Pergamon

Tetrahedron: *Asymmetry* 13 (2002) 595–600

TETRAHEDRON: *ASYMMETRY*

Synthesis of non-racemic β-branched α-(aminoalkyl)-acrylates from naturally occurring amino acids

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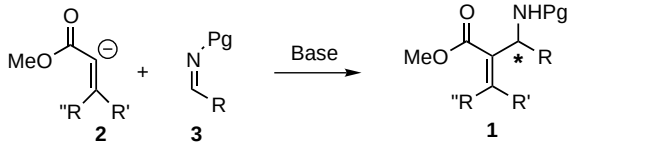
Received 7 March 2002; accepted 18 March 2002

Abstract—Non-racemic Boc-protected γ-stannylated-α-(aminoalkyl)acrylates of (*Z*) geometry have been selectively obtained by addition of stannylcuprate onto propargylamines, followed by reaction with carbon dioxide. Stille coupling has been investigated and a small library of six new β-branched-α-(aminoalkyl)acrylates obtained. These compounds are useful intermediates for the synthesis of new enantiomerically enriched β-amino acids.

1. Introduction

Enantiomerically enriched α-(aminoalkyl)acrylates **1** are synthetically useful building blocks; bearing an array of functional groups, they can be usefully employed for the design and synthesis of biologically important compounds. For instance, they can be easily transformed into 2,3 disubstituted β-amino acids by reduction,[1] addition with Michael donors[2] or through radical alkylation/reduction sequences.[3] In addition α-(aminoalkyl)acrylate analogs can be used for the design and synthesis of taxol and taxotere side chain[4–6] or as building blocks for the synthesis of new β-peptides.[7]

Baylis–Hilmann type condensation[8] is one of the more efficient ways to obtain these compounds through a connective process, formally equivalent to the addition of a vinyl anion **2** to an imine **3** (Scheme 1). Although several asymmetric Baylis–Hillman processes have been studied for the synthesis of enantiomerically pure α-(hydroxyalkyl)acrylates by using chiral auxiliaries,[9,10] the extension to the corresponding α-(aminoalkyl)acrylates is less well documented,[11] especially in the case of β-branched systems. This is probably due to the fact that β-substituted olefinic substrates do not normally undergo the Baylis–Hillman reaction. However, the asymmetric synthesis of *trans*-β-methyl-*N*-(*p*-toluenesulfinyl)-α-(aminoalkyl)acrylates was recently reported[12] by addition of metal dienolates to chiral *p*-toluenesulfinimines,[13,14] followed by cleavage and isomerization reactions. In addition, in a related but more general approach, the synthesis of both *cis*-β-substituted and β,β-substituted *N*-(*p*-toluenesulfinyl)-α-(aminoalkyl) acrylates **1b**,**c**,**d**, was described through the conjugate addition of R_2CuLi to α,β-acetylenic esters to generate an organometallic intermediate, which was then used for nucleophilic addition to chiral *p*-toluenesulfinimines.[15,16]



1a R'=R"=H
1b R'=H R"=Me, Ph, *n*Bu
1c R'=R"=Me
1d R'=Ph R"=Me, Ph, nBu

Scheme 1.

Recently, we have been involved in the synthesis of acrylates and, in particular, we have shown a method for preparing γ-silylated α-methylene-β-alanine **5**, based on the addition of silyl cuprates on propargylamine **4** followed by trapping with CO_2 (Scheme 2).[17]

Desilylation and subsequent esterification with palmitoyl chloride afforded an α-methylene-β-alanine derivative **6** identical to a component of the lipidic extract of the Red Sea sponge *Fasciospongia Cavernosa*.[18] A similar procedure employing a stannylcuprate reagent, yielded the γ-stannyl acrylate **7**.[19] The synthetic utility of **7** was not investigated. Stannylcupration was also

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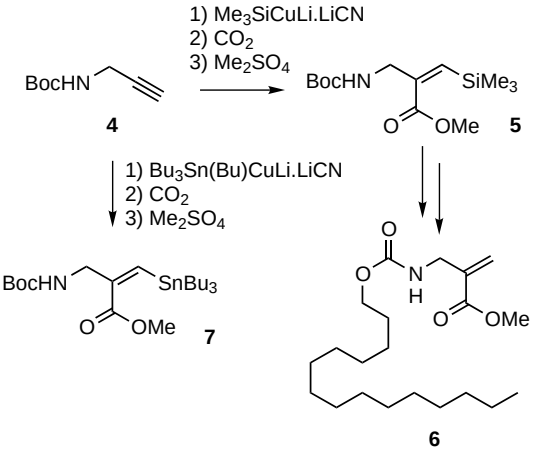
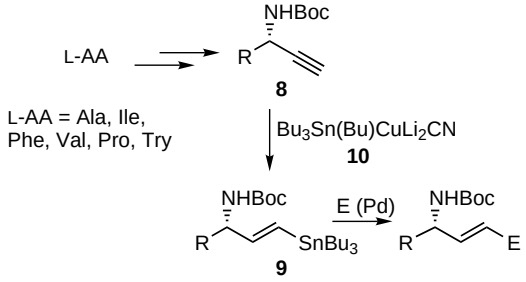


Scheme 2.

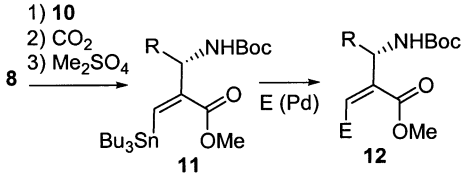
extended to non-racemic propargylic amines **8**, derived from naturally occurring amino acids. Reaction with stannylcuprate **10** yielded the stannylated allylamines **9**, without loss of enantiomeric purity.[20] These compounds proved to be useful three-carbon homologating reagents, the vinyl–tin moiety being able to couple with electrophiles via palladium catalysis (Scheme 3).[21,22]

Hence, we decided to focus on the synthesis of non-racemic β-branched-β-aminoacrylates **12** as a straightforward extension of our methodology. Addition of stannylcuprate **10** on propargylamines **8** followed by carboxylation and esterification would give compounds **11**, which could be transformed into the substituted acrylates **12**. These are, for instance, useful precursors of new 2,3 substituted β-amino acids having a proteinogenic side chain, which are compounds of high synthetic value[23–26] (Scheme 4).

Herein, we report our efforts to develop a new versatile synthesis of non-racemic β-amino-acrylates. These



Scheme 3.



Scheme 4.

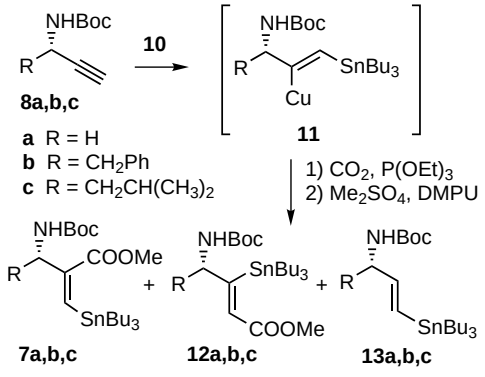
highly functionalized compounds have been obtained from naturally occurring amino acids through stannylated precursors of kind **7**, whose reactivity towards electrophiles has also been investigated.

2. Results and discussion

Achiral **8a** was prepared by protection of commercially available propargylamine with $(t\text{-Boc})_2O$.[19] Non-racemic **8b**,**c** were prepared by transformation of naturally occurring L-phenylalanine and L-leucine into the corresponding aldehydes followed by homologation to the alkyne.[20] Stannylcuprate **10** was prepared as reported[27] and reacted with **8** at −78°C to give intermediate **11** which can be trapped with a suitable electrophile to introduce the carboxylic acid functionality.

It is known that the best conditions for the carboxylation of cuprates involves bubbling CO_2 into the cuprate in the presence of HMPA and $P(OEt)_3$ additives.[28] Although these conditions were already proven to efficiently afford **7a**,[19] we decided to carry out further investigations aiming to avoid toxic HMPA. We were disappointed to observe that when Me_2CO_3 or $CNCO_2Me$ were used no reaction product was detected, even in the presence of additives. After several experiments, however, we were able to establish that heating the reaction mixture at −25°C and bubbling CO_2 in the presence of 1 equivalent of $P(OEt)_3$ gave the best results. The reaction mixture was allowed to warm slowly to room temperature and then stirred overnight. For characterization purposes crude amino acids were transformed into the corresponding esters by treating with Me_2SO_4 in the presence of DMPU as co-solvent (Scheme 5).

Unfortunately variable amounts of non-carboxylated allylamines **13** were present in the crude product, as determined by ^1H NMR analysis. While affecting the final yield of compounds **7**, amines **13** were easily separated by flash chromatography so that the final compounds were obtained with high purity and acceptable yields. Experimental details are reported in Table 1.



Scheme 5.

Table 1. Experimental details for compounds **7a**,**b**,**c**

Starting material	**7**/**13**[a]	**7**/**12**[a]	Yield of **7**[b] (%)	$[\alpha]_D$[c] $CHCl_3$	δ ($CHCl_3$)[d]
8a	70/30	>95/5	45	–	6.91
8b	75/25	>95/5	55	$[\alpha]_D^{20}=1.57$, $c=1.65$	6.60
8c	70/30	>95/5	47	$[\alpha]_D^{20}=32.1$, $c=1.00$	6.79

[a] Determined by ^1H NMR analysis of the crude.
[b] Yield of isolated compounds.
[c] Referred to pure **7**.
[d] Chemical shift observed for the vinylic proton.

As expected, addition of cuprate afforded compounds **7a**,**b**,**c** with high regio- and stereoselectivity and only minor traces of regioisomer **12** were recovered.

The (*Z*)-configuration of the double bond was established by NOE experiments (Fig. 1) and is also in agreement with the chemical shift value observed for the vinylic proton (Table 1), which are very close to those of related compounds of the same geometry.[12,15] The enantiomeric purity of **7b**,**c** was established by ^1H NMR analysis of the diastereomeric Mosher amides prepared by reaction of (*S*)-(+)-α-methoxy-α-(trifluoromethyl)phenylacetyl chloride (MTPACl) with the primary amines derived by deprotection with Me_3SiI.[29] In both cases the e.e. was found to be comparable with that of the starting material **8b**,**c**, confirming that no racemization had occurred under our reaction conditions.

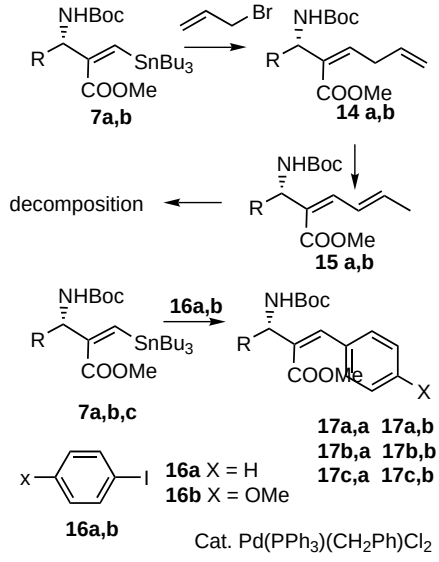
Finally, the reactivity of compounds **7a**,**b**,**c** was investigated. According to the well known Stille procedure,[30] compounds **7a** and **7b** were initially reacted with an excess of allyl bromide in the presence of $Pd(PPh_3)(CH_2Ph)Cl_2$ complex as catalyst (Scheme 6).

Although the corresponding coupling compounds **14a**,**b** were obtained in good yields, they could not be purified as, in both cases, isomerization to the corresponding conjugate diene **15a**,**b** readily occurred, followed by rapid decomposition.

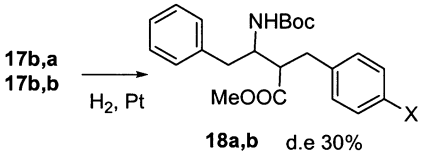
Aryl iodides were next selected to react with compounds **7a**,**b**,**c**. Iodobenzene **16a** and *p*-iodoanisole **16b** were employed and in all cases the coupling proceeded smoothly with retention of configuration at the vinyl–tin bond. The final compounds **17** were isolated in good yields after treatment of the crude mixture with aqueous KF solution and filtration through silica gel. All new compounds were purified and fully characterized.

A small library of six different substituted acrylates was thus obtained, showing the advantage of our method for introducing molecular diversity on the aminoacrylate backbone, while maintaining enantiomeric purity and double bond geometry.

Finally, pure compounds **17b**,**a** and **17b**,**c** were hydrogenated in the presence of a Pt catalyst to yield the corresponding β-amino acids **18a**,**b** in 30% d.e. (Scheme 7). Although the two diastereomers were not separated,



Scheme 6.



Scheme 7.

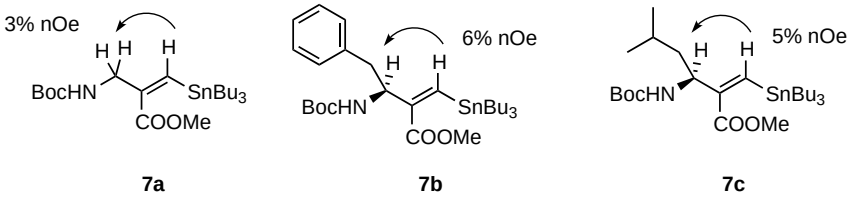


Figure 1.

spectroscopic data were in good agreement with those of related compounds.[31]

3. Conclusion

In conclusion we have presented a method for obtaining a new family of enantiomerically enriched β-amino acrylates as precursors of 2,3 disubstituted β-amino acids, in which the R lateral chain and the absolute configuration at the C(3) stereogenic center can be derived from naturally occurring amino acids, and the lateral chain at C(2) can be varied by coupling with electrophiles. Extensions of the procedure and further synthetic applications are currently under investigation.

4. Experimental

4.1. General methods and materials

All reactions were carried out under a positive pressure of dry nitrogen. Ethereal extracts were dried with Na_2SO_4. Reactions were monitored by TLC on SiO_2; detection was made using a $KMnO_4$ basic solution. Flash column chromatography[32] was performed using glass columns (10–50 mm wide) and SiO_2 230–400 mesh. ^1H NMR spectra were recorded at 200 or 300 MHz. ^{13}C NMR spectra were recorded at 50.3 MHz. Chemical shifts were determined relative to the residual solvent peak ($CHCl_3$ δ 7.26 for ^1H NMR; $CHCl_3$ δ 77.0 for ^{13}C NMR). Coupling constants (J) are reported in Hz. Multiplicities are indicated as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet) and bs (broad singlet). Mass spectra were obtained at a 70 eV ionization potential and are reported in the form m/z (intensity relative to base = 100). Polarimetric measurements were performed in $CHCl_3$ solution at $\lambda = 589$ nm, and the temperature was specified case by case.

Propargylamines **8** were prepared according to the literature.[19,20] THF was dried by distillation over sodium benzophenone ketyl, CH_2Cl_2 and DMPU were dried over $CaCl_2$ and stored over 4 Å molecular sieves. DMF was distilled over calcium hydride and stored over 4 Å molecular sieves. Petroleum ether, unless specified, is the 40–70°C boiling fraction.

4.2. Synthesis of stannylated β-amino acrylates 7. General procedure

Tributyltincuprate **10** was prepared according to the general route described by Lipshutz.[27] Amines **8** were added to −78°C and TLC showed that addition was complete after 15 min. After adding $P(OEt)_3$ (1 equiv.) the reaction mixture was heated at −25°C and CO_2 was bubbled for 1 h. The solution was allowed to slowly reach 0°C and then stirred overnight. DMPU (5 equiv.) and Me_2SO_4 (2 equiv.) were added and left at room temperature for further 24 h. The reaction mixture was hydrolysed with NH_4Cl/NH_4OH buffer solution, extracted with Et_2O, then washed with brine and dried over Na_2SO_4. After solvent evaporation the crude product was analysed by ^1H NMR and then purified by column chromatography.

4.2.1. Methyl 2-{[(*tert*-butoxy)carbonylamino]-methyl}-(2*Z*)-3-tributylstannyl-2-enoate 7a. Amine **8a** (621 mg, 4.0 mmol) was reacted according to the general procedure. After purification (eluent: petroleum ether/ethyl acetate = 10/1) 905 mg of **7a** (45%) were obtained: ^1H NMR (200 MHz) δ: 6.91 [bs, 1H, $J_{Sn,H} = 53.6$ Hz]; 4.80–4.95 [m, 1H]; 4.00–3.90 [m, 2H]; 3.77 [s, 3H]; 1.41 [s, 9H]; 1.35–1.18 [m, 12H]; 0.76–0.83 [m, 15H]. ^{13}C NMR (50.3 MHz) δ: 167.35; 155.44; 150.40; 146.53; 79.27; 53.65; 51.81; 29.07; 28.38; 27.22; 13.60; 11.12. MS m/e: 448 (55); 374 (100). Anal. calcd for $C_{22}H_{43}NO_4Sn$: C, 52.40; H, 8.59; N, 2.78. Found: C, 52.76; H, 8.66; N, 2.71%.

4.2.2. Methyl 2-{(1*S*)-1-[(*tert*-butoxy)carbonylamino]-2-phenylethyl}-(2*Z*)-3-tributylstannyl-prop-2-enoate 7b. Amine **8b** (245 mg, 1.0 mmol) was reacted according to the general procedure. After purification (eluent: petroleum ether/ethyl acetate = 10/1) 324 mg of **7b** (55%) were obtained: ^1H NMR (200 MHz) δ: 7.30–7.05 [m, 5H]; 6.60 [bs, 1H, $J_{Sn,H} = 52.4$ Hz]; 5.22 [bd, 1H, $J = 9.2$ Hz]; 4.84–4.73 [m, 1H]; 3.75 [s, 3H]; 2.98–2.84 [m, 2H]; 1.38 [s, 9H]; 1.40–1.14 [m, 12H]; 0.90–0.83 [m, 15H]. ^{13}C NMR (50.3 MHz) δ: 167.18; 154.89; 151.09; 145.66; 137.80; 129.44; 128.18; 126.34; 79.29; 57.32; 51.74; 41.52; 28.98; 28.29; 27.25; 13.62; 11.06. MS m/e: 538 (12); 57 (100). $[\alpha]_D^{20} = -1.6$ ($c = 1.65$, $CHCl_3$). Anal. calcd for $C_{29}H_{49}NO_4Sn$: C, 58.60; H, 8.31; N. 2.36. Found: C, 58.72; H, 8.43; N, 2.24%.

4.2.3. Methyl 2-{(1*S*)-1-[(*tert*-butoxy)carbonylamino]-2-methylbutyl}-(2*Z*)-3-tributylstannyl-prop-2-enoate 7c. Amine **8c** (422 mg, 2.0 mmol) was reacted according to the general procedure. After purification (eluent: petroleum ether/ethyl acetate = 10/1) 523 mg of **7c** (47%) were obtained: ^1H NMR (200 MHz) δ: 6.79 [bs, 1H, $J_{Sn,H} = 54.2$ Hz]; 5.28–5.10 [m, 1H]; 4.28–4.14 [m, 1H]; 3.74 [s, 3H]; 1.75–1.20 [m, 15H]; 1.45 [s, 9H]; 0.98–0.75 [m, 21H]. ^{13}C NMR (50.3 MHz) δ: 167.37; 155.39; 150.94; 146.30; 79.03; 61.80; 51.70; 37.88; 29.09; 28.40; 27.29; 25.13; 16.46; 13.66; 11.39; 11.22. MS m/e: 504 (17); 57 (100). $[\alpha]_D^{22} = -32.1$ ($c = 1.00$, $CHCl_3$). Anal. calcd for $C_{26}H_{51}NO_4Sn$: C, 55.72; H, 9.17; N, 2.50. Found: C, 55.53; H, 9.21; N, 2.54%.

4.3. Coupling with electrophiles. General procedure

The vinylstannane **7** (1 equiv.) was dissolved in the appropriate solvent (1 mL) and reacted with the electrophile (2 equiv.) in the presence of a catalytic amount (5 mol%) of *trans*-$(PhCH_2)ClPd(PPh_3)_2$. The reaction was left to stir at 50°C for 24 h. Filtration and evaporation of the solvent afforded a crude oil, which was dissolved in ethyl acetate and then stirred for 1 h with a saturated aqueous KF solution. After filtration, the organic layer was washed with brine, dried and evaporated to afford a crude product which was purified by column chromatography.

4.3.1. Methyl (2*Z*)-2-[(*tert*-butoxy)carbonylamino)-methyl])-hexa-2,5-dienoate 14a. The vinylstannane **7a** (201 mg, 0.4 mmol) was dissolved in $CHCl_3$ (1.5 mL) and reacted with allylbromide (70 mg, 0.8 mmol) according to the general procedure. After purification (eluent: petroleum ether/ethyl acetate = 4/1) 73 mg of **14a** (70%) were obtained. Compound **14a** isomerized rapidly into the conjugated isomer **15a**. Compound **14a**: ^{1}H NMR (200 MHz) δ: 6.40–6.10 [m, 1H]; 5.93–5.72 [ddt, 1H, J = 6.6, 10.4, 17.2 Hz]; 5.12–5.00 [m, 2H], 4.91 [bs, 1H]; 3.94–3.85 [bd, 2H, J = 5.4 Hz]; 3.77 [s, 3H]; 3.34–3.24 [m, 2H]; 1.43 [s, 9H]. ^{13}C NMR (50.3 MHz) δ: 166.94; 155.51; 143.07; 135.21; 128.87; 116.00; 79.42; 51.49; 44.12; 44.12; 33.65. MS m/e: 213 (3); 57 (100). Anal. calcd for $C_{13}H_{21}NO_4$: C, 61.16; H, 8.29; N, 4.98. Found: C, 60.90; H, 8.16; N, 5.58%.

4.3.2. Methyl 2-{(1*S*)-1-[(*tert*-butoxy)carbonylamino]-2-phenylethyl}-(2*Z*)-hexa-2,5-dienoate 15b. The vinylstannane **7b** (140 mg, 0.2 mmol) was dissolved in $CHCl_3$ (1.0 mL) and reacted with allylbromide (40 mg, 0.4 mmol) according to the general procedure. After purification (eluent: petroleum ether/ethyl acetate = 7/1) 45 mg of a mixture of **14b** and **15b** (42%) were obtained. Compound **14b**: ^{1}H NMR (200 MHz) δ: 7.38–7.10 [m, 5H]; 5.88 [t, 1H, J = 8.0 Hz]; 5.76–5.58 [m, 1H], 5.24 [bs, 1H]; 5.20–4.86 [m, 2H]; 4.66–4.52 [m, 1H]; 3.80 [s, 3H]; 3.16–3.04 [m, 2H]; 2.98–2.88 [m, 2H]; 1.38 [s, 9H]. MS m/e: 254 (3); 57 (100).

4.3.3. Methyl (2*Z*)-2-[(*tert*-butoxy)carbonylamino-methyl)]-3-phenylprop-2-enoate 17aa. The vinylstannane **7a** (503 mg, 1.0 mmol) was dissolved in acetonitrile (4 mL) and reacted with iodobenzene (400 mg, 2 mmol) according to the general procedure. After purification (eluent: petroleum ether/ethyl acetate = 3/1) 197 mg of **17aa** (68%) were obtained. ^{1}H NMR (200 MHz) δ: 7.38–7.20 [m, 5H]; 6.93 [s, 1H]; 4.96 [bs, 1H]; 4.10–4.00 [m, 2H]; 3.66 [s, 3H]; 1.45 [s, 9H]. ^{13}C NMR (50.3 MHz) δ: 168.45; 155.58; 137.01; 135.32; 134.73; 128.48; 128.28; 128.07; 79.62; 51.69; 44.65; 28.34. MS m/e: 235 (3); 159 (100). Anal. calcd for $C_{16}H_{21}NO_4$: C, 65.96; H, 7.27; N, 4.81. Found: C, 65.73; H, 7.26; N, 4.88%.

4.3.4. Methyl 2-{(1*S*)-1-[(*tert*-butoxy)carbonylamino]-2-phenylethyl}-(2*Z*)-3-phenylprop-2-enoate 17ba. The vinylstannane **7b** (124 mg, 0.2 mmol) was dissolved in acetonitrile (1 mL) and reacted with iodobenzene (80 mg, 0.4 mmol) according to the general procedure. After purification (eluent: petroleum ether/ethyl acetate = 5/1) 59 mg of **17ba** (74%) were obtained. ^{1}H NMR (200 MHz) δ: 7.35–7.19 [m, 5H]; 7.19–7.08 [m, 5H]; 6.60 [bs, 1H]; 5.23 [bd, 1H, J = 11.0 Hz]; 4.78–4.59 [m, 1H]; 3.65 [s, 3H]; 3.10–2.95 [m, 2H]; 1.40 [s, 9H]. ^{13}C NMR (50.3 MHz) δ: 168.87; 154.87; 137.27; 136.37; 135.49; 132.35; 129.51; 128.32; 128.15; 128.04; 126.55; 79.58; 56.74; 51.57; 40.87; 28.28. MS m/e: 290 (5); 190 (100). $[\alpha]_D^{22}$ = +19.4 (c = 0.99, $CHCl_3$). Anal. calcd for $C_{23}H_{27}NO_4$: C, 72.42; H, 7.13; N, 3.67. Found: C, 72.57; H, 7.16; N, 3.76%.

4.3.5. Methyl 2-{(1*S*)-1-[(*tert*-butoxy)carbonylamino]-2-methylbutyl}-(2*Z*)-3-phenylprop-2-enoate 17ca. The vinylstannane **7c** (130 mg, 0.2 mmol) was dissolved in acetonitrile (1 mL) and reacted with iodobenzene (80 mg, 0.4 mmol) according to the general procedure. After purification (eluent: petroleum ether/ethyl acetate = 7/1) 42 mg of **17ca** (54%) were obtained. ^{1}H NMR (200 MHz) δ: 7.38–7.19 [m, 5H]; 6.84 [bs, 1H]; 5.24 [bd, 1H, J = 13.6 Hz]; 4.21–4.08 [m, 1H]; 3.63 [s, 3H]; 1.78–1.46 [m, 1H]; 1.44 [s, 9H]; 1.22–1.00 [m, 2H]; 1.00–0.80 [m, 6H]. ^{13}C NMR (50.3 MHz) δ: 169.35; 155.35; 136.61; 135.57; 133.17; 128.51; 128.25; 128.07; 79.25; 60.80; 51.54; 37.77; 28.37; 16.23; 11.20. MS m/e: 346 (5); 190 (100). $[\alpha]_D^{22}$ = −45.3 (c = 1.05, $CHCl_3$). Anal. calcd for $C_{20}H_{29}NO_4$: C, 69.14; H, 8.41; N, 4.03. Found: C, 69.27; H, 8.46; N, 4.08%.

4.3.6. Methyl (2*Z*)-2-[(*tert*-butoxy)carbonylamino-methyl]-3-(4-methoxyphenyl)prop-2-enoate 17ab. The vinylstannane **7a** (130 mg, 0.2 mmol) was dissolved in acetonitrile (1 mL) and reacted with *p*-iodoanisole (65 mg, 0.3 mmol) according to the general procedure. After purification (eluent: petroleum ether/ethyl acetate = 2/1) 50 mg of **17ab** (67%) were obtained. ^{1}H NMR (200 MHz) δ: 7.27 [d, 2H, J = 8.4 Hz]; 6.88–6.81 [m, 3H]; 4.98 [bs, 1H]; 4.06–3.99 [m, 2H]; 3.80 [s, 3H]; 3.68 [s, 3H]; 1.44 [s, 9H]. ^{13}C NMR (50.3 MHz) δ: 168.46; 159.69; 155.51; 137.27; 130.37; 127.91; 127.51; 113.45; 79.51; 55.20; 51.62; 44.99; 28.37. MS m/e: 265 (31); 189 (100). Anal. calcd for $C_{17}H_{23}NO_5$: C, 63.54; H, 7.21; N, 4.36. Found: C, 63.47; H, 7.45; N, 4.20%.

4.3.7. Methyl 2-{(1*S*)-1-[(*tert*-butoxy)carbonylamino]-2-phenylethyl}-(2*Z*)-3-(4-methoxy-phenyl)prop-2-enoate 17bb. The vinylstannane **7b** (139 mg, 0.2 mmol) was dissolved in acetonitrile (1 mL) and reacted with *p*-iodoanisole (65 mg, 0.3 mmol) according to the general procedure. After purification (eluent: petroleum ether/ethyl acetate = 3/1) 55 mg of **17bb** (52%) were obtained. ^{1}H NMR (200 MHz) δ: 7.35–7.15 [m, 5H]; 7.10 [d, 2H, J = 8.6 Hz]; 6.80 [d, 2H, J = 8.6 Hz]; 6.54 [s, 1H]; 5.20 [bs, 1H]; 4.73–4.56 [m, 1H]; 3.79 [s, 3H]; 3.69 [s, 3H]; 3.04–2.95 [m, 2H]; 1.39 [s, 9H]. ^{13}C NMR (50.3 MHz) δ: 169.03; 159.55; 154.83; 137.37; 136.28; 129.88; 129.46; 128.26; 127.77; 127.46; 126.46; 113.49; 79.55; 57.01; 55.24; 51.58; 41.06; 28.37. MS m/e: 320 (18); 57 (100). $[\alpha]_D^{22}$ = +17.2 (c = 1.04, $CHCl_3$). Anal. calcd for $C_{24}H_{29}NO_5$: C, 70.05; H, 7.10; N, 3.40. Found: C, 69.55; H, 7.32; N, 9.36%.

4.3.8. Methyl 2-{(1*S*)-1-[(*tert*-butoxy)carbonylamino]-2-methylbutyl}-(2*Z*)-3-(4-methoxy-phenyl)prop-2-enoate 17cb. The vinylstannane **7c** (118 mg, 0.2 mmol) was dissolved in acetonitrile (1 mL) and reacted with *p*-iodoanisole (65 mg, 0.3 mmol) according to the general procedure. After purification (eluent: petroleum ether/ethyl acetate = 5/1) 46 mg of **17cb** (63%) were obtained. ^{1}H NMR (200 MHz) δ: 7.19 [d, 2H, J = 8.6 Hz]; 6.83 [d, 2H, J = 8.6 Hz]; 6.77 [bs, 1H]; 5.25 [bd, 1H, J = 9.6 Hz]; 4.18–4.02 [m, 1H]; 3.80 [s, 3H]; 3.66 [s, 3H]; 1.71–1.55 [m, 1H]; 1.43 [s, 9H]; 1.22–1.04 [m, 2H]; 0.96–0.83 [m, 6H]. ^{13}C NMR (50.3 MHz) δ: 169.55; 159.61; 155.41; 136.09; 131.08; 129.99; 129.86; 127.95;

113.58; 79.23; 61.08; 55.24; 51.53; 37.90; 28.40; 25.34; 16.27; 11.23. MS m/e: 320 (10); 220 (100). $[\alpha]_D^{22} = -58.2$ ($c = 1.36$, $CHCl_3$). Anal. calcd for $C_{21}H_{31}NO_5$: C, 66.82; H, 8.28; N, 3.71. Found: C, 66.21; H, 8.36; N, 3.58%.

4.4. Hydrogenation of β-aminoacrylates

Acrylates **17ba**, **17bb** were dissolved in 95% methanol, and hydrogenated (H_2, 1 Atm) over a catalytic amount of Pt on charcoal. The reaction was monitored by GC. After completion, the solution was filtered over Celite and the solvent was evaporated. The diastereomeric excess was determined by calculating the integral ratio of the methyl ester diagnostic signals in the ^1H NMR spectrum of the crude.

4.4.1. Methyl (2*R*,2*S*)-2-benzyl-(3*S*)-3-[(*tert*-butoxy)-carbonylamino]-4-phenyl-butanoate 18a. Compound **17ba** (40 mg, 0.1 mmol) was reacted according to the general procedure. After workup 36 mg of a mixture of *anti* **18a** and *syn* **18a** were obtained in a 30% d.e. Compound **18a**: major isomer, ^1H NMR (200 MHz) δ: 7.28–7.02 [m, 10H]; 5.77 [bd, 1H, $J = 8.6$ Hz]; 4.04–3.91 [m, 1H]; 3.72–3.61 [m, 1H]; 3.60 [s, 3H]; 3.02–2.78 [m, 4H]; 1.42 [s, 9H]. MS m/e: 292 (2); 91 (82); 57 (100).

4.4.2. Methyl (2*R*,2*S*)-2-benzyl-(3*S*)-3-(*tert*-butoxy)-carbonylamino]-4-(4-methoxyphenyl)-butanoate 18b. Compound **17bb** (32 mg, 0.1 mmol) was reacted according to the general procedure. After workup 29 mg of a mixture of *anti* **18b** and *syn* **18b** were obtained in a 30% d.e. Compound **18b**: major isomer, ^1H NMR (200 MHz) δ: 7.28–7.11 [m, 5H]; 6.99 [d, 2H, $J = 8.8$ Hz]; 6.77 [d, 2H, $J = 8.8$ Hz]; 5.57 [bs, 1H, $J = 8.6$ Hz]; 4.02–3.91 [m, 1H]; 3.77 [s, 3H]; 3.72–3.61 [m, 1H]; 3.62 [s, 3H]; 2.91–2.57 [m, 4H]; 1.42 [s, 9H]. MS m/e: 216 (4); 116 (48); 57 (100).

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