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Stereoselective synthesis of β-amino acids via conjugate addition of nitrogen nucleophiles to α,β-unsaturated esters – Recent advances

Review Article

N. Sewald

Institut für Organische Chemie der Universität Leipzig,
Leipzig, Federal Republic of Germany

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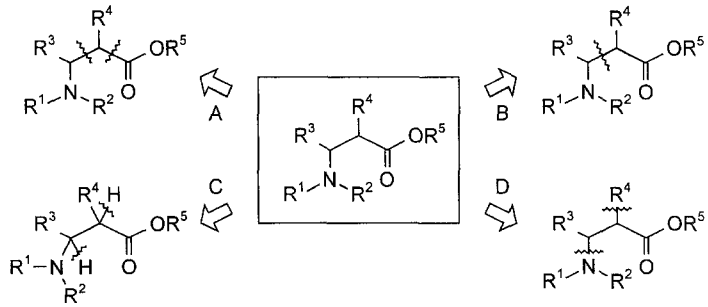
Summary. The latest results concerning the asymmetric synthesis of β-amino acids are reviewed, focussing on methodology involving 1,4-addition of nitrogen nucleophiles to α,β-unsaturated esters. Approaches using both homochiral auxiliaries bound to the enoate and homochiral ammonia equivalents are included as well as alkylations and aldol reactions of enolates derived from homochiral β-amino acids.

Keywords: β-Amino acids – α-Deuterio-β-amino acids – α-Alkyl-β-amino acids – α-Hydroxy-β-amino acids – Conjugate addition – Nitrogen nucleophiles – Homochiral ammonia equivalents – α,β-Unsaturated esters

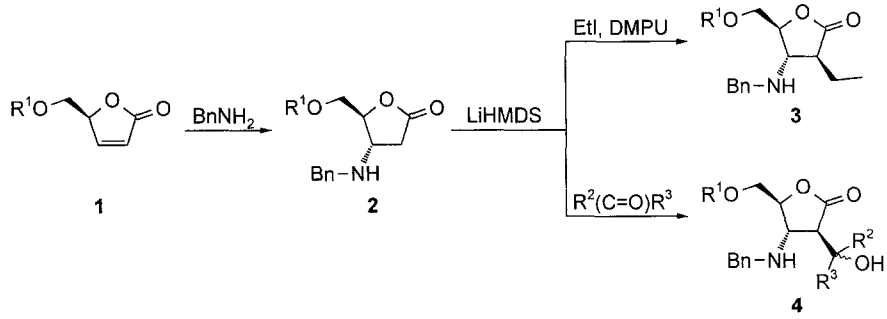
During the last few years the stereoselective synthesis of β-amino acids has gained increasing attention. Although being less abundant than the corresponding α-amino acids, β-amino acids occur in nature both in free form and bound in peptides. A β-amino acid is, for example, a constituent of Jasplakinolide: a cyclodepsipeptide of marine origin, consisting of a polypropionate and a peptide moiety containing (R)-β-tyrosine and bromoabrine (Chu et al., 1991). Astins A, B, or C from *Aster tataricus*, which is widely used in traditional Chinese medicine because of its content of terpenoids and saponins, contain (R)-β-phenylalanine (Jiang et al., 1994). (S)-β-Phenylalanine is also found in the alkaloid dihydroperiphylline (Kaseda et al., 1989) and in the peptide antibiotic andrimid (Fredenhagen et al., 1987).

β-Amino acids are stronger bases and weaker acids compared to α-amino acids (pK_a β-Ala: 3.6, Gly 2.34/β-Ala: 10.36, Gly 9.6) and peptides containing β-amino acids have a different skeleton atom pattern. The incorporation of β-amino acids into biologically active peptides may enhance the activity. Additionally, for instance [β-Asp[1],Val[5]]-Hypertensin II exhibits considerable resistance towards degradation by aminopeptidases (Riniker et al., 1964).

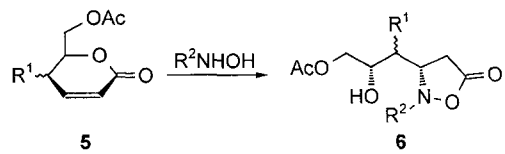
β-Amino acids sometimes show interesting pharmacological properties and serve as precursors e.g. for the synthesis of β-lactams. Stereoselective synthetic pathways to β-amino acids have been summarized in reviews (Cole, 1994; Juaristi et al., 1994), covering references up to 1993. There is a variety of retrosynthetic approaches for these target molecules. Besides homologation of α-amino acids (**A**), enolate additions to imines (**B**), and hydrogenation reactions (**C**), the addition of nitrogen nucleophiles to α,β-unsaturated esters (**D**) is an important strategy.



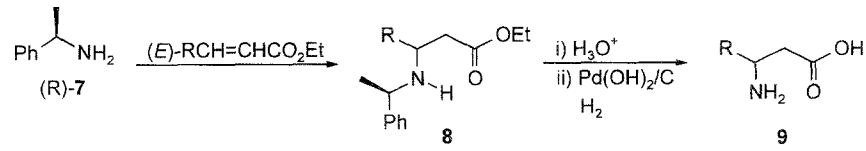
The addition of benzyl amine to the α,β-unsaturated γ-lactone **1** obtained in a multistep procedure from D-mannitol proceeds highly diastereoselective (Collis et al., 1995). The lactone enolate derived from **2** undergoes alkylation (dr 3:1) and aldol reactions.



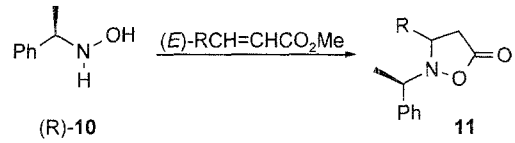
Likewise, the addition of hydroxylamine derivatives to the α,β-unsaturated lactone **5** derived from a carbohydrate gives the isoxazolin-5-one **6** as precursor for the antibiotic negamycin (Socha et al., 1995).



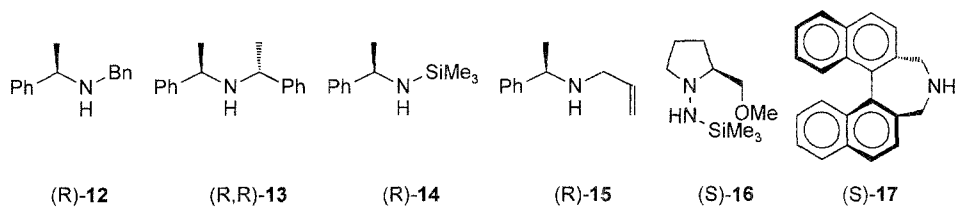
Conjugate addition of homochiral nitrogen nucleophiles to α,β-unsaturated esters represents a versatile methodology for the asymmetric synthesis of β-amino acids. However, as shown in early examples (Furukawa et al., 1977), the addition of scalemic 1-phenylethylamine **7** to enoates proceeds with poor stereoselectivity (**9**: 2–19% ee) and 20–40% overall yield.



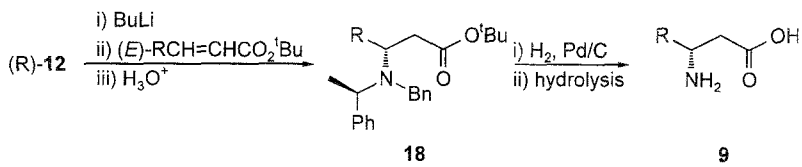
Addition of homochiral hydroxylamine derivatives **10** represents a variant with increased stereoselectivity (38–72% de). The intermediate isoxazolin-5-ones **11** can be cleaved hydrogenolytically (Baldwin et al., 1987).



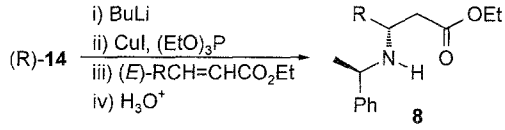
Several metallated amines readily available in both enantiomeric forms are reported to be useful homochiral ammonia equivalents (**12**, **13**: Davies et al., 1991; **14**: Rico et al., 1993; Sewald et al., 1995; **15**: Davies et al., 1995; **16**: Enders et al., 1994; **17**: Hawkins et al., 1994):



Diastereoselective addition of homochiral N-benzyl-phenylethylamine **12** or bis(phenylethyl)amine **13** to α,β-unsaturated esters gives β-amino acids with excellent stereoselectivity (Davies et al., 1991).



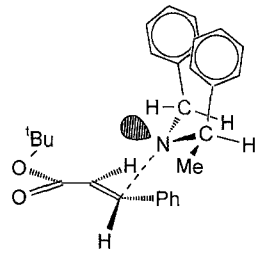
Cuprate reagents are known to suppress the competing 1,2-addition, which gives the corresponding α,β-unsaturated amide, even in the case of α,β-unsaturated methyl or ethyl esters (Yamamoto et al., 1992; Sewald et al., 1995).



Although the C_2-symmetric auxiliary **13** provides excellent results under these conditions, the conjugate addition requires longer reaction times and higher reaction temperatures because of the steric hindrance. Furthermore, the synthesis of **12** or **14** is more straightforward compared to **13**. The diastereoselectivity observed for auxiliaries of the 1-phenylethylamine type (e.g. **12**, **14**) seems to be very high in most cases. Slightly lower asymmetric

induction may originate from insufficient enantiomeric purity (≥94% ee) of commercially available 1-phenylethylamine **7** (Rico et al., 1993).

The high stereoselectivity observed in the conjugate addition of **12** is, according to theoretical calculations, a consequence of the preferred transition state geometry **19**: the enoate reacts from its *s-cis* conformation, lithium is chelated between the carbonyl oxygen and the nitrogen lonepair and the phenyl rings are oriented nearly in parallel. All other transition state geometries have higher energy (Costello et al., 1994).



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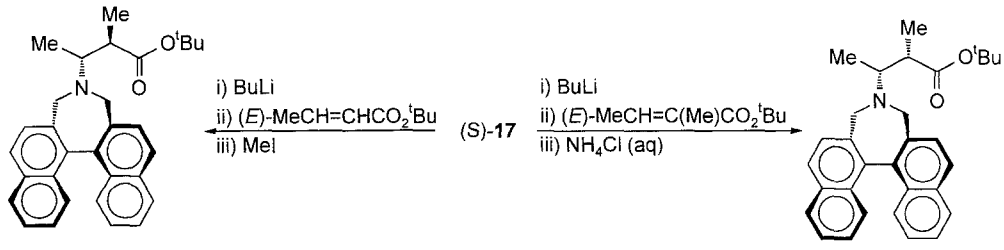
The stereoselectivity of the conjugate addition to α,β-unsaturated esters as well as the stereochemical outcome of the enolate trapping reaction strongly depends on the conformational preference of the enoate. The *s-cis* and *s-trans* conformers of methyl cinnamate are nearly equally populated in the gas phase at 4K, whereas in solution a slight preference of uncomplexed methyl cinnamate for the *s-cis* conformer exists (Shida et al., 1994). The Michael addition of metal amides to uncomplexed α,β-unsaturated esters at low temperature is supposed to proceed through this conformation giving perferentially the intermediate Z-enolate (*vide infra*), as shown by several examples for lithium amides (Asao et al., 1990; Costello et al., 1994; Rico et al., 1993) and lithium amidocuprates (Shida et al., 1992; Sewald et al., 1995).

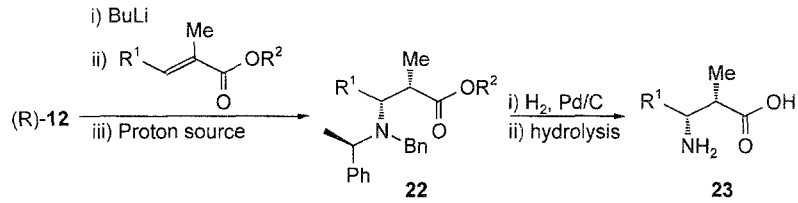
The homochiral binaphthyl based nitrogen nucleophile **17** can also be used for this type of transformation (Hawkins et al., 1994). While *anti* α-methyl β-amino butanoate **20** is obtained on ester enolate trapping with methyl iodide, the corresponding C2-epimer **21** is formed on addition of the homochiral nitrogen nucleophile to tiglate (2-methylcrotonate) and subsequent hydrolysis.



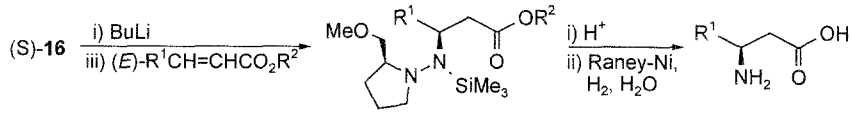
20 **21**

Likewise, stereoselective addition of the Davies auxiliary **12** to α-alkyl α,β-unsaturated esters and subsequent protonation of the intermediate ester enolate with a sterically hindered proton donor gives *syn* α-alkyl substituted β-amino acids **22** with excellent stereocontrol (Davies et al., 1994b). This

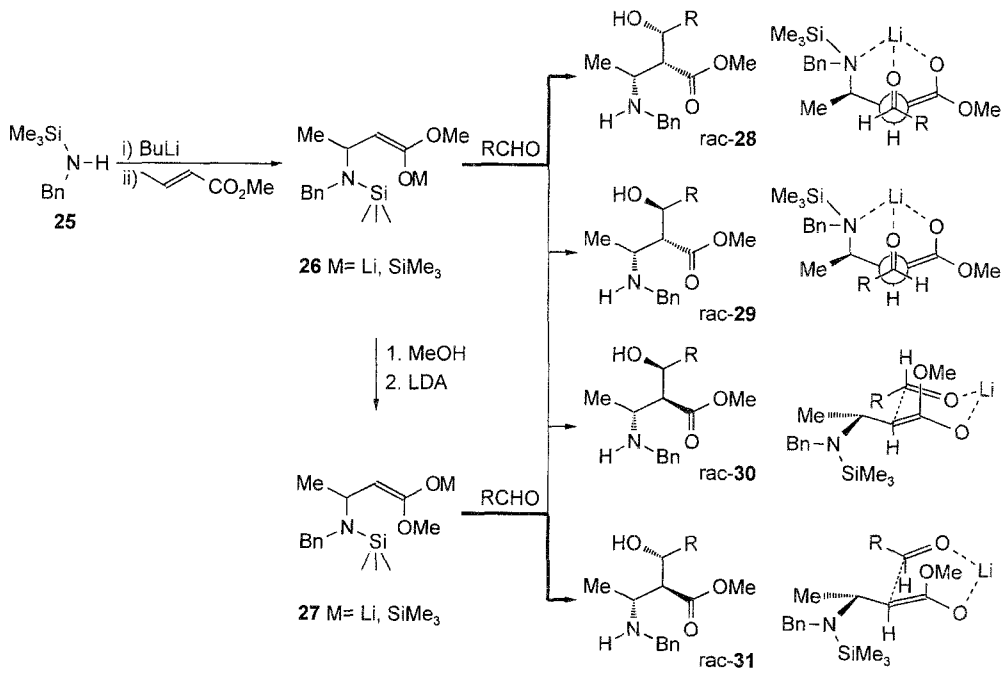
strategy was successfully applied to the asymmetric synthesis of (−)-(1R,2S)-2-aminocyclopentane-1-carboxylic acid (cispentacin) and its cyclohexane analogues (Davies et al., 1994c).



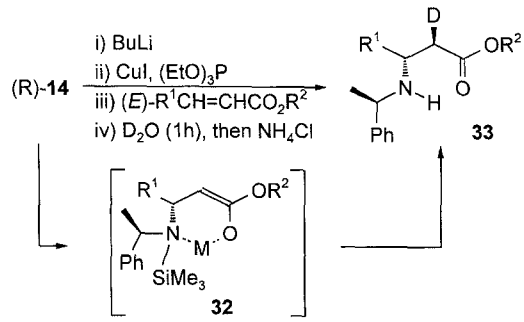
A similar approach utilizes TMS-SAMP/TMS-RAMP ((S)-**16**/(R)-**16**) as homochiral nitrogen nucleophiles forming **24** with de values >93%. Unsilylated SAMP or RAMP yields 1,2-adducts exclusively (Enders et al., 1995b).



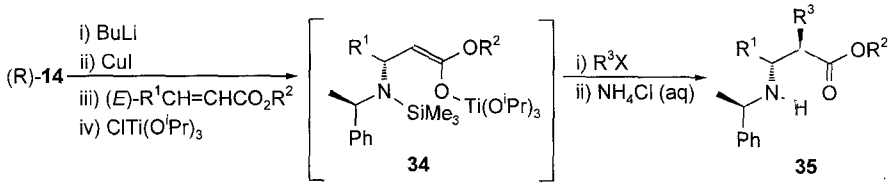
The addition of achiral lithium N-trimethylsilyl benzylamide **25** to methyl crotonate and subsequent trapping of the intermediate ester enolate with trimethylsilyl chloride predominantly gives the Z-configured O-silyl ketene acetal **26**, whereas the E-ketene acetal **27** is formed upon deprotonation of a β-amino acid ester with lithium diisopropylamide followed by O-silylation (Asao et al., 1990). Trapping of the Z- or E-ester enolate with carbon electrophiles, e.g. alkyl halides or aldehydes, yields the corresponding α-alkyl or aldol adducts, respectively. Product **28** dominates in the aldol reaction of the Z-enolate **26** while **31** is preferentially formed from the E-enolate **27** via a skewed chair transition state.



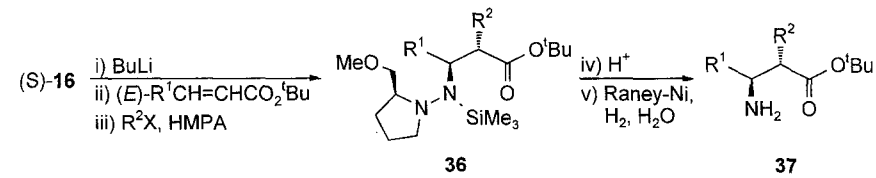
Conjugate addition of homochiral amidocuprates based on N-trimethylsilyl (R)- or (S)-1-phenylethylamine **14**, resp., to α,β-unsaturated esters and subsequent trapping of the intermediate enolate with D_2O proceeds with excellent stereoselectivity (dr > 95:5) providing efficient methodology for the asymmetric synthesis of *anti* configured α-deuterated β-amino acids **33** (Sewald et al., 1995).



The intermediate lithium/copper ester enolates **32** react only slowly with deuterium oxide. They do not react with carbon electrophiles under similar reaction conditions. However, transmetallation of the ester enolate with chlorotriisopropoxytitanium from copper to titanium (**34**) enhances the reactivity towards carbon electrophiles and trapping with carbon electrophiles is then possible in a one-pot reaction; the stereoselectivity varies from good to excellent values favouring the *anti* isomers (Sewald et al., 1996).

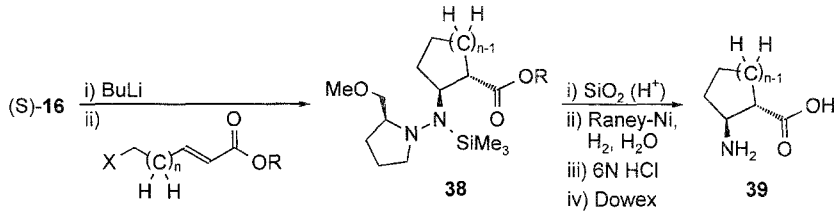


Analogously, the application of TMS-SAMP (S)-**16** or TMS-RAMP (R)-**16** in a tandem Michael addition provides access to *anti* α-alkyl β-amino acids **36** with excellent stereoselectivity (de between 63 and >96%) in moderate to good yields (26–68%). Phenyl substituents in position 3 (R^1 = Ph), however, are reduced to cyclohexyl residues under the reaction conditions necessary to cleave the N-N bond in **36** (Enders et al., 1994).

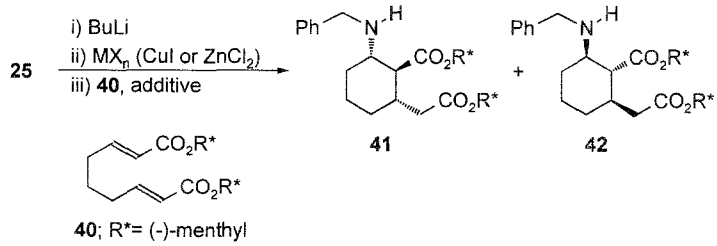


Intramolecular alkylation of the intermediate enolate provides access to *trans* 2-aminocycloalkane-1-carboxylates **39** via this route (Enders et al., 1995a).

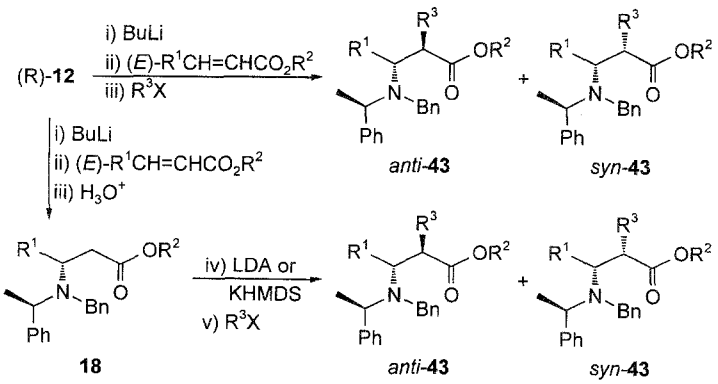
The concept of tandem conjugate addition also works well on Michael addition of the achiral nitrogen nucleophile **25** followed by carbocyclization via Michael addition of the intermediate ester enolate when a chiral auxiliary



is bound to the substrate. The stereoselectivity of this process is highly dependent on the reagent (lithium amide, lithium amidocuprate, lithium amidozincate) and the presence of a bidentate chelating additive, e.g. $ZnCl_2$ or $MgBr_2$. However, according to the results observed, the enoate geometry in **40** is postulated to be *s-cis* even when a chelating additive is used, whereas *s-trans* geometry is involved in several other conjugate additions to complexed enoates. The products **41**, **42** are obtained in 40–87% yield with diastereomeric ratios between 61:39 and 95:5 (Shida et al., 1992).

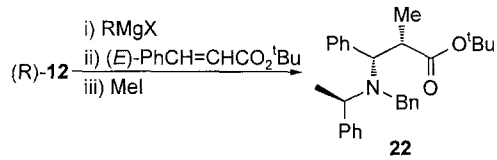


α-Alkyl substituted β-amino acids are also obtained via enolate trapping after Michael addition of metallated N-benzyl (R)- or (S)-phenylethylamine **12**. However, direct trapping of the enolate in most cases gives moderate to good stereoselectivity (dr between 1.2:1 and 13:1). Higher *anti* selectivity is observed (dr between 1:1 and 30:1) in a two-step reaction where the corresponding E-configured ester enolate, formed with LDA starting from the β-amino ester **18**, is alkylated. Hence, the tandem and the stepwise protocol proceed *via* two different enolate geometries. O-Silylation of the intermediate lithium enolates involved in both methods affords two O-silyl ketene acetals with different double bond geometry (Davies et al., 1994a) as predicted by literature precedence (*vide supra*).



Surprisingly, the conjugate addition of achiral lithium dibenzylamide followed by tandem enolate alkylation proceeds highly diastereoselective, whereas application of the stepwise protocol is nearly non-selective in this case. This finding proves the influence of the remote N-1-phenylethyl group on chiral recognition during enolate alkylation.

Tandem conjugate addition/methylation occurs with excellent *syn* selectivity on replacement of the lithium amide based on (R)-**12** by the corresponding magnesium amide (Bunnage et al., 1994a).



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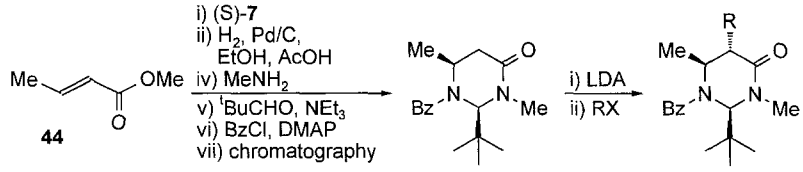
In summary, while the topicity of the Michael addition is identical for 1-phenylethylamine derivatives with different metals, the diastereoselectivity of the ester enolate trapping reaction is strongly governed by both the enolate geometry and the counterion (Li, Cu, Mg).

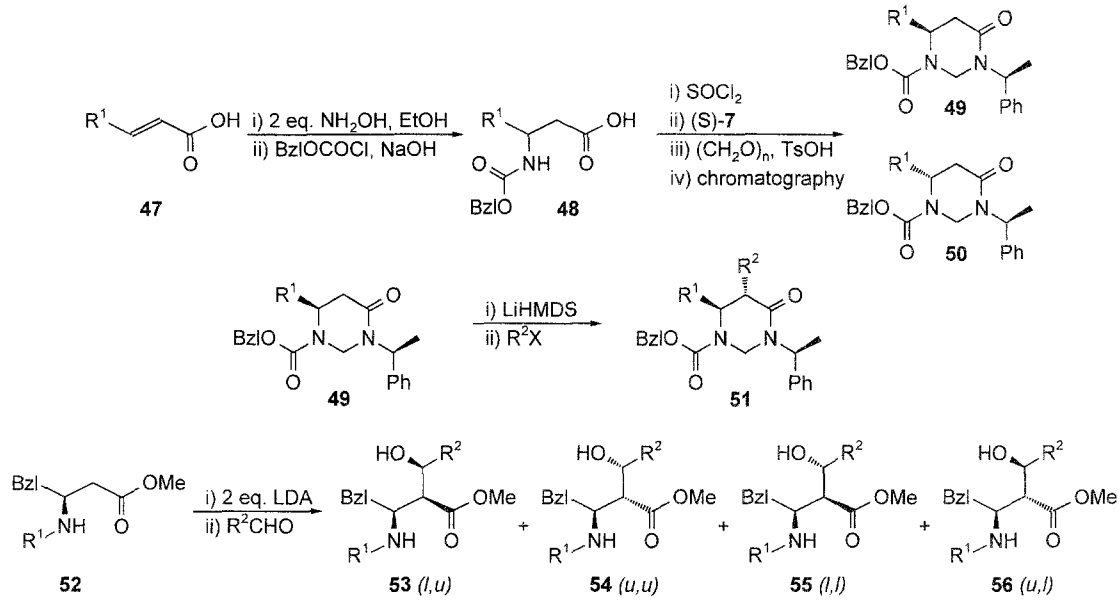
Asymmetric alkylations of enolates derived from perhydropyrimidin-4-ones (cyclic aminals of β-amino acid amides) are also described in the literature. For the preparation of the corresponding starting materials, the strategies rely on conjugate addition of nitrogen nucleophiles (Juaristi et al., 1992: (S)-phenylethylamine to methyl crotonate, 20% de; Braschi et al., 1994: hydroxylamine to α,β-unsaturated acids), followed by ester to amide transformation with subsequent aminal formation using pivalaldehyde (Juaristi et al., 1992) or formaldehyde (Braschi et al., 1994) and finally diastereomeric separation by recrystallization or flash chromatography.

Deprotonation of **45** using LDA and methylation or benzylation gives stereochemically homogeneous products. Hydrolysis is achieved by heating with 6N HCl in a sealed tube to give *anti* α-alkyl substituted β-amino acids (Juaristi et al., 1992). Stereoselective aldol reactions starting from **45** are also reported (Murer et al., 1994).

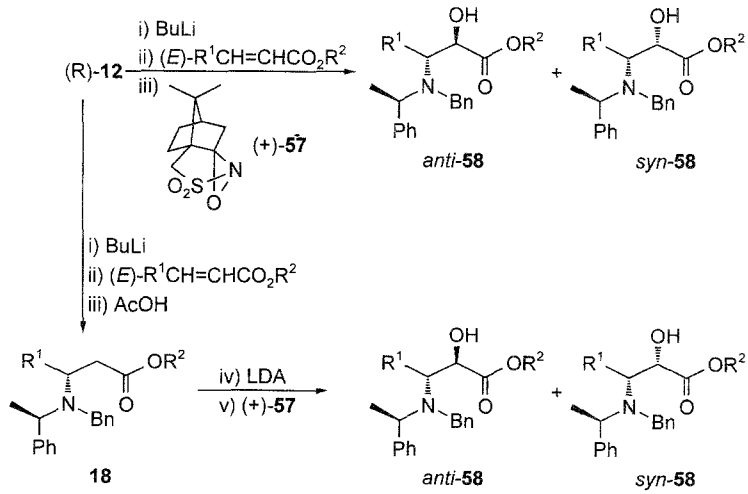


The second type of perhydropyrimidin-4-ones described so far, e.g. **49**, is deprotonated with LiHMDS prior to enolate alkylation. The stereoselectivity of the α-alkylation slightly depends on the steric bulk of the electrophile. While the *trans/cis* ratio for methylations of the enolate derived from **49** ranges from 77:23 to 92:8, no *cis* isomer can be detected on reaction with ethyl iodide or benzyl bromide (Braschi et al., 1994).

Aldol reactions of dilithiated ester enolates derived from protected acyclic β-amino acid derivatives **52** mainly proceed with the relative topicity *lk* under *ul*-1,2 induction clearly favouring the (*l,u*) product **53** (Ettmayer et al., 1994).

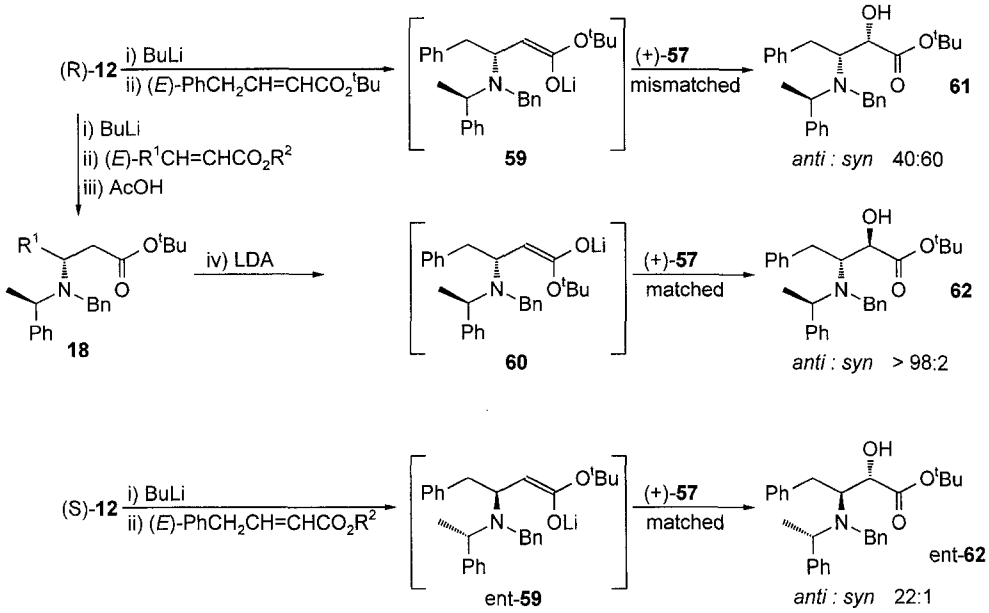


The concept of Michael addition / enolate trapping used for the synthesis of α-alkyl substituted β-amino acids has been extended to electrophilic hydroxylation reactions of the ester enolate. Based on a publication by Davis reporting on stereoselective oxaziridine mediated α-hydroxylation of N-benzoyl β-amino ester enolates, an efficient protocol for the synthesis of isoserine derivatives *anti*-**58** (α-hydroxy β-amino acids) has been elaborated. Although the tandem addition/hydroxylation using the camphorsulfonyloxaziridine **57** proceeds with good diastereoselectivity in the case of cinnamates (R^1 = Ph), only medium yields are obtained in the case of methyl esters because of the competing 1,2 addition which can be excluded on application of ^{t}butyl esters. Earlier literature precedence suggests the stereoselectivity of the hydroxylation to be governed by the 1,2-induction of the homochiral enolate and being less dependent on the absolute configuration of the oxaziridine (Davis et al., 1992). Regardless the fact that different enolate configurations are supposed to dominate in the tandem or in the stepwise protocol, respectively, only a slight divergence in diastereoselectivity



is observed in most cases with (+)-**57** (R^1 = Ph, Me, Et) (Bunnage et al., 1994c).

A higher degree of chirality recognition with the oxaziridine reagent **57** is reported in the case of R^1 = Bzl. Again, the stepwise protocol via **60** is reported to compare most favourably to the tandem protocol via **59** in the synthesis of the allophenylnorstatine derivative *anti*-**61** as a consequence of mismatched reagent pairing in the latter case (**59**/(+)-**57**, Bunnage et al., 1994e). The matched pair ent-**59**/(+)-**57** reacts highly stereoselective also in the tandem reaction.



Several biologically relevant derivatives like N-benzoyl (2S,3R)-3-phenylisoserine (Bunnage et al., 1994d) and (2S,3R)-3-amino-2-hydroxydecanoic acid, a β-amino acid occurring in the pseudopentapeptide microginin (Bunnage et al., 1994b) were synthesized using this methodology in combination with Mitsunobu inversion at C-2.

References

Asao N, Uyehara T, Yamamoto Y (1990) Stereodivergent synthesis of the enolates of a β-amino ester by using lithium N-benzyltrimethylsilylamide. Tetrahedron 46: 4563–4572

Baldwin SW, Aubé J (1987) Asymmetric synthesis with chiral hydroxylamines. Synthesis of optically pure 4-substituted azetidinones. Tetrahedron Lett 28: 179–182

Braschi I, Cardillo G, Tomasini C, Venezia R (1994) Highly diastereoselective alkylation of perhydropyrimidin-4-ones directed toward the synthesis of α-substituted β-amino acids. J Org Chem 59: 7292–7298

Bunnage ME, Davies SG, Goodwin CJ, Walters IAS (1994a) Asymmetric Michael additions of homochiral magnesium amides. Tetrahedron: Asymmetry 5: 35–36

Bunnage ME, Burke AJ, Davies SG, Goodwin CJ (1994b) Asymmetric synthesis of (2S,3R)-3-amino-2-hydroxydecanoic acid: the unknown amino acid component of microginin. Tetrahedron: Asymmetry 5: 203–206

Bunnage ME, Chernega AN, Davies SG, Goodwin CJ (1994c) Asymmetric synthesis of β-amino-α-hydroxy acids via diastereoselective hydroxylation of homochiral β-amino enolates. J Chem Soc Perkin Trans I: 2373–2384

Bunnage ME, Davies SG, Goodwin CJ (1994d) Asymmetric synthesis of the taxol and taxotère C-13 side chain. J Chem Soc Perkin Trans I: 2385–2391

Bunnage ME, Davies SG, Goodwin CJ, Ichihara O (1994e) An expeditious asymmetric synthesis of allophenylnorstatine. Tetrahedron 50: 3975–3986

Chu KS, Negrete GR, Konopelski JP (1991) Asymmetric total synthesis of (+)-jasplakinolide. J Org Chem 56: 5196–5202

Cole DC (1994) Recent stereoselective synthetic approaches to β-amino acids. Tetrahedron 50: 9517–9582

Collis MP, Hockless DCR, Perlmutter P (1995) (4S,5S)-4-Benzylamino-5-[((*tert*-butyl)diphenylsilyl)oxymethyl]-dihydro-2(3*H*)-furanone. A new intermediate for the enantiospecific synthesis of β-aminoesters and β-lactams. Tetrahedron Lett 36: 7133–7136

Costello JF, Davies SG, Ichihara O (1994) Origins of the high stereoselectivity in the conjugate addition of lithium(α-methylbenzyl)benzylamide to *t*-butyl cinnamate. Tetrahedron: Asymmetry 5: 1999–2008

Davies SG, Ichihara O (1991) Asymmetric synthesis of R-β-amino butanoic acid and S-β-tyrosine: homochiral lithium amide equivalents for Michael additions to α,β-unsaturated esters. Tetrahedron: Asymmetry 2: 183–186

Davies SG, Walters IAS (1994a) Asymmetric synthesis of *anti*-α-alkyl-β-amino acids. J Chem Soc Perkin Trans I: 1129–1139

Davies SG, Ichihara O, Walters IAS (1994b) Asymmetric synthesis of *syn*-α-alkyl-β-amino acids. J Chem Soc Perkin Trans I: 1141–1147

Davies SG, Ichihara O, Lenoir I, Walters IAS (1994c) Asymmetric synthesis of (−)-(1R,2S)-cispentacin and related *cis*- and *trans*-2-amino cyclopentane- and cyclohexane-1-carboxylic acids. J Chem Soc Perkin Trans I: 1411–1415

Davies SG, Hedgecock CJR, McKenna JM (1995) A Stereocontrolled approach to 1β-methylcarbapenem. Tetrahedron: Asymmetry 6: 827–830

Davis FA, Reddy RT, Reddy RE (1992) Asymmetric synthesis of sulfinimines: applications to the synthesis of nonracemic β-amino acids and α-hydroxyl-β-amino acids. J Org Chem 57: 6387–6389

Enders D, Bettray W, Raabe G, Runsink J (1994) Diastereo- and enantioselective synthesis of α-substituted β-amino acid esters by tandem Michael-addition/α-alkylation with TMS-SAMP as chiral equivalent of ammonia. Synthesis: 1322–1326

Enders D, Wiedemann J, Bettray W (1995a) Diastereo- and enantioselective synthesis of *trans*-2-amino-cycloalkane-1-carboxylic acids via intramolecular tandem Michael-addition/α-alkylation using TMS-SAMP as chiral equivalent of ammonia. Synlett: 369–371

Enders D, Wahl H, Bettray W (1995b) Enantioselektive Synthese von β-Aminosäuren – TMS-SAMP als chirales Ammoniak-Äquivalent in der azaanalogen Michael-Addition an α,β-ungesättigte Ester. Angew Chem 107: 527–529; Angew Chem Int Ed Engl 34: 455–457

Ettmayer P, Hübner M, Gstach H (1994) Addition of dilithiated methyl-3-aminobutanoate to aldehydes proceeds with *ul*-1,2-induction. Tetrahedron Lett 35: 3901–3904

Fredenhagen A, Tamura SY, Kenny PTM, Komura H, Naya Y, Nakanishi K, Nishiyama K, Sugiura M, Kita H (1987) Andrimid, a new peptide antibiotic produced by an intracellular bacterial symbiont isolated from a brown planthopper. J Am Chem Soc 109: 4409–4411

Furukawa M, Okawara T, Terawaki Y (1977) Asymmetric synthesis of β-amino acids by the addition of chiral amines to C=C double bonds. Chem Pharm Bull Japan 25: 1319–1325

Hawkins JM, Lewis TA (1994) Asymmetric synthesis of *erythro* and *threo* α-substituted β-amino esters. J Org Chem 59: 649–652

Jiang J, Schumacher KK, Joullié MM, Davis FA, Reddy RE (1994) Approaches toward the total syntheses of astins A, B, and C. Tetrahedron Lett 35: 2121–2124

Juaristi E, Escalante J, Lamatsch B, Seebach D (1992) Enantioselective synthesis of β-amino acids. 2. Preparation of the *like* stereoisomers of 2-methyl- and 2-benzyl-3-aminobutanoic acid. J Org Chem 57: 2396–2398

Juaristi E, Quintana D, Escalante J (1994b) Enantioselective synthesis of β-amino acids. Aldrichim Acta 27: 3–11

Kaseda T, Kikuchi T, Kibayashi C (1989) Enantioselective total synthesis of (+)-(S)-dihydroperiphylline. Tetrahedron Lett 30: 4539–4542

Murer P, Rheiner B, Juaristi E, Seebach D (1994) Enantioselective synthesis of β-amino acids. 5. Stereoselective reaction of chiral pyrimidinone enolates with aldehydes. Heterocycles 39: 319–344

Rico JG, Lindmark PJ, Rogers TE, Bovy PR (1993) A highly stereoselective Michael addition to an α,β-unsaturated ester as the crucial step in the synthesis of a novel β-amino acid-containing fibrinogen receptor antagonist. J Org Chem 58: 7948–7951

Riniker B von, Schwyzer R (1964) Synthetische Analoge des Hypertensins. V. α-L-, β-L-, α-D- und β-D-Asp[1]-Val[5]-Hypertensin II; Desamino-Val[5]-Hypertensin II. Helv Chim Acta 47: 2357–2374

Sewald N, Hiller KD, Helmreich B (1995) Asymmetric synthesis of β-amino acids and α-deuterated β-amino acids via conjugate addition of homochiral amidocuprates. Liebigs Ann: 925–928

Sewald N, Hiller KD, Körner M (1996) Highly steroselective synthesis of α-alkyl β-amino acids via tandem Michael addition/ester enolate trapping. A simple one-pot procedure. J Org Chem (submitted)

Shida N, Uyehara T, Yamamoto Y (1992) Asymmetric cyclization via tandem conjugate addition by using metal amide reagents. Importance of the folded orientation of two enoate moieties. J Org Chem 57: 5049–5051

Shida N, Kabuto C, Niwa T, Ebata T, Yamamoto Y (1994) Studies on *s-cis/s-trans* preference of acyclic α,β-unsaturated esters. Reactions, supersonic jet spectroscopy, NOEs, and X-ray analysis. J Org Chem 59: 4068–4075

Socha D, Jurczak M, Chmielewski M (1995) Stereocontrolled entry to negamycin from D-glucose. Tetrahedron Lett 36: 135–138

Yamamoto Y, Asao N, Uyehara T (1992) Amide cuprate reagents as a new class of nitrogen nucleophiles. Application to asymmetric synthesis of β-lactams. J Am Chem Soc 114: 5427–5429

Author's address: Dr. N. Sewald, Institut für Organische Chemie der Universität Leipzig, Talstraße 35, D-04103 Leipzig, Federal Republic of Germany.

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