Asymmetric Synthesis of (2*S*,6*S*)- and *meso*-(2*S*,6*R*)-Diaminopimelic Acids from Enantiopure Bis(sulfinimines)

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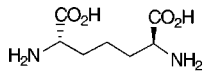
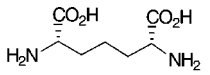
Interest in the development of efficient and versatile routes to enantiopure bis(α-amino acids) stems mainly from their ability to function as substrate-based inhibitors, i.e., antibiotics.[1] In this regard much of the recent interest in this area, particularly by the groups of Vederas,[2] Williams,[3] and others,[4] have been directed at the synthesis of (2*S*,6*S*)-diaminopimelic acid (DAP **1**) and *meso*-(2*S*,2*R*)-diaminopimelic acid (DAP **2**), and their analogues. The reason is that bacterial α-amino acid biosynthesis is dependent upon (*S*,*S*)-DAP **1** which is epimerized to meso-DAP **2** by L,L-DAP epimerase.[1] Stereoselective decarboxylation of **2** affords L-lysine which is essential for the growth of bacteria and plants. In addition, *meso*-**2** is a cross-linking unit of the cell wall peptidoglycan of most Gram-negative and some Gram-positive bacteria and, therefore, responsible, in part, for cell wall integrity.[1,5] DAP-containing peptides also exhibit diverse biological activities[1a] including cytotoxicity[6] and antitumor behavior.[7] We report here a new strategy, based on the sulfinimine (*N*-sulfinyl imine)-mediated asymmetric Strecker synthesis,[8] for the enantioselective synthesis of bis(α-amino acids) which is illustrated for the asymmetric synthesis of DAP **1** and **2**.



(2*S*,6*S*)-**1** DAP



(2*S*,6*R*)-**2** *meso*-DAP

To prepare (2*S*,6*S*)-**1** DAP we need the bis(sulfinimine) derived from the glutaraldehyde. However, all attempts to condense (*S*)-(+)-*p*-toluenesulfinamide (**3**)[9] with anhydrous glutaraldehyde[10] using $Ti(OEt)_4$ and/or 4 Å molecular sieves failed. This result is probably due to the instability of this dialdehyde under the reaction conditions, because bis(sulfinimines) have been prepared from dialdehydes such as terephthaldicarboxaldehyde.[9] With the failure of this approach, the more lengthy procedure, which would be needed anyway for the preparation of *meso*-DAP **2**, was employed as outlined in Scheme 1.

Condensation of 5-(benzyloxy)pentanal (**4**)[10] with (*S*)-(+)-**3** and 4.0 equiv of $Ti(OEt)_4$ for 4 h at reflux afforded a 95% isolated yield of sulfinimine (*S*)-(+)-**5**. The sulfinimine-mediated asymmetric Strecker synthesis involves the addition of ethylaluminum cyanoisopropoxide [EtAl(O-*i*-Pr)CN], generated in situ by addition of *i*-PrOH to diethylaluminum cyanide (Et_2AlCN), to the sulfinimine.[8] Thus treatment of (+)-**5** at −78 °C in THF with 1.5/1.0 equiv of Et_2AlCN/*i*-PrOH gave an 86% yield of α-amino nitrile (+)-**6** in >96% de. Re face addition of "CN" to the sulfinimine C−N bond in (*S*)-**5** is predicted to give (2*S*)-**6** because the sulfinyl group controls the stereoselectivity.[8] This was later confirmed in the synthesis of DAP **1** (vide infra). We next needed to protect the amino group in **6** to avoid cyclization when the second aldehyde **11** was generated. Rapoport has demonstrated the utility of arylsulfonyl substituents as protecting groups for the amino function in α-amino acids.[11] Conversion of **6** to the *N*-tosyl amino nitrile **7** was readily accomplished in 88% yield, without epimerization, by oxidation with 57% *m*-CPBA. Hydrolysis with methanolic-HCl gave the amino acid methyl ester (*S*)-(+)-**8** in 65% yield which was further protected by treatment with NaH/SEM-Cl to give **9**. Hydrogenation (H_2/Pd) gave alcohol **10**, and PCC oxidation gave aldehyde **11** in 69% yield. The sulfinimine (S_S,2*S*)-(+)-**12** was prepared as previously described and treatment with "EtAl(O-*i*-Pr)CN" gave the α-amino nitrile (S_S,2*S*,6*S*)-(+)-**13** in 69% yield and 86% de. Following separation of the diastereoisomers by chromatography and methanolic-HCl hydrolysis, the protected bis(α-amino acid) (2*S*,6*S*)-(+)-**14** was obtained in 84% yield. Removal of the *N*-tosyl group was readily accomplished by refluxing **14** with 48% HBr/PhOH to give the crude product which was purified by ion-exchange chromatog-

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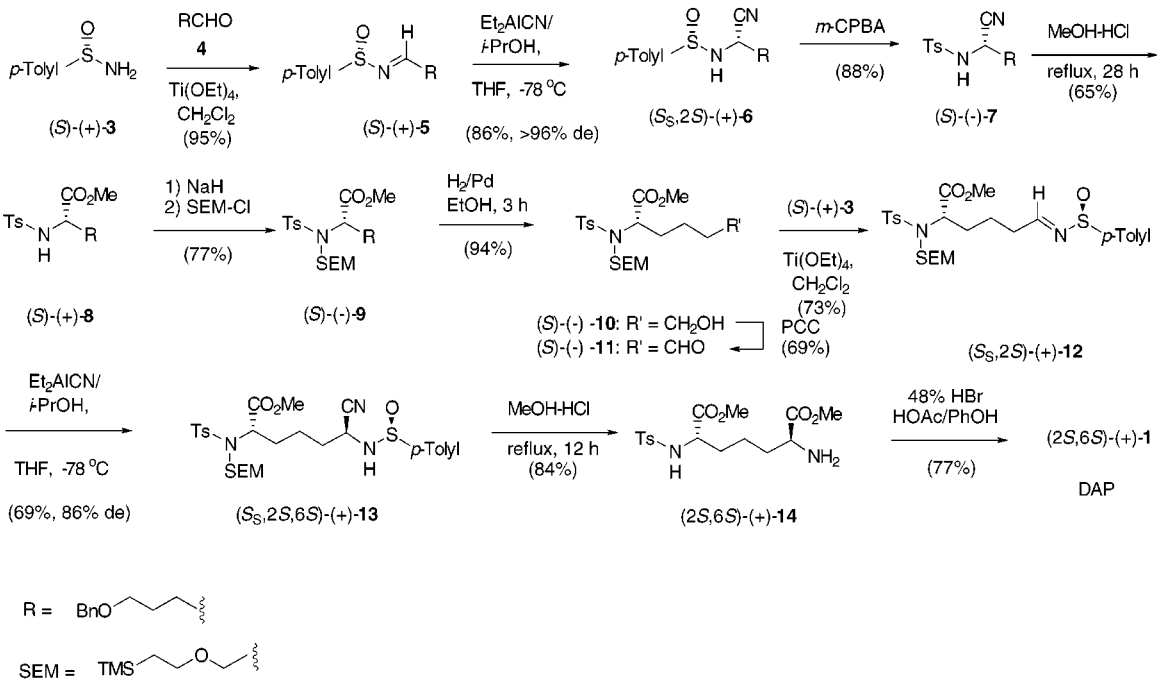
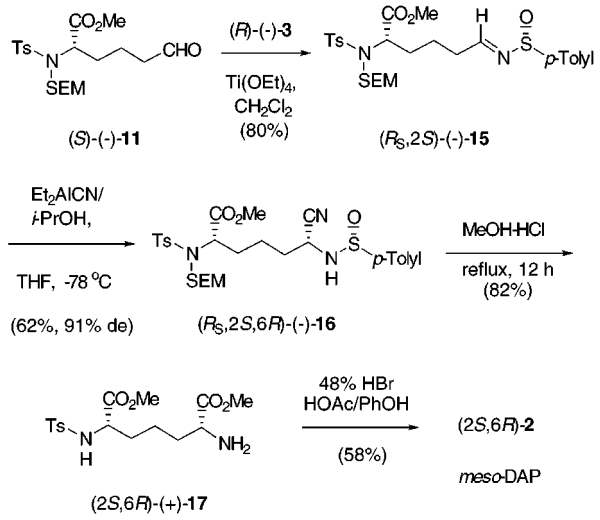
Scheme 1



Scheme 2



raphy affording (2*S*,6*S*)-(+)-**1** in 77% yield. Since earlier studies had demonstrated that these sequences of steps (i.e., protection/deportation) does not lead to racemization (Scheme 1) DAP (+)-**1** is obtained in high enantiomeric purity (>97%). This was confirmed by comparison of its optical rotation with literature values.[3d]

meso-DAP **2** was prepared in a related fashion by condensing sulfinamide (*R*)-(−)-**3** with aldehyde (*S*)-(−)-**11** to give (R_S,2*S*)-(−)-**15** (Scheme 2). Cyanide addition and hydrolysis gave (2*S*,6*R*)-**2** *meso*-DAP **2** in 58% yield.

In summary, a general methodology is demonstrated for the synthesis of bis(α-amino acids) using the sulfinimine-mediated asymmetric Strecker synthesis. The utility of the *N*-tosyl group as an amino acid protecting group is further demonstrated by these transformations as well as the ease with which it is installed using sulfinimine chemistry. Finally, polyfunctionalized α-amino acid sulfinimines such as (S_S,2*S*)-(+)-**12** and (R_S,2*S*)-(−)-**15** offer significant potential for the asymmetric synthesis of structural analogues of DAP because sulfinimines are versatile chiral building blocks for amine, aziridine, 2*H*-azirine, and *β*-amino acid synthesis.[13,1412−14] Studies aimed at demonstrating this potential in the synthesis of improved DAP substrate-based inhibitors is currently underway and will be reported in due course.

Experimental Section

General Procedure. Column chromatography was performed on silica gel, Merck grade 60 (230−400 mesh). Analytical and preparative thin-layer chromatography was performed on precoated silica gel plates (250 and 1000 μm) purchased from Analtech Inc. TLC plates were visualized with UV in an iodine chamber or with phosphomolybdic acid unless noted otherwise. THF was freshly distilled under nitrogen from a purple solution of sodium and benzophenone.

Unless stated otherwise, all reagents were purchased from commercial sources and used without additional purification. (*S*)-(+) and (*R*)-(−)-*p*-toluenesulfinamides (**3**) were prepared as previously described,[9] and 5-(benzyloxy)penanal (**4**) was purchased from Aldrich.

(*S*)-(+)-*N*-(5-Benzyloxyvalerylidene)-*p*-toluenesulfinamide (5). In an oven-dried single-necked 250 mL round-bottom flask equipped with a magnetic stir bar and reflux condenser was placed a solution of **4** (4.6 g, 24 mmol) in CH_2Cl_2 (80 mL). Titanium(IV) ethoxide (20 mL, 96 mmol) was added to the solution followed by the (*S*)-(+)-*p*-toluenesulfinamide **3** (3.72 g, 24 mmol). The reaction mixture was refluxed for 4 h and cooled to 0 °C, H_2O (80 mL) was added, and the solution was filtered through Celite. The phases were separated, and the organic phase was washed with brine (40 mL), dried ($MgSO_4$), and concentrated. Flash chromatography (EtOAc:hexane, 10:90) afforded 7.4 g (95%) of (+)-**5** as an oil: $[\alpha]^{23}_D$ 168.0 (*c* 1.5, $CHCl_3$); IR 1620 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.6−1.8 (m, 5H), 2.4 (s, 3H), 2.45−2.40 (m, 1H), 3.45−3.50 (m, 2H), 4.5 (s, 2H), 7.3−7.4 (m, 7H), 7.6 (d, J = 6.2 Hz, 2H), 8.25 (t, J = 4.8 Hz, 1H); ^{13}C NMR

(12) If some epimerization of one of the stereocenters had occurred, diasteroisomers would have been produced. None was detected by ^1H (500 MHz) NMR.

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($CDCl_3$) δ 22.0, 22.8, 29.8, 36.3, 70.4, 73.5, 125.2, 128.2, 128.3, 129.0, 130.5, 139.0, 142.0, 167.6. HRMS calcd for $C_{19}H_{23}NO_2S$ (M + H) 330.1526. Found 330.1527 (M + H).

(*2S*)-(+)-(2-*N*-*p*-Toluenesulfinamido)-6-(benzyloxy)hexanonitrile (6). In an oven-dried 250 mL two-necked round-bottom flask fitted with a magnetic stir bar under argon balloon was placed a solution of (+)-**5** (3.29 g, 10 mmol) in THF (60 mL), and the solution was cooled to −78 °C. In a separate two-necked 100 mL round-bottom flask fitted with a magnetic stir bar, under an argon balloon was added a solution of diethylaluminum cyanide (15 mL, 15 mmol) and *i*-PrOH (0.76 mL) in THF (30 mL). The reaction mixture was stirred at 0−10 °C for 10 min and cannulated to the solution of (+)-**5** at −78 °C. After the reaction mixture was warmed to room temperature, the solution was stirred for 12 h, cooled to −78 °C, and quenched with sat. NH_4Cl solution (40 mL). The reaction mixture was extracted with EtOAc (3 × 30 mL), and the combined organic phases were washed with brine (30 mL), dried ($MgSO_4$), and concentrated. Flash chromatography (EtOAc:hexane, 20:80) gave 3.0 g (86%) of (+)-**6** as an oil in >96% de; $[\alpha]^{23}_D$ 34.4 (*c* 0.9, $CHCl_3$); IR 3464−3032, 2243 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.55−170 (m, 4H), 1.85 (q, *J* = 7.3 Hz, 2H), 2.43 (s, 3H), 3.5 (t, *J* = 6.2 Hz, 2H), 4.12 (q, *J* = 7.3 Hz, 1H), 4.5 (s, 2H), 4.8 (bs, 1H), 7.3−7.4 (m, 7H), 7.6 (d, *J* = 8 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 22.07, 23.06, 29.5, 35.5, 42.7, 70.4, 73.5, 119.8, 126.8, 128.3, 128.4, 129.1, 130.6, 139.1, 140.4, 142.7. HRMS calcd for $C_{20}H_{24}N_2O_2S$ (M + H) 357.1642. Found 357.1636 (M + H).

(*2S*)-(−)-(2-*N*-*p*-Toluenesulfonamido)-6-(benzyloxy)hexanonitrile (7). In a single-necked 100 mL round-bottom flask fitted with a magnetic stir bar, under argon, was placed a solution of (+)-(**6**) (2.85 g, 8 mmol) in CH_2Cl_2 (40 mL). *m*-Chloroperbenzoic acid (57%) (2.75 g, 16 mmol) was added, and the solution was stirred at room temperature for 4.5 h at which time the reaction mixture was washed with sodium thiosulfate solution (50 mL) and sat. sodium bicarbonate (30 mL), dried ($MgSO_4$), and concentrated. Filtration through a short column of silica gel afforded 2.63 g (88%) of (−)-**7**; mp 77 °C; $[\alpha]^{23}_D$ −23.9 (*c* 1.7, $CHCl_3$); IR 3650−3030 (b), 2241, 1597, 1450 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.5−1.7 (m, 4H), 1.85 (q, *J* = 7.3 Hz, 2H), 2.43 (s, 3H), 3.46 (t, *J* = 5.9 Hz, 2H), 4.23 (m, 1H), 4.5 (s, 2H), 5.0 (d, *J* = 9.5 Hz, 1H); 7.3−7.4 (m, 7H), 7.7 (d, *J* = 8 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 21.0, 21.5, 28.0, 32.8, 43.8, 69.1, 72.4, 117.2, 126.7, 127.1, 127.2, 127.9, 129.5, 135.7, 137.8, 143.9. Anal. Calcd for $C_{20}H_{24}N_2O_3S$: C, 64.49; H, 6.49; N, 7.52. Found: C, 64.15; H, 6.41; N, 7.40.

Methyl (*2S*)-(+)-(*N*-*p*-Toluenesulfonamido)-6-(benzyloxy)-hexonate (8). In a single-necked 100 mL round-bottom flask equipped with a magnetic stir bar, reflux condenser, and calcium chloride drying tube was placed a solution of (−)-**7** (2.1 g, 6 mmol) in (4 M) methanolic-HCl (60 mL). The reaction mixture was refluxed for 28 h. The progress of the reaction was monitored by TLC by the disappearance of the starting material. The solution was cooled to 0 °C and carefully neutralized by addition of pyridine. Concentration gave a residue which was dissolved in CH_2Cl_2 (80 mL), washed with water (2 × 20 mL) and brine (30 mL), dried ($MgSO_4$), and concentrated. Flash chromatography (EtOAc:hexane, 20:80) gave 1.63 g (65%) of (+)-**8**; mp 38 °C; $[\alpha]^{23}_D$ 14.9 (*c* 2, $CHCl_3$); IR 3472−3080, 1741, 1599, 1452 cm^{-1}; ^1H NMR δ 1.4−1.7 (m, 6H), 2.4 (s, 3H), 3.42 (m, 2H), 3.47 (s, 3H), 3.9 (m, 1H), 4.5 (s, 2H), 5.1 (d, *J* = 9.5 Hz, 1H), 7.25−7.40 (m, 7H), 7.7 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR δ 22.2, 22.4, 29.6, 33.8, 53.0, 56.3, 70.5, 73.6, 127.9, 128.2, 128.3, 129.0, 130.3, 137.5, 139.2, 144.3, 172.9. HRMS calcd for $C_{21}H_{27}NO_5S$ (M + Na) 428.1519. Found (M + Na) 428.1507.

Methyl (*2S*)-(−)-*N*-(*p*-Toluenesulfonamido-trimethylsilyl(ethoxy)methyl)-6-(benzyloxy)hexonate (9). In an oven-dried two-necked 250 mL round-bottom flask equipped with a magnetic stir bar under an argon balloon was placed a solution of NaH (0.22 g, 4.8 mmol), prewashed with *n*-hexane (3 × 15 mL), in dry DMF (25 mL) and cooled to 0 °C. A solution of (+)-**8** (1.29 g, 3.2 mmol) in dry DMF (20 mL) was slowly added. The solution was stirred at 0 °C for 5 min and trimethylsilyl(ethoxy)-methyl chloride (0.56 mL, 3.2 mmol) (Aldrich) was added and the solution stirred for 5 min. At this time the reaction mixture was quenched with brine (60 mL) and extracted with EtOAc (3 × 30 mL), and the organic phases combined, washed with brine (20 mL), dried ($MgSO_4$), and concentrated. Flash chromatography (EtOAc:hexane, 15:85) gave 1.32 g, (77%) of (−)-**9** as an oil; $[\alpha]^{23}_D$ −4.0 (*c* 0.3, $CHCl_3$); IR 1744, 1597, 1454 cm^{-1}; ^1H NMR δ (s, 9H), 0.8 (m, 2H), 1.30−1.95 (m, 7H), 2.40 (s, 3H), 3.42 (m, 2H), 3.49 (s, 3H), 3.6 (m, 1H), 4.38 (m, 1H), 4.5 (s, 2H), 4.9 (s, 2H), 7.2−7.4 (m, 7H), 7.75 (d, *J* = 8 Hz, 2H); ^{13}C NMR δ.1, 18.5, 22.5, 23.8, 30.0, 31.6, 52.5, 59.8, 67.0, 70.2, 73.2, 76.5, 128.2, 128.3, 128.9, 130.0, 138.5, 139.2, 144.0, 172.5. Anal. Calcd for $C_{27}H_{41}NO_6SSi$: C, 60.53; H, 7.71; N, 2.61. Found: C, 60.53; H, 7.51; N, 2.34.

Methyl (*2S*)-(−)-*N*-(*p*-Toluenesulfonamido-trimethylsilyl(ethoxy)methyl)-6-hydroxyhexanoate (10). In an oven dried two necked 100 mL round-bottom flask equipped with a magnetic stir bar under a hydrogen balloon was placed a suspension of (10%) Pd/C (0.12 g) in ethanol (40 mL). A solution of (−)-**9** (1.2 g, 2.4 mmol) in ethanol (20 mL) was added, and the reaction mixture was stirred for 3 h at room temperature at which time the solution was filtered and concentrated. The residue was dissolved in EtOAc (60 mL), washed with brine (20 mL), dried ($MgSO_4$) and concentrated. Flash chromatography (EtOAc:hexane, 25:75) afforded 1.0 g (94%) of (−)-**10** as an oil.; $[\alpha]^{23}_D$ −9.0 (*c* 0.5, $CHCl_3$); IR 3723−3029, 1744, 1597, 1450 cm^{-1}; ^1H NMR δ (s, 9H), 0.8−0.9 (m, 2H), 1.30−1.65 (m, 6H), 1.8−1.9 (m, 2H), 2.4 (s, 3H), 3.45 (s, 3H), 3.6 (m, 2H), 4.4 (m, 1H), 4.95 (s, 2H), 7.25 (d, *J* = 8.06 Hz, 2H), 7.7 (d, *J* = 8.06 Hz, 2H); ^{13}C NMR δ.1, 19.2, 22.5, 23.0, 31.5, 32.5, 52.3, 59.1, 62.2, 66.4, 77.0, 127.8, 130.0, 138.2, 145.0, 172.6. HRMS calcd for $C_{20}H_{35}NO_6SSi$ (M + Na) 468.1834. Found 468.1852.

Methyl (*2S*)-(−)-*N*-(*p*-Toluenesulfonamido-trimethylsilyl(ethoxy)methyl)-6-formylhexanoate (11). In an oven-dried single-necked 100 mL round-bottom flask fitted with a magnetic stir bar under argon balloon was placed a solution of (−)-**10** (0.8 g, 1.8 mmol) in CH_2Cl_2 (30 mL). Pyridinium chlorochromate (0.39 g, 1.8 mmol) was added, and the solution was stirred for 1 h at room temperature. At this time the reaction mixture was diluted with ether (30 mL), filtered through silica gel, and concentrated. Flash chromatography (EtOAc:hexane, 10:90) gave 0.55 g (69%) of (−)-**11** as an oil; $[\alpha]^{23}_D$ −7.7 (*c* 0.78, $CHCl_3$); IR 1744, 1597 cm^{-1}; ^1H NMR 0 (s, 9H); 0.86 (m, 3H), 1.6−1.9 (m, 5H), 2.4 (s, 3H), 3.45 (s, 3H), 3.57−3.59 (m, 2H); 4.3 (m, 1H), 4.9 (s, 2H), 7.27 (d, *J* = 8 Hz, 2H), 7.7 (d, *J* = 8 Hz, 2H); 9.7 (s, 1H); ^{13}C NMR 0, 18.5, 19.3, 22.2, 30.6, 43.6, 52.7, 59.0, 66.5, 76.4, 128.2, 130.0, 138.0, 145.0, 172.0, 202.3.

Methyl (2*S*)-(+)-*N*-(*p*-Toluenesulfonamido-trimethylsilyl(ethoxy)methyl)-6-ene-*N*-(*S*)-(*p*-toluenesulfinamido)-hexanoate (12). The sulfinimine was prepared as described earlier and flash chromatography (EtOAc:hexane, 10:90) gave 0.465 g (80%) of (+)-**12** as an oil; $[\alpha]^{23}_D$ 66.3 (*c* 0.4, $CHCl_3$); IR 1744, 1620, 1450 cm^{-1}; ^1H NMR δ (s, 9H), 0.8−0.9 (m, 2H), 1.6−2.0 (m, 5H), 2.4 (2s, 6H), 2.41 (m, 1H), 3.45 (s, 3H), 3.6 (m, 2H), 4.4 (m, 1H), 4.9 (s, 2H), 7.27 (2d, *J* = 8 Hz, 4H), 7.55 (d, *J* = 8 Hz, 2H), 7.75 (d, *J* = 8 Hz, 2H), 8.2 (t, *J* = 4.5 Hz, 1H); ^{13}C NMR δ 18.5, 22.0, 22.2, 22.5, 30.6, 35.8, 52.7, 59.0, 66.4, 76.3, 125.3, 128.2, 130.0, 130.4, 138.0, 142.5, 142.6, 144.2, 166.9, 171.9. HRMS calcd for $C_{27}H_{40}N_2O_6S_2Si$ (M + Na) 603.1985. Found 603.1994 (M + Na).

Methyl (2*S*)-(+)-*N*-(*p*-Toluenesulfonamido-trimethylsilyl(ethoxy)methyl)-(6*S*)-(nitrile-*N*-((*S*)-*p*-toluenesulfinimido))hexanoate (13). The amino nitrile was prepared as described earlier and flash chromatography (EtOAc:hexane, 20:80) afforded 0.22 g (69%) of (+)-**13** as an oil: $[\alpha]^{23}_D$ 24.39 (*c* 2.05, $CHCl_3$); IR 3420−3055, 2243, 1746, 1597, 1444 cm^{-1}; ^1H NMR δ (s, 9H), 0.9 (m, 2H), 1.5−2.0 (m, 6H), 2.46 (2s, 6H), 3.5 (s, 3H), 3.6 (m, 2H), 4.05 (d, *J* = 7 Hz, 1H), 4.38 (t, *J* = 7.3 Hz, 1H), 4.9 (m, 3H), 7.3 (d, *J* = 8.1 Hz, 2H), 7.78 (d, *J* = 8.1 Hz, 2H); ^{13}C NMR δ, 18.6, 22.1, 22.2, 30.1, 34.8, 41.8, 52.8, 58.7, 66.7, 76.3, 119.4, 126.8, 128.3, 130.2, 130.7, 137.9, 140.3, 142.9, 144.4, 171.7. HRMS calcd for $C_{28}H_{41}N_3O_6S_2Si$ (M + Na) 630.2095. found 630.2103 (M + Na).

Methyl (2*S*,6*S*)-(+)-2-*N*-(*p*-Toluenesulfonamido)-6-amino-bishexanoate (14). In a single-necked 100 mL round-bottom flask fitted with a magnetic stir bar and a condenser was placed a solution of (+)-**13** (0.14 g, 0.22 mmol) in (4 M) methanolic-HCl (15 mL), and the solution was refluxed for 12 h. The reaction mixture was cooled to 0 °C, carefully neutralized with pyridine (pH indicator paper), and concentrated and the residue dissolved in EtOAC (15 mL). The organic phase was washed with brine (10 mL), dried ($MgSO_4$), and concentrated to give 0.068 g (84%)

of (+)-**14** as an oil: $[\alpha]^{23}_D$ 15 (*c* 0.4, $CHCl_3$); IR 3469−3069, 1736, 1597, 1439 cm^{-1}; ^1H NMR δ 1.2−2.0 (m, 6H), 2.4 (s, 3H), 3.44 (s, 3H), 3.45 (m, 1H), 3.7 (s, 3H), 3.95 (m, 1H), 5.2−5.4 (bs, 1H), 7.3 (d, J = 8 Hz, 2H), 7.7 (d, J = 8 Hz, 2H); ^{13}C NMR δ 22.2, 22.5, 33.0, 34.5, 52.5, 53.0, 54.5, 56.0, 127.5, 130.0, 137.4, 144.7, 172.6, 177. HRMS calcd for $C_{16}H_{24}N_2O_6S$ (M + Na) 395.1264. Found 395.1252 (M + Na).

(2*S*,6*S*)-(+)-Diaminopimilic Acid (1). In an one-necked 50 mL round-bottom flask equipped with a magnetic stir bar and a reflux condenser was placed a solution of (+)-**14** (0.048 g, 0.13 mmol) in 48% HBr in acetic acid (12 mL) and phenol (20 mg). The reaction mixture was refluxed for 10 h, cooled to 0 °C, and washed with ether (10 mL). The aqueous phase was loaded on to Dowex-50 ion-exchange resin, and eluted with H_2O (70 mL) followed by 10% NH_4OH (150 mL) solution to give 0.019 g (77%) of **1**; mp 309−312 °C; $[\alpha]^{23}_D$ 42.7 (*c* 1.1, 1 N HCl); (lit.[3d] $[\alpha]^{23}_D$ 44.5 (*c* 0.95, 1 N HCl); ^1H NMR: δ 1.2−1.45 (m, 2H), 1.5−1.9 (m, 4H), 3.45−3.75 (m, 2H).

Methyl (2*S*)-(−)-*N*-(*p*-Toluenesulfonamido-trimethylsilyl(ethoxy)methyl)-6-ene-*N*-(*R*)-(*p*-toluenesulfinamido)-hexanoate (15). Prepared from (*S*)-(−)-**11** and (*R*)-(−)-**3** and purified by flash chromatography (EtOAc:hexane, 10:90) to give 0.315 g (73%) of (−)-**15** as an oil; $[\alpha]^{23}_D$ −93.18 (*c* 1.1, $CHCl_3$); IR 1744, 1620, 1450 cm^{-1}; ^1H NMR δ (s, 9H), 0.8 (m, 2H), 1.5−1.9 (m, 5H), 2.35 (2s, 6H), 2.4 (m, 1H), 3.39 (m, 1H), 3.4 (s, 3H), 3.5 (m, 1H), 4.35 (m, 1H), 4.85 (s, 2H), 7.25 (2d, J = 8.8 Hz, 4H), 7.5 (d, J = 8.1 Hz, 2H), 7.7 (d, J = 8.1 Hz, 2H); 8.15 (t, J = 4 Hz, 1H); ^{13}C NMR δ, 18.5, 22.0, 22.1, 22.4, 30.6, 35.8, 52.6, 59.0, 66.4, 76.3, 125.2, 128.2, 130.0, 130.4, 138.1, 142.2, 142.5, 144.2, 166.8, 171.8. HRMS calcd for $C_{27}H_{40}N_2O_6S_2Si$ (M + Na) 603.1985. Found (M + Na) 603.1995.

Methyl (2*S*)-(−)-*N*-(*p*-toluenesulfonamido-trimethylsilyl(ethoxy)methyl)-(6*R*)-(nitrile-*N*-((*S*)-*p*-toluenesulfinimido))hexanoate (16). Flash chromatography (EtOAc:hexane, 20:80) gave 0.170 g (62%) of (−)-**16** as an oil; $[\alpha]^{23}_D$ −21.33 (*c* 0.45, $CHCl_3$); IR 3395−3079, 2245, 1740 cm^{-1}; ^1H NMR δ (s, 9H), 1.0−1.8 (m, 8H), 2.25 (2s, 6H), 3.3−3.4 (m, 5H), 3.95 (m, 1H), 4.2 (m, 1H), 4.8 (s, 2H), 5.25 (m, 1H), 7.2 (2d, J = 7.9 Hz, 4H), 7.45 (d, J = 8 Hz, 2H), 7.6 (d, J = 8 Hz, 2H); ^{13}C NMR δ 18.4, 21.5, 21.9, 30.2, 34.7, 41.9, 52.6, 58.7, 66.4, 76.2, 119.2, 126.6, 128.1, 129.9, 130.5, 137.8, 140.1, 142.7, 144.2, 171.6. HRMS calcd for $C_{28}H_{41}N_3O_6S_2Si$ (M + Na) 630.2095. Found 630.2104 (M + Na).

Methyl (2*S*,6*R*)-(+)-2-*N*-(*p*-Toluenesulfonamido)-6-aminobishexanoate (17). Flash chromatography (EtOAc:*n*-hexane 30:70) gave 0.055 g (82%) of (+)-**17** as an oil; $[\alpha]^{23}_D$ 2.0 (*c* 0.5, $CHCl_3$); IR 3434−3044, 1740, 1597, 1439 cm^{-1}; ^1H NMR δ 1.3−1.8 (m, 6H), 2.38 (s, 3H), 3.4 (m, 4H), 3.65 (s, 3H), 3.85 (m, 1H), 7.25 (d, J = 8.1 Hz, 2H), 7.65 (d, J = 8.1 Hz, 2H); ^{13}C NMR δ 21.8, 22.1, 33.4, 34.5, 52.7, 53.0, 54.6, 56.2, 127.8, 130.2, 137.5, 144.2, 172.7, 176.7. HRMS calcd for $C_{16}H_{24}N_2O_6S$ (M + Na) 395.1264. Found 395.1253 (M + Na).

***meso*-(2*S*,6*R*)-Diaminopimilic Acid (2)**. Yield 0.011 g (58%); mp: >312 °C (dec). ^1H NMR δ 1.2−1.4 (m, 2H), 1.5−1.8 (m, 4H), 3.4−3.7 (m, 2H). Spectral properties were identical to literature values.[3d]

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Supporting Information Available: ^1H, ^{13}C, and IR spectra for compounds (+)-**5**, (+)-**6**, (−)-**7**, (+)-**8**, (−)-**9**, (−)-**10**, (−)-**11**, (+)-**12**, (+)-**13**, (+)-**14**, (−)-**15**, (−)-**16**, and (+)-**17**. This material is available free of charge via the Internet at http://pubs.acs.org.

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