α-amination of racemic α,α-disubstituted aldehydes with azodicarboxylates under enamine catalysis. We had previously found that this amination reaction proceeded well with these sterically demanding carbonyl substrates and furnished enantiomerically enriched α,α-disubstituted amino aldehydes in good yields and moderate to excellent stereoselectivities.[18] This publication discloses the scope and the limitations of this procedure in detail.

Results and Discussion

The required aldehydes are either commercially available, or – in the case of α-substituted α-aryl aldehydes – can be easily prepared in one of the following manners. Starting with the corresponding acetophenones, one possibility is to perform a Wittig reaction with methoxymethyl(triphenyl)-phosphonium chloride, leading to enol ethers which can be cleaved with mineral acids.[19] In the case of acid labile acetophenones, epoxidation with trimethylsulfoxonium iodide,[20] followed by Meinwald rearrangement with weak Lewis acids,[21] results in the required α,α-disubstituted aldehydes. The acetophenones required in either case are commercially available, rendering both methods easy and of practical use.

Wittig olefination of the substituted acetophenones **1** with methoxymethyltriphenylphosphonium chloride and *n*-butyllithium or sodium *tert*-butoxide was performed at –78 °C in THF. After warming up to room temperature, simple removal of the byproduct triphenylphosphane oxide by filtration or in some cases by column chromatography afforded the corresponding enol ethers **2** in moderate to excellent yield (Table 1).

Table 1. Reaction of acetophenones $R^1C(O)R^2$ (**1**) with methoxymethyl(triphenyl)phosphonium chloride at –78 °C in THF and subsequent hydrolysis of resulting enol ethers $R^1R^2C{=}CHOMe$ (**2**) with hydrobromic acid at 0 °C in acetone/water.



R^1	R^2	Enol ether	Yield [%]	Aldehyde	Yield [%]
Me	2-naphthyl	**2b**	69	**3b**	74
Me	3-OMe-C_6H_4	**2c**	75	**3c**	71
Me	4-OMe-C_6H_4	**2d**	84	**3d**	81
Me	4-CO_2Me-C_6H_4	**2e**	56	**3e**	55
Me	4-F-C_6H_4	**2f**	95	**3f**	92
Me	4-Cl-C_6H_4	**2g**	85	**3g**	80
Me	4-Br-C_6H_4	**2h**	88	**3h**	73
Me	4-CF_3-C_6H_4	**2i**	93	**3i**	93
Me	4-NO_2-C_6H_4	**2j**	37	**3j**	94
Me	4-CN-C_6H_4	**2k**	96	**3k**	92
Me	3,5-OMe-C_6H_3	**2l**	77	**3l**	88
Me	$–(CH_2)_5–$	**2m**	32	**3m**	27
Me	2-thiophenyl	**2n**	86	**3n**	65
Et	Ph	**2o**	79	**3o**	56

Although it would be bold to derive a general tendency, it was observed that electron- deficient aromatic ring systems gave the best results. One exception was the 4-ni-

trophenyl-substituted aldehyde **1j**, which resulted in the formation of many side products and thus a low yield in the desired enol ether.

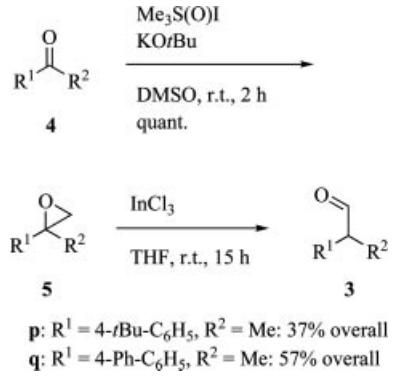
The cleavage of the enol ether **2** was achieved by acidic hydrolysis with mineralic acid in aqueous acetone, and subsequent spontaneous tautomerization to the desired aldehydes **3**. Several acids and additives were tested for this reaction, such as hydrochloric acid, hydrochloric acid in combination with sodium or potassium iodide, sulfuric acid in combination with potassium iodide, acetic acid and *p*-toluenesulfonic acid, as well as different Lewis acids like boron tribromide, boron trifluoride diethyl etherate, titanium tetrachloride, and aluminium trichloride. The temperature was varied between –78 °C and room temperature. Most of these attempts, however, resulted in low yields, and the best results were accomplished when using hydrobromic acid at 0 °C. Neutralization and purification by flash chromatography on silica delivered the racemic α-alkyl-α-aryl aldehydes **3** in moderate to high yield.

For acid-labile acetophenones a different strategy had to be used. The process started with the conversion of the carbonyl group to an epoxide with trimethylsulfoxonium iodide and potassium *tert*-butoxide in dry DMSO at room temperature. Subsequent Meinwald rearrangement with indium trichloride gave the corresponding aldehydes in moderate yield (Scheme 3). This procedure was applied to the interesting 1-indanone, which represents an annulated acetophenone derivative, and was found to be a very reactive and stereoselective substrate in the Mannich reaction.[22] For this system, the Wittig olefination-acidic hydrolysis protocol failed because the second step resulted in the complete decomposition of the initial Wittig product, which was formed in quantitative yield. Unfortunately, all other attempts failed as well; only starting material could be recovered, or complete decomposition was observed. Heteroaromatic ring systems such as furanyl or pyrrolyl derivatives could not be built up either by Wittig or by epoxidation reactions. The reason for this was that the required acidic hydrolysis or the basic epoxidation conditions were both too stressful for these sensitive molecules. Surprisingly, the *para*-phenyl and *tert*-butyl-substituted acetophenones **4p**,**q** did not react at all in the Wittig olefination, and were therefore synthesized through Corey–Chaikovsky reaction and subsequent rearrangement of the epoxide to give the corresponding aldehydes **3p** and **3q** in moderate yield.

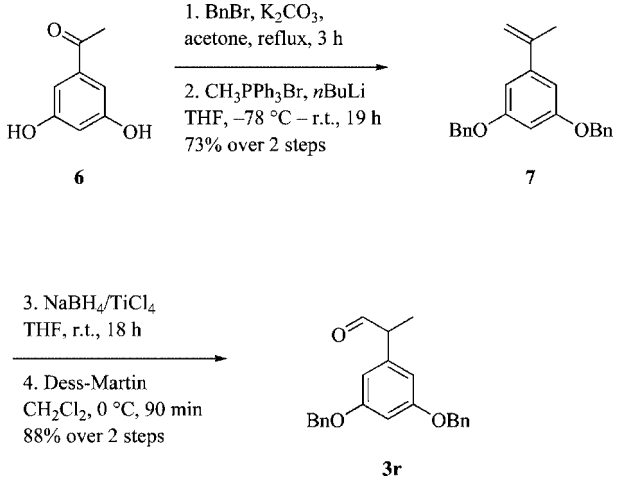
For the preparation of the 3,5-dibenzyloxy-substituted aldehyde **3r**, a third procedure was applied, because the acidic cleavage of the benzyl-protected enol ether arising from the Wittig reaction between the benzyl-protected derivative of **6** and methoxymethyl(triphenyl)phosphonium bromide could not be achieved (Scheme 4). Instead, olefination to give the styrene derivative **7** and subsequent hydroboration led to the primary alcohol, which was finally oxidized with Dess–Martin periodinane to the desired aldehyde **3r**.

With the required α,α-disubstituted aldehydes in hand, the proline-catalyzed asymmetric amination reaction using diethyl azodicarboxylate (DEAD, **8**) and dibenzyl azodicarboxylate (DBAD, **9**) was examined. Thus, 50 mol-% of the amino acid acting as the catalyst and 1 equiv. of the carbonyl compound **3** were treated with 1.5 equiv. of azodicarboxylate at 0 °C (Table 3). During the screening of the catalyst loading, the amount of proline was successfully reduced to 20 mol-% without significantly affecting the yield and stereoselectivity, although longer reaction times had to be applied. The completion of the reaction could be easily monitored by the ceasing color of the azodicarboxylate. The reaction was then quenched with water, and the aqueous phase extracted with organic solvents to deliver the α-aminated aldehydes **10** which were then purified by column chromatography. By treating the initial reaction mixture with a slight excess of sodium borohydride, the 2-hydrazino alcohols **11** were obtained, which in most cases underwent intramolecular substitution to form the stable oxazolidinones **12**.

The influence of different solvents was tested in the reaction of hydratropaldehyde (**3a**) with DEAD (Table 2). While in ethyl acetate and DMF no conversion was observed, acetonitrile, dichloromethane, DMSO, and 1,4-dioxane proved to be suitable solvents to provide the aldehyde **10a** in mod-



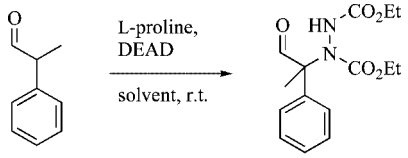
Scheme 3. Epoxidation of acetophenones $R^1C(O)R^2$ (**1p**,**q**) with trimethylsulfoxonium iodide in DMSO and rearrangement of epoxide $R^1COCH_2R^2$ (**5p**,**q**) with indium chloride in THF.



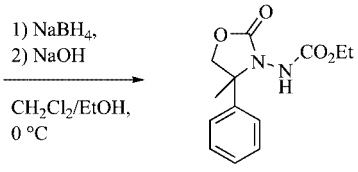
Scheme 4. Protection, Wittig olefination, hydroboration, and final oxidation of 3,5-dihydroxyacetophenone (**6**) to 2-[3,5-bis(benzyloxy)phenyl]propionaldehyde (**3r**).

erate to good enantioselectivities. Even though a maximum yield of 87% was obtained in dioxane, dichloromethane was used in the following experiments because it provided **10a** in 80% *ee*. The α-amination can also be performed as a neat reaction by simply adding the azodicarboxylate to a mixture of L-proline and the aldehyde. Under these conditions, very similar yields were obtained, whereas the enantioselectivity was significantly lower than in dichloromethane.

Table 2. Solvent screening in the reaction of hydratropaldehyde **3a** with DEAD under catalysis of L-proline.[a]



3a **10a**



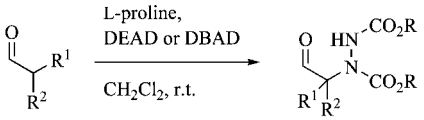
12a

Solvent	Yield[b] [%]	*ee*[c] [%]
Acetonitrile	77	66
Dichloromethane	62	80
DMF	no reaction	–
DMSO	64	72
1,4-Dioxane	87	67
Ethyl acetate	no reaction	–
Neat	83	62

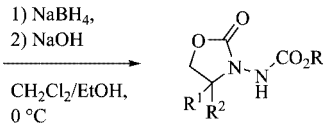
[a] Reaction conditions: 1 equiv. of aldehyde, 0.5 equiv. of L-proline, 1.5 equiv. of DEAD. [b] Isolated yields. [c] Determined by HPLC analysis of **10a** using a chiral stationary phase (Chiralcel AD); see Exp. Sect. for details.

The bulkier dibenzyl azodicarboxylate (DBAD) was used in the reaction with **3a** to evaluate the influence of the carbamate substituent on the stereoselectivity (Table 3, Entry 10). Due to the higher lability of the benzyloxycarbonyl group, the cyclization of the alcohol **11a** to give the oxazolidinone **12a** proceeded quantitatively without additional basic treatment of the crude product. In the case of diethyl azodicarboxylate, the corresponding alcohols were transformed into the oxazolidinones by addition of sodium hydroxide to the crude reaction mixture. In both cases, the formation of the oxazolidinones facilitated the determination of the level of stereoselectivity and was therefore conducted rather than the isolation of the amino alcohols. The selectivity found to be 81% *ee* in the case of DBAD, and thus very similar to that using DEAD. For this reason, mainly DBAD was employed as the aminating reagent in the following reactions. Moreover, its advantages include the introduction of the easily removable Cbz-protecting group as well as an aromatic chromophore into the product, the latter facilitating HPLC analysis.

Table 3. L-Proline-catalyzed asymmetric α-amination of α,α-disubstituted aldehydes with azodicarboxylates towards α-amino aldehydes **10** and oxazolidinones **12**.[a]



10 R = Et, Bn



12 R = Et, Bn

Entry	R^1	R^2	Aldehyde	Reagent	Product	Yield[b] [%]	*ee*[c] [%]
1	Me	Me	**3s**	DEAD	**10s-Et**	83	–
2	Me	Me	**3s**	DBAD	**10s-Bn**	85	–
3	Me	Et	**3t**	DEAD	**10t**	52	28
4	Me	Pr	**3u**	DEAD	**10u-Et**	60	–[d]
5	Me	Pr	**3u**	DBAD	**10u-Bn**	60	39
6	Et	Et	**3v**	DEAD	**10v-Et**	55	–
7	Et	Et	**3v**	DBAD	**10v-Bn**	51	–
8	Et	Bu	**3w**	DBAD	**10w**	35	4
9	Me	Ph	**3a**	DEAD	**10a-Et**	62	80
10	Me	Ph	**3a**	DBAD	**10a-Bn**	83	81
11	Me	2-Naph	**3b**	DEAD	**10b**	54	86
12	Me	3-OMe-C_6H_4	**3c**	DEAD	**10c**	62	83
13	Me	4-OMe-C_6H_4	**3d**	DEAD	**10d**	87	76
14	Me	4-CO_2Me-C_6H_4	**3e**	DEAD	**10e**	50	82
15	Me	4-F-C_6H_4	**3f**	DEAD	**10f-Et**	26	68
16	Me	4-F-C_6H_4	**3f**	DBAD	**10f-Bn**	29	35
17	Me	4-Cl-C_6H_4	**3g**	DBAD	**10g**	86	61
18	Me	4-Br-C_6H_4	**3h**	DBAD	**10h**	70	79
19	Me	4-CF_3-C_6H_4	**3i**	DEAD	**10i-Et**	19	–[d]
20	Me	4-CF_3-C_6H_4	**3i**	DBAD	**10i-Bn**	40	–[d]
21	Me	4-NO_2-C_6H_4	**3j**	DEAD	**10j-Et**	99	36
22	Me	4-NO_2-C_6H_4	**3j**	DBAD	**10j-Bn**	99	56
23	Me	4-CN-C_6H_4	**3k**	DBAD	**10k**	62	53
24	Me	3,5-OMe-C_6H_3	**3l**	DEAD	**10l**	63	85
25	Me	3,5-OBn-C_6H_3	**3r**	DBAD	**10r**	58	73
26	Me	–$(CH_2)_5$–	**3m**	DEAD	**10m**	26	–
27	Me	2-thiophenyl	**3n**	DBAD	**10n**	60	70
28	Me	4-Ph-C_6H_4	**3o**	DBAD	**10o**	53	84
29	Et	Ph	**3p**	DEAD	**10p**	59	80

[a] Reaction conditions: 1 equiv. of aldehyde, 0.5 equiv. of L-proline, 1.5 equiv. of DEAD or DBAD. [b] Isolated yields. [c] Determined by HPLC analysis of **10** using a chiral stationary phase (Chiralcel AD); see Exp. Sect. for details. [d] The *ee* could not be determined by GC or HPLC with chiral stationary phase.

The amination reaction was further evaluated by reaction of different aliphatic and aromatic racemic chiral aldehydes, as well as alicyclic cyclohexanecarbaldeyde with DEAD and DBAD to yield the configurationally stable α-amino aldehydes **10** or their corresponding oxazolidinones **12** (Table 3). In cases, where mixtures of **10** and **12** were obtained, complete formation of the oxazolidinone was achieved by treating the crude product with methanolic sodium hydroxide solution prior to isolation. Because most of the phenylpropionaldehyde derivatives with electron-withdrawing groups were found to be sensitive to air and moist-

ure, and decomposed even under a protective atmosphere within a few days, 50 mol% of L-proline were used in order to shorten the reaction time and to prevent background reactions.

The symmetric aliphatic aldehydes **3s** and **3v** showed very similar yields in the reaction with DEAD and DBAD. A longer chain length resulted in lower conversion, which can be explained by the increasing steric demand. While the reaction of non-aromatic chiral α-alkyl aldehydes **3t** and **3u** displayed only moderate enantioselectivities (28% and 39% *ee*, respectively), a significant improvement in terms of stereoselectivity could be observed when chiral α-alkyl-α-aryl-substituted aldehydes were used. In these cases, the bulky aromatic substituent seems to improve the level of stereo-differentiation between the two α-substituents. Depending on the aromatic substitution pattern, the corresponding hydrazides were obtained in moderate to good enantiomeric excess: from 53% *ee* in the case of *para*-cyanophenyl-substituted aldehyde **3k** up to 86% *ee* in the 2-naphthyl-substituted substrate **3b**. Surprisingly, the *para*-nitro derivative **3j** reacted almost quantitatively, but only with moderate levels of stereoselectivity. The presence of electron-donating groups resulted in remarkably consistent enantioselectivity, whereas electron-withdrawing substituents lowered the yield as well as the stereoselectivity. We suggest that in some cases, L-proline is thought to act more like a sub-stoichometric base rather than in a true catalytic way. With the exception of the 2-(*para*-fluorophenyl)propionaldehyde (**3f**), which reacted with DBAD in poor enantioselectivity (35% *ee*), the average stereoselectivity in reactions of electron-deficient aromatic aldehydes was found to be around 60% *ee* and thus clearly lower than the stereoselectivity observed for electron-rich aromatic aldehydes. This is presumably due to the very fast formation of a stabilized enol that competes as a nucleophile with the desired enamine for the azodicarboxylate. Control experiments in the absence of the catalyst confirmed this assumption: The racemic α-aminated products were obtained in moderate yields after one day. This background reaction which was observed especially for push-pull substituents like the nitro group significantly lowered the level of stereoselectivity, whereas the unsubstituted phenylpropionaldehyde did not react at all in the absence of the catalyst. Deviations from the average 80% *ee* of the unsubstituted phenylpropionaldehyde **3a** to higher and lower values are most likely attributed to electronic affects stabilizing or destabilizing certain transition states.

With the idea in mind that the more rigid four-membered ring analog of proline, L-2-azetidinecarboxylic acid, would improve the level of stereoselectivity, this catalyst was tested in the α-amination reaction. However, in all cases lower *ee* values around 50% were observed, with the exception of the *para*-methoxycarbonyl derivative **3c**, which gave the product in 78% *ee*, but still remained below the levels obtained in the analogous reaction catalyzed by L-proline. This decrease in selectivity can most probably be explained by a different set of geometrical parameters as a result of the varying ring sizes of the catalysts. This will most likely lead to an impairment of the coordination of the azodicarboxylate by the enamine in the transition state. Extensive studies onto the mechanism of proline-catalyzed aldol and Mannich reactions[23,24] revealed the formation of an *E*-enamine between the aldehyde and proline – with the enamine bond *anti* to the carboxylic moiety – followed by the addition of the electrophile. In this transition state, the favorable *re* attack on the *anti*-enamine induces facial selectivity due to the carboxylic acid transferring its proton to the azodicarboxylate to compensate negative charge. This model is consistent with the experimentally determined configuration of the amination products.[17,18]

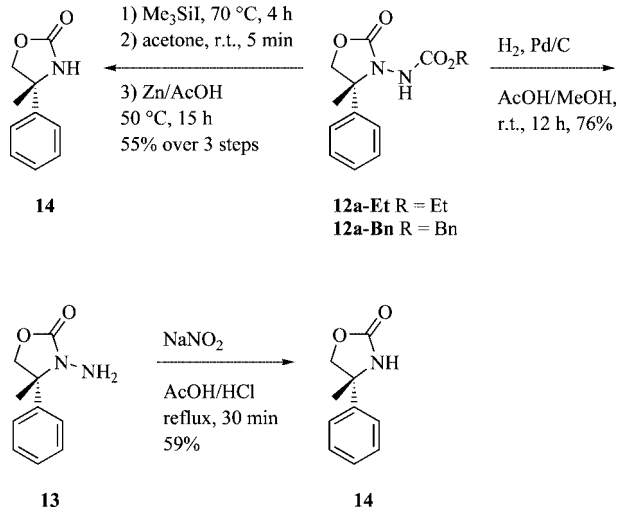
The observation of an accelerating reaction rate and a positive nonlinear effect for the proline-catalyzed α-amination of α-unbranched aldehydes with azodicarboxylates, as well as the α-aminoxylation with nitroso benzene, initiated more detailed investigations into the reaction mechanism by Blackmond et al.[25,26] The initial assumption of the formation of a more efficient catalytic species during the reaction could not be confirmed. DFT calculations indicated instead the formation of a three-point hydrogen-bound complex upon separation of the catalyst from the product, which exposes the nitrogen lone pair to attack by a new substrate molecule in contrast to the two-point hydrogen-bound complex conceivable for aldol reactions. This helps to increase the active concentration of the else poorly soluble catalyst, and to channel it into the catalytic cycle. Because the reaction times for the proline-catalyzed α-amination of α,α-disubstituted aldehydes are considerably elongated in comparison to α-unbranched species (within several days in contrast to few hours), it can be concluded that the aforementioned acceleration does not occur in that case. This might be either due to the presence of an additional methyl-group in α-position, preventing the formation of complementary three-point hydrogen bound complexes, or, on the other hand, shielding the nitrogen lone pair from attack within these complexes.

Cleavage of the hydrazide moiety was demonstrated on the Cbz-protected oxazolidinone **12a-Bn** as well as on the ethoxycarbonyl derivative **12a-Et** (Scheme 5). Removal of the benzyloxycarbonyl group in **12a-Bn** was accomplished by hydrogenation at ambient conditions using 10% Pd/C in methanol/acetic acid. Treatment of hydrazide **13** with sodium nitrite in a 3:1 mixture of acetic acid and hydrochloric acid resulted in the cleavage of the hydrazide moiety and the formation of the unprotected oxazolidinone **14** within 30 min.

Reaction of the *N*-amino oxazolidinone **12a-Et** with trimethylsilyl iodide in acetonitrile, followed by addition of acetone and zinc dust in acetic acid gave the oxazolidinone **14** in good yield.

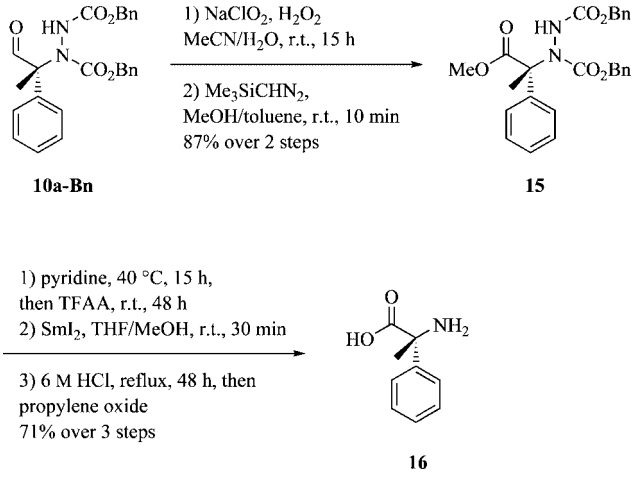
The absolute configuration of oxazolidinone **14** was assigned to be (*R*) by comparison with known optical rotation values.[27] This is consistent with the proposed transition state.[25,26]

In addition to the α-amino aldehydes **10** and their corresponding oxazolidinones, another class of great interest are the non-proteogenic α-amino acids which can be obtained



Scheme 5. Deprotection of the hydrazides **12a-Bn** and **12a-Et** towards the unprotected oxazolidinone **14**.

from those precursors. Removal of the Cbz group to yield the unprotected amino acid was demonstrated on aldehyde **10a-Bn** (Scheme 6). Mild oxidation with sodium chlorite in acetonitrile, followed by subsequent treatment of the resulting acid with diazomethane gave the fully protected amino acid derivative **15** in almost quantitative yield. Applying a one-pot trifluoroacetylation-selective benzyloxycarbonyl deprotection protocol[28] provided the trifluoromethylhydrazine. Cleavage of the N–N bond was then carried out with SmI_2 using a procedure slightly modified from the one originally reported by Friestad.[29] Subsequent hydrolysis of the ester functionality gave the α,α-disubstituted phenylglycine derivative **16**.



Scheme 6. Conversion of aldehyde **10a-Bn** towards protected α-amino acid methyl ester **15**, and cleavage of protecting groups.

Conclusions

In summary, we presented an efficient and convenient method to open access to configurationally stable α,α-disubstituted α-amino aldehydes, oxazolidinones, and α-amino acids. Starting from simple and easily available racemic aldehydes, the α-aminated products were obtained in up to 86% *ee* and moderate to excellent yield using azodicarboxylates as the nitrogen source These products could further be converted into both the corresponding α-amino alcohols and, depending on the residue of the azodicarboxylates and the reaction conditions, into the oxazolidinones. On the other hand, oxidation towards the carboxylic acids and cleavage of the hydrazide bond under mild conditions delivered the free α,α-disubstituted methyl phenylglycine derivative.

Experimental Section

General Methods: Flash chromatography (FC) was carried out using Merck silica gel 60 (230–400 mesh). TLC was carried out on silica gel coated aluminium sheets with fluorescence indicator (silica gel 60 F_{254}) by Merck. ^1H NMR spectra were recorded at 250 MHz with Bruker AC300, at 300 MHz with Bruker DP300 and at 400 MHz with Bruker DP400 and with Bruker AM400, the ^{13}C NMR spectra were recorded at 75 MHz and 100 MHz, respectively. The chemical shifts are reported in ppm relative to the solvent residual peak.[30] Mass spectra were recorded with Kratos MS50, on Finnigan MAT 90 (EI-MS, HRMS), Thermo Quest Finnigan MAT 95 XL (EI-MS) or Kratos Concept 1H (FAB). Elemental analysis was carried out with Elementar Vario EL and with Heraeus CHN-O-Rapid. HPLC was performed with Agilent 1100 Series using Diacel Chiralpak AS (250 × 4.6 mm) or Diacel Chiracel OD (250 × 4.00 mm, 10 μM). Rotational values were determined with a Perkin–Elmer 241 Polarimeter at λ = 589 nm (sodium D-line). The concentration *c* is given in [g/100 mL]. The *ee* and *de* values were determined by comparison with the racemic products obtained by application of DL-proline as catalyst.

Materials: All reagents available from commercial sources (Acros, Aldrich, Fluka, Lancaster, Merck) were used without further purification.

General Procedure (GP 1) for the Synthesis of 2-Aryl-1-methoxy-1-propenes and 2-Cyclohexyl-1-methoxy-1-propene (2m). Method A:[31] A suspension of 1.5 equiv. of methoxymethyl(triphenyl)phosphonium chloride in abs. THF (12 mL/mmol acetophenone) is carefully treated under argon with 1.5 equiv. of a 2.5 M solution of *n*-butyllithium in hexane or 1.5 equiv. of sodium *tert*-butoxide at –78 °C. The resulting orange to red suspension is stirred for 30 min at –78 °C, the cooling bath removed and the mixture stirred for another 30 min at room temperature. After cooling to –78 °C again 1 equiv. of the acetophenone is added either as pure liquid or as a solution in abs. THF. The reaction mixture is left stirring in the cooling bath to warm to room temperature (typically within 18 h). The reaction is then quenched with water (5 mL/mmol acetophenone), the organic phase separated and the aqueous phase extracted twice with diethyl ether (3 mL/mmol acetophenone). The combined organic phases are washed with brine and dried with magnesium sulfate. Evaporation of the solvent delivers an oily product which is purified by flash chromatography on silica.

Method B: A suspension of 1.3 equiv. of sodium hydride in DMSO (0.5 mL/mmol acetophenone) is heated under argon to 40 °C for 7 h. The suspension is then diluted with an equal volume of abs. THF, cooled to 0 °C and treated in small portions with 1 equiv. of (methoxymethyl)triphenylphosphonium chloride. After stirring for 1 h at 0 °C, 1 equiv. of the acetophenone is added either as pure liquid or as a solution in abs. THF. The reaction mixture is stirred

at 0 °C for another 1.5 h, then at room temperature for 1 h. The reaction is then quenched by careful addition of water at 0 °C. The aqueous phase is extracted three times with diethyl ether (3 mL/mmol acetophenone). The combined organic phases are washed with brine, dried with magnesium sulfate, and the solvent is removed by evaporation. The residue is purified by flash chromatography on silica.

1-Methoxy-2-(2′-naphthyl)propene (2b): The product was synthesized according to GP 1, Method B, employing 2-acetonaphthone (0.851 g, 5.00 mmol). Flash chromatography on silica (diethyl ether/pentane, 1:30) delivered 0.682 g (3.44 mmol, 69%) of a mixture of *E*- and *Z*-**2b** (*E*/*Z* ratio = 2.26:1, as determined by comparison of the integrals of the methyl signals in the ^{1}H NMR spectrum) as a colorless oil. R_f = 0.29 (diethyl ether/pentane, 1:20). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.94, 2.01 (2d, J = 1.4 Hz, 3 H, CR_2CH_3), 3.63, 3.67 (2s, 3 H, CHROCH_3), 6.12, 6.50 (2q, J = 1.3 Hz, 1 H, CHROCH$_3$), 7.27–7.38 (m, 2 H, C$^{3'}$H$_{ar}$/C$^{7'}$H$_{ar}$), 7.41 (dd, J = 8.6, 1.9 Hz, 1 H, C$^{9'}$H$_{ar}$), 7.59 (d, J = 1.5 Hz, 1 H, C$^{1'}$H$_{ar}$), 7.63 –7.85 (m, 3 H, C$^{4'}$H$_{ar}$/C$^{6'}$H$_{ar}$/C$^{8'}$H$_{ar}$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 12.5, 18.5 (CR_2CH_3), 60.0, 60.3 (RCHOCH_3), 110.9, 114.4 (CR_2CH_3), 123.0, 123.6, 125.1, 125.3, 125.7, 125.7, 126.1, 126.5, 127.1, 127.4, 127.5, 127.7, 127.7, 128.1 (14 × C$_{ar}$H), 132.1, 133.5, 133.8, 136.0, 137.9 (5C$_{q,ar}$), 144.5, 145.2 (RCHOCH$_3$) ppm. IR (KBr): $\tilde{\nu}$ = 3053 cm^{-1} (m, ν[CH$_{ar}$]), 2989, 2940 (w, m, ν[CH]), 2837 (m, ν[OCH$_3$]), 1647, 1596 (m, m, ν[C–C$_{ar}$]), 1504 (m), 1472 (m, δ[OCH$_3$]), 1457, 1385 (m, m, δ[CH]), 1360 (w), 1338 (m), 1275, 1236, 1223 (m, m, m, ν[C$_{ar}$–O–C]), 1168 (m), 1139, (m), 1075, 1038 (m, w, ν[C$_{ar}$–O–C]), 1006 (m), 860 (m), 834, 820, 770, 744 (m, m, w, m, δ[CH$_{ar}$]) cm^{-1}. MS (EI, II, 70 eV): *m*/*z* (%) = 198 (100) [M$^+$], 183 (24) [M$^+$ – CH$_3$], 155 (46) [C$_{12}$H$_{11}^+$], 128 (8) [C$_{10}$H$_8^+$]. HRMS (II) calcd. for $C_{14}H_{14}O$ 198.1045, found 198.1045. $C_{14}H_{14}O$ (198.26): calcd. C 84.81, H 7.12, found C 84.72, H 7.15.

1-Methoxy-2-(3′-methoxyphenyl)propene (2c): The product was synthesized according to GP 1, Method B, employing 3-methoxyacetophenone (0.733 g, 4.88 mmol). Flash chromatography on silica (diethyl ether/pentane, 1:20) delivered 0.649 g (3.64 mmol, 75%) of a mixture of *E*- and *Z*-**2c** (*E*/*Z* ratio = 1.06:1, as determined by comparison of the integrals of the methyl signals in the ^{1}H NMR spectrum) as a colorless oil. R_f = 0.35 (diethyl ether/pentane, 1:20). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.83, 1.90 (2d, J = 1.3 and 1.4 Hz, 3 H, CR_2CH_3), 3.58, 3.63 (2s, 3 H, CHROCH_3), 3.72 (s, 3 H, C$_{ar}$OCH$_3$), 6.03, 6.34 (2q, J = 1.4, 1 H, CHROCH$_3$), 6.62–6.69 (m, 1 H, CH$_{ar}$), 6.75–6.85 (m, 1 H, CH$_{ar}$), 7.08–7.18 (m, 2 H, CH$_{ar}$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 12.7, 18.5 (CR_2CH_3), 55.3, 55.3 (C$_{ar}$OCH_3), 60.0, 60.3 (RCHOCH_3), 110.8, 114.5 (CR_2CH_3), 111.2, 111.2 (C$^{4'}$$_{ar}$H), 111.5, 113.7 (C$^{2'}$$_{ar}$H), 117.7, 120.2 (C$^{6'}$$_{ar}$H), 128.9, 129.3 (C$^{5'}$$_{ar}$H), 139.9, 142.4 ($C^{1'}$$_{ar}CR_2$), 145.0, 145.5 (R$C$HOCH$_3$), 159.4, 159.8 ($C_{ar}OCH_3$) ppm. IR (KBr): $\tilde{\nu}$ = 2933 cm^{-1} (w, ν[CH]), 2834 (w, ν[OCH$_3$]), 1658, 1595, 1577, 1490 (w, vw, vw, w, ν[C–C$_{ar}$]), 1463, 1375 (w, vw, δ[CH]), 1223 (m, ν[C$_{ar}$–O–C]), 1121 (m, ν[C–O–C]), 1072 (w, ν[C$_{ar}$–O–C]) cm^{-1}. MS (EI, II, 70 eV): *m*/*z* (%) = 178 (100) [M$^+$], 163 (14) [M$^+$ – CH$_3$], 135 (23) [C$_9$H$_{11}$O$^+$], 105 (9) [C$_8$H$_9^+$], 91 (7) [C$_7$H$_7^+$], 77 (6) [C$_6$H$_5^+$]. HRMS (II) *m*/*z* calcd. for $C_{11}H_{14}O_2$ 178.0994, found: 178.0995. $C_{11}H_{14}O_2$ (178.23): calcd. C 74.13, H 7.92; found C 73.91, H 7.95.

1-Methoxy-2-(4′-methoxyphenyl)propene (2d): The product was synthesized according to GP 1, Method A, employing 4-methoxyacetophenone (1.544 g, 10.2 mmol). Flash chromatography on silica (diethyl ether/pentane, 1:80) delivered 1.334 g (7.46 mmol, 73%) of a mixture of *E*- and *Z*-**2d** (*E*/*Z* ratio = 1.62:1, as determined by comparison of the integrals of the methyl signals in the ^{1}H NMR spectrum) as a colorless oil. R_f = 0.23 (diethyl ether/pentane, 1:80). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.80, 1.88 (2d, J = 1.3 and 1.4 Hz, 3 H, CR_2CH_3), 3.55, 3.59 (2s, 3 H, CHROCH_3), 3.69, 3.70 (s, 3 H, C$_{ar}$OCH$_3$), 5.95, 6.22 (2q, J = 1.2 and 1.3 Hz, 1 H, CHROCH$_3$), 6.76, 6.79 (2d, J = 9.0 Hz, 2 H, C$^{3'}$H$_{ar}$), 7.13, 7.47 (2d, J = 9.0 Hz, 2 H, C$^{2'}$H$_{ar}$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 12.9, 18.5 (CR_2CH_3), 55.3, 55.4 (C$_{ar}$OCH_3), 59.9, 60.1 (RCHOCH_3), 110.6, 114.3 (CR_2CH_3), 113.5, 114.0 (C$^{3'}$$_{ar}$H), 126.2, 128.7 (C$^{2'}$$_{ar}$H), 131.2, 133.4 ($C^{1'}$$_{ar}CR_2$), 143.7, 144.2 (R$C$HOCH$_3$), 157.9, 158.2 ($C^{4'}$$_{ar}OCH_3$) ppm. IR (KBr): $\tilde{\nu}$ = 3039 cm^{-1} (vw, ν[CH$_{ar}$]), 2934 (w, ν[CH]), 2835 (w, ν[OCH$_3$]), 2056 (vw), 1676, 1653, 1605, 1512 (w, m, m, m, ν[C–C$_{ar}$]), 1463, 1441, 1416 (w, w, w, δ[CH]), 1377 (w, δ[OCH$_3$]), 1358 (w), 1294, 1248, 1222 (m, m, m, ν[C$_{ar}$–O–C]), 1180, 1133, 1114 (m, m, m, ν[C–O–C]), 1078, 1033 (w, m, ν[C$_{ar}$–O–C]), 1008 (w), 956 (vw), 828, 808 (m, w, δ[CH$_{ar}$]), 744 (vw), 722 (w) cm^{-1}. MS (EI, II, 70 eV): *m*/*z* (%) = 178 (100) [M$^+$], 163 (64) [M$^+$ – CH$_3$], 135 (64) [C$_9$H$_{11}$O$^+$], 105 (9) [C$_8$H$_9^+$], 91 (19) [C$_7$H$_7^+$], 77 (7) [C$_6$H$_5^+$]. HRMS (II) *m*/*z* calcd. for $C_{11}H_{14}O_2$ 178.0994, found 178.0992. $C_{11}H_{14}O_2$ (178.23): calcd. C 74.13, H 7.92; found C 73.96, H 7.95.

1-Methoxy-2-(4′-methoxycarbonylphenyl)propene (2e): The product was synthesized according to GP 1, Method B, employing 4-methoxycarbonylacetophenone (0.891 g, 5.00 mmol). Flash chromatography on silica (diethyl ether/pentane, 1:9) delivered 0.575 g (2.79 mmol, 56%) of a mixture of *E*- and *Z*-**2e** (*E*/*Z* ratio = 1.35:1, as determined by comparison of the integrals of the methyl signals in the ^{1}H NMR spectrum) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.93, 1.99 (2d, J = 1.3 Hz, 3 H, CR_2CH_3), 3.71, 3.75 (2s, 3 H, CHROCH_3), 3.90 (s, 3 H, RCO$_2$CH$_3$), 6.21, 6.57 (2q, J = 1.3 Hz, 1 H, CHROCH$_3$), 7.35, 7.68 (2ddd, J = 8.7, 1.9, 1.9 Hz, 2 H, C$^{2'}$H$_{ar}$), 7.94, 7.98 (2ddd, J = 8.6, 1.8, 1.8 and 8.8, 1.9, 1.9 Hz, 2 H, C$^{3'}$H$_{ar}$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.3, 18.1 (CR_2CH_3), 52.0, 52.0 (RCO$_2$$CH_3$), 60.3, 60.5 (RCHO$CH_3$), 110.0, 113.8 ($CR_2CH_3$), 124.5, 127.4 (C$^{3'}$$_{ar}$H), 127.4, 127.4 ($C^{4'}$$_{ar}CO_2$), 129.3, 129.8 (C$^{2'}$$_{ar}$H), 143.2, 145.5 ($C^{1'}$$_{ar}CR_2$), 146.7, 147.1 (R$C$HOCH$_3$), 167.2, 167.3 (R$CO_2CH_3$) ppm. IR (KBr): $\tilde{\nu}$ = 2947 cm^{-1} (m, ν[CH]), 2844 (m, ν[OCH$_3$]), 1796 (w), 1706 (m, ν[CO]), 1647, 1603 (m, s, ν[C–C$_{ar}$]), 1561 (m), 1510 (m), 1436 (m, δ[CH]), 1415 (m, δ[OCH$_3$]), 1365 (m, δ[CH]), 1321 (m), 1280, 1231 (s, m, ν[C$_{ar}$–O–C]), 1193, 1117 (s, m, ν[C–O–C]), 1078, 1037, 1017 (m, w, m, ν[C$_{ar}$–O–C]), 983 (m), 971 (m), 944 (m), 866 (m), 850, 829 (m, m, δ[CH$_{ar}$]), 775 (m) cm^{-1}. MS (EI, II, 70 eV): *m*/*z* (%) = 206 (100) [M$^+$], 175 (23) [M$^+$ – OCH$_3$], 159 (6) [C$_{10}$H$_7$O$_2^+$], 147 (3) [M$^+$ – CO$_2$CH$_3$], 131 (9) [C$_9$H$_7$O$^+$], 119 (10), 103 (8) [C$_8$H$_7^+$], 91 (6) [C$_7$H$_7^+$], 77 (5) [C$_6$H$_5^+$], 59 (7). HRMS (II) *m*/*z* calcd. for $C_{12}H_{14}O_3$ 206.0943; found 206.0945. $C_{12}H_{14}O_3$ (206.24): calcd. C 69.88, H 6.84; found C 69.76, H 6.85.

2-(4′-Fluorophenyl)-1-methoxypropene (2f): The product was synthesized according to GP 1, Method A, employing 4-fluoroacetophenone (1.392 g, 10.0 mmol). Flash chromatography on silica (diethyl ether/pentane, 1:100) delivered 1.581 g (9.51 mmol, 95%) of a mixture of *E*- and *Z*-**2f** (*E*/*Z* ratio = 1.39:1, as determined by comparison of the integrals of the methyl signals in the ^{1}H NMR spectrum) as a colorless oil. R_f = 0.80 (diethyl ether/pentane, 1:100). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.81, 1.88 (2d, J = 1.2 Hz, 3 H, CR_2CH_3), 3.58, 3.63 (2s, 3 H, CHROCH_3), 6.01, 6.25 (2q, J = 1.2 Hz, 1 H, CHROCH$_3$), 6.88, 6.94 (2d, J = 8.8 Hz, 2 H, C$^{3'}$H$_{ar}$), 7.15, 7.18 (2d, J = 5.2 and 5.4 Hz, 2 H, C$^{2'}$H$_{ar}$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 12.9, 18.5 (CR_2CH_3), 60.9, 60.3 (RCHOCH_3), 109.9, 113.8 (CR_2CH_3), 114.8, 115.2 (d, J = 21.2 Hz, C$^{3'}$$_{ar}$H), 126.5, 129.2 (d, J = 7.7 Hz, C$^{2'}$$_{ar}$H), 133.7, 134.0 ($C^{1'}$$_{ar}CR_2$), 144.5, 145.0 (R$C$HOCH$_3$), 161.1, 161.5 (d, J = 244.5 Hz, $C^{4'}$$_{ar}$F) ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ =

–113.1 ppm. IR (KBr): $\tilde{\nu}$ = 3048 cm^{-1} (vw, ν[CH_{ar}]), 2934, 2860 (w, w, ν[CH]), 2834 (w, ν[OCH_3]), 1655, 1601, 1509 (w, w, m, ν[C–C_{ar}]), 1457, 1406 (w, vw, δ[CH]), 1377 (vw, δ[OCH_3]), 1276, 1259, 1225 (w, w, m, ν[C_{ar}–O–C]), 1135 (w), 1101 (w), 1076 (w, ν[C_{ar}–O–C]), 1011 (w), 981 (vw), 829 (w, δ[CH_{ar}]), 749, 720 (w, w, ν[CHal]) cm^{-1}. MS (EI = 70 eV): *m*/*z* (%) = 166 (100) [M^+], 151 (44) [$M^+ – CH_3$], 123 (5). HRMS (EI) *m*/*z* calcd. for $C_{10}H_{11}FO$ 166.0794; found 166.0797. $C_{10}H_{11}FO$ (166.19): calcd. C 72.27, H 6.67; found C 72.41, H 6.74.

2-(4′-Chlorophenyl)-1-methoxypropene (2g): The product was synthesized according to GP 1, Method B, employing 4-chloroacetophenone (3.092 g, 20.00 mmol). Flash chromatography on silica (diethyl ether/pentane, 1:80) delivered 3.123 g (17.10 mmol, 85%) of a mixture of *E*- and *Z*-**2g** (*E*/*Z* ratio = 1.31:1, as determined by comparison of the integrals of the methyl signals in the ^1H NMR spectrum) as a yellow oil. R_f = 0.73 (diethyl ether/pentane, 1:80). ^1H NMR (400 MHz, $CDCl_3$): δ = 1.69, 1.76 (2d, *J* = 1.3 Hz, 3 H, CR_2CH_3), 3.47, 3.55 (2s, 3 H, CHROCH_3), 5.93, 6.18 (q, *J* = 1.3 Hz, 1 H, C*H*ROCH$_3$), 6.94, 7.16 (2d, *J* = 8.7, 2 H, $C^{2'}H_{ar}$), 7.22, 7.29 (2d, *J* = 8.7 Hz, 2 H, $C^{3'}H_{ar}$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 12.2, 17.9 (CR_2CH_3), 59.7, 60.2 (RCHOCH_3), 109.4, 113.3 (CR_2CH_3), 125.7, 128.2 ($C^{3'}{}_{ar}H$), 131.3, 131.9 ($C^{2'}{}_{ar}H$), 132.2, 134.5 ($C^{4'}{}_{ar}Cl$), 134.8, 135.2 ($C^{1'}{}_{ar}CR_2$), 137.1, 139.4 (R*C*HOCH$_3$) ppm. IR (KBr): $\tilde{\nu}$ = 3096, 3069 cm^{-1} (w, vw, ν[CH_{ar}]), 2981 (vw), 2935 (w, ν[CH]), 2841 (vw, ν[OCH_3]), 1686, 1589, 1490 (m, m, w, ν[C–C_{ar}]), 1428 (w, δ[CH]), 1397 (w, δ[OCH_3]), 1358 (w), 1261, 1176, 1094, (m, w, m, ν[C_{ar}–O–C]), 1013 (w), 959 (w), 829 (w, δ[CH_{ar}]), 762 (w, ν[CHal]) cm^{-1}. MS (EI, II, 70 eV): *m*/*z* (%) = 184 (2) [M^+], 169 (1), 167 (3) [M^+-CH_3], 156 (25), 154 (63) [$C_9H_{10}Cl^+$], 141 (60), 139 (100) [$C_8H_8Cl^+$], 113 (24), 111 (60) [$C_6H_5Cl^+$], 77 (14), 75 (47) [$C_3H_5Cl^+$]. HRMS *m*/*z* calcd. for $C_{10}H_{11}{}^{37}ClO$ 184.0469, found: 184.0477. $C_{10}H_{11}Cl$ (182.65): calcd. C 65.76, H 6.07; found C 65.91, H 5.97.

2-(4′-Bromophenyl)-1-methoxypropene (2h): The product was synthesized according to GP 1, Method B, employing 4-bromoacetophenone (1.990 g, 10.00 mmol). Flash chromatography on silica (diethyl ether/pentane, 1:80) delivered 1.998 g (8.80 mmol, 88%) of a mixture of *E*- and *Z*-**2h** (*E*/*Z* ratio = 1.25:1, as determined by comparison of the integrals of the methyl signals in the ^1H NMR spectrum) as a yellow oil. R_f = 0.58 (diethyl ether/pentane, 1:100). ^1H NMR (400 MHz, $CDCl_3$): δ = 1.72, 1.79 (2d, *J* = 1.3 Hz, 3 H, CR_2CH_3), 3.52, 3.56 (2s, 3 H, CHROCH_3), 5.97, 6.25 (q, *J* = 1.3 Hz, 1 H, C*H*ROCH$_3$), 7.00, 7.26 (2d, *J* = 8.6 and 8.7 Hz, 2 H, $C^{2'}H_{ar}$), 7.23, 7.32 (2d, *J* = 8.6 and 8.7 Hz, 2 H, $C^{3'}H_{ar}$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 12.4, 18.1 (CR_2CH_3), 60.0, 60.3 (RCHOCH_3), 109.6, 113.4 (CR_2CH_3), 119.4, 119.6 ($C^{4'}{}_{ar}Br$), 126.5, 129.1 ($C^{3'}{}_{ar}H$), 130.9, 131.3 ($C^{2'}{}_{ar}H$), 133.6, 133.8 ($C^{1'}{}_{ar}CR_2$), 137.2, 139.6 (R*C*HOCH$_3$) ppm. IR (KBr): $\tilde{\nu}$ = 3102 cm^{-1} (w, ν[CH_{ar}]), 2981 (w), 2934 (w, ν[CH]), 2831 (w, ν[OCH_3]), 1687, 1588, 1489 (m, w, m, ν[C–C_{ar}]), 1454, 1428 (w, w, δ[CH]), 1396 (w, δ[OCH_3]), 1360 (w), 1265, 1186, 1076, (w, w, m, ν[C_{ar}–O–C]), 1010 (m), 980 (w), 823 (m, δ[CH_{ar}]), 748, 722 (w, w, ν[CHal]) cm^{-1}. MS (EI, II, 70 eV): *m*/*z* (%) = 229, 227 (3) [M^+], 200, 198 (16) [$C_9H_{10}Br^+$], 185 (43), 183 (65) [$C_8H_7Br^+$], 157, 155 (16) [$C_6H_5Br^+$], 75 (100). HRMS *m*/*z* calcd. for $C_{10}H_{11}Br$ 225.9993, found: 225.9991. $C_{10}H_{11}Br$ (227.10): calcd. C 52.89, H 4.88; found C 52.67, H 4.95.

Methoxy-2-(4′-trifluoromethylphenyl)propene (2i): The product was synthesized according to GP 1, Method A, employing 4-trifluoromethylacetophenone (2.932 g, 15.50 mmol). Flash chromatography on silica (diethyl ether/pentane, 1:100) delivered 3.131 g (14.50 mmol, 93%) of a mixture of *E*- and *Z*-**2i** (*E*/*Z* ratio = 1.24:1, as determined by comparison of the integrals of the methyl signals in the ^1H NMR spectrum) as a colorless oil. R_f = 0.85 (diethyl ether/pentane, 1:100). ^1H NMR (400 MHz, $CDCl_3$): δ = 1.85, 1.91 (2d, *J* = 1.3 Hz, 3 H, CR_2CH_3), 3.63, 3.67 (2s, 3 H, CHROCH_3), 6.12, 6.43 (2q, *J* = 1.3 Hz, 1 H, C*H*ROCH$_3$), 7.32, 7.39 (2d, *J* = 8.2 Hz, 2 H, $C^{3'}H_{ar}$), 7.63, 7.68 (2d, *J* = 8.1 Hz, 2 H, $C^{2'}H_{ar}$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 12.3, 18.0 (CR_2CH_3), 60.1, 60.4 (RCHOCH_3), 109.5, 113.3 (CR_2CH_3), 123.8, 123.9 (q, *J* = 271.6 Hz, $C^{4'}{}_{ar}CF_3$), 125.8, 126.3 (q, *J* = 3.5 Hz, $C^{3'}{}_{ar}H$), 126.7, 127.2 ($C^{2'}{}_{ar}H$), 127.5 (q, *J* = 32.5 Hz, $C^{4'}{}_{ar}CF_3$), 133.7, 133.9 ($C^{1'}{}_{ar}CR_2$), 145.8, 146.7 (R*C*HOCH$_3$) ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ = –62.6 ppm. IR (KBr): $\tilde{\nu}$ = 3078 cm^{-1} (w, ν[CH_{ar}]), 2938 (w, ν[CH]), 2841 (w, ν[OCH_3]), 1652, 1614, 1511, 1489 (w, w, w, ν[C–C_{ar}]), 1459 (w, δ[CH]), 1411 (w, δ[OCH_3]), 1327 (m), 1264, 1228, 1211 (w, w, w, w, ν[C_{ar}–O–C]), 1165, 1113, 1080, 1015 (w, w, ν[C_{ar}–O–C]), 950 (vw), 835 (w, δ[CH_{ar}]), 764 (w, ν[CHal]) cm^{-1}. MS (EI = 70 eV): *m*/*z* (%) = 216 (83) [M^+], 201 (19) [$M^+ – CH_3$], 173 (100) [$C_9H_8F_3^+$], 145 (34) [$C_7H_4F_3^+$], 103 (47), 77 (11) [$C_6H_5^+$]. HRMS (EI) *m*/*z* calcd. for $C_{11}H_{11}F_3O$ 216.0762, found 216.0757. $C_{11}H_{11}F_3O$ (216.20): calcd. C 72.27, H 6.67; found C 72.41, H 6.74.

1-Methoxy-2-(4′-nitrophenyl)propene (2j): The product was synthesized according to GP 1, Method B, employing 4-nitroacetophenone (0.826 g, 5.00 mmol). Flash chromatography on silica (diethyl ether/pentane mixtures) delivered 0.175 g (0.906 mmol, 37%) of a yellow oil. R_f = 0.44 (diethyl ether/pentane, 1:10). ^1H NMR (400 MHz, $CDCl_3$): δ = 2.00 (d, *J* = 1.3 Hz, 3 H, CR_2CH_3), 3.8 (s, 3 H, CHROCH_3), 6.66 (q, *J* = 1.3 Hz, 1 H, C*H*ROCH$_3$), 7.41 (ddd, *J* = 9.3, 2.4, 2.3 Hz, 2 H, $C^{2'}H_{ar}$), 8.13 (ddd, *J* = 9.3, 2.4, 2.3 Hz, 2 H, $C^{3'}H_{ar}$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 12.2 (CR_2CH_3), 60.6 (RCHOCH_3), 113.1 (CR_2CH_3), 123.9 ($C^{3'}{}_{ar}H$), 124.8 ($C^{2'}{}_{ar}H$), 145.8 ($C^{1'}{}_{ar}CR_2$), 147.7 ($C^{4'}{}_{ar}NO_2$), 148.7 (R*C*HOCH$_3$) ppm. IR (KBr): $\tilde{\nu}$ = 3105, 3081, 3020 (vw, w, w, ν[CH_{ar}]), 2967, 2938 (w, m, ν[CH]), 2841 (w, ν[OCH_3]), 1744 (w), 1722 (w), 1639, 1589 (m, m, ν[C–C_{ar}]), 1507 (m, ν[NO_2]), 1455 (w, δ[CH]), 1416 (w, δ[OCH_3]), 1392 (w, δ[CH]), 1349 (m, δ[NO_2]), 1300, 1238 (m, m, ν[C_{ar}–O–C]), 1189 (w), 1146 (m), 1111 (m), 1074, 1036 (m, w, ν[C_{ar}–O–C]), 1004 (w), 945 (w), 847, 822 (m, w, δ[CH_{ar}]), 780 (w), 752 (m) cm^{-1}. MS (EI, II, 70 eV): *m*/*z* (%) = 193 (100) [M^+], 161 (9), 147 (5) [$M^+ – NO_2$], 132 (23) [$M^+ – CH_3 – NO_2$], 115 (10) [$C_9H_7^+$], 103 (12) [$C_8H_7^+$], 91 (7) [$C_7H_7^+$], 77 (8) [$C_6H_5^+$]. HRMS *m*/*z* calcd. for $C_{10}H_{11}NO_3$ 193.0739, found: 193.0741. $C_{10}H_{11}NO_3$ (193.20): calcd. C 62.17, H 5.74, N 7.25; found C 62.28, H 5.85, N 7.31.

2-(4′-Cyanophenyl)-1-methoxypropene (2k): The product was synthesized according to GP 1, Method B, employing 4-cyanoacetophenone (2.468 g, 17.00 mmol). Flash chromatography on silica (diethyl ether/pentane, 1:5) delivered 2.827 g (16.30 mmol, 96%) of a mixture of *E*- and *Z*-**2k** (*E*/*Z* ratio = 1.17:1, as determined by comparison of the integrals of the methyl signals in the ^1H NMR spectrum) as a yellow oil. R_f = 0.42 (diethyl ether/pentane, 1:5). ^1H NMR (400 MHz, $CDCl_3$): δ = 1.84, 1.90 (2d, *J* = 1.3 Hz, 3 H, CR_2CH_3), 3.66, 3.70 (2s, 3 H, CHROCH_3), 6.18, 6.51 (q, *J* = 1.3 Hz, 1 H, C*H*ROCH$_3$), 7.29, 7.50 (2d, *J* = 8.7, 2 H, $C^{2'}H_{ar}$), 7.47, 7.64 (2d, *J* = 8.7 Hz, 2 H, $C^{3'}H_{ar}$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 12.0, 17.8 (CR_2CH_3), 60.4, 60.6 (RCHOCH_3), 108.7, 108.8 ($C^{4'}{}_{ar}CN$), 108.9, 113.0 (CR_2CH_3), 119.4, 119.5 ($C^{4'}{}_{ar}CN$), 124.9, 127.8 ($C^{3'}{}_{ar}H$), 131.6, 132.1 ($C^{2'}{}_{ar}H$), 143.0, 145.4 (R*C*HOCH$_3$), 147.6, 147.8 ($C^{1'}{}_{ar}CR_2$) ppm. IR (KBr): $\tilde{\nu}$ = 3104 cm^{-1} (vw, ν[CH_{ar}]), 2935 (w, ν[CH]), 2839 (w, ν[OCH_3]), 2223 (m, ν[CN]), 1647, 1601 (m, m, ν[C–C_{ar}]), 1506 (w), 1456 (w, δ[CH]), 1410 (w, δ[OCH_3]), 1265, 1228, 1208 (w, m, m, ν[C_{ar}–O–C]), 1180 (w), 1138 (m), 1115 (m), 1074 (m, ν[C_{ar}–O–C]), 1008 (w), 982 (vw), 944 (vw), 855, 832 (w, m, δ[CH_{ar}]) cm^{-1}. MS (EI, II, 70 eV): *m*/*z* (%)

= 173 (100) [M^+], 158 (16) [M^+-CH_3], 143 (8) [$C_{10}H_9N^+$], 130 (55) [$C_9H_8N^+$], 116 (6) [$C_8H_6N^+$], 103 (19) [$C_7H_5N^+$], 77 (8) [$C_6H_5^+$]. HRMS *m*/*z* calcd. for $C_{11}H_{11}NO$ 173.0840; found 173.0836. $C_{11}H_{11}NO$ (173.21): calcd. C 76.28, H 6.40, N 8.09; found C 76.42, H 6.35, N 7.99.

2-(3′,5′-Dimethoxyphenyl)-1-methoxypropene (2l): The product was synthesized according to GP 1, Method B, employing 3,5-dimethoxyacetophenone (0.901 g, 5.00 mmol). Flash chromatography on silica (diethyl ether/pentane, 1:15) delivered 0.799 g (3.84 mmol, 77%) of a mixture of *E*- and *Z*-**2l** (*E*/*Z* ratio = 1.03:1, as determined by comparison of the integrals of the methyl signals in the ^{1}H NMR spectrum) as a colorless oil. R_f = 0.31 (diethyl ether/pentane, 1:20). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.91, 1.98 (2d, *J* = 1.3 Hz, 3 H, CR_2CH_3), 3.68, 3.72 (2s, 3 H, $CHROCH_3$), 3.80 (s, 6 H, $C_{ar}OCH_3$), 6.12, 6.44 (2q, *J* = 1.2 and 1.3 Hz, 1 H, $CHROCH_3$), 6.33, 6.35 (2t, *J* = 2.4 Hz, 1 H, $C^{4'}H_{ar}$), 6.48, 6.82 (2d, *J* = 2.3 Hz, 2 H, $C^{2'}H_{ar}$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.7, 18.5 (CR_2CH_3), 55.3, 55.4 ($C_{ar}OCH_3$), 60.0, 60.3 ($RCHOCH_3$), 98.0, 98.4 ($C^{4'}{}_{ar}H$), 103.6, 106.1 ($C^{2'}{}_{ar}H$), 110.8, 114.6 (CR_2CH_3), 140.4, 143.0 ($C^{1'}{}_{ar}CR_2$), 145.2, 145.6 ($RCHOCH_3$), 160.5, 160.9 ($C_{ar}OCH_3$) ppm. IR (KBr): $\tilde{\nu}$ = 2997, 2935 cm^{-1} (w, m, ν[CH]), 2836 (w, ν[OCH_3]), 1653, 1591 (m, m, ν[C–C_{ar}]), 1458, 1422, 1377 (m, m, w, δ[CH]), 1355 (w), 1336 (w), 1311 (w), 1297 (w), 1235, 1204 (w, m, ν[C_{ar}–O–C]), 1155, 1100 (m, w, ν[C–O–C]), 1067, 1051, 1013 (m, m, w, ν[C_{ar}–O–C]), 981 (w), 928 (w), 835, 692 (w, w, δ[CH_{ar}]) cm^{-1}. MS (EI, II, 70 eV): *m*/*z* (%) = 208 (100) [M^+], 193 (18) [M^+ – CH_3], 179 (8), 165 (12) [$C_{10}H_{13}O_2^+$], 150 (6), 126 (15), 105 (5) [$C_8H_9^+$], 91 (5) [$C_7H_7^+$], 77 (5) [$C_6H_5^+$]. HRMS (II) *m*/*z* calcd. for $C_{12}H_{16}O_3$ 208.1099, found 208.1099. $C_{12}H_{16}O_3$ (208.25): calcd. C 69.21, H 7.74; found C 69.12, H 7.83.

2-Cyclohexyl-1-methoxypropene (2m): The product was synthesized according to GP 1, Method B, employing cyclohexyl methyl ketone (0.631 g, 5.00 mmol). Flash chromatography on silica (diethyl ether/pentane, 1:50) delivered 0.377 g of a mixture of *E*- and *Z*-**2m** (*E*/*Z* ratio = 2.08:1, as determined by comparison of the integrals of the methyl signals in the ^{1}H NMR spectrum) as a colorless oil, also containing impurities of triphenylphosphane. By comparison of the ^{1}H integrals the purity was determined to be 35%, amounting to a yield of 0.245 g (1.59 mmol, 32%) of **2m**. The product was used in the next reaction without further purification. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.98 –1.29 (m, 6 H, $C^{3'}H_2$/$C^{4'}H_2$), 1.34 –1.74 (m, 7 H, $C^{2'}H_2$/$C^{1'}H$/CR_2CH_3), 3.42, 3.45 (2s, 1 H, $CHROCH_3$), 5.56–5.61, 5.68–5.73 (2m, 1 H, $CHROCH_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 10.9, 13.9 (CR_2CH_3), 26.4, 26.5 ($C^{4'}H_2$), 26.9, 27.1 ($C^{3'}H_2$), 30.9, 32.2 ($C^{2'}H_2$), 59.3, 59.4 ($RCHOCH_3$), 119.5, 119.7 (CR_2CH_3), 140.7, 141.3 ($RCHOCH_3$) ppm.

1-Methoxy-2-(2-thiophenyl)propene (2n): The product was synthesized according to GP 1, Method A, employing 2-acetylthiophene (3.785 g, 30.0 mmol). Flash chromatography on silica (diethyl ether/pentane, 1:50) delivered 3.980 g (25.80 mmol, 86%) of a mixture of *E*- and *Z*-**2n** (*E*/*Z* ratio = 2.56:1, as determined by comparison of the integrals of the methyl signals in the ^{1}H NMR spectrum) as a brown oil. R_f = 0.34 (diethyl ether/pentane, 1:50). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.89, 1.91 (2d, *J* = 1.3 and 1.2 Hz, 3 H, CR_2CH_3), 3.62, 3.69 (2s, 3 H, $CHROCH_3$), 6.00, 6.48 (2q, *J* = 1.3 and 1.2 Hz, 1 H, $CHROCH_3$), 6.76, 6.98 (2dd, *J* = 3.6, 1.0 Hz, 1 H, CH_{ar}), 6.85, 6.86 (d, *J* = 3.6 Hz, 1 H, CH_{ar}), 6.92, 7.13 (2dd, *J* = 5.2, 1.2 Hz, 1 H, CH_{ar}) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.1, 17.4 (CR_2CH_3), 60.0 ($RCHOCH_3$), 107.3, 109.9 (CR_2CH_3), 121.1, 121.2 ($C_{ar}H$), 123.0, 124.1 ($C_{ar}H$), 125.9, 127.2 ($C_{ar}H$), 132.5, 133.8 ($C^{1'}{}_{ar}CR_2$), 143.3, 144.5 ($RCHOCH_3$) ppm. IR (KBr): $\tilde{\nu}$ = 3103 cm^{-1} (vw, ν[CH_{ar}]), 2985, 2935 (w, w, ν[CH]), 2831 (vw, ν[OCH_3]), 1662, 1517 (m, w, ν[C–C_{ar}]), 1450, 1414 (w, m, δ[CH]), 1357 (w, δ[OCH_3]), 1274, 1237, 1194, 1090 (m, m, w, m, ν[C–O–C]), 857 (w), 705 (m) cm^{-1}. MS (EI, II, 70 eV): *m*/*z* (%) = 154 (74) [M^+], 141 (100) [M^+ – CH_3], 111 (92), 97 (10) [$C_5H_5S^+$], 75 (53). HRMS (II) *m*/*z* calcd. for $C_8H_{10}OS$ 154.0452, found 154.0455. $C_8H_{10}OS$ (154.23): calcd. C 62.30, H 6.54; found C 62.18, H 6.60.

1-Methoxy-2-phenyl-1-butene (2o): The product was synthesized according to GP 1, Method B, employing propiophenone (0.671 g, 5.00 mmol). Flash chromatography on silica (diethyl ether/pentane, 1:60) delivered 0.638 g (3.93 mmol, 79%) of a mixture of *E*- and *Z*-**2o** (*E*/*Z* ratio = 1:1, as determined by comparison of the integrals of the methyl signals in the ^{1}H NMR spectrum) as a colorless oil [the NMR spectra show impurities of triphenylphosphane]. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.03 (t, *J* = 7.5 Hz, 3 H, RCH_2CH_3), 2.35, 2.55 (2dq, *J* = 7.4, 1.2 and 7.5, 0.6 Hz, 2 H, RCH_2CH_3), 3.65, 3.71 (2s, 3 H, $CHROCH_3$), 6.10, 6.29 (t, *J* = 1.1 Hz and s, 1 H, $CHROCH_3$), 7.17–7.24 (m, 1 H, $C^{4'}H_{ar}$), 7.28–7.38 (m, 4 H, $C^{2'}H_{ar}$/$C^{3'}H_{ar}$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.3, 14.3 (RCH_2CH_3), 20.4, 25.9 (RCH_2CH_3), 60.0, 60.1 ($RCHOCH_3$), 118.6, 121.7 (CR_2CH_2R), 126.0, 126.2 ($C^{4'}{}_{ar}H$), 128.1, 128.3 ($C^{3'}{}_{ar}H$), 133.8, 134.0 ($C^{2'}{}_{ar}H$), 137.4, 137.7 ($C^{1'}{}_{ar}CR_2$), 143.8, 144.9 ($RCHOCH_3$) ppm. IR (KBr): $\tilde{\nu}$ = 3053 cm^{-1} (vw, ν[CH_{ar}]), 2965, 2931 (w, w, ν[CH]), 2873 (vw), 2835 (vw, ν[OCH_3]), 1648, 1598, 1496 (vw, w, vw, ν[C–C_{ar}]), 1459 (vw, δ[CH]), 1435 (vw, δ[OCH_3]), 1384 (vw, δ[CH]), 1314 (vw), 1258, 1222, 1204 (vw, w, w, ν[C_{ar}–O–C]), 1134 (w), 1101 (vw), 1077, 1027 (vw, vw, ν[C_{ar}–O–C]), 1001 (vw), 908 (vw), 848 (vw), 761, 744, 695 (vw, vw, w, δ[CH_{ar}]) cm^{-1}.

General Procedure (GP 2) for the Synthesis of 2-Arylpropionaldehydes and 2-Cyclohexylpropionaldehyde (3m):[30] A solution of the 2-aryl-1-methoxypropene or 2-cyclohexyl-1-methoxypropene (**2m**) obtained by general procedure 1 (GP 1) in acetone/water, 4:1 is treated at 0 °C with 1 mL of 48% aqueous hydrobromic acid and stirred for 1 d. The addition of hydrobromic acid and stirring at room temperature is repeated until the TLC indicates complete consumption of the enol ether. The reaction mixture is then neutralized by addition of saturated aqueous sodium carbonate solution, most of the acetone removed by evaporation and the remaining aqueous phase extracted three times with diethyl ether. The combined organic phases are washed with brine, dried with magnesium sulfate, and the solvent is removed by evaporation. The residue is purified by flash chromatography on silica.

2-(2′-Naphthyl)propionaldehyde (3b): The product was synthesized according to GP 2, employing **2b** (0.636 g, 3.21 mmol). Flash chromatography on silica (diethyl ether/pentane, 1:30) delivered 0.441 g (2.39 mmol, 74%) of a colorless solid. R_f = 0.36 (diethyl ether/pentane, 1:20); m.p. 89 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.55 (d, *J* = 7.1 Hz, 3 H, CHR_2CH_3), 3.81 (dq, *J* = 7.0, 1.3 Hz, 1 H, CHR_2CH_3), 7.33 (dd, *J* = 8.5, 1.8 Hz, 1 H, $C^{9'}H_{ar}$), 7.46 – 7.35 (m, 2 H, $C^{6'}H_{ar}$/$C^{7'}H_{ar}$), 7.68 (d, *J* = 1.4 Hz, 1 H, $C^{1'}H_{ar}$), 7.80–7.89 (m, 3 H, $C^{3'}H_{ar}$/$C^{4'}H_{ar}$/$C^{6'}H_{ar}$), 9.77 (d, *J* = 1.4 Hz, 1 H, CHO) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.8 (CHR_2CH_3), 53.3 (CHR_2CH_3), 126.3, 126.3, 126.6, 127.3, 127.9, 127.9, 129.0 (7 × $C_{ar}H$), 132.9 ($C^{10'}{}_{ar}H$), 133.8 ($C^{5'}{}_{ar}H$), 135.3 ($C^{1'}{}_{ar}CHR_2$), 201.1 (CHO) ppm. IR (KBr): $\tilde{\nu}$ = 3057 cm^{-1} (m, ν[CH_{ar}]), 2976, 2935, 2875 (m, m, m, ν[CH]), 2819, 2719 (m, m, ν[C(O)H]), 2293 (vw), 1936 (w), 1734 (s, ν[CO]), 1682 (m), 1631, 1599, 1506 (m, m, m, ν[C–C_{ar}]), 1453, 1389 (m, m, δ[CH]), 953 (m), 901 (m), 866, 826, 752, 700 (m, m, m, w, δ[CH_{ar}]) cm^{-1}. MS (EI, II, 70 eV): *m*/*z* (%) = 184 (25) [M^+], 155 (100) [M^+ – CHO], 141 (42), 128 (9), 115 (6).

HRMS (II) calcd. for $C_{13}H_{12}O$ 184.0888; found 184.0886. $C_{13}H_{12}O$ (184.23): calcd. C 84.75, H 6.57; found C 84.62, H 6.45.

2-(3′-Methoxyphenyl)propionaldehyde (3c): The product was synthesized according to GP 2, employing **2c** (1.093 g, 6.12 mmol). Flash chromatography on silica (diethyl ether/pentane, 1:20) delivered 0.709 g (4.32 mmol, 71%) of a colorless oil. R_f = 0.26 (diethyl ether/pentane, 1:50). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.44 (d, J = 7.0 Hz, 3 H, $CHR_2C\mathit{H}_3$), 3.59 (dq, J = 7.1, 1.4 Hz, 1 H, $C\mathit{H}R_2CH_3$), 3.81 (s, 3 H, $C_{ar}OCH_3$), 6.75 (dd, J = 2.1 Hz, 1 H, $C^{2'}H_{ar}$), 6.80 (d, J = 7.5 Hz, 1 H, $C^{4'}H_{ar}$), 6.84 (ddd, J = 8.3, 2.6, 0.9 Hz, 1 H, $C^{6'}H_{ar}$), 7.30 (dd, J = 7.9 Hz, 1 H, $C^{5'}H_{ar}$), 9.68 (d, J = 1.5 Hz, 1 H, CHO) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.6 ($CHR_2C\mathit{H}_3$), 53.1 ($C\mathit{H}R_2CH_3$), 55.4 ($C_{ar}O\mathit{C}H_3$), 112.9, 114.3, 120.7, 130.2 ($C_{ar}H$), 139.4 ($\mathit{C}^{1'}{}_{ar}CHR_2$), 160.3 ($\mathit{C}^{3'}{}_{ar}OCH_3$), 201.0 (CHO) ppm. IR (KBr): $\tilde{\nu}$ = 3063, 3029 cm^{-1} (vw, vw, ν[CH_{ar}]), 2961, 2931, 2872 (w, vw, vw, ν[CH]), 2813 (vw, ν[OCH_3]), 1724 (w, ν[CO]), 1600, 1492 (vw, vw, ν[C–C_{ar}]), 1454, 1386, 1369 (vw, vw, vw, δ[CH]), 1224, 1074 (vw, vw, ν[C_{ar}–O–C]) cm^{-1}. MS (EI, II, 70 eV): m/z (%) = 164 (27) [M$^+$], 135 (100) [M$^+$ – CHO], 121 (10) [$C_8H_9O^+$], 105 (18) [$C_8H_9^+$], 91 (12) [$C_7H_7^+$], 77 (13) [$C_6H_5^+$]. HRMS (II) m/z calcd. for $C_{10}H_{11}O_2$ 164.0837, found: 164.0842.

2-(4′-Methoxyphenyl)propionaldehyde (3d): The product was synthesized according to GP 2, employing **2d** (0.479 g, 2.69 mmol). Flash chromatography on silica (diethyl ether/pentane, 1:9) delivered 0.358 g (2.18 mmol, 81%) of a colorless oil. R_f = 0.30 (diethyl ether/pentane, 1:6). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.42 (d, J = 7.0 Hz, 3 H, $CHR_2C\mathit{H}_3$), 3.58 (dq, J = 7.1, 1.4 Hz, 1 H, $C\mathit{H}R_2CH_3$), 3.81 (s, 3 H, $C_{ar}OCH_3$), 6.91 (d, J = 8.7 Hz, 2 H, $C^{3'}H_{ar}$), 7.13 (d, J = 8.5 Hz, 2 H, $C^{2'}H_{ar}$), 9.68 (d, J = 1.5 Hz, 1 H, CHO) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.8 ($CHR_2\mathit{C}H_3$), 52.3 ($\mathit{C}HR_2CH_3$), 55.4 ($C_{ar}O\mathit{C}H_3$), 114.7 ($C^{3'}{}_{ar}H$), 129.5 ($C^{2'}{}_{ar}H$), 129.8 ($\mathit{C}^{1'}{}_{ar}CHR_2$), 159.2 ($\mathit{C}^{4'}{}_{ar}OCH_3$), 201.2 (CHO) ppm. IR (KBr): $\tilde{\nu}$ = 2974 cm^{-1} (w, ν[CH_{ar}]), 2935 (w, ν[CH]), 2836 (w, ν[OCH_3]), 2717 (w, ν[C(O)H]), 1720 (w, ν[CO]), 1676, 1611, 1584, 1513 (w, w, w, m, ν[C–C_{ar}]), 1464, 1421, 1372 (w, w, w, δ[CH]), 1303 (w), 1248 (m, ν[C_{ar}–O–C]), 1179 (m), 1118 (w), 1033 (m, ν[C_{ar}–O–C]), 866, 830 (m, w, δ[CH_{ar}]), 728 (ww) cm^{-1}. MS (EI, II, 70 eV): m/z (%) = 164 (12) [M$^+$], 135 (100) [M$^+$ – CHO], 120 (5) [$C_8H_8O^+$], 105 (10) [$C_8H_9^+$], 91 (6) [$C_7H_7^+$], 77 (8) [$C_6H_5^+$]. HRMS (II) m/z calcd. for $C_{10}H_{11}O_2$ 164.0837, found 164.0841. $C_{10}H_{11}O_2$ (164.20): calcd. C 73.15, H 7.37; found C 73.22, H 7.30.

2-(4′-Methoxycarbonylphenyl)propionaldehyde (3e): The product was synthesized according to GP 2, employing **2e** (0.600 g, 2.91 mmol). Flash chromatography on silica (diethyl ether/pentane, 1:4) delivered 0.310 g (1.61 mmol, 55%) of a colorless solid. –^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.47 (d, J = 7.1 Hz, 3 H, $CHR_2C\mathit{H}_3$), 3.70 (dq, J = 7.1, 0.9 Hz, 1 H, $C\mathit{H}R_2CH_3$), 3.91 (s, 3 H, RCO_2CH_3), 7.28 (d, J = 8.1 Hz, 2 H, $C^{2'}H_{ar}$), 8.04 (d, J = 8.5 Hz, 2 H, $C^{3'}H_{ar}$), 10.01 (d, J = 1.3 Hz, 1 H, CHO) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.7 ($CHR_2\mathit{C}H_3$), 52.3 ($R\mathit{C}O_2CH_3$), 53.1 ($\mathit{C}HR_2CH_3$), 128.5 ($C^{2'}{}_{ar}H$), 129.6 ($\mathit{C}^{1'}{}_{ar}CHR_2$), 130.4 ($C^{3'}{}_{ar}H$), 143.0 ($\mathit{C}^{4'}{}_{ar}CO_2$), 166.8 ($R\mathit{C}O_2CH_3$), 200.3 (CHO) ppm.

2-(4′-Fluorophenyl)propionaldehyde (3f): The product was synthesized according to GP 2, employing **2f** (1.504 g, 9.0 mmol). Flash chromatography on silica (diethyl ether/pentane, 1:100) delivered 1.260 g (8.30 mmol, 92%) of a colorless oil. R_f = 0.40 (diethyl ether/pentane, 1:100). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.36 (d, J = 7.1 Hz, 3 H, $CHR_2C\mathit{H}_3$), 3.57 (q, J = 7.1 Hz, $C\mathit{H}R_2CH_3$), 6.93 (d, J = 8.8 Hz, 2 H, $C^{3'}H_{ar}$), 7.16 (d, J = 5.4 Hz, 2 H, $C^{2'}H_{ar}$), 9.58 (d, J = 1.3 Hz, 1 H, CHO) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.8 ($CHR_2C\mathit{H}_3$), 52.2 ($C\mathit{H}R_2CH_3$), 116.1 (d, J = 20.9 Hz, $C^{3'}{}_{ar}H$), 129.9 (d, J = 7.8 Hz, $C^{2'}{}_{ar}H$), 133.4 ($\mathit{C}^{1'}{}_{ar}CR_2$), 163.4 (d, J = 246.0 Hz, $\mathit{C}^{4'}{}_{ar}F$), 200.8 (CHO) ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ = –113.3 ppm. IR (KBr): $\tilde{\nu}$ = 3044 cm^{-1} (w, ν[CH_{ar}]), 2979, 2936, 2879 (w, w, w, ν[CH]), 2819, 2721 (w, w, ν[C(O)H]), 1892 (vw), 1723 (s, ν[CO]), 1687 (w), 1603 (m, ν[C–C_{ar}]), 1510 (s), 1457, 1439, 1417, 1390, 1373, (w, w, w, w, w, δ[CH]), 1225 (s), 1160 (m), 1070 (w), 1015 (m), 835 (s, δ[CH_{ar}]), 722 (m, ν[CHal]) cm^{-1}. MS (EI, II, 70 eV): m/z (%) = 152 (8) [M$^+$], 123 (100) [M$^+$ – CHO], 103 (29) [M$^+$ – CHO – HF], 77 (8) [$C_6H_5^+$]. HRMS (EI) m/z calcd. for C_9H_9FO 152.0637, found 152.0640. C_9H_9FO (152.17): calcd. C 71.04, H 5.96; found C 71.23, H 6.02.

2-(4′-Chlorophenyl)propionaldehyde (3g): The product was synthesized according to GP 2, employing **2g** (3.105 g, 17.0 mmol). Flash chromatography on silica (diethyl ether/pentane, 1:80) delivered 2.293 g (13.60 mmol, 80%) of a colorless oil. R_f = 0.55 (diethyl ether/pentane, 1:80). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.36 (d, J = 7.1 Hz, 3 H, $CHR_2C\mathit{H}_3$), 3.55 (dq, J = 7.1, 1.0 Hz, $C\mathit{H}R_2CH_3$), 7.07 (d, J = 8.4 Hz, 2 H, $C^{3'}H_{ar}$), 7.27 (d, J = 8.5 Hz, 2 H, $C^{2'}H_{ar}$), 9.58 (d, J = 1.3 Hz, 1 H, CHO) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.7 ($CHR_2C\mathit{H}_3$), 52.3 ($C\mathit{H}R_2CH_3$), 129.3 ($C^{3'}{}_{ar}H$), 129.7 ($C^{2'}{}_{ar}H$), 133.5 ($C^{4'}{}_{ar}Cl$), 136.7 ($\mathit{C}^{1'}{}_{ar}CR_2$), 200.5 (CHO) ppm. IR (KBr): $\tilde{\nu}$ = 3050 cm^{-1} (w, ν[CH_{ar}]), 2979, 2934, 2877 (w, vw, vw, ν[CH]), 2818, 2719 (vw, ν[C(O)H]), 1900 (vw), 1726 (m, ν[CO]), 1597 (w), 1493 (m, ν[C–C_{ar}]), 1457, 1410, 1372 (w, m, vw, δ[CH]), 1093 (m), 1014 (m), 897 (w), 866 (w), 825 (m, ν[CHal]) cm^{-1}. MS (EI, II, 70 eV): m/z (%) = 170 (5), 168 (14) [M$^+$], 154 (5), 152 (12) [M$^+$ – CH_3], 141 (32), 139 (100) [M$^+$ – CHO], 105 (3), 104 (7) [$C_8H_8^+$], 103 (41), 77 (13) [$C_6H_5^+$]. HRMS (EI) m/z calcd. for C_9H_9ClO 168.0342, found 168.0345. C_9H_9ClO (168.62): calcd. C 64.11, H 5.38; found C 64.22, H 5.41.

2-(4′-Bromophenyl)propionaldehyde (3h): The product was synthesized according to GP 2, employing **2h** (1.817 g, 8.0 mmol). Flash chromatography on silica (diethyl ether/pentane, 1:80) delivered 1.244 g (5.84 mmol, 73%) of a colorless oil. R_f = 0.60 (diethyl ether/pentane, 1:80). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.36 (d, J = 7.1 Hz, 3 H, $CHR_2C\mathit{H}_3$), 3.54 (dq, J = 7.1, 0.9 Hz, $C\mathit{H}R_2CH_3$), 7.01 (d, J = 8.3 Hz, 2 H, $C^{3'}H_{ar}$), 7.43 (d, J = 8.4 Hz, 2 H, $C^{2'}H_{ar}$), 9.58 (d, J = 1.3 Hz, 1 H, CHO) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.6 ($CHR_2C\mathit{H}_3$), 52.4 ($C\mathit{H}R_2CH_3$), 121.6 ($C^{4'}{}_{ar}Br$), 130.0 ($C^{3'}{}_{ar}H$), 132.2 ($C^{2'}{}_{ar}H$), 136.7 ($\mathit{C}^{1'}{}_{ar}CR_2$), 200.4 (CHO) ppm. IR (KBr): $\tilde{\nu}$ = 3052 cm^{-1} (vw, ν[CH_{ar}]), 2978, 2934, 2876 (w, vw, vw, ν[CH]), 2817, 2718 (vw, ν[C(O)H]), 1900 (vw), 1726 (m, ν[CO]), 1591 (vw), 1489 (m, ν[C–C_{ar}]), 1456, 1406, 1372 (w, m, w, δ[CH]), 1074 (m), 1026 (m), 895 (w), 865 (w), 820 (m, ν[CHal]) cm^{-1}. MS (EI, II, 70 eV): m/z (%) = 214, 212 (19) [MH$^+$], 185 (86), 183 (83) [$C_8H_9Br^+$], 104 (100) [$C_8H_8^+$], 77 (17) [$C_6H_5^+$]. HRMS (EI) m/z calcd. for C_9H_9BrO 211.9837, found 211.9839. C_9H_9BrO (152.17): calcd. C 50.73, H 4.26; found C 50.89, H 4.19.

2-(4′-Trifluoromethylphenyl)propionaldehyde (3i): The product was synthesized according to GP 2, employing **2i** (3.033 g, 14.0 mmol). Flash chromatography on silica (diethyl ether/pentane, 1:100) delivered 2.631 g (13.0 mmol, 93%) of a colorless oil. R_f = 0.45 (diethyl ether/pentane, 1:100). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.50 (d, J = 7.1 Hz, 3 H, $CHR_2C\mathit{H}_3$), 3.74 (q, J = 7.1 Hz, $C\mathit{H}R_2CH_3$), 7.36 (d, J = 8.2 Hz, 2 H, $C^{3'}H_{ar}$), 7.65 (d, J = 8.1 Hz, 2 H, $C^{2'}H_{ar}$), 9.71 (d, J = 1.3 Hz, 1 H, CHO) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.6 ($CHR_2C\mathit{H}_3$), 52.7 ($C\mathit{H}R_2CH_3$), 124.1 (q, J = 272.0 Hz, $C^{4'}{}_{ar}CF_3$), 126.0 (q, J = 3.6 Hz, $C^{3'}{}_{ar}H$), 128.7 ($C^{2'}{}_{ar}H$), 129.9 (q, J = 32.5 Hz, $\mathit{C}^{4'}{}_{ar}CF_3$), 141.8 ($\mathit{C}^{1'}{}_{ar}CR_2$), 200.1 (CHO) ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ = –62.5 ppm. IR (KBr): $\tilde{\nu}$ = 2984, 2939 cm^{-1} (w, w, ν[CH]), 1726 (w, ν[CO]), 1693 (w), 1620 (m, ν[C–C_{ar}]), 1512 (vw), 1457, 1420 (w, w, δ[CH]), 1327 (s), 1265 (w), 1166 (m), 1123 (s), 1069 (m), 1016 (m), 840 (m, δ[CH_{ar}]), 739, 720 (w,

w, ν[CHal]) cm^{-1}. MS (EI, II, 70 eV): *m/z* (%) = 202 (6) [M^+], 173 (100) [M^+ – CHO], 159 (29) [$C_6H_8F_3^+$], 133 (19) [M^+ – CHF_3]. HRMS (EI) *m/z* calcd. for $C_{10}H_9F_3O$ 202.0605, found 202.0607. $C_{10}H_9F_3O$ (202.17): calcd. C 59.41, H 4.49; found C 59.27, H 4.41.

2-(4′-Nitrophenyl)propionaldehyde (3j): The product was synthesized according to GP 2, employing **2j** (0.146 g, 0.756 mmol). Flash chromatography on silica (diethyl ether/pentane, 1:2) delivered 0.127 g (0.710 mmol, 94%) of a yellow solid. R_f = 0.42 (diethyl ether/pentane, 1:5); m.p. 39 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.51 (d, J = 7.2 Hz, 3 H, CHR_2CH_3), 3.78 (br. q, J = 7.1 Hz, 1 H, CHR_2CH_3), 7.39 (ddd, J = 8.9, 2.1, 2.0 Hz, 2 H, $C^{2'}H_{ar}$), 8.23 (ddd, J = 9.1, 2.3, 2.1 Hz, 2 H, $C^{3'}H_{ar}$), 9.71 (d, J = 1.1 Hz, 1 H, CHO) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.8 (CHR_2CH_3), 52.8 (CHR_2CH_3), 124.3 ($C^{3'}{}_{ar}H$), 129.3 ($C^{2'}{}_{ar}H$), 145.3 ($C^{1'}{}_{ar}CHR_2$), 147.6 ($C^{4'}{}_{ar}NO_2$), 199.4 (CHO) ppm. IR (KBr): ṽ = 3113, 3081, 2983 (m, m, m, ν[CH_{ar}]), 2939, 2878, 2842 (m, m, m, ν[CH]), 2739 (m, ν[C(O)H]), 1727 (m, ν[CO]), 1605 (m, ν[C–C_{ar}]), 1519 (s, ν[NO_2]), 1458, 1419, 1397 (m, m, m, δ[CH]), 1349, 1319 (s, m, ν[NO_2]), 1184 (m), 1110 (m), 1031 (m), 1014 (m), 855 (m, δ[CH_{ar}]), 751 (m) cm^{-1}. MS (EI, II, 70 eV): *m/z* (%) = 179 (11) [M^+], 150 (100) [M^+ – CHO], 134 (3) [M^+ – CHO – O], 120 (7) [M^+ – CHO – NO], 104 (15) [M^+ – CHO – NO_2], 92 (10) [$C_6H_6N^+$], 77 (10) [$C_6H_5^+$]. HRMS (II) calcd. for $C_9H_9NO_3$ 179.0582, found: 179.0583. $C_9H_9NO_3$ (179.17): calcd. C 60.33, H 5.06, N 7.82; found C 60.22, H 5.12, N 7.75.

2-(4′-Cyanophenyl)propionaldehyde (3k): The product was synthesized according to GP 2, employing **2k** (2.598 g, 15.0 mmol). Flash chromatography on silica (diethyl ether/pentane, 1:30) delivered 2.197 g (13.80 mmol, 92%) of a yellow oil. R_f = 0.38 (diethyl ether/pentane, 1:5). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.49 (d, J = 7.1 Hz, 3 H, CHR_2CH_3), 3.74 (q, J = 7.1 Hz, CHR_2CH_3), 7.35 (d, J = 8.4 Hz, 2 H, $C^{3'}H_{ar}$), 7.68 (d, J = 8.4 Hz, 2 H, $C^{2'}H_{ar}$), 9.70 (d, J = 0.9 Hz, 1 H, CHO) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.5 (CHR_2CH_3), 52.9 (CHR_2CH_3), 111.5 ($C^{4'}{}_{ar}CN$), 118.5 ($C^{4'}{}_{ar}CN$), 129.2 ($C^{2'}{}_{ar}H$), 132.8 ($C^{3'}{}_{ar}H$), 143.2 ($C^{1'}{}_{ar}CR_2$), 199.6 (CHO) ppm. IR (KBr): ṽ = 3058 cm^{-1} (m, ν[CH_{ar}]), 2979, 2936, 2879 (m, m, m, ν[CH]), 2825, 2724 (m, w, ν[C(O)H]), 2229 (vs, ν[CN]), 1926 (vw), 1724 (vs, ν[CO]), 1607, 1504 (s, s, ν[C–C_{ar}]), 1456, 1438, 1414 (m, m, m, δ[CH]), 1294 (w), 1180 (m), 1120 (m), 1069 (m), 1018 (m), 898 (m), 836 (s, δ[CH_{ar}]), 749 (m) cm^{-1}. MS (EI, II, 70 eV): *m/z* (%) = 159 (21) [M^+], 145 (9) [M^+ – CH_3], 130 (100) [M^+ – CHO], 116 (14) [$C_8H_6N^+$], 103 (21) [$C_7H_5N^+$], 77 (6) [$C_6H_5^+$]. HRMS (EI) *m/z* calcd. for $C_{10}H_9NO$ 159.0684, found 159.0686. $C_{10}H_9NO$ (159.18): calcd. C 75.45, H 5.70, N 8.80; found C 75.64, H 5.85, N 8.68.

2-(3′,5′-Dimethoxyphenyl)propionaldehyde (3l): The product was synthesized according to GP 2, employing **2l** (0.72 g, 3.46 mmol). Flash chromatography on silica (diethyl ether/pentane, 1:15 to 1:5) delivered 0.59 g (3.04 mmol, 88%) of a colorless oil. R_f = 0.16 (diethyl ether/pentane, 1:15). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.41 (d, J = 7.2 Hz, 3 H, CHR_2CH_3), 3.54 (dq, J = 7.1, 1.3 Hz, 1 H, CHR_2CH_3), 3.78 (s, 6 H, $C_{ar}OCH_3$), 6.35 (d, J = 2.3 Hz, 2 H, $C^{2'}H_{ar}$), 6.39 (t, J = 2.3 Hz, 1 H, $C^{4'}H_{ar}$), 9.64 (d, J = 1.3 Hz, 1 H, CHO) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.4 (CHR_2CH_3), 53.2 (CHR_2CH_3), 55.4 ($C_{ar}OCH_3$), 99.4 ($C^{4'}{}_{ar}H$), 106.5 ($C^{2'}{}_{ar}H$), 140.4 ($C^{1'}{}_{ar}CHR_2$), 161.4 ($C_{ar}OCH_3$), 200.8 (CHO) ppm. IR (KBr): ṽ = 2976, 2937 cm^{-1} (w, w, ν[CH]), 2836 (vw, ν[OCH_3]), 2720 (vw, ν[C(O)H]), 1722 (m, ν[CO]), 1601, 1585, 1491 (w, w, w, ν[C–C_{ar}]), 1455, 1391 (w, w, δ[CH]), 1263, 1043 (w, w, ν[C_{ar}–O–C]) cm^{-1}. MS (EI, II, 70 eV): *m/z* (%) = 194 (50) [M^+], 165 (100) [M^+ – CHO], 150 (42) [M^+ – CHO – CH_3], 135 (11) [M^+ – CHO – $2CH_3$], 105 (8) [$C_8H_9^+$], 91 (6) [$C_7H_7^+$], 77 (6) [$C_6H_5^+$]. HRMS (II) calcd. for $C_{11}H_{14}O_3$ 194.0943, found 194.0936.

2-Cyclohexylpropionaldehyde (3m): The product was synthesized according to GP 2, employing **2m** (0.204 g, 1.32 mmol). Aqueous workup delivered 0.050 g (0.359 mmol, 27%) of a colorless oil. The crude product contained minor impurities of triphenylphosphane/triphenylphosphane oxide. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.98–1.34 (m, 4 H, 2 × CH_2), 1.04 (d, J = 7.1 Hz, 3 H, CHR_2CH_3), 1.56–1.80 (m, 7 H, 3 × CH_2/CHR_2CH_3), 2.20 (ddq, J = 7.0, 5.8, 2.1 Hz, 1 H, CHR_2CH_3), 9.71 (d, J = 2.4 Hz, 1 H, CHO) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 10.2 (CHR_2CH_3), 26.4 (CH_2), 26.5 (CH_2), 26.6 (CH_2), 29.4 (CH_2), 31.3 (CH_2), 38.7 [$CH(CH_2)_5$], 52.0 (CHR_2CH_3), 205.9 (CHO) ppm. IR (KBr): ṽ = 2928 cm^{-1} (w, ν[CH]), 1853 (w), 1709 (w, ν[CO]), 1484, 1438, 1380 (vw, w, vw, δ[CH]) cm^{-1}. MS (EI, I, 70 eV): *m/z* (%) = 140 (4) [M^+], 122 (6) [M^+ – H_2O], 82 (44) [$C_6H_{10}^+$], 69 (48) [$C_4H_5O^+$], 58 (100) [$C_3H_6O^+$], 55 (68) [$C_3H_3O^+$]. HRMS (I) calcd. for $C_{11}H_{12}O_3$ 140.1201; found 140.1195.

2-(Thiophen-2-yl)propionaldehyde (3n): The product was synthesized according to GP 2, employing **2n** (3.085 g, 20.0 mmol). Flash chromatography on silica (diethyl ether/pentane, 1:20) delivered 1.823 g (13.0 mmol, 65%) of a brown oil. R_f = 0.25 (diethyl ether/pentane, 1:20). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.52 (d, J = 7.2 Hz, 3 H, CHR_2CH_3), 3.63 (dq, J = 7.2, 1.3 Hz, 1 H, CHR_2CH_3), 6.84 (dd, J = 3.6, 1.0 Hz, 1 H, CH_{ar}), 6.85 (d, J = 3.6 Hz, 1 H, CH_{ar}), 7.01 (dd, J = 5.2, 1.0 Hz, 1 H, CH_{ar}), 9.56 (d, J = 1.3 Hz, 1 H, CHO) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.3 (CHR_2CH_3), 58.5 (CHR_2CH_3), 120.2 ($C_{ar}H$), 124.5 ($C_{ar}H$), 126.8 ($C_{ar}H$), 135.8 ($C^{1}{}_{ar}CHR_2$), 198.5 (CHO) ppm. IR (KBr): ṽ = 3066, 3002 cm^{-1} (w, w, ν[CH_{ar}]), 2965 (w, ν[CH]), 2819, 2722 (m, w, ν[C(O)H]), 1725 (w, ν[CO]), 1666, 1554, 1512 (w, w, m, ν[C–C_{ar}]), 1461, 1403 (w, w, δ[CH]), 1313 (w), 1179 (m), 866 (m), 756, 721 (w, w) cm^{-1}. MS (EI, II, 70 eV): *m/z* (%) = 140 (7) [M^+], 111 (100) [M^+ – CHO], 97 (23) [$C_5H_5S^+$], 75 (45) [$C_6H_5^+$]. HRMS (II) *m/z* calcd. for C_7H_8OS 140.0296, found 140.0299. C_7H_8OS (140.20): calcd. C 59.97, H 5.75; found C 60.10, H 5.84.

2-Phenylbutyraldehyde (3o): The product was synthesized according to GP 2, employing **2o** (0.582 g, 3.5 mmol). Flash chromatography on silica (diethyl ether/pentane mixtures) delivered 0.291 g (1.96 mmol, 56%) of a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.91 (dd, J = 7.1 Hz, 3 H, RCH_2CH_3), 1.77 (ddq, J = 14.1, 7.5, 7.4 Hz, 1 H, $RCHHCH_3$), 2.12 (ddq, J = 14.2, 7.2, 7.0 Hz, 1 H, $RCHHCH_3$), 3.41 (ddd, J = 8.1, 6.5, 1.8 Hz, 1 H, CHR_2CHO), 7.20 (ddd, J = 6.5, 1.7, 1.7 Hz, 2 H, $C^{4'}H_{ar}$), 7.26–7.42 (m, 3 H, $C^{2'}H_{ar}$/$C^{3'}H_{ar}$), 9.68 (d, J = 2.1 Hz, 1 H, CHO) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.8 (RCH_2CH_3), 23.1 (RCH_2CH_3), 61.1 (CHR_2CH_2), 127.6 ($C^{4'}{}_{ar}H$), 129.0 ($C^{3'}{}_{ar}H$), 129.1 ($C^{2'}{}_{ar}H$), 136.5 ($C^{1'}{}_{ar}CHR_2$), 201.1 (CHO) ppm.

1-(4′-*tert*-Butylphenyl)-1-methyloxirane (5p). General Procedure (GP3): A mixture of trimethylsulfoxonium iodide (2.96 g, 13.4 mmol) and potassium *tert*-butoxide (1.50 g, 13.4 mmol) is dissolved in 20 mL of dry DMSO and treated at room temperature under argon with 4-*tert*-butylacetophenone (1.76 g, 10.0 mmol). The mixture is stirred for 2 h at room temperature, the reaction quenched by addition of 100 mL of water and the aqueous phase extracted once with 30 mL of diethyl ether and twice 30 mL of ethyl acetate. The combined organic phases are dried with sodium sulfate and the solvent is removed by evaporation. The crude product is immediately employed in the next step.

2-(Biphenyl-4-yl)-2-methyloxirane (5q): The product was synthesized according to GP 3, employing 4′-biphenylacetophenone (1.962 g, 10.0 mmol). Aqueous workup delivered 2.082 g (9.90 mmol, 99%) of a colorless solid. The analytical pure product was used in the next step without further purification. R_f = 0.33

(diethyl ether/pentane, 1:30). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.67 (s, 3 H, CR_2CH_3), 2.76 (d, J = 5.4 Hz, 1 H, $CHHCR_2$), 2.92 (d, J = 5.4 Hz, 1 H, $CHHCR_2$), 7.26 (t, J = 7.4 Hz, 1 H, $C^{4''}H_{ar}$), 7.35 (m, 4 H, CH_{ar}), 7.49 (m, 4 H, CH_{ar}) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.8 (CR_2CH_3), 56.7 (CR_2CH_3), 57.2 ($CHHCR_2$), 125.8 ($C^{2'}{}_{ar}H$), 127.1 ($C^{2''}{}_{ar}H$), 127.1 ($C^{3'}{}_{ar}H$), 127.4 ($C^{4''}{}_{ar}H$), 128.8 ($C^{3''}{}_{ar}H$), 140.3 ($C^{4'}{}_{ar}Ph$), 140.5 ($C^{1'}{}_{ar}CR_2$), 140.7 ($C^{1''}{}_{ar}$) ppm. IR (KBr): $\tilde{\nu}$ = 3062, 3032 cm^{-1} (m, m, ν[CH_{ar}]), 2977, 2933 (m, m, ν[CH]), 1678, 1600, 1581, 1486 (w, w, w, m, ν[C–C_{ar}]), 1447, 1407 (m, m, δ[CH]), 1161, 1120, 1101, 1066, 1038 (m, m, m, m, m, ν[C–O–C]), 833 (m, δ[CH_{ar}]), 763 (m) cm^{-1}. MS (EI, II, 70 eV): m/z (%) = 210 (95) [M^+], 196 (5) [$M^+ - CH_3$], 181 (100) [$C_{14}H_{13}^+$], 167 (21) [$C_{13}H_{11}^+$], 152 (32), 133 (28). HRMS (EI) m/z calcd. for $C_{15}H_{14}O$ 210.1047, found 201.1042. $C_{15}H_{14}O$ (210.27): calcd. C 85.68, H 6.71; found C 85.62, H 6.66.

2-(4′-*tert*-Butylphenyl)propionaldehyde (3p). General Procedure (GP4): A solution of the crude product **5p** in 10 mL abs. THF is added at room temperature under argon to a stirred suspension of indium(III) chloride (1.33 g, 6.00 mmol). After 1 h TLC indicates complete reaction and the reaction is quenched with brine and extracted three times with diethyl ether. The combined organic phases are dried with sodium sulfate and the solvent is removed by evaporation. Flash chromatography on silica (diethyl ether/pentane, 1:25) delivers 707.6 mg (3.72 mmol, 37% with respect to 4-*tert*-butylacetophenone) of a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.32 [s, 9 H, $C(CH_3)_3$], 1.44 (d, J = 7.1 Hz, 3 H, CHR_2CH_3), 3.61 (dq, J = 7.1, 1.3 Hz, 1 H, CHR_2CH_3), 7.15 (ddd, J = 8.5, 2.0, 2.0 Hz, 2 H, $C^{3'}H_{ar}$), 7.41 (ddd, J = 8.7, 2.2, 2.0 Hz, 2 H, $C^{2'}H_{ar}$), 9.68 (d, J = 1.5 Hz, 1 H, CHO) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.7 (CHR_2CH_3), 31.5 [$C(CH_3)_3$], 34.7 [$C(CH_3)_3$], 52.7 (CHR_2CH_3), 126.2 ($C^{3'}{}_{ar}H$), 128.1 ($C^{2'}{}_{ar}H$), 134.7 ($C^{1'}{}_{ar}CHR_2$), 150.6 [$C^{4'}{}_{ar}C(CH_3)_3$], 201.4 (CHO) ppm.

2-(Biphenyl-4-yl)propionaldehyde (3q): The product was synthesized according to GP 4, employing **5q** (1.998 g, 9.50 mmol). Flash chromatography on silica (diethyl ether/pentane, 1:50) delivered 1.140 g (5.42 mmol, 57%) of a colorless solid. R_f = 0.35 (diethyl ether/pentane, 1:50). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.51 (d, J = 7.1 Hz, 3 H, CHR_2CH_3), 3.71 (q, J = 7.1 Hz, CHR_2CH_3), 7.26 (m, 9 H, CH_{ar}), 9.74 (d, J = 0.9 Hz, 1 H, CHO) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.6 (CHR_2CH_3), 52.7 (CHR_2CH_3), 127.1 ($C^{2'}{}_{ar}H$), 127.4 ($C^{4''}{}_{ar}H$), 127.8 ($C^{2''}{}_{ar}H$), 128.7 ($C^{3'}{}_{ar}H$), 128.8 ($C^{3''}{}_{ar}H$), 136.7 ($C^{4'}{}_{ar}Ph$), 136.8 ($C^{1'}{}_{ar}CR_2$), 140.5 ($C^{1''}{}_{ar}$), 201.0 (CHO) ppm. IR (KBr): $\tilde{\nu}$ = 3056 cm^{-1} (m, ν[CH_{ar}]), 2978, 2929 (m, m, ν[CH]), 1950 (vw), 1721 (m, ν[CO]), 1603, 1520, 1486 (m, m, s, ν[C–C_{ar}]), 1450, 1405 (m, m, δ[CH]), 1267 (m), 1180 (m), 1075 (m), 1008 (m), 839 (s, δ[CH_{ar}]), 765 (s), 733 (m) cm^{-1}. MS (EI, II, 70 eV): m/z (%) = 210 (11) [M^+], 196 (30) [$M^+ - CH_3$], 181 (100) [M^+ – CHO], 165 (14), 152 (34), 77 (7) [$C_6H_5^+$]. HRMS (EI) m/z calcd. for $C_{15}H_{14}O$ 210.1045, found 210.1048. $C_{15}H_{14}O$ (210.27): calcd. C 85.68, H 6.71; found C 85.63, H 6.67.

General Procedure for the Synthesis of [*N*,*N*′-Bis(alkyloxycarbonyl)-hydrazino]-Substituted Aldehydes (GP 5): A suspension of the amino acid L-proline or L-azetidinecarboxylic acid as the catalyst (50 mol-% with respect to the aldehyde) in dichloromethane (7.5 to 10 mL/mmol aldehyde) is stirred at room temperature for 30 min, followed by addition of 1.0 or 1.5 equiv. of the aldehyde **3** at 0 °C. After 1 h of stirring at room temperature 1.0 to 1.2 equiv. of the azodicarboxylate **8** or **9** is added and the mixture stirred at room temperature under argon until the color of the azodicarboxylate has disappeared. The reaction is then quenched by addition of water and the aqueous phase extracted three times with diethyl ether. The combined organic phases are dried with magnesium sulfate and the solvent is removed by evaporation. Subsequent flash chromatography on silica with adequate mixtures of diethyl ether/pentane delivers the product as an oil or solid.

2-[*N*,*N*′-Bis(ethoxycarbonyl)hydrazino]-2-methylpropionaldehyde (10s-Et): The reaction was carried out according to GP 5 using L-proline (0.288 g, 2.50 mmol), isobutyraldehyde (**3s**) (0.433 g, 6.00 mmol) and diethyl azodicarboxylate (**8**) (0.871 g, 5.00 mmol) in 10 mL of dichloromethane within 3 d. Column chromatography on silica (diethyl ether/pentane, 1:1) delivered 1.020 g (4.15 mmol, 83%) of a white solid. R_f = 0.44 (diethyl ether/pentane, 1:1); m.p. 64 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.17–1.30 (m, 12 H, OCH_2CH_3, CR_3CH_3), 4.08–4.21 (m, 4 H, OCH_2CH_3 rotamers), 6.51, 6.58 (br. s, 1 H, NH rotamers), 9.38, 9.45 (s, 1 H, CHO rotamers) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.3, 14.4 (OCH_2CH_3), 20.3 (CR_3CH_3), 62.4, 63.1 (OCH_2CH_3), 67.3 (CR_3CH_3), 155.8, 156.8 (NCO_2R), 198.5 (CHO) ppm. IR (KBr): $\tilde{\nu}$ = 3569, 3307 cm^{-1} (vw, m, ν[NH]), 2986, 2939 (m, w, ν[CH]), 2817 (w, ν[C(O)H]), 1737 (s, ν[CO]), 1706 (s), 1516 (m, δ[NH]), 1469, 1411, 1381 (m, m, m, δ[CH]), 1344 (m), 1257, 1232, 1098, 1056 (m, m, m, m, ν[C–O–C]), 1019 (w). MS (EI): m/z (%) = 272 (36) [M^+ – CHO], 145 (100) [$C_6H_{13}N_2O_2^+$], 130 (21) [$C_6H_{12}NO_2^+$], 99 (54), 56 (36). HRMS (EI): m/z calcd. for $C_{10}H_{18}N_2O_5$ – CHO 218.1267, found 218.1272. $C_{10}H_{18}N_2O_5$ (246.26): calcd. C 48.77, H 7.37, N 11.38; found C 48.47, H 7.19, N 11.30.

2-[*N*,*N*′-Bis(benzyloxycarbonyl)hydrazino]-2-methylpropionaldehyde (10s-Bn): The reaction was carried out according to GP 5 using L-proline (0.288 g, 2.50 mmol), isobutyraldehyde (**3s**) (0.433 g, 6.00 mmol) and dibenzyl azodicarboxylate (**9**) (1.491 g, 5.00 mmol) in 20 mL of dichloromethane within 3 d. Column chromatography on silica (diethyl ether/pentane, 1:1) delivered 1.148 g (4.25 mmol, 85%) of a white solid. R_f = 0.45 (diethyl ether/pentane, 1:1); m.p. 79 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.19, 1.31 (s, 6 H, CR_3CH_3 rotamers), 5.05–5.12 (m, 4 H, OCH_2Ph rotamers), 6.53, 6.67 (br. s, 1 H, NH rotamers), 7.18–7.25 (m, 10 H, CH_{ar}), 9.29, 9.44 (s, 1 H, CHO rotamers) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.2 (CR_3CH_3), 67.6 (CR_3CH_3), 68.1, 68.7 (OCH_2Ph), 128.2, 128.5, 128.6, 128.7 ($C_{ar}H$), 135.2, 135.4 ($C^{1'}{}_{ar}CH_2R$), 155.6, 156.6 (NCO_2R), 198.3 (CHO) ppm. IR (KBr): $\tilde{\nu}$ = 3295 cm^{-1} (m, ν[NH]), 3065, 3035, 2996 (m, m, m, ν[CH_{ar}]), 2951, 2829 (m, w, ν[CH]), 1744 (m, ν[CO]), 1672 (m, ν[C–C_{ar}]), 1526 (m, δ[NH]), 1498 (w, ν[C–C_{ar}]), 1457, 1420, 1389 (w, m, w, δ[CH]), 1355 (m), 1287, 1248, 1225, 1098, 1049 (w, m, m, m, ν[C–O–C]), 1029 (w), 1010 (w). MS (EI): m/z (%) = 341 (4) [M^+ – CHO], 297 (10), 192 (4) [$C_{11}H_{14}NO_2^+$], 148 (3), 91 (100) [$C_7H_7^+$]. HRMS (EI): m/z calcd. for $C_{20}H_{22}N_2O_5$ 370.1529, found 370.1524. $C_{20}H_{22}N_2O_5$ (370.40): calcd. C 64.85, H 5.99, N 7.56; found C 65.04, H 6.07, N 7.48.

(+)-2-[*N*,*N*′-Bis(ethoxycarbonyl)hydrazino]-2-methylpentanal (10u-Et): The reaction was carried out according to GP 5 using L-proline (0.288 g, 2.50 mmol), 2-methylpentanal (**3u**) (0.601 g, 6.00 mmol) and diethyl azodicarboxylate (**8**) (0.871 g, 5.00 mmol) in 10 mL of dichloromethane within 3 d. Column chromatography on silica (diethyl ether/pentane, 1:2) delivered 0.820 g (3.00 mmol, 60%) of a colorless oil. The *ee* value could not be determined by GC or HPLC with chiral stationary phase. R_f = 0.54 (diethyl ether/pentane, 1:1). $[a]_D^n$ = +5.34 (c = 1.00, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.71 (t, J = 7.3 Hz, 3 H, RCH_2CH_3), 1.04 (t, J = 7.1 Hz, 3 H, OCH_2CH_3), 1.06 (t, J = 7.4 Hz, 3 H, OCH_2CH_3), 1.07–1.11 (m, 2 H, RCH_2R), 1.34–1.68 (m, 2 H, RCH_2R), 1.48–1.62 (m, 3 H, CR_3CH_3), 3.96–4.06 (m, 4 H, OCH_2CH_3 rotamers), 6.35 (br. s, 1 H, NH), 9.29, 9.33 (s, 1 H, CHO rotamers) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.3, 14.4, 14.5 (RCH_2CH_3, OCH_2CH_3), 16.9 (RCH_2CH_3), 17.3 (CR_3CH_3), 36.0 (RCH_2R),

62.4, 63.1 (OCH_2CH_3), 69.9 (CR_3CH_3), 156.0, 156.8 (NCO_2R), 198.9 (CHO) ppm. IR (KBr): $\tilde{\nu}$ = 3315 cm^{-1} (m, ν[NH]), 2962, 2936, 2875 (m, m, w, ν[CH]), 1744 (m, ν[CO]), 1510 (m, δ[NH]), 1467 (m), 1371, 1324 (m, m, δ[CH]), 1239, 1096, 1070 (m, m, m, ν[C–O–C]), 1018 (m), 868 (vw), 766 (w). MS (EI): *m/z* (%) = 274 (37) [M^+], 229 (7) [$C_{10}H_{17}N_2O_4^+$], 176 (100), 130 (38). HRMS (EI): *m/z* calcd. for $C_{12}H_{26}N_2O_5$ 274.1529, found 274.1531. $C_{12}H_{26}N_2O_5$ (274.31): calcd. C 52.54, H 8.08, N 10.21; found C 54.66, H 87.98, N 12.19.

(+)-2-[*N*,*N*′-Bis(benzyloxycarbonyl)hydrazino]-2-methylpentanal (10u-Bn): The reaction was carried out according to GP 5 using L-proline (0.288 g, 2.50 mmol), 2-methylpentanal (**3u**) (0.601 g, 6.00 mmol) and dibenzyl azodicarboxylate (**9**) (1.491 g, 5.00 mmol) in 10 mL of dichloromethane within 3 d. Column chromatography on silica (diethyl ether/pentane, 1:2) delivered 1.220 g (3.01 mmol, 60%) of a colorless oil with 35% *ee*. R_f = 0.56 (diethyl ether/pentane, 1:1); HPLC (Chiralcel OD, *n*-heptane/2-propanol 90:10, 0.7 mL/min): R_t(maj) = 16.6 min, R_t(min) = 12.8 min. $[a]_D^n$ = +3.45 (*c* = 1.00, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.81 (t, *J* = 7.2 Hz, 3 H, RCH_2CH_3), 1.13–1.26 (m, 4 H, RCH_2R), 1.53–1.78 (m, 3 H, CR_3CH_3), 4.92–5.17 (m, 4 H, OCH_2Ph rotamers), 6.31, 6.49 (br. s, 1 H, NH rotamers), 7.19–7.27 (m, 10 H, CH_{ar}), 9.31, 9.48 (s, 1 H, CHO rotamers) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.4, 16.9 (RCH_2CH_3, CR_3CH_3), 18.3 (RCH_2CH_3), 36.0, (RCH_2R), 68.1, 69.0 (OCH_2Ph), 70.1 (CR_3CH_3), 128.1, 128.2, 128.5, 128.6 128.7 ($C_{ar}H$), 135.2, 135.3 ($C^{1''}{}_{ar}CH_2R$), 155.8, 156.6 (NCO_2R), 197.7, 198.6 (CHO rotamers) ppm. IR (KBr): $\tilde{\nu}$ = 3330 cm^{-1} (m, ν[NH]), 3089, 3064, 3035, 2974 (vw, w, w, w, ν[CH_{ar}]), 2880, 2736 (w, vw, ν[CH]), 1958 (vw), 1746 (m, ν[CO]), 1679 (m, ν[C–C_{ar}]), 1585, 1516 (w, m, δ[NH]), 1456, 1414, 1390 (m, m, w, δ[CH]), 1352 (m), 1292, 1280, 1231, 1196, 1159, 1115, 1071, 1038 (m, m, m, w, w, w, w, w, ν[C–O–C]), 1002 (vw), 970(w), 865 (vw), 827 (vw), 780, 758 (w, w, δ[CH_{ar}]) cm^{-1}. MS (EI): *m/z* (%) = 369 (49) [M^+ – CHO], 325 (64), 220 (37) [$C_{13}H_{18}NO_2^+$], 91 (100) [$C_7H_7^+$]. HRMS (EI): *m/z* calcd. for $C_{22}H_{26}N_2O_5$ 398.1842, found 398.1848. $C_{22}H_{26}N_2O_5$ (398.45): calcd. C 66.32, H 6.58, N 7.03; found C 66.59, H 6.50, N 6.99.

2-[*N*,*N*′-Bis(ethoxycarbonyl)hydrazino]-2-ethylbutyraldehyde (10v-Et): The reaction was carried out according to GP 5 using L-proline (0.288 g, 2.50 mmol), 2-ethylbutyraldehyde (**3v**) (0.601 g, 6.00 mmol) and diethyl azodicarboxylate (**8**) (0.871 g, 5.00 mmol) in 10 mL of dichloromethane within 4 d. Column chromatography on silica (diethyl ether/pentane, 1:1) delivered 0.760 g (2.77 mmol, 55%) of a white solid. R_f = 0.62 (diethyl ether/pentane, 1:1); m.p. 85 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.74 (t, *J* = 7.5 Hz, 3 H, RCH_2CH_3), 0.76 (t, *J* = 7.5 Hz, 3 H, RCH_2CH_3), 1.18 (t, *J* = 7.1 Hz, 3 H, OCH_2CH_3), 1.24 (t, *J* = 7.1 Hz, 3 H, OCH_2CH_3), 1.55–1.65 (m, 1 H, $RCHHCH_3$), 1.68–1.77 (m, *J* = 7.5 Hz, 1 H, $RCHHCH_3$), 1.82–1.90 (m, 2 H, RCH_2CH_3), 4.09–4.23 (m, 4 H, OCH_2CH_3 rotamers), 6.32, 6.37 (br. s, 1 H, NH rotamers), 9.37, 9.45 (s, 1 H, CHO rotamers) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 7.3 (RCH_2CH_3), 7.7 (RCH_2CH_3), 14.3 (OCH_2CH_3), 14.4 (OCH_2CH_3), 22.3 (RCH_2CH_3), 62.4 (OCH_2CH_3), 63.1 (OCH_2CH_3), 73.0 (CR_3CH_3), 156.0 (NCO_2R), 157.0 (NCO_2R), 198.0 (CHO) ppm. IR (KBr): $\tilde{\nu}$ = 3299 cm^{-1} (w, ν[NH]), 2980, 2943, 2885 (m, w, w, ν[CH]), 1734 (m, ν[CO]), 1707 (m), 1516 (w, δ[NH]), 1465, 1407, 1378 (w, m, m, δ[CH]), 1342, 1320, 1242, 1206, 1175, 1101, 1056 (m, m, m, w, w, m, m, ν[C–O–C]), 1010 (w). MS (EI): *m/z* (%) = 245 (51) [M^+ – CHO], 201 (16), 173 (100) [$C_7H_{13}N_2O_3^+$], 157 (14) [$C_7H_{13}N_2O_2^+$], 145 (17), 130 (21), 127 (36), 84 (12), 56 (51). HRMS (EI): *m/z* calcd. for $C_{12}H_{22}N_2O_5$ – CHO 246.1580, found 246.1578. $C_{12}H_{22}N_2O_5$ (274.31): calcd. C 52.54, H 8.08, N 10.21; found C 52.50, H 7.91, N 10.16.

2-[*N*,*N*′-Bis(benzyloxycarbonyl)hydrazino]-2-ethylbutyraldehydes (10v-Bn): The reaction was carried out according to GP 5 using L-proline (0.288 g, 2.50 mmol), 2-ethylbutyraldehyde (**3v**) (0.601 g, 6.00 mmol) and dibenzyl azodicarboxylate (**9**) (1.491 g, 5.00 mmol) in 10 mL of dichloromethane within 4 d. Column chromatography on silica (diethyl ether/pentane, 1:1) delivered 1.015 g (2.55 mmol, 51%) of a white solid. R_f = 0.60 (diethyl ether/pentane, 1:1); m.p. 96 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.71 (t, *J* = 7.6 Hz, 3 H, RCH_2CH_3), 0.78 (t, *J* = 7.6 Hz, 3 H, RCH_2CH_3), 1.61–1.76 (m, 2 H, RCH_2CH_3), 1.80–1.89 (m, 2 H, RCH_2CH_3), 5.07–5.14 (m, 4 H, OCH_2Ph rotamers), 6.20, 6.40 (br. s, 1 H, NH rotamers), 7.21–7.31 (m, 10 H, CH_{ar}), 9.27, 9.47 (s, 1 H, CHO rotamers) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.7 (RCH_2CH_3), 24.9 (RCH_2CH_3), 47.6 (RCR_3CH_2), 68.2, 69.3 (OCH_2Ph), 128.2, 128.3, 128.5, 128.7, 128.8 ($C_{ar}H$), 134.9, 135.6 ($C^{1'}{}_{ar}CH_2R$), 153.2, 155.6 (NCO_2R), 197.2 (CHO) ppm. IR (KBr): $\tilde{\nu}$ = 3303 cm^{-1} (m, ν[NH]), 3059, 3031, 2987 (m, m, m, ν[CH_{ar}]), 2955, 2834 (w, w, ν[CH]), 1741 (m, ν[CO]), 1669 (w, ν[C–C_{ar}]), 1521 (m, δ[NH]), 1489 (w, ν[C–C_{ar}]), 1461, 1417, 1381 (w, m, m, δ[CH]), 1343 (m), 1301, 1243, 1211, 1096, 1060 (m, m, m, m, w, ν[C–O–C]), 1026 (w), 1009 (w). MS (EI): *m/z* (%) = 369 (11) [M^+ – CHO], 325 (19), 263 (34) [$C_{14}H_{19}N_2O_3^+$], 220 (21) [$C_{13}H_{18}NO_2^+$], 176 (9), 91 (100) [$C_7H_7^+$]. HRMS (EI): *m/z* calcd. for $C_{22}H_{26}N_2O_5$ 398.1842, found 398.1846. $C_{22}H_{26}N_2O_5$ (398.45): calcd. C 66.32, H 6.58, N 7.03; found C 66.28, H 6.66, N 7.11.

(+)-2-[*N*,*N*′-Bis(ethoxycarbonyl)hydrazino]-2-(3′-methoxyphenyl)-propionaldehyde (10c): The reaction was carried out according to GP 5 using L-proline (0.057 g, 0.49 mmol), 2-(3′-methoxyphenyl) propionaldehyde (**3c**) (0.165 g, 1.01 mmol) and diethyl azodicarboxylate (**8**) (0.190 g, 1.09 mmol) in 7.5 mL of dichloromethane within 4 d. Flash chromatography on silica (diethyl ether/pentane, 1:2) delivered 0.257 g (0.63 mmol, 62%) of a light yellow oil in 83% *ee*. R_f = 0.34 (diethyl ether/pentane, 1:2); HPLC (Chiracel OD, *n*-heptane/2-propanol 80:20, 0.6 mL/min): R_t(maj) = 18.5 min, R_t(min) = 24.0 min. $[a]_D^n$ = +44.95 (*c* = 1.21, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.13 (t, *J* = 7.0 Hz, 3 H, OCH_2CH_3), 1.21 (t, *J* = 7.1 Hz, 3 H, OCH_2CH_3), 1.61, 1.78 (br. s, 3 H, CR_3CH_3 rotamers), 3.81 (s, 3 H, $C_{ar}OCH_3$), 4.06–4.28 (m, 2 H, OCH_2CH_3 rotamers), 4.14 (q, *J* = 7.1 Hz, 2 H, OCH_2CH_3), 6.23, 6.42 (br. s, 1 H, NH rotamers), 6.86 (dd, *J* = 8.5, 1.3 Hz, 1 H, $C^{4'}H_{ar}$), 6.89–7.13 (m, 2 H, $C^{2'}H_{ar}$/$C^{6'}H_{ar}$), 7.31 (dd, *J* = 7.8, 7.8 Hz, 1 H, $C^{5'}H_{ar}$), 9.58, 9.75 (br. s, 1 H, CHO rotamers) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.4, 14.5 (OCH_2CH_3), 17.6 (CR_3CH_3), 55.4 ($C_{ar}OCH_3$), 62.4 (OCH_2CH_3), 63.4 (OCH_2CH_3), 73.3 (CR_3CH_3), 113.3, 113.5, 119.2, 130.2 ($C_{ar}H$), 138.5 ($C^{1'}{}_{ar}CR_3$), 156.2, 156.4 (NCO_2R), 159.3 ($C^{3'}{}_{ar}OCH_3$), 192.9 (CHO) ppm. IR (KBr): $\tilde{\nu}$ = 3301 cm^{-1} (m, ν[NH]), 2983, 2939 [m, w, ν[CH]], 2838 (w, ν[OCH_3]), 1732 (s, ν[CO]), 1600, 1584, 1491 (m, m, m, ν[C–C_{ar}]), 1467, 1378 (m, m, δ[CH]), 1243, 1048 (m, m, ν[C–O–C]) cm^{-1}. MS (EI, II, 70 eV): *m/z* (%) = 338 (4) [M^+], 309 (23) [M^+ – CHO], 265 (24) [$C_{13}H_{18}N_2O_4^+$], 237 (100) [$C_{12}H_{17}N_2O_3^+$], 221 (34) [$C_{11}H_{12}N_2O_3^+$], 191 (44) [$C_{10}H_{11}N_2O_2^+$], 176 (21) [$C_9H_8N_2O_2^+$], 163 (29) [$C_9H_{11}N_2O^+$], 148 (62) [$C_8H_8N_2O^+$], 135 (48), 107 (10) [$C_7H_7O^+$], 104 (14), 77 (15) [$C_6H_5^+$]. HRMS (II): *m/z* calcd. for $C_{16}H_{22}N_2O_6$ – CHO 309.1450, found 309.1445. $C_{16}H_{22}N_2O_6$ (338.36): calcd. C 56.80, H 6.55, N 8.28; found C 56.23, H 6.90, N 8.38.

(+)-2-[*N*,*N*′-Bis(ethoxycarbonyl)hydrazino]-2-(4′-fluorophenyl)-propionaldehyde (10f-Et): The reaction was carried out according to GP 5 using L-proline (0.115 g, 1.00 mmol), 2-(4-fluorophenyl)-propionaldehyde (**3f**) (0.304 g, 2.00 mmol) and diethyl azodicarboxylate (**8**) (0.348 g, 2.00 mmol) in 5 mL of dichloromethane within 5 d. Column chromatography on silica (diethyl ether/pentane, 1:2)

delivered 0.111 g (0.34 mmol, 17%) of a colorless oil with 68% *ee*. R_f = 0.50 (diethyl ether/pentane, 1:1); HPLC (Chiralpak AS, *n*-heptane/2-propanol 95:05, 0.6 mL/min): R_t(maj) = 26.5 min, R_t(min) = 29.5 min. $[a]_D^n$ = +34.12 (*c* = 1.00, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.20 (t, *J* = 7.1 Hz, 6 H, OCH_2CH_3), 1.63 (s, 3 H, CR_3CH_3), 4.13 (q, *J* = 7.1 Hz, 4 H, OCH_2CH_3), 6.75 (br. s, 1 H, NH rotamers), 6.91–7.38 (m, 4 H, CH_{ar}), 10.66, 10.72 (s, 1 H, CHO rotamers) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 14.4 (OCH_2CH_3), 26.9 (CR_3CH_3), 62.3, 62.8 (OCH_2CH_3), 77.3 (CR_3CH_3), 115.2, 115.4 ($C^{3'}{}_{ar}H$), 126.3, 126.6 ($C^{2'}{}_{ar}H$), 131.0 ($C^{1'}{}_{ar}CR_3$), 155.5, 158.4 (NCO_2R), 162.1 (d, *J* = 246.7 Hz, $C^{4'}{}_{ar}F$), 196.8 (CHO) ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ = –114.3 ppm. IR (KBr): $\tilde{\nu}$ = 3245 cm^{-1} (m, ν[NH]), 3040 (m, ν[CH_{ar}]), 2990, 2916, 2872 (m, m, w, ν[CH]), 2768 (w), 1752 (m, ν[CO]), 1698 (m), 1532 (m, δ[NH]), 1481 (m), 1448, 1358 (w, w, δ[CH]), 1249, 1112, 1069 (m, w, m, ν[C–O–C]), 1021 (w), 901 (w), 838 (w, δ[CH_{ar}]), 783, 760 (w, w, ν[CHal]) cm^{-1}. MS (EI): *m*/*z* (%) = 297 (16) [M^+ – CHO], 225 (61) [$C_{11}H_{15}FN_2O_2^+$], 210 (26) [$C_{11}H_{13}FNO_2^+$], 176 (100), 123 (93), 104 (91) [$C_8H_8^+$]. HRMS (EI): *m*/*z* calcd. for $C_{15}H_{19}FN_2O_5$ – CHO 297.1251, found 297.1252. $C_{15}H_{19}FN_2O_5$ (326.32): calcd. C 55.21, H 5.87, N 8.58; found C 55.44, H 5.98, N 8.45.

(+)-2-[*N*,*N*′-Bis(benzyloxycarbonyl)hydrazino]-2-(4′-fluorophenyl)-propionaldehyde (10f-Bn): The reaction was carried out according to GP 5 using L-proline (0.115 g, 1.00 mmol), 2-(4-fluoro-phenyl) propionaldehyde (**3f**) (0.304 g, 2.00 mmol) and dibenzyl azodicarboxylate (**9**) (0.597 g, 2.00 mmol) in 5 mL of dichloromethane within 5 d. Column chromatography on silica (diethyl ether/pentane, 1:2) delivered 0.260 g (0.58 mmol, 29%) of a colorless oil with 35% *ee*. R_f = 0.39 (diethyl ether/pentane, 1:2); HPLC (Chiralpak AS, *n*-heptane/2-propanol 80:20, 0.6 mL/min): R_t(maj) = 18.9 min, R_t(min) = 23.4 min. $[a]_D^n$ = +15.66 (*c* = 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.68–1.83 (m, 3 H, CR_3CH_3 rotamers), 5.10–5.19 (m, 4 H, OCH_2Ph rotamers), 6.80, 6.90 (br. s, 1 H, NH rotamers), 7.01–7.40 (m, 14 H, CH_{ar}), 9.63, 9.76 (s, 1 H, CHO rotamers) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 17.9 (CR_3CH_3), 68.1, 69.0 (OCH_2Ph), 72.8 (CR_3CH_3), 115.8, 116.0, 128.2, 128.5, 128.6, 128.7 ($C_{ar}H$), 131.1 ($C^{1'}{}_{ar}CR_3$), 135.0, 135.3 ($C^{1''}{}_{ar}CH_2R$), 156.0, 156.3 (NCO_2R), 162.5 (d, *J* = 248.2 Hz, $C^{4'}{}_{ar}F$), 192.1 (CHO) ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ = –113.3 ppm. IR (KBr): $\tilde{\nu}$ = 3293 cm^{-1} (m, ν[NH]), 3066, 3034 (w, w, ν[CH_{ar}]), 2955, 2898 (w, w, ν[CH]), 2714 (w), 1737 (m, ν[CO]), 1603 (w), 1511 (m, δ[NH]), 1455, 1422, 1348 (w, m, m, δ[CH]), 1240, 1166, 1104, 1062 (m, w, w, m, ν[C–O–C]), 1002 (w), 913 (w), 833 (w, δ[CH_{ar}]), 820, 739 (w, w, ν[CHal]) cm^{-1}. MS (EI): *m*/*z* (%) = 421 (7) [M^+ – CHO], 377 (11), 287 (14) [$C_{16}H_{16}FN_2O_2^+$], 272 (9) [$C_{16}H_{15}FNO_2^+$], 91 (100) [$C_7H_7^+$]. HRMS (EI): *m*/*z* calcd. for $C_{25}H_{23}FN_2O_5$ – CHO 421.1564, found 421.1566. $C_{25}H_{23}FN_2O_5$ (450.46): calcd. C 66.66, H 5.15, N 6.22; found C 66.36, H 5.20, N 6.40.

(+)-2-[*N*,*N*′-Bis(benzyloxycarbonyl)hydrazino]-2-(4′-chlorophenyl)-propionaldehyde (10g): The reaction was carried out according to GP 5 using L-proline (0.115 g, 1.00 mmol), 0.337 g (2.00 mmol) of 2-(4-chlorophenyl)propionaldehyde (**3g**) and of dibenzyl azodicarboxylate (**9**) (0.895 g, 3.00 mmol) in 15 mL of dichloromethane within 3 d. Column chromatography on silica (diethyl ether/pentane, 1:2) delivered 0.800 g (1.71 mmol, 86%) of a colorless oil with 61% *ee*. R_f = 0.42 (diethyl ether/pentane, 1:2); HPLC (Chiralpak AS, *n*-heptane/2-propanol 75:25, 0.5 mL/min): R_t(maj) = 33.4 min, R_t(min) = 26.3 min. $[a]_D^n$ = +24.15 (*c* = 1.00, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.56–1.70 (m, 3 H, CR_3CH_3 rotamers), 5.02–5.10 (m, 4 H, OCH_2Ph rotamers), 6.37, 6.51 (br. s, 1 H, NH rotamers), 7.13–7.31 (m, 14 H, CH_{ar}), 9.52, 9.65 (s, 1 H, CHO rotamers) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.9 (CR_3CH_3), 66.9, 68.0 (OCH_2Ph), 71.7 (CR_3CH_3), ($C^{4'}{}_{ar}Cl$), 127.2, 127.5, 127.6, 127.9, 128.1, 128.7 ($C_{ar}H$), 133.4 ($C^{1'}{}_{ar}CR_3$), 134.1, 134.4 ($C^{1''}{}_{ar}CH_2R$), 138.6 ($C^{4'}{}_{ar}Cl$), 154.8, 155.1 (NCO_2R), 191.5 (CHO) ppm. IR (KBr): $\tilde{\nu}$ = 3090 cm^{-1} (w, ν[CH_{ar}]), 3065 (m, ν[NH]), 3034 (m, ν[CH_{ar}]), 2957, 2897, 2840 (w, w, ν[CH]), 2715 (w), 1956 (vw), 1881 (w), 1725 (m, ν[CO]), 1588 (m, ν[C–C_{ar}]), 1494 (m, δ[NH]), 1455, 1402 (m, m, δ[CH]), 1343 (m), 1237, 1179, 1097, 1061 (m, m, m, m, ν[C–O–C]), 1013 (m), 983 (w), 909 (w), 828 (w, δ[CH_{ar}]), 741 (m, ν[CHal]) cm^{-1}. MS (EI): *m*/*z* (%) = 437 (1) [M^+ – CHO], 303 (3) [$C_{16}H_{16}ClN_2O_2^+$], 288 (2) [$C_{16}H_{15}ClNO_2^+$], 139 (11), 121 (11), 91 (100) [$C_7H_7^+$]. HRMS (EI): *m*/*z* calcd. for $C_{25}H_{23}ClN_2O_5$ – CHO 437.1268, found 437.1271. $C_{25}H_{23}ClN_2O_5$ (466.91): calcd. C 64.31, H 4.97, N 6.00; found C 64.09, H 5.03, N 5.97.

(+)-2-[*N*,*N*′-Bis(benzyloxycarbonyl)hydrazino]-2-(4′-bromophenyl)-propionaldehyde (10h): The reaction was carried out according to GP 5 using L-proline (0.288 g, 2.50 mmol), 2-(4-bromophenyl)propionaldehyde (**3h**) (1.065 g, 5.00 mmol) and dibenzyl azodicarboxylate (**9**) (1.491 g, 5.00 mmol) in 20 mL of dichloromethane within 3 d. Column chromatography on silica (diethyl ether/pentane, 1:2) delivered 1.800 g (3.52 mmol, 70%) of a colorless oil with 79% *ee*. R_f = 0.39 (diethyl ether/pentane, 1:2); the *ee* was determined by GC with chiral stationary phase: R_t(min) = 34.5 min, R_t(maj) = 35.2 min. $[a]_D^n$ = +36.87 (*c* = 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.55–1.68 (m, 3 H, CR_3CH_3 rotamers), 5.01–5.08 (m, 4 H, OCH_2Ph rotamers), 6.43, 6.53 (br. s, 1 H, NH rotamers), 7.10–7.40 (m, 14 H, CH_{ar}), 9.51, 9.64 (s, 1 H, CHO rotamers) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 17.9 (CR_3CH_3), 68.2, 69.1 (OCH_2Ph), 72.9 (CR_3CH_3), 122.7 ($C^{4'}{}_{ar}Br$), 128.5, 128.6, 128.7, 129.9 ($C_{ar}H$), 131.9, 132.1 ($C^{3'}{}_{ar}H$), 134.9 ($C^{1'}{}_{ar}CR_3$), 135.2, 135.5 ($C^{1''}{}_{ar}CH_2R$), 155.8, 156.1 (NCO_2R), 192.7 (CHO) ppm. IR (KBr): $\tilde{\nu}$ = 3301 cm^{-1} (m, ν[NH]), 3090 (w), 3065, 3033 (w, m, ν[CH_{ar}]), 2957, 2897 (w, w, ν[CH]), 1956 (vw), 1726 (m, ν[CO]), 1587, 1498 (m, w, ν[C–C_{ar}]), 1455, 1397 (m, m, δ[CH]), 1344 (m), 1265, 1179, 1066, (m, m, m, ν[C–O–C]), 1029 (m), 1010 (m), 976 (w), 912 (w), 825 (w, δ[CH_{ar}]), 748 (m, ν[CHal]) cm^{-1}. MS (EI): *m*/*z* (%) = 483/481 (1) [M^+ – CHO], 349/347 (1/2) [$C_{16}H_{16}BrN_2O_2^+$], 300 (5), 185/183 (4/5) [$C_7H_7BrN^+$], 121 (26), 107 (12), 91 (100) [$C_7H_7^+$]. HRMS (EI): *m*/*z* calcd. for $C_{25}H_{23}BrN_2O_5$ – CHO 481.0763, found 481.0766. $C_{25}H_{23}BrN_2O_5$ (511.36): calcd. C 58.72, H 4.53, N 5.48; found C 58.43, H 4.54, N 5.68.

(+)-2-[*N*,*N*′-Bis(ethoxycarbonyl)hydrazino]-2-(4′-trifluoromethyl-phenyl)propionaldehyde (10i-Et): The reaction was carried out according to GP 5 using L-proline (0.230 g, 2.00 mmol), 2-(4-trifluoromethylphenyl)propionaldehyde (**3i**) (0.809 g, 4.00 mmol) and diethyl azodicarboxylate (**8**) (0.697 g, 4.00 mmol) in 10 mL of dichloromethane within 5 d. Column chromatography on silica (diethyl ether/pentane, 1:2) delivered 0.280 g (0.74 mmol, 19%) of a colorless oil. The *ee* could not be determined by GC or HPLC with chiral stationary phase. R_f = 0.6 (diethyl ether/pentane, 1:1). $[a]_D^n$ = +45.67 (*c* = 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.28 (t, *J* = 7.2 Hz, 6 H, OCH_2CH_3), 1.72 (s, 3 H, CR_3CH_3), 4.21 (q, *J* = 7.2 Hz, 4 H, OCH_2CH_3), 6.87, 6.90 (br. s, 1 H, NH rotamers), 7.57 – 7.66 (m, 4 H, CH_{ar}), 10.75, 10.83 (s, 1 H, CHO rotamers) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.3 (OCH_2CH_3), 26.6 (CR_3CH_3), 62.7, 63.0 (OCH_2CH_3), 98.6 (CR_3CH_3), 125.1, 125.2, 125.4 ($C_{ar}H$), 123.9 (q, *J* = 275.0 Hz, $C^{4'}{}_{ar}CF_3$), 129.9 (q, *J* = 32.4 Hz, $C^{4'}{}_{ar}CF_3$), 130.4 ($C^{1'}{}_{ar}CR_3$), 158.2, 159.0 (NCO_2R), 197.4 (CHO) ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ = –62.6 ppm. IR (KBr): $\tilde{\nu}$ = 3245 cm^{-1} (m, ν[NH]), 3039 (m, ν[CH_{ar}]), 2990, 2955, 2915 (w, w, w, ν[CH]), 1752 (m, ν[CO]), 1620 (w, ν[C–C_{ar}]), 1532 (m, δ[NH]), 1448, 1412 (w, w, δ[CH]), 1329 (m), 1245, 1169, 1128, 1068 (w, w, w, w, ν[C–O–C]), 901 (w), 846 (w, δ[CH_{ar}]), 783 (w, ν[CHal]) cm^{-1}. MS (EI): *m*/*z* (%) = 347 (7) [M^+ – CHO], 303 (7),

275 (60) [$C_{12}H_{14}F_3N_2O_2^+$], 205 (79), 188 (29) [$C_9H_9F_3N$], 173 (100) [$C_9H_8F_3$], 145 (45) [$C_7H_4F_3^+$]. HRMS (EI): *m/z* calcd. $C_{16}H_{19}F_3N_2O_5$ – CHO 347.1219, found 347.1217. $C_{16}H_{19}F_3N_2O_5$ (376.33): calcd. C 51.07, H 5.09, N 7.44; found C 50.92, H 5.17, N 7.52.

(+)-2-[*N*,*N*′-Bis(benzyloxycarbonyl)hydrazino]-2-(4′-trifluoromethylphenyl)propionaldehyde (10i-Bn): The reaction was carried out according to GP 5 using L-proline (0.230 g, 2.00 mmol), 2-(4-trifluoromethylphenyl)propionaldehyde (**3i**) (0.809 g, 4.00 mmol) and dibenzyl azodicarboxylate (**9**) (1.491 g, 5.00 mmol) in 10 mL of dichloromethane within 3 d. Column chromatography on silica (diethyl ether/pentane, 1:2) delivered 0.780 g (1.56 mmol, 40%) of a colorless oil. The *ee* could not be determined by GC or HPLC with chiral stationary phase. R_f = 0.6 (diethyl ether/pentane, 1:1). $[a]_D^n$ = +39.73 (*c* = 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.68–1.80 (m, 3 H, CR_3CH_3), 5.09–5.22 (m, 4 H, OCH_2Ph), 6.61–6.85 (m, 1 H, NH rotamers), 7.31–7.65 (m, 4 H, CH_{ar}), 9.68, 9.80 (s, 1 H, CHO rotamers) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 26.8 (CR_3CH_3), 68.3, 69.1 (OCH_2Ph), 72.9 (CR_3CH_3), 124.6, 124.9, 125.1 ($C_{ar}H$), 125.2 (q, *J* = 269.0 Hz, $C^{4'}{}_{ar}CF_3$), 129.9 (q, *J* = 32.0 Hz, $C^{4'}{}_{ar}CF_3$), 134.8, 135.1 ($C^{1''}{}_{ar}CH_2R$), 141.1 ($C^{1'}{}_{ar}CR_3$), 155.8, 156.2 (NCO_2R), 192.9 (CHO) ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ = –62.9 ppm. IR (KBr): $\tilde{\nu}$ = 3301 cm^{-1} (m, ν[NH]), 3067, 3035 (m, m, ν[CH_{ar}]), 2959, 2899, 2841 (m, w, w, ν[CH]), 2290 (vw), 1955 (vw), 1726 (m, ν[CO]), 1619 (m, ν[C–C_{ar}]), 1587 (m, δ[NH]), 1500 (m, ν[C–C_{ar}]), 1454, 1410 (m, m, δ[CH]), 1327 (m), 1167, 1066 (m, m, ν[C–O–C]), 1016 (m), 983 (w), 910 (w), 845 (m, δ[CH_{ar}]), 745 (m, ν[CHal]) cm^{-1}. MS (EI): *m/z* (%) = 471 (3) [M^+ – CHO], 427 (15), 337 (12) [$C_{17}H_{16}F_3N_2O_2^+$], 322 (5) [$C_{17}H_{15}F_3NO_2^+$], 173 (27) [$C_9H_8F_3^+$], 91 (100) [$C_7H_7^+$]. HRMS (EI) *m/z* calcd. for $C_{26}H_{23}F_3N_2O_5$ – CHO 471.1531, found 471.1535. $C_{26}H_{23}F_3N_2O_5$ (500.47): calcd. C 62.40, H 4.63, N 5.60; found C 62.69, H 4.70, N 5.51.

(+)-2-[*N*,*N*′-Bis(ethoxycarbonyl)hydrazino]-2-(4′-nitrophenyl)-propionaldehyde (10j-Et): The reaction was carried out according to GP 5 using L-proline (0.115 g, 1.00 mmol), 2-(4-nitrophenyl)propionaldehyde (**3j**) (0.394 g, 2.00 mmol) and of diethyl azodicarboxylate (**8**) (0.479 g, 2.75 mmol) in 5 mL of dichloromethane within 2 d. Column chromatography on silica (diethyl ether/pentane, 1:1) delivered 0.600 g (1.70 mmol, 85%) of a yellow solid (36% *ee*). R_f = 0.36 (diethyl ether/pentane, 1:1); m.p. 41 °C; HPLC (Chiralcel OD, *n*-heptane/2-propanol 90:10, 0.7 mL/min): R_t(maj) = 11.5 min, R_t(min) = 10.1 min. $[a]_D^n$ = +7.22 (*c* = 1.00, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.24 (t, *J* = 7.1 Hz, 3 H, OCH_2CH_3), 1.31 (t, *J* = 7.1 Hz, 3 H, OCH_2CH_3), 1.71, 1.74 (br. s, CR_3CH_3 rotamers), 4.17, 4.28 (q, *J* = 7.1 Hz, 2 H, OCH_2CH_3 rotamers), 6.86, 7.07 (br. s, 1 H, NH rotamers), 7.62 (d, *J* = 8.5 Hz, 2 H $C^{2'}H_{ar}$), 8.19 (m, *J* = 8.7 Hz, 2 H, $C^{3'}H_{ar}$), 9.65, 9.74 (s, 1 H, CHO rotamers) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.2, 14.4 (OCH_2CH_3), 19.4 (CR_3CH_3), 62.3, 63.6 (OCH_2CH_3), 72.5 (CR_3CH_3), 123.7 ($C^{3'}{}_{ar}H$), 127.7 ($C^{2'}{}_{ar}H$), 145.1 ($C^{1'}{}_{ar}CR_3$), 147.3 ($C^{4'}{}_{ar}NO_2$), 155.8, 157.0 (NCO_2R), 193.5, 194.6 (CHO rotamers) ppm. IR (KBr): $\tilde{\nu}$ = 3307 cm^{-1} (m, ν[NH]), 3081 (vw, ν[CH_{ar}]), 2885, 2940, 2871 (w, w, w, ν[CH]), 2721 (vw), 2459 (vw), 1727 (m, ν[CO]), 1606 (w), 1521 (m, ν[NO_2]), 1407 (w, δ[CH]), 1346 (m, δ[NO_2]), 1095, 1064 (w, w, ν[C–O–C]), 1014 (w), 922 (w), 856 (w, δ[CH_{ar}]), 767 (w) cm^{-1}. MS (EI): *m/z* (%) = 354 (15) [M^+ + H], 324 (4) [M^+ – CHO], 252 (100) [$C_{11}H_{14}N_3O_4^+$], 165 (40) [$C_8H_9N_2O_2^+$], 117 (64). HRMS (EI): *m/z* calcd. for $C_{15}H_{19}N_3O_7$ + H 354.1301, found 354.1305. $C_{15}H_{19}N_3O_7$ (353.33): calcd. C 50.99, H 5.42, N 11.89; found C 50.92, H 5.56, N 11.58.

(+)-2-[*N*,*N*′-Bis(benzyloxycarbonyl)hydrazino]-2-(4′-nitrophenyl)propionaldehyde (10j-Bn): The reaction was carried out according to GP 5 using L-proline (0.173 g, 1.50 mmol), 2-(4-nitrophenyl)propionaldehyde (**3j**) (0.493 g, 2.50 mmol) and dibenzyl azodicarboxylate (**9**) (1.193 g, 4.00 mmol) in 10 mL of dichloromethane within 2 d. Column chromatography on silica (diethyl ether/pentane, 1:1) delivered 1.184 g (2.48 mmol, 99%) of a yellow solid with 56% *ee*. R_f = 0.38 (diethyl ether/pentane, 1:1); m.p. 39 °C; HPLC (Chiralcel OD, *n*-heptane/2-propanol 90:10, 0.7 mL/min): R_t(maj) = 34.7 min, R_t(min) = 52.1 min. $[a]_D^n$ = +12.92 (*c* = 1.00, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.62, 1.69 (br. s, 3 H, CR_3CH_3 rotamers), 5.03–5.10 (m, 4 H, OCH_2Ph rotamers), 6.51, 6.68 (br. s, 1 H, NH rotamers), 7.19–8.07 (m, 14 H, CH_{ar}), 9.61, 9.71 (s, 1 H, CHO rotamers) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 19.4 (CR_3CH_3), 68.0, 69.2 (OCH_2Ph), 72.7 (CR_3CH_3), 123.8, 127.6, 128.2, 128.5, 128.6, 128.7 ($C_{ar}H$), 134.7, 135.4 ($C^{1''}{}_{ar}CH_2R$), 144.6 ($C^{1'}{}_{ar}CR_3$), 147.4 ($C^{4'}{}_{ar}NO_2$), 155.6, 156.4 (NCO_2R), 192.2 (CHO) ppm. IR (KBr): $\tilde{\nu}$ = 3288 cm^{-1} (m, ν[NH]), 3034 (w, ν[CH_{ar}]), 2899, 2834 (w, w, ν[CH]), 2720 (vw), 2455 (vw), 1953 (vw), 1744 (m, ν[CO]), 1695, 1674 (m, m, ν[C–C_{ar}]), 1606 (w), 1519 (m, ν[NO_2]), 1456, 1425 (m, m, δ[CH]), 1345 (m, δ[NO_2]), 1292, 1262, 1235, 1157, 1112, 1062 (m, m, m, w, w, m, ν[C–O–C]), 1003 (w), 960 (w), 918 (w), 855 (w, δ[CH_{ar}]), 740 (m) cm^{-1}. MS (EI): *m/z* (%) = 448 (1) [M^+ – CHO], 314 (10) [$C_{16}H_{16}N_3O_4^+$], 91 (100) [$C_7H_7^+$]. HRMS (EI): *m/z* calcd. for $C_{25}H_{23}N_3O_7$ – CHO 448.1508, found 448.1505. $C_{25}H_{23}N_3O_7$ (477.47): calcd. C 62.89, H 4.86, N 8.80; found C 62.72, H 4.97, N 8.77.

(+)-2-[*N*,*N*′-Bis(benzyloxycarbonyl)hydrazino]-2-(4′-cyanophenyl)-propionaldehyde (10k): The reaction was carried out according to GP 5 using L-proline (0.230 g, 2.00 mmol), 2-(4-cyanophenyl)propionaldehyde (**3k**) (0.637 g, 4.00 mmol) and dibenzyl azodicarboxylate (**9**) (1.491 g, 5.00 mmol) in 20 mL of dichloromethane within 3 d. Column chromatography on silica (diethyl ether/pentane, 1:2) delivered 1.135 g (2.48 mmol, 62%) of a colorless oil with 53% *ee*. R_f = 0.56 (diethyl ether/pentane, 2:1); HPLC (Chiralcel OD, *n*-heptane/2-propanol 90:10, 1.0 mL/min): R_t(maj) = 51.1 min, R_t(min) = 42.9 min. $[a]_D^n$ = +12.62 (*c* = 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.55–1.66 (m, 3 H, CR_3CH_3 rotamers), 5.02–5.14 (m, 4 H, OCH_2Ph rotamers), 6.62, 6.72 (br. s, 1 H, NH rotamers), 7.21–7.51 (m, 14 H, CH_{ar}), 9.57, 9.68 (s, 1 H, CHO rotamers) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 19.0 (CR_3CH_3), 68.4, 69.2 (OCH_2Ph), 72.8 (CR_3CH_3), 112.0 ($C^{4'}{}_{ar}CN$), 118.4 ($C^{4'}{}_{ar}CN$), 125.7 ($C^{2'}{}_{ar}H$), 127.5, 128.0, 128.3, 128.6, 128.7 ($C_{ar}H$), 132.5 ($C^{3'}{}_{ar}H$), 134.0 ($C^{1'}{}_{ar}CR_3$), 134.7, 135.1 ($C^{1''}{}_{ar}CH_2R$), 155.6, 155.9 (NCO_2R), 192.9 (CHO) ppm. IR (KBr): $\tilde{\nu}$ = 3300 cm^{-1} (m, ν[NH]), 3065 (w), 3034 (m, ν[CH_{ar}]), 2898, 2835 (w, w, ν[CH]), 2229 (m, ν[CN]), 1956 (vw), 1737 (m, ν[CO]), 1608 (w, ν[C–C_{ar}]), 1587 (w), 1500 (m, δ[NH]), 1455, 1402 (m, w, δ[CH]), 1342 (m), 1234, 1179, 1060 (m, m, m, ν[C–O–C]), 981 (w), 909 (w), 839 (w, δ[CH_{ar}]), 743 (m) cm^{-1}. MS (EI): *m/z* (%) = 428 (1) [M^+ – CHO], 300 (13), 145 (14) [$C_9H_9N_2^+$], 130 (44) [$C_9H_8N^+$], 91 (100) [$C_7H_7^+$]. HRMS (EI): *m/z* calcd. for $C_{26}H_{23}N_3O_5$ – CHO 428.1610, found 428.1609. $C_{26}H_{23}N_3O_5$ (457.48): calcd. C 68.26, H 5.07, N 9.19; found C 68.44, H 5.14, N 9.24.

(+)-2-[*N*,*N*′-Bis(benzyloxycarbonyl)hydrazino]-2-(3′,5′-dibenzyloxyphenyl)propionaldehyde (10r): The reaction was carried out according to GP 5 using L-proline (0.029 g, 0.25 mmol), 2-(3′,5′-dibenzyloxyphenyl)propionaldehyde **3r** (0.175 g, 0.51 mmol) and dibenzyl azodicarboxylate (**9**) (0.181 g, 0.61 mmol) in 5.0 mL of dichloromethane within 7 d. Flash chromatography on silica (diethyl ether/pentane, 1:2) delivered 0.188 g (0.29 mmol, 58%) of a colorless solid in 72% *ee*. R_f = 0.62 (diethyl ether/pentane, 2:1); m.p. 126 °C; HPLC (Chiracel OD, *n*-heptane/2-propanol 90:10, 0.5 mL/min): R_t(maj) = 58.8 min, R_t(min) = 63.8 min. $[a]_D^n$ = +5.12 (*c* = 0.195, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.69, 1.76 (2 ×br.

s, 3 H, CR_3CH_3 rotamers), 4.99, 5.12 (br. s, 8 H, OCH_2Ph rotamers), 6.03, 6.86 (2br. s, 1 H, NH rotamers), 6.57 (br. s, 3 H, $C^{2'}H_{ar}/C^{4'}H_{ar}$), 7.08–7.49 (m, 20 H, Bn-CH_{ar}), 9.53, 9.70 (2br. s, 1 H, CHO rotamers) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 17.4 (CR_3CH_3), 68.1, 69.0 (OCH_2Ph), 70.3 ($C^{3'}{}_{ar}OCH_2$), 73.6 (CR_3CH_3), 101.9 ($C^{4'}{}_{ar}H$), 106.7 ($C^{2'}{}_{ar}H$), 127.7, 128.3, 128.3, 128.6, 128.6, 128.7, 128.8 (Bn-$C_{ar}H$), 135.2, 135.5 ($C^{1''}{}_{ar}CH_2R$), 136.7 ($C_{ar}OCH_2C_{ar}$), 138.9 ($C^{1'}{}_{ar}CR_3$), 156.0, 156.2 (NCO_2R), 160.5 ($C^{3'}{}_{ar}OBn$), 191.9 (CHO) ppm. IR (KBr): $\tilde{\nu}$ = 3321 cm^{-1} (w, ν[NH]), 3065, 3036 (vw, w, $\nu[CH_{ar}]$), 2917 (vw, ν[CH]), 2864 (vw, $\nu[OCH_2]$), 1752 (w, ν[CO]), 1730 (w, ν[CO]), 1596, 1519 (w, w, ν[C–C_{ar}]), 1455, 1442, 1383 (w, δ[CH]), 1253, 1227, 1054, 1035 (w, w, w, w, ν[C–O–C]) cm^{-1}. MS (EI, II, 70 eV): *m*/*z* (%) = 644 (5) [M^+], 571 (22), 481 (5) [M^+ – CO–CO_2Bn], 330 (6) [$C_{22}H_{18}O_3{}^+$], 181 (7), 91 (100) [$C_7H_7{}^+$]. HRMS (II): *m*/*z* calcd. for $C_{39}H_{36}N_2O_7$ 644.2523; found 644.2522. $C_{39}H_{36}N_2O_7$ (644.71): calcd. C 72.66, H 5.63, N 4.35; found C 72.48, H 5.72, N 4.24.

(+)-2-[*N*,*N*′-Bis(benzyloxycarbonyl)hydrazino]-2-(thiophen-2-yl)propionaldehyde (10n): The reaction was carried out according to GP 5 using L-proline (0.058 g, 0.50 mmol), 2-(thiophen-2-yl)propionaldehyde (**3n**) (0.140 g, 1.00 mmol) and dibenzyl azodicarboxylate (**9**) (0.447 g, 1.50 mmol) in 20 mL of dichloromethane within 3 d. Column chromatography on silica (diethyl ether/pentane, 1:2) delivered 0.232 g (0.53 mmol, 53%) of a brown oil with 70% *ee*. R_f = 0.35 (diethyl ether/pentane, 1:1); HPLC (Chiralpak AS, *n*-heptane/2-propanol 75:25, 0.5 mL/min): R_t(maj) = 31.5 min, R_t(min) = 40.5 min. $[a]_D^n$ = +27.52 (*c* = 1.00, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ = 1.54–1.78 (m, 3 H, CR_3CH_3 rotamers), 5.00–5.10 (m, 4 H, OCH_2Ph rotamers), 6.25, 6.48 (br. s, 1 H, NH rotamers), 6.92–7.25 (m, 13 H, CH_{ar}), 9.39, 9.50 (s, 1 H, CHO rotamers) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 19.4 (CR_3CH_3), 68.1, 69.1 (OCH_2Ph), 71.2 (CR_3CH_3), 98.5 ($C^{4'}{}_{ar}H$), 124.5 ($C^{5'}{}_{ar}H$), 126.6, 126.7, 127.3, 128.2, 128.6 ($C_{ar}H$), 128.7 ($C^{3'}{}_{ar}H$), 135.0, 135.3 ($C^{1''}{}_{ar}CH_2R$), 139.9 ($C^{2'}{}_{ar}CR_3$), 155.7, 156.1 (NCO_2R), 191.1 (CHO) ppm. IR (KBr): $\tilde{\nu}$ = 3301 cm^{-1} (m, ν[NH]), 3065 (w), 3033 (m, $\nu[CH_{ar}]$), 2957, 2897, 2831 (w, w, w, ν[CH]), 1958 (vw), 1727 (m, ν[CO]), 1608 (w, ν[C–C_{ar}]), 1587 (w), 1499 (m, δ[NH]), 1455, 1401 (m, m, δ[CH]), 1343 (m), 1238, 1177, 1060 (m, m, m, ν[C–O–C]), 983 (w), 910 (w), 853 (w, $\delta[CH_{ar}]$), 740 (m, ν[CS]) cm^{-1}. MS (EI): *m*/*z* (%) = 409 (4) [M^+ – CHO], 365 (3), 275 (5) [$C_{14}H_{15}N_2O_2S^+$], 91 (100) [$C_7H_7{}^+$]. HRMS (EI): *m*/*z* calcd. for $C_{23}H_{22}N_2O_5S$ – CHO 409.1222, found 409.1224. $C_{23}H_{22}N_2O_5S$ (438.50): calcd. C 63.00, H 5.06, N 6.39; found C 63.31, H 5.14, N 6.43.

(+)-2-[*N*,*N*′-Bis(benzyloxycarbonyl)hydrazino]-2-(4′-biphenyl-4-yl)-propionaldehyde (10o): The reaction was carried out according to GP 5 using L-proline (0.058 g, 0.50 mmol), 2-(4-biphenyl)propionaldehyde (**3o**) (0.210 g, 1.00 mmol) and dibenzyl azodicarboxylate (**9**) (0.447 g, 1.50 mmol) in 20 mL of dichloromethane within 3 d. Column chromatography on silica (diethyl ether/pentane, 1:3) delivered 0.305 g (0.60 mmol, 60%) of a colorless oil with 84% *ee*. R_f = 0.45 (diethyl ether/pentane, 1:3); HPLC (Chiralpak AS, *n*-heptane/2-propanol 70:30, 1.0 mL/min): R_t(maj) = 41.8 min, R_t(min) = 51.8 min. $[a]_D^n$ = +22.23 (*c* = 1.00, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ = 1.64–1.78 (m, 3 H, CR_3CH_3 rotamers), 5.00–5.19 (m, 4 H, OCH_2Ph rotamers), 6.29, 6.50 (br. s, 1 H, NH rotamers), 7.18–7.23 (m, 10 H, CH_{ar}), 7.29 (t, *J* = 7.3 Hz, 2 H, CH_{ar}), 7.37 (t, *J* = 7.5 Hz, 3 H, CH_{ar}), 7.49 (t, *J* = 8.1 Hz, 4 H, CH_{ar}), 9.56, 9.72 (s, 1 H, CHO rotamers) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 17.7 (CR_3CH_3), 68.2, 69.0 (OCH_2Ph), 73.3 (CR_3CH_3), 127.1 ($C^{2'}{}_{ar}H$), 127.4 ($C^{4''}{}_{ar}H$), 127.7, 127.8 ($C^{4'''}{}_{ar}H$), 128.2, 128.5, 128.6 ($C_{ar}H$), 128.9 ($C^{3''}{}_{ar}H$), 135.0, 135.1, 135.5 ($C^{1'}{}_{ar}CR_3$), 140.2 ($C^{4'}{}_{ar}Ph$), 141.3 ($C^{1''}{}_{ar}Ph$), 156.0, 156.4 (NCO_2R), 192.5 (CHO) ppm. IR (KBr): $\tilde{\nu}$ = 3421 cm^{-1} (w), 3255 (m, ν[NH]), 3064, 3028, (m, m, $\nu[CH_{ar}]$), 2954, 2851 (m, m, ν[CH]), 1805 (w), 1725 (m, ν[CO]), 1697 (m, ν[C–C_{ar}]), 1604 (m), 1526 (m, δ[NH]), 1497 (m, ν[C–C_{ar}]), 1456, 1436, 1404 (m, m, m, δ[CH]), 1351 (m), 1238, 1180, 1140, 1123, 1066, 1051 (m, m, m, m, m, m, ν[C–O–C]), 1029 (m), 1008 (m), 987 (m), 960 (w), 943 (m), 904 (m), 850, 826 (m, m, $\delta[CH_{ar}]$), 764 (m), 734 (m). MS (EI): *m*/*z* (%) = 479 (3) [M^+ – CHO], 435 (9), 345 (10) [$C_{22}H_{21}N_2O_2{}^+$], 196 (34), 181 (100) [$C_{13}H_{11}N^+$], 152 (85), 127 (14), 121 (97), 91 (66) [$C_7H_7{}^+$]. HRMS (EI): *m*/*z* calcd. for $C_{31}H_{28}N_2O_5$ – CHO 479.1970, found 479.1969. $C_{31}H_{28}N_2O_5$ (508.56): calcd. C 73.21, H 5.55, N 5.51; found C 73.36, H 5.47, N 5.45.

Acknowledgments

Financial support from the DFG (SPP 1085, CFN) and the BMBF is gratefully acknowledged.

[1] For reviews, see the following: a) R. M. Williams, J. A. Hendrix, *Chem. Rev.* **1992**, *92*, 889; b) T. Wirth, *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 225; c) D. Seebach, A. R. Sting, M. Hoffmann, *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 2708.
[2] a) J. E. Baldwin, V. Lee, C. J. Schofield, *Heterocycles* **1992**, *34*, 903; b) W. D. Shrader, C. K. Marlowe, *Bioorg. Med. Chem. Lett.* **1995**, *5*, 2207; c) R. Badorrey, C. Cativiela, M. D. Diaz-de-Villegas, J. A. Galvez, *Tetrahedron: Asymmetry* **1995**, *6*, 2787; d) R. J. Boyce, G. C. Mulqueen, G. Pattenden, *Tetrahedron* **1995**, *51*, 7321; e) E. Gershonov, R. Granoth, E. Tzehoval, Y. Gaoni, M. Fridkin, *J. Med. Chem.* **1996**, *39*, 4833.
[3] a) J. S. Bedingfield, M. C. Kemp, D. E. Jane, H. W. Tse, P. J. Roberts, J. C. Watkins, *Br. J. Pharmacol.* **1995**, *116*, 3323; b) N. Sekiyama, Y. Hayashi, S. Nakanishi, D. E. Jane, H. W. Tse, E. F. Birse, J. C. Watkins, *Br. J. Pharmacol.* **1996**, *117*, 1493.
[4] J. R. Cronin, S. Pizzarello, *Adv. Space Res.* **1999**, *23*, 293.
[5] J.-P. Mazaleyrat, M. Wakselman, F. Formaggio, M. Crisma, C. Toniolo, *Tetrahedron Lett.* **1999**, *40*, 6245.
[6] S. Abele, D. Seebach, *Eur. J. Org. Chem.* **2000**, 1–15 and references herein.
[7] a) S. H. Lee, E. K. Lee, *Bull. Korean Chem. Soc.* **2001**, *22*, 551; b) E. Vedejs, S. C. Fields, R. Hayashi, S. R. Hitchcock, D. R. Powell, M. R. Schrimpf, *J. Am. Chem. Soc.* **1999**, *121*, 2460; c) C. Spino, C. Gobdout, *J. Am. Chem. Soc.* **2003**, *125*, 12106.
[8] For a review, see: K. Maruoka, T. Ooi, *Chem. Rev.* **2003**, *103*, 3013 and references cited therein.
[9] a) C. Gennari, L. Colombo, G. Bertolini, *J. Am. Chem. Soc.* **1986**, *108*, 6394; b) D. A. Evans, T. C. Britton, R. L. Dorow, J. F. Dellaria Jr, *J. Am. Chem. Soc.* **1986**, *108*, 6395; c) L. A. Trimble, J. C. Vederas, *J. Am. Chem. Soc.* **1986**, *108*, 6397; d) W. Oppolzer, R. Moretti, *Helv. Chim. Acta* **1986**, *69*, 1923.
[10] a) U. Schöllkopf, *Pure Appl. Chem.* **1983**, *55*, 1799; b) Y. Hsiao, L. S. Hegedus, *J. Org. Chem.* **1997**, *62*, 3586; c) L. Zhang, J. M. Finn, *J. Org. Chem.* **1995**, *60*, 5719; d) A. B. Smith, A. B. Benowitz, D. A. Favor, P. A. Sprengeler, R. Hirschmann, *Tetrahedron Lett.* **1997**, *38*, 3809.
[11] a) D. B. Berkowitz, M. K. Smith, *J. Org. Chem.* **1995**, *60*, 1233; b) M. Ihara, M. Takahashi, H. Niitsuma, N. Taniguchi, K. Yasui, K. Fukumoto, *J. Org. Chem.* **1989**, *54*, 5413.
[12] a) D. Ma, H. Tian, G. Zou, *J. Org. Chem.* **1999**, *64*, 120; b) F. A. Davis, S. Lee, H. Zhang, D. L. Fanelli, *J. Org. Chem.* **2000**, *65*, 8704; c) P. Vachal, E. N. Jacobsen, *Org. Lett.* **2000**, *2*, 867.
[13] T. K. Chakraborty, K. A. Hussain, G. V. Reddy, *Tetrahedron* **1995**, *51*, 9179.
[14] A. A. Cordi, J.-M. Lacoste, F. L. Borgne, Y. Herve, L. Vaysse-Ludot, J.-J. Descombes, C. Courchay, M. Laubie, T. J. Verbeuren, *J. Med. Chem.* **1997**, *40*, 2931 and references cited therein.

[15] a) S. Yamasaki, T. Iida, M. Shibasaki, *Tetrahedron* **1999**, *55*, 8857; b) K. Juhl, N. Gathergood, K. A. Jørgensen, *Angew. Chem.* **2001**, *113*, 3083; *Angew. Chem. Int. Ed.* **2001**, *40*, 2995; c) W. Notz, K. Sakthivel, T. Bui, C. F. Barbas III, *Tetrahedron Lett.* **2001**, *42*, 199; d) A. Cordova, W. Notz, G. Zhong, J. M. Betancort, C. F. Barbas III, *J. Am. Chem. Soc.* **2002**, *124*, 1842; e) A. Cordova, S.-I. Watanabe, F. Tanaka, W. Notz, C. F. Barbas III, *J. Am. Chem. Soc.* **2002**, *124*, 1866; f) N. S. Chowdari, D. B. Ramachary, C. F. Barbas III, *Synlett* **2003**, 1906; g) W. Notz, F. Tanaka, S.-I. Watanabe, N. S. Chowdari, R. Thayumanavan, C. F. Barbas III, *J. Org. Chem.* **2003**, *68*, 9624; h) B. List, P. Pojarliev, W. T. Biller, H. J. Martin, *J. Am. Chem. Soc.* **2002**, *124*, 827; i) A. J. A. Cobb, D. M. Shaw, S. V. Ley, *Synlett* **2004**, 558; j) W. Zhuang, S. Saaby, K. A. Jørgensen, *Angew. Chem. Int. Ed.* **2004**, *43*, 476; k) N. S. Chowdari, J. T. Suri, C. F. Barbas III, *Org. Lett.* **2004**, *6*, 2507.

[16] a) A. Bogevig, K. Juhl, N. Kumaragurubaran, W. Zhuang, K. A. Jørgensen, *Angew. Chem. Int. Ed.* **2002**, *41*, 1790; b) N. Kumaragurubaran, K. Juhl, W. Zhuang, A. Bogevig, K. A. Jørgensen, *J. Am. Chem. Soc.* **2002**, *124*, 6254; c) B. List, *J. Am. Chem. Soc.* **2002**, *124*, 5656; d) H. Iwamura, S. P. Mathew, D. G. Blackmond, *J. Am. Chem. Soc.* **2004**, *126*, 11770.

[17] a) B. List, *J. Am. Chem. Soc.* **2002**, *124*, 5656; b) A. Bøgevig, K. Juhl, N. Kumaragurubaran, W. Zhuang, K. A. Jørgensen, *Angew. Chem.* **2002**, *114*, 1868; *Angew. Chem. Int. Ed.* **2002**, *41*, 1790. For a review see: R. O. Duthaler, *Angew. Chem.* **2003**, *115*, 1005; *Angew. Chem. Int. Ed.* **2003**, *42*, 975.

[18] H. Vogt, S. Vanderheiden, S. Bräse, *Chem. Commun.* **2003**, 2448.

[19] S. Danishefsky, D. F. Harvey, *J. Am. Chem. Soc.* **1985**, *107*, 6647.

[20] a) E. J. Corey, M. Chaykovsky, *J. Am. Chem. Soc.* **1962**, *84*, 867; b) E. J. Corey, M. Chaykovsky, *J. Am. Chem. Soc.* **1962**, *84*, 3782; c) E. J. Corey, M. Chaykovsky, *J. Am. Chem. Soc.* **1965**, *87*, 1353.

[21] M. Lemaire, I. Karame, M. L. Tommasino, *Tetrahedron Lett.* **2003**, *44*, 7687.

[22] a) N. S. Chowdari, J. T. Suri, C. F. Barbas III, *Org. Lett.* **2004**, *6*, 2507; b) A. Cordova, S.-I. Watanabe, F. Tanaka, W. Notz, C. F. Barbas III, *J. Am. Chem. Soc.* **2002**, *124*, 1866; c) A. Cordova, W. Notz, G. Zhong, J. M. Betancort, C. F. Barbas III, *J. Am. Chem. Soc.* **2002**, *124*, 1842; d) R. Thayumanavan, F. Tanaka, C. F. Barbas III, *Org. Lett.* **2004**, *6*, 3541.

[23] a) S. Bahmanyar, K. N. Houk, *J. Am. Chem. Soc.* **2001**, *123*, 12911; b) S. Bahmanyar, K. N. Houk, *J. Am. Chem. Soc.* **2001**, *123*, 11273; c) L. Hoang, S. Bahmanyar, K. N. Houk, B. List, *J. Am. Chem. Soc.* **2003**, *125*, 16; d) S. Bahmanyar, K. N. Houk, H. J. Martin, B. List, *J. Am. Chem. Soc.* **2003**, *125*, 2475.

[24] S. Bahmanyar, K. N. Houk, *Org. Lett.* **2003**, *5*, 1249.

[25] a) H. Iwamura, S. P. Mathew, D. G. Blackmond, *J. Am. Chem. Soc.* **2004**, *126*, 11770; b) H. Iwamura, S. P. Mathew, D. G. Blackmond, *J. Am. Chem. Soc.* **2004**, *126*, 16312.

[26] S. P. Mathew, H. Iwamura, D. G. Blackmond, *Angew. Chem. Int. Ed.* **2004**, *43*, 3317.

[27] H. Pietsch, *Tetrahedron Lett.* **1972**, *27*, 2789 {$[a]_D^n$ = +107.2 (*c* = 3, CH_3OH), (*S*)-enantiomer; found: $[a]_D^n$ = –84.3 (*c* = 1, $CHCl_3$)}.

[28] J. T. Suri, D. D. Steiner, C. F. Barbas III, *Org. Lett.* **2005**, *7*, 3885.

[29] H. Ding, G. K. Friestad, *Org. Lett.* **2004**, *6*, 637.

[30] H. E. Gottlieb, V. Kotlyar, A. Nudelman, *Org. Chem.* **1997**, *62*, 7512.

[31] S. Danishefsky, D. F. Harvey, *J. Am. Chem. Soc.* **1985**, *107*, 6647.

Received: July 27, 2006
Published Online: November 3, 2006

