# Barbier-Type Diastereoselective Allylation of α-Amino Aldehydes with an Enantiopure 2-Sulfinylallyl Building Block

Francesc Márquez,[†,‡] Raúl Montoro,[‡] Amadeu Llebaria,[‡] Elena Lago,[§] Elies Molins,[§] and Antonio Delgado*[,†,‡]

*Universitat de Barcelona, Facultat de Farmàcia, Unitat de Química Farmacèutica, (Unitat Associada al CSIC) Avgda. Joan XXIII, s/n, 08028 Barcelona, Spain, Research Unit on Bioactive Molecules (RUBAM), Departament de Química Orgànica Biològica, Institut d'Investigacions Químiques i Ambientals de Barcelona (IIQAB-C.S.I.C), Jordi Girona 18-26, 08034 Barcelona, Spain, and Institut de Ciència de Materials de Barcelona (CSIC), Campus Universitari de Bellaterra, E-08193 Cerdanyola, Spain*

*adelgado@far.ub.es*

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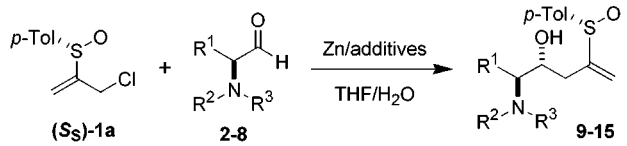
**Abstract:** An optimized procedure for the diastereoselective allylation under aqueous Barbier conditions of a series of α-amino aldehydes with our new chiral building block ($S_s$)-3-chloro-2-(*p*-tolylsulfinyl)-1-propene [($S_s$)-**1a**] to afford enantiomerically pure sulfinylamino alcohols in good yields and diastereoselectivites is reported. High levels of diastereoinduction can be achieved from α-amino aldehydes configurationally related to natural α-amino acids.

In our ongoing studies on the use of sulfoxides as chiral auxiliaries in organic synthesis,[1−3] we have described ($S_s$)-3-chloro-2-(*p*-tolylsulfinyl)-1-propene [($S_s$)-**1a**] as a new chiral building block[4] and its application for the diastereoselective allylation of aldehydes under environmentally friendly Barbier conditions.[4,5] As far as the aldehyde component is concerned, an interesting variation to widen the potential of diversity inherent to this allylation process relies on the use of enantiopure α-amino aldehydes as reaction partners. In this context, the use of α-amino aldehydes in organic synthesis has increased over the last years due to the development of efficient preparative methods from the corresponding α-amino acids or derivatives thereof.[6] Along this line, we wish to present our results on the allylation of enantiopure α-amino aldehydes with ($S_s$)-**1a** under optimized Barbier conditions (Scheme 1).Even though allylation of enantiopure α-amino aldehydes with simple allyl derivatives under Barbier conditions has been the subject of several interesting reports,[7] the use of ($S_s$)-**1a** as allylating agent is attractive. Thus, by the proper choice of the configuration of the starting α-amino aldehyde, a matched double diastereoinduction can be envisaged. In addition, the resulting sulfinylamino alcohols are versatile synthetic intermediates in which the vinyl sulfinyl moiety can be used, inter alia, as acceptor in inter or intramolecular Michael additions[8] with a vast array of nucleophiles.

**Scheme 1**




Due to the chiral nature of both reactive counterparts (α-amino aldehyde and sulfinyl allylic chloride), preliminary experiments were aimed at determining the "matched" pair in this allylation system. The serine-derived Garner's aldehyde (**2**) and its enantiomer (*ent*-**2**) were chosen for this purpose. Thus, allylation of each of the above enantiomers with ($S_s$)-**1a** under identical conditions afforded higher diastereoinduction from L-amino aldehyde **2** (Table 1, entries 1 and 5). Therefore, α-amino aldehydes derived from natural α-amino acids were used throughout this work. In addition, the dramatic effect of the chiral sulfoxide in this allylation system was made evident from achiral sulfone **1b**, whose reaction with α-amino aldehyde **2** afforded adduct **16** in remarkable lower diastereoselectivity (Table 1, entries 3 and 4). However, chirality on both reaction partners seems to be a requirement to reach high levels of diastereoinduction, since achiral *N*,*N*-diprotected glycinal derivative **3** (Table 2, entry 1) gave rise to a modest diastereomeric ratio in comparison with the remaining enantiopure *N*,*N*-diprotected amino aldehydes used in this study (see Table 2, entries 3−6).

Initial experiments with Garner's aldehyde **2** and ($S_s$)-**1a** under our previously described Barbier conditions,[4] afforded the diastereomeric adducts **9** (Table 1, entry 1). The configuration of the new stereogenic center for each diastereomer was unambiguously determined by X-ray diffraction analysis (see Supporting Information). Thus, the new stereogenic center on the major diastereomer was assigned as *R*, in agreement with our previous studies on the allylation of ($S_s$)-**1a** with simple aldehydes.[5] According to our working hypothesis, the observed diastereoinduction in this allylation system can be explained as a result of the competition between two major transition states, that is, an open-chain one and a cyclic one, each of them leading to a different diastereomer (Scheme 2). To address this issue, differences in metal coordination on both types of transition states were considered. Thus, while single metal−sulfoxide and metal−carbonyl coordinations take place in the open transition states, a double intramolecular metal−carbo-

* Corresponding author. Fax: int +34-932045904.
† Universitat de Barcelona.
‡ Institut d'Investigacions Químiques i Ambientals de Barcelona.
§ X-ray diffraction analysis: Institut de Ciència de Materials de Barcelona.

(1) Villar, J. M.; Delgado, A.; Llebaria, A.; Moretó, J. M.; Molins, E.; Miravitlles, C. *Tetrahedron* **1996**, *52*, 10525−10546.
(2) Henrich, M. L.; Delgado, A.; Molins, E.; Roig, A.; Llebaria, A. *Tetrahedron Lett.* **1999**, *40*, 4259−4262.
(3) For the use of sulfoxides as chiral auxiliaries in organic synthesis, see: Carreño, M. C. *Chem. Rev.* **1995**, *95*, 1717−1760.
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(5) Márquez, F.; Llebaria, A.; Delgado, A. *Tetrahedron Asymm.* **2001**, *12*, 1625−1634.
(6) Steurer, S.; Podlech, J. *Eur. J. Org. Chem.* **1999**, 1551−1560, and references therein.
(7) Allylations with **Zn**: (a) Rübsam, F.; Seck, S.; Giannis, A. *Tetrahedron* **1997**, *53*, 2823−2834. (b) Gryko, D.; Jurczak, J. *Helv. Chim. Acta* **2000**, *83*, 2705−2711. (c) Hanessian, S.; Park, H.; Yang, R. Y. *Synlett* **1997**, *4*, 353−354. **Sn**: refs 7a and 7b. **In**: ref 6 and (d) Paquette, L. A.; Mitzel, T. M.; Isaac, M. B.; Crasto, C. F.; Schomer, W. W. *J. Org. Chem.* **1997**, *62*, 4293−4301. (e) Steurer, S.; Podlech, J. *Adv. Synth. Catal.* **2001**, *343*, 251−254
(8) We have already reported on the synthesis of enantioenriched (*S*)-nicotine based on intramolecular Michael addition from a sulfinylamino alcohol has been reported (see ref 5).

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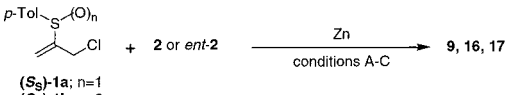
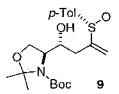
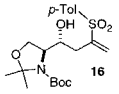
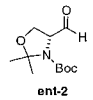
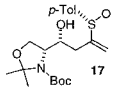
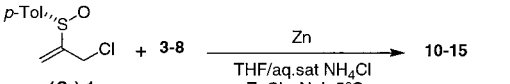
**Table 1. Allylation of Serinal Derivatives 2 and *ent*-2**

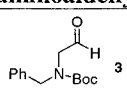
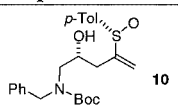
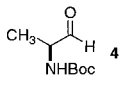
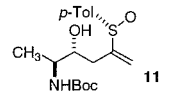
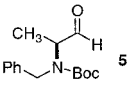
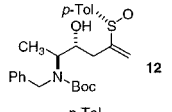
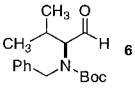
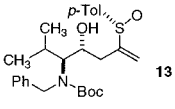
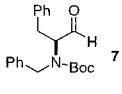
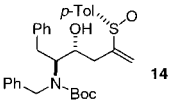
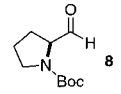
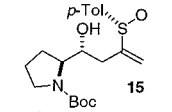



| entry | halide | aminoaldehyde | conditions[a] | product[b] | dr[c] | yield (%) |
|---|---|---|---|---|---|---|
| 1 | 1a |  2 | A |  9 | 80 : 20 | 77 |
| 2 | 1a | 2 | B | 9 | 85 : 15 | 65 |
| 3 | 1a | 2 | C | 9 | 88 : 12 | 75 |
| 4 | 1b | 2 | C |  16 | 60 : 40 | 82 |
| 5 | 1a |  ent-2 | A |  17 | 60 : 40 | 75 |

[a] (A): Zn dust (1.3 equiv), sat $NH_4Cl$/THF (6:1), rt; (B): Zn dust (1.3 equiv.), $ZnCl_2$ (2 equiv), sat $NH_4Cl$/THF (6:1), rt; (C): Zn dust (1.3 equiv), $ZnCl_2$ (2 equiv), NaI (3 equiv), sat $NH_4Cl$/THF (6:1), 5 °C. [b] Major diastereomer shown. [c] Diastereomeric ratio calculated by $^1H$ NMR from crude reaction mixtures.

**Table 2. Allylation of α-Aminoaldehydes 3−8 with ($S_S$)-1a**

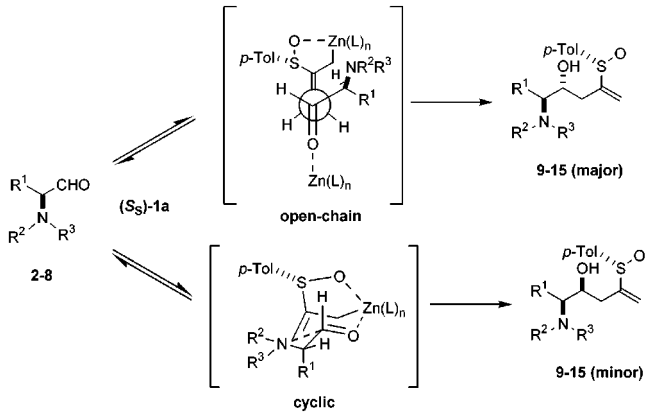



| entry | α-aminoaldehyde | product[a] | dr[b] | yield (%) |
|---|---|---|---|---|
| 1 |  3 |  10 | 75 : 25 | 90 |
| 2 |  4 |  11 | 75 : 25 | 82 |
| 3 |  5 |  12 | 93 : 7 | 70 |
| 4 |  6 |  13 | 88 : 12 | 75 |
| 5 |  7 |  14 | 93 : 7 | 75 |
| 6 |  8 |  15 | 91 : 9 | 79 |

[a] Major diastereomer shown. [b] Diastereomeric ratio calculated by $^1H$ NMR from crude reaction mixture.

nyl chelation can be postulated for the cyclic ones.[9] As a result, an efficient approach to favor the operation of the open transition state would rely on the use of an external Lewis acid for an additional carbonyl coordination. In this context, the use of $ZnCl_2$ (2 equiv) gave rise to an increase on the diastereoselectivity in comparison with an standard system with no external additives (compare entries 1 and 2, Table 1). Moreover, since the Lewis acidity of Zn, and thus its coordination ability, can be decreased by coordination with iodide ions,[5,10] we were pleased to observe that the highest diastereoselectivity in the allylation of **2** with ($S_s$)-**1a** was achieved by the combination of NaI (3 equiv) and $ZnCl_2$ (2 equiv) (entry 3, Table 1). All these results are consistent with the preference for an open-chain transition state model in this allylation process.[11]

**Scheme 2**




These results led us to examine the suitability of other α-amino aldehydes as allylation partners for ($S_s$)-**1a**. In this context, it is well established that the tendency of α-amino aldehydes toward racemization can be greatly reduced, or even avoided, by the proper choice of protecting groups on the nitrogen atom.[12−14] Moreover, the effect of nitrogen protection (*N*-monoprotected vs *N*,*N*-diprotected derivatives) on the diastereoselectivity of the allylations of α-amino aldehydes is well precedented in the literature.[7a,b,d,15] In general, *N*-monoprotected derivatives afford lower diastereoselectivities than *N*,*N*-diprotected ones due to the competition between a chelation-controlled Cram model and a nonchelating Felkin−Ahn model.[16] This trend was also observed in our allylation system when comparing alaninal derivatives **4** and **5** (Table 2, entries 2 and 3). As expected, the diastereoselectivity on the allylation of *N*-monoprotected **4** was lower than that observed from **5**, albeit the sense of diastereoinduction was not reversed. In this case, the operation of a chelation-controlled open-chain model, as depicted

(9) A seven-membered cyclic transition state has been proposed for the Lewis acid-catalyzed allylation of 2-(arylsulfinyl)allyl tributylstannanes with aldehydes under strictly anhydrous conditions (see Mortlock, S. V.; Thomas, E. J. *Tetrahedron* **1998**, *54*, 4663−4672).

(10) Ito, A.; Kishida, M.; Kurusu, Y.; Masuyama, Y. *J. Am. Chem. Soc.* **2000**, *65*, 494−498.

(11) This model is also valid to explain the observed diastereoinduction in the allylation of *ent*-**2** (Table 1, entry 5). Thus, the *R* configuration of the new stereocenter in the major diastereomer of **17** was inferred from X-ray diffraction analysis of the minor diastereomer (see Supporting Information). The lower diastereoinduction observed from *ent*-**2** in comparison with **2** can be explained by the higher contribution of the cyclic transition state (see Scheme 2) as a result of the steric bias imposed by the opposite configuration of amino aldehyde *ent*-**2** in the open-chain transition state.

(12) Rapoport, H.; Lubell, W. D. *J. Am. Chem. Soc.* **1987**, *109*, 236−239.

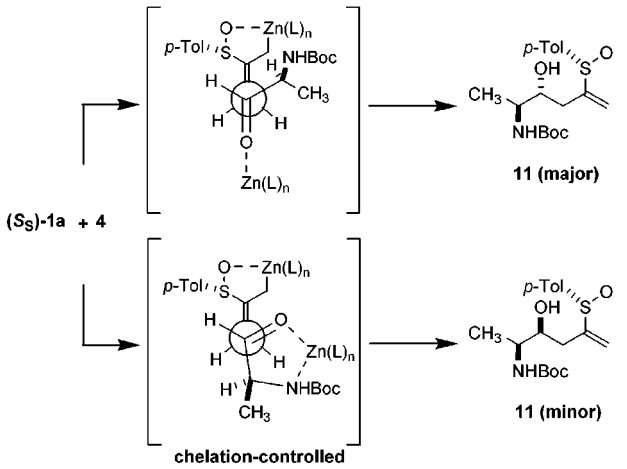
(13) Garner, P.; Park, J. M. *J. Org. Chem.* **1987**, *52*, 2361−2364.

(14) Reetz, M. T. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 1531−1545.

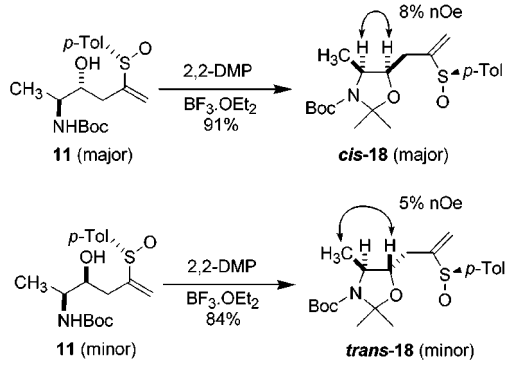
(15) Gryko, D.; Urbanczyk-Lipkoska, Z.; Jurczak, J. *Tetrahedron* **1997**, *53*, 13373−13382.

(16) In some cases a reversal in the diastereoselectivity between *N*-mono- and *N*,*N*-diprotected amino aldehydes has been observed (see ref 7b, and references therein).

**Scheme 3**




**Scheme 4**




in Scheme 3, would also account for the formation of the minor diastereomer of **11**.

Configurational assignments of diastereomers **11** were carried out by their independent conversion into oxazolidines **18** and NOE measurements from selected protons (Scheme 4).

Finally, a small representative series of *N*,*N*-diprotected α-amino aldehydes **6**−**8** was chosen to show the scope of this allylation system (Table 2, entries 4−6). In all cases, the expected allylation adducts **13**−**15** were obtained in good yields and diastereoselectivities and the configuration of the major diastereomer was inferred from the above considerations. It is worth mentioning, that the stereochemical integrity of the α-amino aldehyde was preserved in all the examples here studied, as evidenced by the observation (by $^1$H NMR of crude mixtures) of only two diastereomers instead of four, as it would be expected if epimerization of the α-amino aldehyde had taken place.[17]

In summary, an optimized procedure for the diastereoselective allylation of a series of α-amino aldehydes with ($S_S$)-**1a** under aqueous Barbier conditions to afford enantiomerically pure sulfinylamino alcohols in good yields and diastereoselectivites is reported. The diastereoselectivity of the process has been optimized by a judicious choice of additives and reaction conditions. Interestingly, α-amino aldehydes configurationally related to natural α-amino acids afford "matched" diastereoinduction with ($S_S$)-**1a** as a counterpart.

(17) The stereochemical integrity of the sulfinyl allylic chloride in this allylation system had been previously proven (see ref 5).

Further studies addressed at the exploitation of the synthetic potential of these building blocks are currently underway in our laboratory and will reported in due course.

## Experimental Section

Melting points are uncorrected. FT-IR spectra are reported in cm$^{-1}$. $^1$H and $^{13}$C NMR spectra were obtained in $CDCl_3$ solutions at 200 MHz (for $^1$H) and 50 MHz (for $^{13}$C), respectively, unless otherwise indicated. Chemical shifts are reported in delta ($\delta$) units, parts per million (ppm) relative to the singlet at 7.24 ppm of $CDCl_3$ for $^1$H and in ppm relative to the center line of a triplet at 77.0 ppm of $CDCl_3$ for $^{13}$C. Solvents were distilled prior to use and dried by standard methods.[18] Usual reaction workup consists of extraction of the aqueous phase with an organic solvent, washings with brine, drying of the extracts over $Na_2SO_4$, filtration, and evaporation to dryness. A detailed experimental procedure for the synthesis of ($S_S$)-**1a** is described in ref 5. For the synthesis of aldehyde **6**, see Supporting Information.

**General Procedure for the Allylation of Aldehydes with ($S_S$)-1a.** NaI (670 mg, 4.5 mmol) is added portionwise to a solution of ($S_S$)-**1a** (320 mg, 1.5 mmol) in THF (1 mL) under Ar. After stirring for 5 min at room temperature, a solution of the requisite aldehyde (1.5 mmol) in THF (0.5 mL) was added followed by portionwise addition of $ZnCl_2$ (610 mg, 3 mmol) and sat. aqueous $NH_4Cl$ solution (7.5 mL). The reaction mixture was then cooled in an ice−water bath, and Zn dust (150 mg, 2.3 mmol) was added portionwise. After stirring at 0 °C for 2 h, the reaction mixture was extracted with $CH_2Cl_2$/$Et_2O$ (1:2, 10 mL) and worked up in the usual way to obtain an oil which was purified by flash chromatography to give the desired sulfinylamino alcohol.

**Compound 9.** Obtained from aldehyde **2**[13] in 75% yield as a 80:20 mixture of diastereomers. HRMS, calcd for $C_{21}H_{31}NO_5S$: 409.192295. Found: 409.192614. Major diastereomer: $[\alpha]_D$ +11.8 (*c*, 0.51, $CHCl_3$); mp: 106−107 °C. IR (film): 3380; 1695, 1049. $^1$H NMR (300 MHz, $C_6D_6$, 60 °C): 1.30 (s, 9H, $C(CH_3)_3$); 1.39 (s, 3H, $CH_3$); 1.54 (s, 3H, $CH_3$); 1.97 (s, 3H, $CH_3$Ar); 2.16 (dd, 1H, $J_1$ = 9 Hz, $J_2$ = 15 Hz); 2.48 (dd, 1H, $J_1$ = 10.3 Hz, $J_2$ = 15 Hz,); 3.58 (dd, 1H, $J_1$ = 6.6 Hz, $J_2$ = 9 Hz, $CH_2O$); 3.84−4.00 (m, 4H); 5.7 (broad. 1H, =$CH_2$); 5.92 (s, 1H, =$CH_2$); 6.88 (2H, AA′ of AA′BB′: $J$ = 7.8 Hz and H arom *m*-SO); 7.47 (BB′ of AA′BB′, 2H, $J$ = 7.8 Hz, and H arom. *o*-SO). $^{13}$C NMR (75.4 MHz, $C_6D_6$, 60 °C): 21.0, 27.0, 28.3, 32.8, 62.2, 65.0, 71.7, 80.2, 94.4, 120.6, 125.4, 129.9, 140.8, 141.1, 153.6, 190.0. For X-ray coordinates, see below. Minor diastereomer: $[\alpha]_D$ −50.0 (*c*, 0.72, acetone); mp: 121−122 °C. IR (film): 3350, 1697, 1054. $^1$H NMR (300 MHz, $C_6D_6$, 60 °C): 1.25 and 1.30 (3H, rotamers), 1.39 (9H), 1.53 (3H), 1.97 and 1.94 (3H), 2.27 (1H), 2.45 (1H), 3.70 (1H), 3.91−4.14 (3 × 1H), 4.88 (1H), 5.42 (1H), 5.71 and 5.75 (1H, rotamers), 6.85−6.89 (2H), 7.42 and 7.43 (2H, rotamers). $^{13}$C NMR (75.4 MHz, $C_6D_6$, 60 °C): 21.0, 27.0, 28.3, 28.4, 33.0, 61.4, 64.2, 71.6, 80.0, 94.4, 121.6, 125.1, 130.0, 141.2. For X-ray coordinates, see below.

**Compound 10.** Obtained from aldehyde **3**[19] in 90% yield as a 75:25 mixture of diastereomers. HRMS, calcd for $C_{24}H_{31}NO_4S$: 429.197369. Found: 429.198013, $[\alpha]_D$ +10.0 (*c*, 0.25, $CHCl_3$); IR (film): 3392, 2976, 2928, 1692, 1048. Major diastereomer: $^1$H NMR (200 MHz, $CDCl_3$): 1.42 (s, 9H, $(CH_3)_3$), 2.02−2.37 (m, 2H), 3.01−3.35 (m, 2H), 3.95 (m, 1H), 4.20−4.71 (m, 2H, $CH_2$Ar), 5.75 (broad, 1H, =$CH_2$), 6.08 (broad, 1H, =$CH_2$), 7.11−7.44 (m, 9H). $^{13}$C NMR (75.4 MHz, $CDCl_3$): Major diastereomer: 21.4, 28.3, 34.3, 52.2, 80.9, 122.2, 125.1, 127.2, 128.5, 129.9, 138.1, 138.2, 141.7, 151.9, 156.9.

**Compound 11.** Obtained from aldehyde **4**[20] in 82% yield as a 75:25 mixture of diastereomers. HRMS, calcd for $C_{18}H_{28}NO_4S$ ($M^+$ + 1): 354.173905. Found: 354.172827. Major diastereomer: $[\alpha]_D$ +28.2 (*c*, 0.62, acetone). IR (film): 3458, 1710, 1045.

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$^1$H NMR (300 MHz, $C_6D_6$, 60 °C): 0.95 (d, 3H, $J$ = 6.9 Hz, 3H), 1.40 (s, 9H, $C(CH_3)_3$), 1.97 (s, 3H), 2.09 (dd, 1H, $J_1$ = 7,5 Hz, $J_2$ = 15,3 Hz), 2.26 (ddd, 1H, $J_1$ = 0.9 Hz, $J_2$ = 4.2 Hz, $J_3$ = 15.3 Hz,), 3.54−3.79 (m, 3 × 1H), 4.50 (d, 1H, $J$ = 8.4 Hz), 5.55 (s, 1H, =$CH_2$), 5.82 (s, 1H, =$CH_2$), 6.89 (AA′ of AA′BB′, 2H, $J$ = 8 Hz), 7.43 (BB′ of AA′BB′, 2H, $J$ = 8 Hz). $^{13}$C NMR (75.4 MHz, $C_6D_6$): 16.0, 21.0, 28.4, 33.3, 50.6, 73.0, 78.7, 121.7, 125.3, 129.9, 139.9, 141.1, 152.4, 155.8. Minor diastereomer: $[\alpha]_D$ −60.3 (*c*, 1.25, acetone). IR (film): 3436, 1708, 1048, 1029. $^1$H NMR (300 MHz, $C_6D_6$, 60 °C): 1.14 (d, 3H, $J$ = 6.6 Hz), 1.35 (s, 9H, $C(CH_3)_3$), 1.97 (s, 3H), 2.08−2.25 (m, 2H), 3.41 (dt, 1H, $J_1$ = 1.8 Hz, $J_2$ = 9 Hz), 3.77 (m, 1H), 4.85 (d, 1H, $J$ = 9.6 Hz), 4.99 (broad, 1H, NH), 5.14 (s, 1H, =$CH_2$), 5.55 (s, 1H, =$CH_2$), 6.88 (AA′ of AA′BB′, 2H, $J$ = 8 Hz), 7.34 (BB′ of AA′BB′, 2H, $J$ = 8 Hz). $^{13}$C NMR (75.4 MHz, $C_6D_6$): 19.1, 21.0, 28.4, 36.6, 50.7, 73.9, 78.2, 123.7, 124.8, 130.0, 139.0, 141.1, 153.7, 155.9.

**Compound 12:** Obtained from aldehyde **5**[20] in 70% yield as a 93:7 mixture of diastereomers. HRMS, calcd for $C_{25}H_{33}NO_4S$: 443.213031. Found: 443.213234; $[\alpha]_D$ +50.0 (*c*, 0.45, acetone); mp: 94−96 °C. Major diastereomer: IR (film): 3390, 1687, 1029. $^1$H NMR (300 MHz, $C_6D_6$, 60 °C): 1.17 (d, 3H, $J$ = 6.9 Hz), 1.32 (s, 9H, $C(CH_3)_3$), 1.98 (s, 3H, $CH_3$), 2.11 (dd, 1H, $J_1$ = 7.5 Hz, $J_2$ = 15.3 Hz), 2.33 (dd, 1H, $J_1$ = 4,5 Hz, $J_2$ = 15.3 Hz), 3.67 (m, 1H), 4.02 (m, 1H), 4.28 (m, 2H), 5.44 (s, 1H, =$CH_2$), 5.90 (s, 1H, =$CH_2$), 6.89 (AA′ of AA′BB′, 2H, $J$ = 8 Hz), 7.02−7.20 (m, 5H), 7.44 (BB′ of AA′BB′, 2H, $J$ = 8 Hz). $^{13}$C NMR (75.4 MHz, $C_6D_6$, 60 °C): 21.0, 28.4, 34.6, 50.7, 58.3, 73.2, 80.0, 125.5, 127.2, 127.8, 128.6, 129.9, 140.0, 140.7, 141.1, 153.5, 156.4. Minor diastereomer (selected signals from the mixture of diastereomers): $^1$H NMR (300 MHz, $C_6D_6$, 60 °C): 1.12 (d, 3H, $J$ = 6,9 Hz), 1.27 (s, 9H, $C(CH_3)_3$), 4.43 (A of AB, 1H, $J$ = 16 Hz), 4.60 (B of AB, 1H, $J$ = 16 Hz), 5.39 (s, 1H, =$CH_2$), 5.77 (s, 1H, =$CH_2$).

**Compound 13.** Obtained from aldehyde **6** in 75% yield as a 88:12 mixture of diastereomers. HRMS, calcd for $C_{27}H_{37}NO_4S$: 471.2443162. Found: 471.242911; $[\alpha]_D$ +6.78 (*c*, 0.56, $CHCl_3$). IR (film): 3382, 1687, 1031. Major diastereomer: $^1$H NMR (200 MHz, $CDCl_3$): 0.75−1.05 (broad, 6H, $(CH_3)_2$ rotamers), 1.42 (s, 9H, $(CH_3)_3$), 1.72 (m, 1H), 2.01−2.19 (m, 2H), 2.36 (s, 3H), 3.95 (broad, 1H), 4.09 (broad, 1H, A of AB), 4.41 (broad, 1H), 4.61 (broad, 1H, B of AB), 5.48 (broad, 1H, =$CH_2$), 5.91 (broad, 1H, =$CH_2$), 7.32−7.42 (m, 9H). $^{13}$C NMR (50.3 MHz, $CDCl_3$): 20.2, 20.6, 28.3, 34.6, 54.1, 69.3, 74.1, 80.4, 119.8, 125.3, 125.5, 127.2, 127.7, 128.6, 129.7, 138.5, 141.1, 152.1, 156.7. Minor diastereomer (selected signals from the mixture of diastereomers): $^1$H NMR (200 MHz, $CDCl_3$): 3.39 (s, 3H), 5.67 (broad, 1H, =$CH_2$), 6.02 (broad, 1H, =$CH_2$).

**Compound 14.** Obtained from aldehyde **7**[21] in 75% yield as a 93:7 mixture of diastereomers. HRMS, calcd for $C_{31}H_{37}NO_4S$: 519.2443162. Found: 519.245881. $[\alpha]_D$ −7.18 (*c*, 0.97, $CHCl_3$). IR (film): 3419, 3041, 2921, 2850, 1654, 1250, 1178. Major diastereomer: $^1$H NMR (200 MHz, $CDCl_3$): 1.46 (broad, 9H, $(CH_3)_3$), 1.94 (m, 1H), 2.25 (m, 1H), 2.38 (s, 3H), 2.88 (m, 1H), 3.13 (m, 1H), 3.23 (m, 1H), 3.32 (broad, 1H), 3.93 (broad, 1H), 4.36 (m, 1H), 5.25 (s, 1H, =$CH_2$), 5.81 (s, 1H, =$CH_2$), 7.01−7.44 (m, 14H); $^{13}$CNMR (50.3 MHz, $CDCl_3$): 21.2, 28.3, 31.2, 33.2, 53.9, 65.1, 73.7, 80.7, 119.9, 125.1, 126.1, 127.0, 127.2, 127.8, 128.3, 128.4, 129.2, 129.6, 129.8, 137.9, 141.4, 151.6, 157.0. Minor diastereomer (selected signals from the mixture of diastereomers): $^1$H NMR (200 MHz, $CDCl_3$): 3.85 (m, 1H), 3.32 (m, 1H).

**Compound 15.** Obtained from commercially available aldehyde **8** in 79% yield as a 91:9 mixture of diastereomers. HRMS, calcd for $C_{20}H_{29}NO_4S$: 379.181731. Found: 379.182965. Major diastereomer: $[\alpha]_D$ +30 (*c*, 1.14, acetone). IR (film): 3405, 1689, 1045. $^1$H NMR (300 MHz, $C_6D_6$, 60 °C): 1.17−1.68 (m, 4H), 1.38 (s, 9H, $C(CH_3)_3$), 1.98 (s, 3H), 2.07 (dd, 1H, $J_1$ = 8.7 Hz, $J_2$ = 15.6 Hz), 2.35 (m, 1H), 3.03 (m, 1H), 3.28 (broad, 1H), 3.78 (broad, 1H), 4.00 (m, 1H), 5.75 (broad, 1H, =$CH_2$), 5.97 (broad, 1H, =$CH_2$), 6.90 (AA′ of AA′BB′, 2H, $J$ = 8 Hz), 7.43 (BB′ of AA′BB′, 2H, $J$ = 8 Hz). $^{13}$C NMR (75.4 MHz, $C_6D_6$): 21.0, 24.1, 27.2, 28.5, 32.2, 47.8, 62.8, 71.9, 79.3, 119.7, 125.5, 129.8, 141.0, 141.5, 154.0. Minor diastereomer: $^1$H NMR (300 MHz, $C_6D_6$, 60 °C): 1.39 (s, 9H, $C(CH_3)_3$), 1.88−1.94 (m, 1H), 1.97 (s, 3H), 2.14−2.24 (m, 1H), 3.67−3.72 (m, 1H), 3.87−3.94 (m, 1H), 5.53 (broad, 1H, =$CH_2$), 5.83 (broad, 1H, =$CH_2$), 7.35 (AA′ of AA′BB′, 2H, $J$ = 8,1 Hz). $^{13}$C NMR (75.4 MHz, $C_6D_6$): 25.7, 29.9, 28.5, 34.1, 46.9, 62.0, 74.5, 116.9, 125.3, 141.2, 154.9.

**Compound 16.** Obtained from condensation of aldehyde **2** with sulfone **1b** in 82% yield as a 60:40 mixture of diastereomers following the above general procedure. HRMS, calcd for $C_{21}H_{31}NO_6S$: 425.187210. Found: 425.188823. IR (film): 3501, 1697, 1366, 1135. Major diastereomer: $^1$H NMR (300 MHz, $C_6D_6$, 60 °C): 1.30 (s, 9H, $C(CH_3)_3$); 1.37−1.53 (m, 6H); 1.91 (s, 3H), 2.23−2.34 (m, 1H), 2.54−2.62 (m, 1H), 3.56−3.67 (m, 1H), 3.83 (broad, 1H), 3.82−4.40 (m, 3 × 1H), 5.78 (broad, 1H, =$CH_2$), 6.38 (broad, 1H, =$CH_2$), 6.83 (AA′ of AA′BB′, 2H, $J$ = 8,1 Hz), 7.30−7.77 (m, 2H). $^{13}$C NMR (75.4 MHz, $C_6D_6$, 60 °C): 21.1, 26.9, 28.3, 33.9, 62.4, 65.2, 71.9, 80.5, 94.5, 125.4, 125.7, 128.7, 129.9, 137.2, 144.0, 148.6. Most relevant signals for the minor diastereomer (taken from the mixture of isomers): $^1$H NMR: 1.90 (s, 3H), 4.18 (broad, 1H), 6.35 (broad, 1H, =$CH_2$). $^{13}$CNMR: 28.4, 64.3, 144.2, 148.4.

**Compound 17.** Obtained from commercially available aldehyde *ent*-**2b** in 75% yield as a 60:40 mixture of diastereomers. HRMS, calcd for $C_{21}H_{31}NO_5S$: 409.192295. Found: 409.192990. Major diastereomer: $[\alpha]_D$ +92.4 (*c*, 0.80, acetone); mp: 105−108 °C. IR (film): 3382, 1697, 1052. $^1$H NMR (300 MHz, $C_6D_6$, 60 °C): 1.26 and 1.30 (s, 3H, rotamers), 1.39 (s, 9H, $C(CH_3)_3$), 1.53 (s, 3H), 1.98 (s, 3H), 2.12 (dd, 1H, $J_1$ = 9.6 Hz, $J_2$ = 15 Hz), 2.40−2.50 (m, 1H), 3.58−3.64 (m, 1H), 3.91−4.14 (m, 3 × 1H), 4.21 (broad, 1H, OH), 5.61 (broad, 1H, =$CH_2$), 5.95 (broad, 1H, =$CH_2$), 6.91 (AA′ of AA′BB′, 2H, $J$ = 8,1 Hz), 7.49 (BB′ of AA′BB′, 2H, $J$ = 8,1 Hz). $^{13}$C (75.4 MHz, $CDCl_3$): 21.3, 24.0, 26.4 and 27.0 (rotamers); 28.2, 32.6, 61.5, 64.4, 71.9, 81.2, 94.0 and 94.2 (rotamers), 119.8, 125.3, 129.9, 140.8, 141.1, 151.4, 154. Minor diastereomer: $[\alpha]_D$ +9.7 (*c*, 0.75, acetone; mp: 88−90 °C. IR (film): 3382, 1050, 1014. $^1$H NMR (300 MHz, $C_6D_6$, 60 °C): 1.25 (s, 9H, $C(CH_3)_3$), 1.39 and 1.47 (s, 3H rotamers), 1.64 (s, 3H); 1.96 (s, 3H); 2.22 (dd, 1H, $J_1$ = 10.2 Hz, $J_2$ = 14.7 Hz), 2.40 (d, 1H, $J_1$ = 14.7 Hz), 3.61 (dd, 1H, $J_1$ = 5.7 Hz, $J_2$ = 9 Hz), 3.71−3.85 (m, 2 × 1H), 4.07 (broad, 1H), 4.70 (broad, 1H), 5.36 (broad, 1H, =$CH_2$), 5.68 (broad, 1H, =$CH_2$), 6.86 (AA′ of AA′BB′, 2H, $J$ = 8,1 Hz), 7.39 (BB′ of AA′BB′, 2H, $J$ = 8,1 Hz). $^{13}$C NMR (75.4 MHz, $CDCl_3$): 21.3, 26.4, 28.2, 33.9 and 34.8 (rotamers), 61.6, 64.7 and 65.5 (rotamers), 71.7, 80.0 and 80.7, 94.1, 122.3 and 123.6 (rotamers), 124.9, 129.9, 137.9, 141.6, 152.4. For X-ray coordinates, see below.

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**Supporting Information Available:** Experimental details for the synthesis of aldehyde **6** and oxazolidines *cis*- and *trans*-**18**; copies of $^1$H and/or $^{13}$C NMR spectra for compounds **9**−**12** and **14**−**18**; X-ray coordinates for **9** (major isomer), **9** (minor isomer), and **17** (minor isomer). This material is available free of charge via the Internet at http://pubs.acs.org.

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