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Diastereoselective addition of vinylmagnesium halides to variously N-mono- and N,N-diprotected L-alaninals

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Abstract: Diastereoselective C_2-elongation processes of N-mono- **1a–c** and N,N-diprotected **1d–f** L-alaninals, using vinylmagnesium bromide and chloride, are described. A substantial difference between effects of the N-protecting groups replacing either one or two amino protons was observed. © 1997 Elsevier Science Ltd. All rights reserved.

α-Amino aldehydes are versatile chirons, frequently used in asymmetric syntheses of amino sugars[1–4] and other natural products.[5–7] Stereoselective elongation of the carbon skeleton is the central point of such syntheses.[8–10] We recently described several C_3- and C_4-elongations of α-amino aldehydes *via* addition of allyltrimethylsilane,[11] the Barbier type reactions,[12] high pressure [4+2] cycloaddition,[13,14] Lewis acid-mediated cyclocondensation,[14,15] and furyllithium addition.[16] When we used N,N-diprotected α-amino aldehydes instead of N-monoprotected ones, the direction of asymmetric induction was reversed. We explained this was a result of substantial changes in the nature of the amino group: from steric to chelating character.[17]

We considered it very interesting, especially from the synthetic point of view, to study another type of elongation, namely addition of vinylmagnesium halides to variously N-protected α-amino aldehydes. All six α-amino aldehydes **1a–f** were obtained from two independent routes: (1) from the respective α-amino alcohols, using the TEMPO oxidation method[11,18,19] and (2) from methyl esters of the respective α-amino acids, using the DIBAL reduction method.[20–22] In all additions of vinylmagnesium bromide **2a** to α-amino aldehydes **1a–f**, obtained *via* route (1), mixtures of *syn*-**3** and *anti*-**4** diastereoisomeric products were obtained (Scheme 1, Table 1). Throughout this paper we follow *syn/anti* convention as proposed by Masamune *et al.*[23,24]

1a R^1 = H, R^2 = Boc
1b R^1 = H, R^2 = Cbz
1c R^1 = H, R^2 = Ts
1d R^1 = Bn, R^2 = Boc
1e R^1 = Bn, R^2 = Cbz
1f R^1 = Bn, R^2 = Ts

2a X=Br
2b X=Cl

3a **3b** **3c** **3d** **3e** **3f**

4a **4b** **4c** **4d** **4e** **4f**

Scheme 1.

Addition of vinylmagnesium bromide **2a** to N-monoprotected α-amino aldehydes **1a–c** (Table 1, Entries 1–3) yielded mixtures of diastereoisomers **3** and **4**, with a preference for the *syn*-product **3**, but the diastereoselectivity was rather low, accordingly to the literature data.[25,26] Similar addition of

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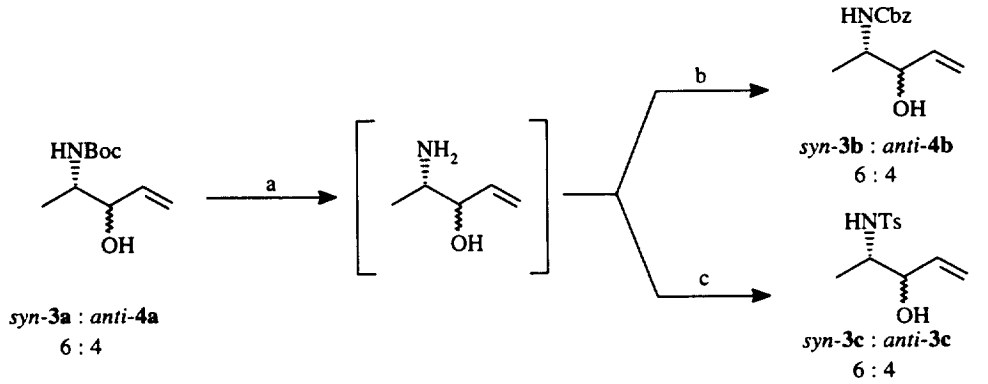
Table 1. Addition of **2a** to α-amino aldehydes **1a–f**

Entry	α-Amino Aldehyde	VinylMgBr [n equiv.]	Temperature [0°C]	Yield [%]	*syn:anti* 3:4
1	**1a**	9	4	90	58:42
2	**1b**	9	4	65	78:22
3	**1c**	9	23	70	60:40
4	**1d**	4	-78	55	31:69
5	**1e**	2.5	-78	62	23:77
6	**1f**	4	-78	56	11:89

N,N-diprotected L-alaninals **1d–f** (Entries 4–6) afforded better diastereoselectivity, with a preference for the *anti*-product **4**.

N-Monoprotected diastereoisomeric adducts **3a–c** and **4a–c** were inseparable by any chromatographic method tried. Therefore, an integration of signals, derived from the methyl groups in the ^{1}H NMR spectra, was used for determination of a *syn/anti* ratio in these cases. For N,N-diprotected adducts, however, a *syn/anti* ratio was determined *via* high performance liquid chromatography (HPLC) using a Nucleosil 100 column. Moreover, the preparative version of this HPLC method allowed us to separate diastereoisomeric mixtures and to obtain compounds **3d–f** and **4d–f** in diastereoisomerically pure form.

After the determination of the extent of asymmetric induction, we studied its direction. In the case of N-monoprotected adducts *syn*-**3a** and *anti*-**4a**, their relative configurations were established on the basis of the literature data.[27] For other inseparable mixtures **3b+4b** and **3c+4c**, chemical correlations with a mixture **3a+4a** of known configuration of the major diastereoisomer *syn*-**3a**, were used as shown in Scheme 2.



syn-**3a** : *anti*-**4a** 6 : 4

syn-**3b** : *anti*-**4b** 6 : 4

syn-**3c** : *anti*-**3c** 6 : 4

Scheme 2. Reaction conditions: (a) TFA, CH_2Cl_2, RT; (b) CbzCl, $NaHCO_3$, AcOEt, 0°C; (c) TsCl, Et_3N, CH_2Cl_2, 0°C to RT.

Among the diastereoisomerically pure N,N-diprotected adducts **3d–f** and **4d–f**, the major product of the addition of bromide **2a** to aldehyde **1e**, the compound **4e** formed single crystals suitable for X-ray analysis which was used for the final proof of the structure and stereochemistry (Figure 1).

For remaining pairs of the diastereoisomeric products of additions of bromide **2a** to aldehydes **1d** and **1f**, configurations were established *via* chemical correlations shown in Scheme 3. A mixture of diastereoisomers of unknown configuration **3d** and **4d** (3:7) was transformed independently into a 3:7 mixture of diastereoisomers *syn*-**3e** and *anti*-**4e**, and into a 3:7 mixture of diastereoisomers of unknown configuration **3f** and **4f** (Scheme 3).

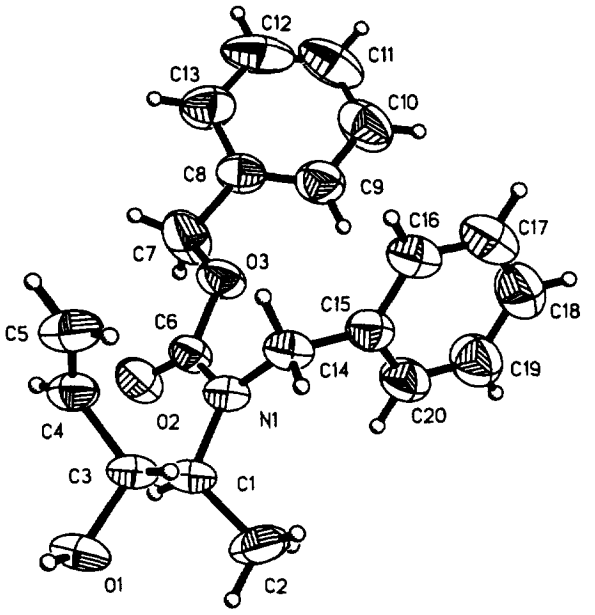
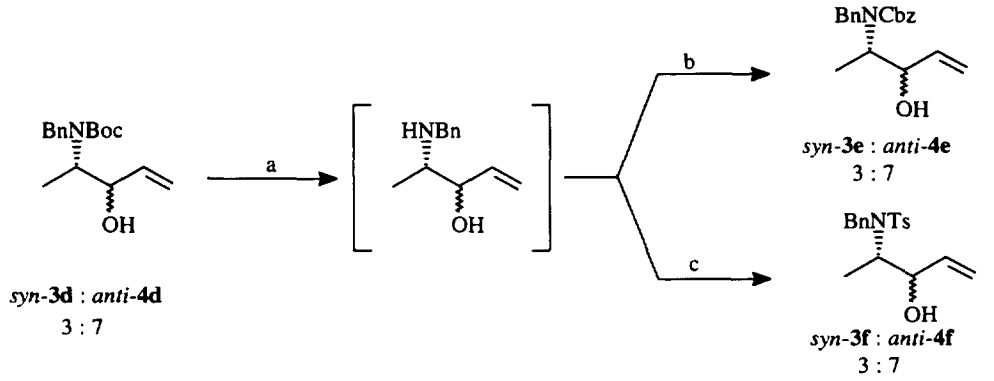


Figure 1. ORTEP Diagram of the molecule of compound *anti*-**4e**.



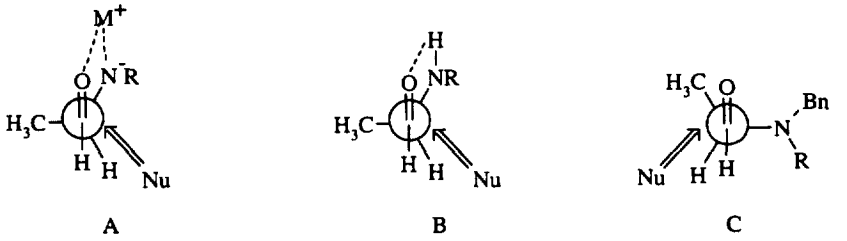
syn-**3d** : *anti*-**4d**
3 : 7

syn-**3e** : *anti*-**4e**
3 : 7

syn-**3f** : *anti*-**4f**
3 : 7

Scheme 3. Reaction conditions: (a) TFA, CH_2Cl_2, RT; (b) CbzCl, $NaHCO_3$, AcOEt, 0°C; (c) TsCl, Et_3N, CH_2Cl_2, 0°C to RT.

In conclusion, *syn*-diastereoselectivity was observed for all additions with N-monoprotected L-alaninals,[25–27] independent of the protecting group used, whereas for N,N-diprotected L-alaninals only *anti*-diastereoselectivity[28] was observed. The direction of asymmetric induction is in agreement with commonly accepted stereochemical models, as shown in Scheme 4.



Scheme 4.

Table 2. Addition of **2b** to α-amino aldehydes **1a–f** obtained *via* DIBAL reduction

Entry	α-Amino Aldehyde	Temperature [0°C]	Yield [%]	*syn:anti* **3:4**
1	**1a**	0	40	79:21
2	**1b**	0	56	80:20
3	**1c**	0	31	87:13
4	**1d**	0	0	-
5	**1e**	0→RT	13	26:74
6	**1f**	0→RT	3	19:81

In the case of N-monoprotected α-amino aldehydes **1a–c**, addition of vinylmagnesium bromide **2a** led to *syn*-adducts, according to the chelation-controlled cyclic Cram model A,[29] formed as a consequence of deprotonation of alaninals in the first step, which is similar to the hydrogen-bonding cyclic transition state B. To achieve *anti*-diastereoselection, the Felkin–Anh model C[30,31] should operate, what is favorable in the case of additions to N,N-diprotected L-alaninals **1d–f**.

Relatively poor results of the above-presented Grignard additions, especially in the case of N-monoprotected L-alaninals, prompted us to turn our attention to other modified Grignard procedures. Recently, Ibuka *et al.*[27] reacted aldehyde **1a** with vinylmagnesium chloride **2b**,[32] and observed a moderate *syn*-diastereoselectivity (7:3). When this addition was performed in a one-pot manner, following the DIBAL reduction of the corresponding methyl ester, the *syn*-diastereoselectivity rose substantially. This behavior was explained by enhanced chelation of the aldehyde by aluminum. Therefore we decided to follow this procedure for both N-monoprotected **1a–c** and N,N-diprotected **1d–f** α-amino aldehydes (Scheme 1, Table 2). Our results confirm those published by Ibuka *et al.*[27] In the case of N-monoprotected L-alaninals **1a–c**, where formation of α-chelate is possible, higher asymmetric induction was observed (Entries 1–3). In the case of N,N-diprotected L-alaninals **1d–f** α-chelation is impossible and asymmetric induction is similar to that observed for regular addition of vinylmagnesium bromide **2a** (Entries 5 and 6). Moreover, the reaction yield is very low, and for aldehyde **1d** we did not detected any reaction product **3d** or **4d** (Entry 4).

Solution of the problem under consideration calls for further studies, extended for other C_2-elongation procedures, which are now in progress.

Experimental

General

Melting points were determined using a Kofler hot stage apparatus and are uncorrected. Optical rotations were recorded using a JASCO DIP-360 polarimeter with a thermally jacketed 10 cm cell. ^{1}H NMR spectra were recorded using a Bruker AM 500 (500 MHz) spectrometer, and ^{13}C NMR spectra were recorded also using a Bruker AM 500 (125 MHz) spectrometer. All chemical shifts are quoted in parts per million relative to tetramethylsilane (δ, 0.00 ppm), and coupling constants (J) are measured in Hertz. IR spectra were obtained on a Perkin–Elmer 1640 FTIR spectrophotometer in KBr pellets. Mass spectra were recorded on an AMD-604 Intectra instrument using the electron impact (EI) technique. Single-crystal X-ray diffraction analysis was performed on an Enraf–Nonius MACH 3 diffractometer. Flash-column chromatography was performed according to Still *et al.*[33] on silica gel (Kieselgel-60, Merck, 200–400 mesh).

Addition of vinylmagnesium halides to N-protected L-*alaninals* ***1a–f****. General procedures*

A. Addition of vinylmagnesium bromide ***2a***

A precooled solution of vinylmagnesium bromide **2a** (2.5–9 mmol, 2.5–9 mL, 1M in THF) was added dropwise under argon to a cold (−78°C), stirred solution of an α-amino aldehyde (1 mmol in 8 mL of dry THF). After stirring at the temperature given in Table 1, for several hours (TLC control), a saturated aqueous solution of ammonium chloride (10 mL) was added, and the reaction mixture was allowed to reach room temperature (if necessary) then extracted with Et_2O (3×10 mL). The combined extracts were washed with brine (10 mL), dried ($MgSO_4$) and evaporated *in vacuo*. Flash chromatography (hexanes:EtOAc 9:1 to 1:1) afforded a mixture of *syn* and *anti* diastereoisomers.

B. Addition of vinylmagnesium chloride ***2b*** *in the presence of DIBAL*

A precooled solution of DIBAL (2 mmol, 1.3 mL, 1.5 M in toluene) was added dropwise under argon to a cold (−78°C) stirred solution of an α-amino methyl ester (1 mmol) in methylene chloride (0.75 mL). Stirring was continued at −78°C for three hours, and additionally at −20°C for 30 min. After cooling (−78°C) of the reaction mixture, a precooled solution of vinylmagnesium chloride **2b** (3 mmol, 1.8 mL, 15% in THF) was added dropwise under argon, and stirring was continued for 30 min. The reaction temperature was then increased to 0°C and the reaction mixture was stirred for an additional three hours and then diluted with 1 M hydrochloric acid (5 mL), and extracted with Et_2O (3×5 mL). The combined extracts were washed with brine (5 mL), dried ($MgSO_4$) and evaporated *in vacuo*. Flash chromatography was performed analogously as in the former case.

Analytical and spectral data for a 1.5:1 mixture of syn-***3a*** *and* anti-***4a***

ν_{max}(film)/cm^{-1}: 3404; 2978; 1690; 1507; 1367; 1249; 1171; 1053. δ_H (200 MHz; $CDCl_3$); 6.0–5.8 (m, 1H); 5.37 (t, J=1.6, 0.2H); 5.35 (t, J=1.6, 0.4H); 5.3–5.2 (m, 1.4H); 4.8–4.6 (m, 1H); 4.3–4.1 (m, 0.4H); 4.08 (m, 0.6H); 3.9–3.6 (m, 1H); 2.95 (s, 0.4H); 2.63 (s, 0.6H); 1.44 (s, 9H); 1.17 (d, J=6.9, 1.8H); 1.09 (d, J=6.9, 1.2H) δ_C (125 MHz; $CDCl_3$): 137.9; 136.9; 116.6; 116.5; 50.7; 29.7; 28.3; 17.5; 15.3; 10.2. m/z (LSIMS): 224 $(M+Na)^+$; 202 $(M+H)^+$. (LSIMS HR) calculated for $C_{10}H_{20}NO_3$ $(M+H)^+$ 202.1443. Found 202.1449.

Analytical and spectral data for a 1.8:1 mixture of syn-***3b*** *and* anti-***4b***

ν_{max}(film)/cm^{-1}: 3412; 2978; 1695; 1532; 1454; 1340; 1247; 1053; 990; 740; 698. δ_H (500 MHz, $CDCl_3$): 7.3–7.2 (m, 5H); 5.9–5.7 (m, 1H); 5.4–5.3 (m, 1H); 5.3–5.2 (m, 1H); 5.2–5.1 (m, 1H); 5.1–5.0 (m, 2H); 4.18 (bs, 0.4H); 3.99 (bs, 0.6H); 3.9–3.7 (m, 1H); 3.51 (bs, 1H); 1.14 (d, J=6.8, 2H); 1.05 (d, J=6.9, 1H). δ_C (125 MHz, $CDCl_3$): 156.4; 156.2; 137.7; 136.9; 136.3; 136.2; 128.2; 128.2; 127.9; 127.8; 127.7; 116.2; 116.1; 75.1; 74.7; 60.3; 50.9; 50.8; 20.7; 17.2; 14.5; 13.9. Anal. Calcd for $C_{14}H_{23}NO_3$: C, 66.38%; H, 7.23%; N, 5.96%. Found: C, 66.28%; H, 7.29%; N, 5.86%.

Analytical and spectral data for a 1.6:1 mixture of syn-***3c*** *and* anti-***4c***

ν_{max}(film)/cm^{-1}: 3499; 3279; 2981; 1598; 1431; 1382; 1326; 1160; 1092; 994; 942; 815; 665. δ_H (500 MHz, $CDCl_3$): 7.8–7.7 (m, 2H); 7.3 (m, 2H); 5.8–5.7 (m, 1H); 5.50 (d, J=8.4, 0.4H); 5.44 (d, J=8.0, 0.6H); 5.27 (dt, J_t=17.2, J_d=1.5, 0.4H); 5.26 (dt, J_t=17.2, J_d=1.3, 0.6H); 5.18 (dt, J_t=10.6, J_d=1.4, 0.4H); 5.13 (dt, J_t=10.5, J_d=1.2, 0.6H); 4.2–4.1 (m, 0.4H); 3.93 (m, 0.6H); 3.39 (m, 0.4H); 3.3–3.2 (m, 0.6H); 2.98 (s, 1H); 2.41 (s, 3H); 1.00 (d, J=6.7, 1.8H); 0.93 (d, J=6.9, 1.2H). δ_C (125 MHz, $CDCl_3$): 143.3; 143.2; 137.6; 136.8; 136.2; 129.6; 129.5; 127.0; 126.9; 117.6; 116.8; 75.6; 74.7; 53.8; 53.6; 21.3; 17.4; 15.0. Anal. Calcd for $C_{12}H_{17}NO_3S$: C, 56.47%; H, 6.67%; N, 5.49%; S, 12.65%. Found: C, 56.24%; H, 6.84%; N, 5.29%; S,12.65%.

Analytical and spectral data for syn-***3d***

δ_H (500 MHz, $CDCl_3$): 7.3–7.2 (m, 5H); 5.76 (ddd, J_1=17.1, J_2=10.6, J_3=5.9, 1H); 5.20 (dt, J_d=17.2, J_t=1.6, 1H); 5.09 (d, J=10.5, 1H); 4.5–4.3 (m, 3H); 3.63 (m, 1H); 1.43 (s, 9H); 1.17 (d, J=7.1, 3H). δ_C

(125 MHz, $CDCl_3$): 139.1; 138.6; 128.3; 127.1; 127.0; 115.5; 80.4; 75.9; 58.8; 51.3; 28.3; 11.7. Anal. Calcd for $C_{17}H_{25}NO_3$: C, 70.07%; H, 8.65%; N, 4.81%. Found: C, 69.98%; H, 8.76%;N, 4.78%.

Analytical and spectral data for anti-***4d***

ν_{max} (film)/cm^{-1}: 3444; 3087; 2974; 2931; 1688; 1668; 1496; 1453; 1408; 1366; 1335; 1249; 1167; 1013; 923; 733; 699. $[\alpha]_D^{20}$=+2.8 (c 1.1, $CHCl_3$); δ_H (500 MHz, $CDCl_3$): 7.3–7.2 (m, 5H); 5.76 (ddd, J_1=17.1 Hz, J_2=10.4 Hz, J_3=6.1 Hz, 1H); 5.30 (d, J=17.1 Hz, 1H); 5.14 (d, J=10.4 Hz, 1H); 4.60–4.42 (m, 1H); 4.33–4.25 (m, 1H); 3.75–3.65 (m, 1H); 1.43 (s, 9H); 1.20–1.12 (m, 3H). δ_C (125 MHz, $CDCl_3$): 139.1; 138.7; 138.6; 128.4; 127.4; 127.1; 127.0; 115.8; 80.6; 75.6; 58.5; 51.0; 50.9; 28.4; 15.2. Anal. Calcd for $C_{17}H_{25}NO_3$: C, 70.07%; H, 8.65%; N, 4.81%. Found: C, 69.82%; H, 8.79%; N, 4.69%.

Analytical and spectral data for syn-***3e***

ν_{max} (film)/cm^{-1}: 3431; 2979; 1679; 1496; 1453; 1418; 1333; 1234; 1100; 1015; 734; 698. $[\alpha]_D^{20}$=−0.2 (c 1.2, $CHCl_3$). δ_H (500 MHz, $CDCl_3$): 7.4–7.2 (m, 10H); 5.74 (ddd, J_1=17.0, J_2=10.6, J_3=6.3, 1H); 5.3–5.1 (m, 4H); 4.7–4.5 (m, 1H); 4.5–4.3 (m, 1H); 4.11 (t, J=6.5, 1H); 3.78 (bs, 1H); 1.2–1.1 (m, 3H). δ_C (125 MHz, $CDCl_3$): 157.3; 146.4; 138.4; 136.4; 128.4; 128.3; 128.2; 127.9; 127.8; 127.4; 127.2; 120.2; 116.1; 75.2; 67.4; 58.8; 50.7; 15.0. Anal. Calcd for $C_{20}H_{23}NO_3$: C, 73.82%; H, 7.12%; N, 4.30%. Found: C, 73.75%; H, 7.24%; N, 4.35%.

Analytical and spectral data for anti-***4e***

ν_{max} (KBr)/cm^{-1}: 3433; 2926; 1670; 1477; 1417; 1332; 1278; 1216; 1126; 1065; 1015; 950; 732; 696. $[\alpha]_D^{20}$=−3.4 (c 1.0, $CHCl_3$). M.p. 63–64°C. δ_H (500 MHz, $CDCl_3$): 7.4–7.2 (m, 10H); 5.8–5.7 (s, 1H); 5.3–5.1 (m, 4H); 4.58 ($d_{A\ B/2}$, J=15.1, 1H); 4.41 ($d_{A\ B/2}$, J=16.2, 1H); 4.34 (bs, 1H); 3.88 (bs, 1H); 3.62 (bs, 1H); 1.19 (d, J=7.0, 3H). δ_C (125 MHz, $CDCl_3$): 138.4; 138.2; 128.6; 128.5; 128.1; 127.9; 127.3; 120.3; 125.8; 75.8; 67.5; 59.5; 51.3; 11.5. Anal. Calcd for $C_{20}H_{23}NO_3$: C, 73.82%; H, 7.12%; N, 4.30%. Found: C, 73.74%; H, 7.18%; N, 4.31%.

Crystal data and measurement conditions are given in Table 3. The positions of the H-atoms bonded to carbon atoms were generated from assumed geometries. The structure was solved by the SHELXS86[34] and refined with the SHELXL93[35] programs. Lists of the fractional atomic coordinates and isotropic thermal parameters, bond lengths and angles have been deposited at the Cambridge Crystallographic Data Centre.

Analytical and spectral data for syn-***3f***

ν_{max} (KBr)/cm^{-1}: 3433; 2926; 1670; 1477; 1417; 1332; 1278; 1216; 1126; 1065; 1015; 950; 732; 696. $[\alpha]_D^{20}$=−3.4 (c 1.0, $CHCl_3$). M.p. 63–64°C. δ_H (500 MHz, $CDCl_3$): 7.4–7.2 (m, 10H); 5.8–5.7 (s, 1H); 5.3–5.1 (m, 4H); 4.58 ($d_{A\ B/2}$, J=15.1, 1H); 4.41 ($d_{A\ B/2}$, J=16.2, 1H); 4.34 (bs, 1H); 3.88 (bs, 1H); 3.62 (bs, 1H); 1.19 (d, J=7.0, 3H). δ_C (125 MHz, $CDCl_3$): 138.4; 138.2; 128.6; 128.5; 128.1; 127.9; 127.3; 120.3; 125.8; 75.8; 67.5; 59.5; 51.3; 11.5. Anal. Calcd for $C_{19}H_{23}NO_3S$: C, 73.82%; H, 7.12%; N, 4.30%. Found: C, 73.74%; H, 7.18%; N, 4.31%.

Analytical and spectral data for anti-***4f***

ν_{max} (KBr)/cm^{-1}: 3515; 2976; 1597; 1456; 1320; 1158; 1086; 999; 854; 733; 654. $[\alpha]_D^{20}$=+26.5 (c 1.0, $CHCl_3$). M.p. 93–94°C. δ_H (500 MHz, $CDCl_3$): 7.69 (m, 2H); 7.38 (m, 2H); 7.30 (m, 5H); 5.8–5.9 (m, 1H); 5.06 (d, J=1.5, 1H); 5.04 (dt, J_d=7.2, J_t=1.5, 1H); 4.62 ($d_{A\ B/2}$, J=15.8, 1H); 4.28 ($d_{A\ B/2}$, J=15.8, 1H); 4.12 (bs, 1H); 3.87 (m, 1H); 2.42 (s, 3H); 1.76 (d, J=3.42, 1H); 0.98 (d, J=7.1, 3H). δ_C (125 MHz, $CDCl_3$): 143.37; 138.1; 138.0; 137.8; 129.7; 128.5; 128.1; 127.5; 127.0; 116.1; 75.4; 58.4; 48.6; 21.4; 11.7. Anal. Calcd for $C_{19}H_{23}NO_3S$: C, 66.09%; H, 6.67%; N, 4.06%. Found: C, 66.09%; H, 6.67%; N, 3.96%.

Table 3. Crystal data and measurement conditions for compound *anti*-**4e**

Identification code	*anti*-**4e**
Empirical formula	$C_{20}\ H_{23}\ N\ O_3$
Formula weight	325.39
Temperature (K)	293(2)
Wavelength (Å)	1.54178
Crystal system	monoclinic
Space group	$P2_1$
Unit cell dimensions (Å, °):	
a	6.8759(5)
b	7.6082(6)
c	17.5002(10)
β	97.770(3)
Volume $(Å)^3$	907.09(11)
Z	2
Density (calculated) ($Mg\ m^{-3}$)	1.191
Absorption coefficient (mm^{-1})	0.639
F(000)	348
Crystal size (mm)	0.14 x 0.17 x 0.21
θ-range for data collection (°)	2.55 to 74.85
Index ranges	$0 \le h \le 8, 0 \le k \le 9, -21 \le l \le 21$
Reflections collected	1909
Independent reflections	1769 [R(int) = 0.0153]
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	1769 / 1 / 219
Goodness-of-fit on F^2	1.094
Final R indices [$I>2\sigma(I)$]	$R_1 = 0.0648$, $wR_2 = 0.1544$
R indices (all data)	$R_1 = 0.0657$, $wR_2 = 0.1559$
Absolute structure parameter	-0.1(4)
Extinction coefficient	0.006(2)
Largest diff. peak and hole (e. $Å^{-3}$)	0.330 and -0.298

Chemical correlations

Removal of the tert-butoxycarbonyl protecting group

To a stirring at room temperature solution of N-Boc-protected or N-Bn-N-Boc-protected adduct (1 mmol) in methylene chloride (5 mL), was added dropwise trifluoroacetic acid (5 mmol). Stirring was continued at room temperature until the substrate disappeared (TLC). Then the reaction mixture was diluted with saturated $NaHCO_3$ (10 mL) and extracted with methylene chloride (3×5 mL). The combined extracts were washed with brine (10 mL), dried ($MgSO_4$) and concentrated *in vacuo*. The crude product was immediately used in the next reaction.

N-Protection with the tosyl and carbobenzoxy groups

Introduction of the tosyl[36] or carbobenzoxy[37] protecting group was carried out according to the known literature procedures.

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