spores/mL) of *Botrytis cinerea* (incubated on potato dextrose agar medium at 25 °C for 15 d) by leaf spray on all sides until just before runoff. The plants were then held in lighted dew chamber (20 ± 2 °C) for an additional 4–5 d and rated on the disease severity.

Test 3. Evaluation of activity against tomato late blight was done by foliage spray to run off onto 14-day-old tomato plants grown in 5-cm polyvinyl pots. After the spray deposit had dried for 1 day, the treated plants were inoculated by spraying with a suspension of zoosporangia (1×10^5 zoosporangia/mL; incubated on V-8 juice agar medium at 20 °C for 2 weeks). The plants were then held in lighted dew chamber (20 ± 2 °C) for an additional 4 d and rated on the disease severity.

Test 4. Evaluation of activity against barley powdery mildew was made by foliage spray of the first leaf of wheat (cultivar, Chukwang) grown in polyvinyl pots (diameter, 5 cm) for 7 d. After the spray deposit dried, plants were dusted with a uredospores colonied on the second leaf and placed in a moist chamber at 20 °C for 24 h. One day after inoculation, plants were moved to the plant growth chamber (20 °C, 70% relative humidity) to induce disease. The plants were then held in growth chamber (20 ± 2 °C) for an additional 10 d and rated on the disease severity.

Acknowledgment. We are grateful to the National Science Foundation (Grant CHE-9108231) for partial support of this research. M.J.K. is recipient of Alfred P. Sloan Research (1987–1991) and NIH RCDA (1989–1994; ES00182) fellowships.

Supplementary Material Available: X-ray crystallographic data for *cis*-6-(2-chlorophenyl)-4-methyl-4*H*,6*H*-furo[3,4-*c*]isoxazole (**5f'**), (*R**,*S**)-3-[chloro(2-chlorophenyl)methyl]-4-(1-hydroxyethyl)isoxazole (**6f'**), and (*R**,*S**)-3-[bromo(2-chlorophenyl)methyl]-4-(1-hydroxymethyl)isoxazole (**7f**) (21 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

Asymmetric Synthesis of 2,6-Diaminopimelic Acids

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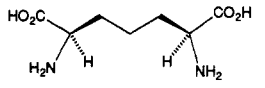
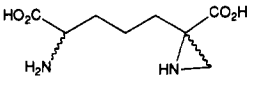
The preparations of (*R*,*R*)-2,6-diaminopimelic acid, (*S*,*S*)-2,6-diaminopimelic acid, (*S*,*R*)-2,6-diaminopimelic acid, and (*S*,*S*)-2,7-diaminosuberic acid are described. The synthesis of mono-N-protected (*S*,*R*)-2,6-diaminopimelic acid is also described.

Introduction

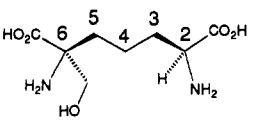
Diaminopimelic acid (**1**, DAP) is an important, naturally occurring amino acid biosynthesized in bacteria and higher plants.[1] L,L- and *meso*-DAP serve as the penultimate biosynthetic precursor of the essential amino acid L-lysine. *meso*-DAP functions as a cross-linking constituent of virtually all Gram-negative and some Gram-positive bacterial peptidoglycan and also serves to anchor various membrane-associated macromolecules, such as lipoprotein to the cell wall. Recognition of the pivotal roles DAP plays in microbial metabolism[2] and cell wall structure has resulted in an increased level of interest in possible means to selectively disrupt the DAP biosynthetic pathway. A flurry of recent papers[3] on the synthesis of DAP and, more significantly, structural analogs of DAP that can function as substrate-based inhibitors of key biosynthetic transformations attests to the potential importance of the DAP/lysine pathway as a viable target for antibiotic design. Recent studies in several laboratories demonstrate that a number of compounds, which inhibit the formation or metabolism of 2,6-diaminopimelic acid in bacteria possess antibiotic activity.[4] Since mammals lack the diaminopimelate pathway and require L-lysine in their diet,[5] specific inhibitors of the enzymes along this route are potential antimicrobial and herbicidal agents that should display low mammalian host toxicity. Thus, the potential importance of inhibiting the DAP pathway through the design and synthesis of functionalized DAP analogs renders this class of amino acids an attractive and worthy synthetic problem. A recent example is the (stereorandom) preparation of the aziridino DAP (**2**, "AZIDAP") that was shown[6] to be a potent inhibitor of L,L-DAP epimerase and exhibits antimicrobial activity.



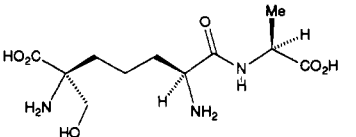
R,S-1



2



3



4

Despite the apparent simplicity of these amino acids, there were no stereochemically unambiguous syntheses of *meso*-DAP nor asymmetric syntheses of (*S*,*S*)-DAP prior to 1992. Two recent exceptions are the synthesis of β-

(1) Patte, J.-C. In *Amino Acids: Biosynthesis and Genetic Regulation*; Hermann, K. M., Somerville, R. L., Eds.; Addison-Wesley: Reading, MA, 1983; pp 213–218.

(2) Certain bacteria bypass the L,L form of DAP by means of *meso*-DAP D-dehydrogenase: (a) Bartlett, A. T. M.; White, P. J. *J. Gen. Microbiol.* **1985**, *131*, 2145. (b) Misono, H.; Ogasawara, M.; Nagasaki, S. *Agric. Biol. Chem.* **1986**, *50*, 2729.

(3) (a) Berges, D. A.; DeWolf, W. E., Jr.; Dunn, G. L.; Grappel, S. F.; Newman, D. J.; Taggart, J. J.; Gilvarg, C. *J. Med. Chem.* **1986**, *29*, 89. (b) Berges, D. A.; DeWolf, W. F., Jr.; Dunn, G. L.; Newman, D. J.; Schmidt, S. J.; Taggart, J. J.; Gilvarg, C. *J. Biol. Chem.* **1986**, *261*, 6160. (c) Kelland, J. G.; Arnold, L. D.; Palcic, M. M.; Pickard, M. A.; Vederas, J. C. *J. Biol. Chem.* **1986**, *261*, 13216. (d) Girodeau, J.-M.; Agouridas, C.; Masson, M.; Pineau, R.; LeGoffic, F. *J. Med. Chem.* **1986**, *29*, 1023. (e) Lam, L. K. P.; Arnold, L. D.; Kalantar, T. H.; Kelland, J. G.; Lane-Bell, P. M.; Palcic, M. M.; Pickard, M. A.; Vederas, J. C. *J. Biol. Chem.* **1988**, *263*, 11814. (f) Baumann, R. J.; Bohme, E. H.; Wiseman, J. S.; Vaal, M.; Nichols, J. S. *Antimicrob. Agents Chemother.* **1988**, *32*, 1119. (g) Bohme, E. H.; Gerhart, F.; Higgins, W. U.S. Patent 4,7300,006, 1988; *Chem. Abstr.* **1988**, *109*, 6981m. (h) O'Donnell, M. J.; Bruder, W. A.; Eckrich, T. M.; Shullenberger, D. F.; Staten, G. S. *Synthesis* **1984**, 127. (i) Wade, R.; Birnbaum, S. M.; Winitz, M.; Koegel, R. J.; Greenstein, J. P. *J. Am. Chem. Soc.* **1957**, *79*, 648. (j) Assche, I.; Soroka, M.; Haemers, A.; Hooper, M.; Blanot, D.; van Heijenoort, J. *Eur. J. Med. Chem.* **1991**, *26*, 505.

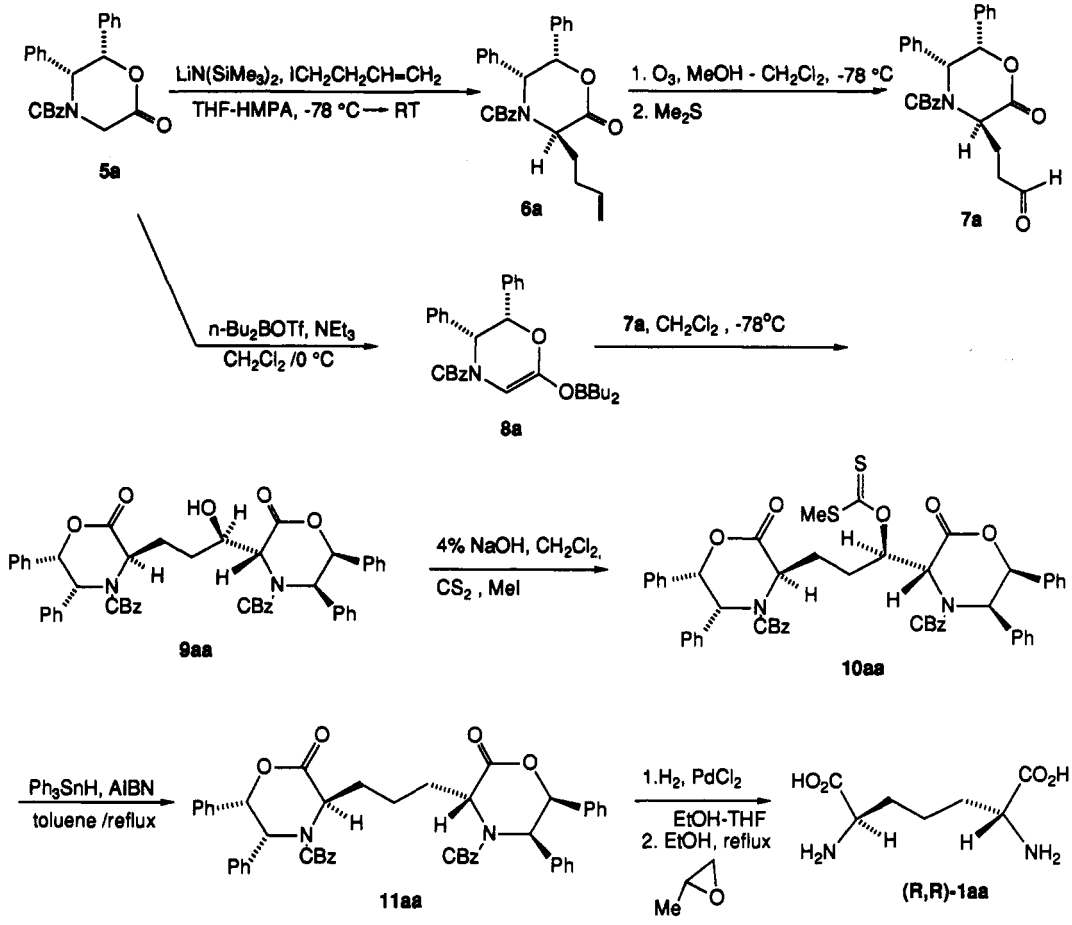
(4) See also references in: Lin, Y.; Myhrman, R.; Schrag, M. L.; Gelb, M. H. *J. Biol. Chem.* **1988**, *263*, 1622.

(5) Jouanneau, J.; Stragier, P.; Bouvier, J.; Patte, J.-C.; Yaniv, M. *Eur. J. Biochem.* **1985**, *146*, 173 and references cited therein.

(6) (a) Gerhart, F.; Higgins, W.; Tardif, C.; Ducep, J.-B. *J. Med. Chem.* **1990**, *33*, 2157. (b) Higgins, W.; Tardif, C.; Richaud, C.; Krivanek, M. A.; Cardin, A. *Eur. J. Biochem.* **1989**, *186*, 137.

0022-3263/92/1957-6519$03.00/0

Scheme I



fluoro-DAP by Vederas and Gelb,[7a] β-hydroxy DAP and, very recently, (*S,S*)-DAP and related analogs by Bold and associates.[7b,c] In addition, our laboratory[8a] and an Oxford group[8b] recently reported the asymmetric synthesis of 2,6-diamino-6-(hydroxymethyl)pimelic acid (**3**) which is a constituent of the natural antibiotic *N*-(2,6-diamino-6-(hydroxymethyl)pimelyl)-L-alanine (**4**).[9] Using much the same approach, we report herein stereochemically unambiguous asymmetric syntheses of three stereoisomers of diaminopimelic acid.

Results and Discussion

We have previously reported[10] on the utility of the diphenyloxazinones (**5/12**) as versatile templates from which both electrophilic[11] and nucleophilic[12] C–C bond-forming strategies can be employed to access a variety of nonproteinogenic α-amino acids. In selecting a strategy to accomplish the key coupling of two optically pure glycinates to a three-carbon tether, we found that employment of the enol borane aldol couplings reported by Miller[13] on these oxazinone systems proved to be attractive. While this approach mandates the deoxygenation of a β-hydroxy construct to obtain the parent DAP systems, we desired an approach that would also install functionality in the connecting propyl chain for the ultimate purpose of providing starting materials for further elaboration into potential k_{cat} inhibitors of DAP biosynthesis. We have also explored an enolate alkylation coupling protocol that utilizes improved enolate alkylation conditions recently disclosed by Baldwin and associates in a similar system[8b] that is also effective for the construction of the requisite DAP stereoisomers.

As shown in Scheme I, the commercially available[14] lactone **5** was treated with homoallyl iodide in the presence of lithium bis(trimethylsilyl)amide to give the homoallyl oxazinone **6** in 47% yield.[8a] This substance was ozonized and then quenched with dimethyl sulfide to afford the aldehyde **7** in 79–84% yield. Preparation of the boron enolate of **5** according to Miller[13] followed by aldol condensation with the aldehyde **7** in methylene chloride at low temperature gave the β-hydroxy dilactone **9** (55–62%,

(7) (a) Gelb, M. H.; Lin, Y.; Pickard, M. A.; Song, Y.; Vederas, J. C. *J. Am. Chem. Soc.* **1990**, *112*, 4932. (b) Bold, G.; Duthaler, R. O.; Riediker, M. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 497. (c) Bold, G.; Allmendinger, T.; Herold, P.; Moesch, L.; Schar, H.-P.; Duthaler, R. O. *Helv. Chim. Acta* **1992**, *75*, 865. See also: (d) Sundharadas, G.; Gilvarg, C. *J. Biol. Chem.* **1966**, *241*, 3276.

(8) (a) Williams, R. M.; Im, M.-N.; Cao, J. *J. Am. Chem. Soc.* **1991**, *113*, 6976. See also: (b) Baldwin, J. E.; Lee, V.; Schofield, C. J. *Synlett* **1992**, 249.

(9) Shoji, J.; Hinoo, H.; Kato, T.; Nakauchi, K.; Matsuura, S.; Mayama, M.; Yasuda, Y.; Kawamura, Y. *J. Antibiot.* **1981**, *34*, 374.

(10) (a) Williams, R. M. *Aldrichimica Acta* **1992**, *25*, 11. See also: (b) Williams, R. M. *Synthesis of Optically Active α-Amino Acids*; Pergamon: Oxford, 1989.

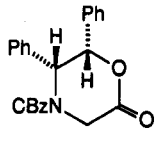
(11) (a) Sinclair, P. J.; Zhai, D.; Reibenspies, J.; Williams, R. M. *J. Am. Chem. Soc.* **1986**, *108*, 1103. (b) Williams, R. M.; Sinclair, P. J.; Zhai, D.; Chen, D. *J. Am. Chem. Soc.* **1988**, *110*, 1547. (c) Sinclair P. J. Ph.D. Thesis, Colorado State University, 1987. (d) Williams, R. M.; Zhai, D.; Sinclair, P. J. *J. Org. Chem.* **1986**, *51*, 5021. (e) Williams, R. M.; Sinclair, P. J.; Zhai, W. *J. Am. Chem. Soc.* **1988**, *110*, 482. (f) Williams, R. M.; Zhai, W. *Tetrahedron* **1988**, *44*, 5425. (g) Zhai, D.; Zhai, W.; Williams, R. M. *J. Am. Chem. Soc.* **1988**, *110*, 2501. (h) Williams, R. M.; Hendrix, J. A. *J. Org. Chem.* **1990**, *55*, 3723.

(12) (a) Williams, R. M.; Im, M.-N. *Tetrahedron Lett.* **1989**, *29*, 6075. (b) Williams, R. M.; Im, M.-N. *J. Am. Chem. Soc.* **1991**, *113*, 9276.

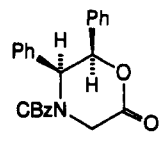
(13) Reno, D. S.; Lotz, B. T.; Miller, M. J. *Tetrahedron Lett.* **1990**, *31*, 827.

(14) Lactones **5** are commercially available from Aldrich Chemical Co.; **5a**, catalog no. 33-185-6; **5b**, catalog no. 33, 187-2; **5c**, catalog no. 33-185-6; **5d**, catalog no. 33-181-3.

Table I



5a



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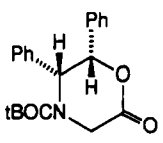
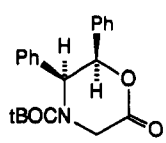


5c



5d

entry	substrates	aldol (% 9)	xanthate (% 10)	reduction (% 11)	% DAP	% ee
1	**5a/5b**	55	73	73	>99 (*R,R*)-**1aa**	>99
2	**5b/5b**	62	82	62	>99 (*S,S*)-**1bb**	>99
3	**5d/5b**	61	74	79	nd[a]	
4	**5d/5a**	56	71	83	72 (*S,R*)-**17da**	>99

[a] This substrate was not processed to the final amino acid.

Scheme I). Although ultimately unimportant for the synthesis of DAP, the diastereoselectivity of the aldol condensation was excellent. Out of a total of four possible diastereoisomers, only two were observable in the crude reaction mixture. The small vicinal coupling constants (~1.9 Hz) for the C-2/C-3 (DAP numbering) methines for **9** is in accord with the anti selectivity observed by Miller[13] and subsequently by us[8a] in the synthesis of **3** in related aldolizations. Both sets of aldolizations support a Zimmerman–Traxler chair-type transition state predominantly from the face of the oxazinone anti to the two phenyl rings with the aldehyde methine oriented toward the inside of the oxazinone ring. The stereoselective preparation of such β-hydroxy-DAP derivatives should provide useful substrates from which additional DAP analogs might be prepared.

Next, the reductive functional transformation of the β-hydroxy group was examined to obtain the requisite deoxygenation products. As in the synthesis of **3**, this proved to be very difficult since this alcohol moiety is very hindered and is prone to β-elimination. Many attempts at activating the hydroxyl for hydride displacement resulted in either no reaction or α,β-dehydrogenation.[8a] After extensive experimentation, an improved procedure utilized[8a] in the synthesis of **3** was found which simply involves stirring **9** in 4% NaOH/methylene chloride in the presence of carbon disulfide and methyl iodide; the xanthate ester **10** is obtained in good yield with little or no detectable elimination product. Radical reduction[15] of **10** with triphenyltin hydride in hot toluene afforded the reduction product **11** in 62–83% yield with no detectable loss of stereochemical integrity at the adjacent methine position.[8a] Finally, catalytic hydrogenolysis of **11** proceeded in essentially quantitative yield to afford (*R,R*)-diaminopimelic acid. Following the same protocol, (*S,S*)-diaminopimelic acid was synthesized by employing 2 equiv of the antipodal lactone **5b**. The results for the couplings examined are collected in Table I.

Syntheses of potential synthetic immunostimulants[16] derived from substructures of bacterial cell walls and small peptides containing DAP or analogs of DAP that would be expected to facilitate the transport of such substances across cell walls requires the selective manipulation of the terminal amino and carboxyl residues. This is a particularly difficult regiochemical problem for the synthesis of peptides derived from meso-DAP. The synthesis of *meso*-diaminopimelic acid can be realized by essentially the same protocol used above, except that both **5a** and **5b** were employed. As an approach to solving the general problem of selectively manipulating the *meso*-DAP system, we have synthesized a differentially protected *N*-t-BOC-(*R,S*)-DAP isomer by employing the *N*-t-BOC glycinate **5d**. By selecting the appropriate absolute stereochemistry and N-protection from the glycinates **5a–d**, in principle, any differentially protected DAP stereoisomer can be synthesized by following the general protocol described. As shown in Scheme II, the corresponding mono-*N*-t-BOC-DAP isomer (*S,R*)-**17da** has been prepared by following essentially the same experimental protocol as that outlined above. The only difference between these routes (Schemes I and II) is the final dissolving metal reduction of bis-lactone **16da** to the corresponding mono-*N*-t-BOC product **17da**.

Table II

entry	substrate[a]	% yield of alkylation product (18)	enolate substrate[b]	% yield of bis-lactone product
1	**5b**	44 (**18b**)	**5c**	27 (**16cb**)
2	**5d**	54 (**18d**)	**5a**	24 (**16da**)
3	**5b**	44 (**18b**)	**5b**	22 (**11bb**)
4	**5a**	45 (**18a**)	**5a**	20 (**11a**)

[a] This refers to the glycinate used in the alkylation/Finklestein sequence to produce the 3′-iodides **18**. [b] This refers to the glycinates (**5**) used to alkylate the 3′-iodides (**18**).

Recently, Baldwin and associates[8b] have described an improved procedure for the enolate alkylation of glycinates **5**. In applying this method to the DAP syntheses, the direct enolate coupling between a 3′-halopropyl derivatized glycinate and a second glycinate enolate can be realized, albeit in moderate yields. An example is illustrated in Scheme III. Enolate alkylation of **5** with 3-chloro-1-iodopropane followed by Finkelstein replacement provides the iodides **18** in moderate yield as single (anti)diastereomers. Addition of the iodide to a preformed solution of enolate derived from **5** in the presence of 15-crown-5 ether proceeds with excellent diastereofacial selectivity but in modest yield to afford the bis-lactones **11** or **16** (Table II). These substances were found to be identical to the products obtained from the radical deoxygenation protocol described in Schemes I and II. As such, these substances can be processed to the corresponding DAP isomers as described above.

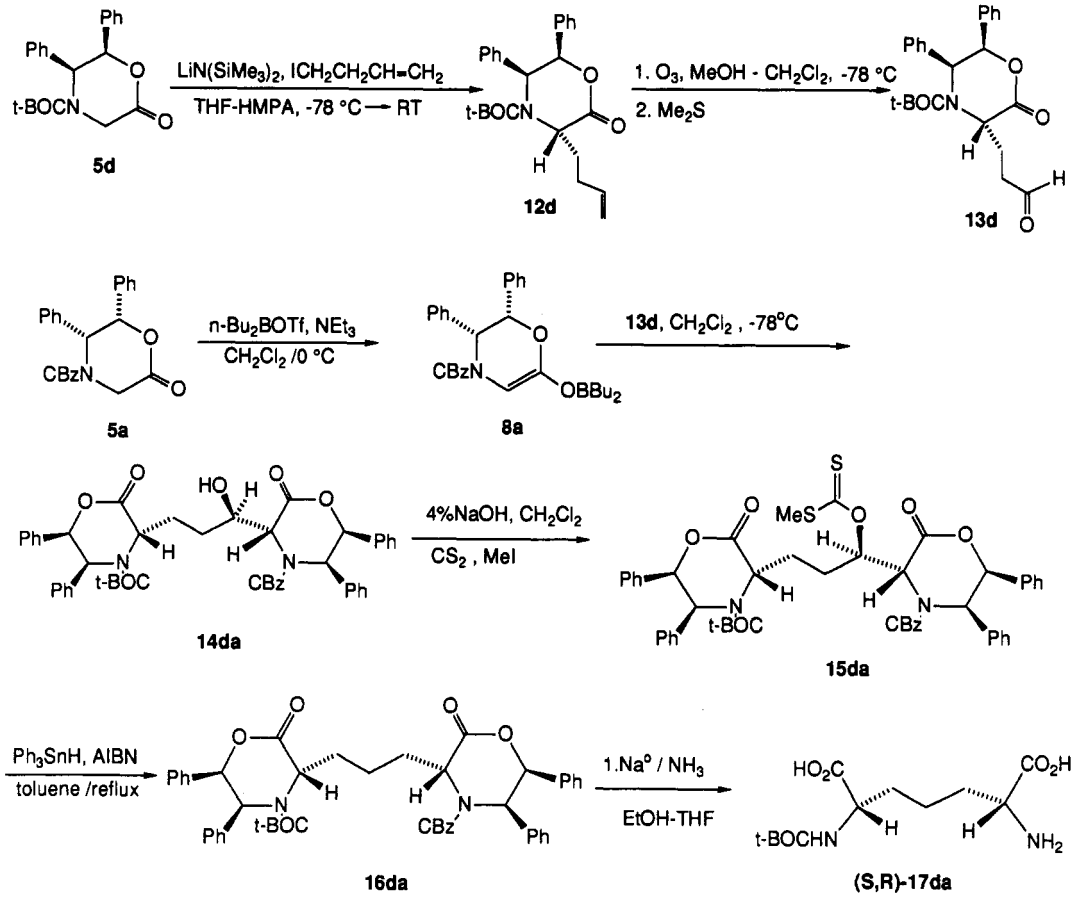
The optical purity of each diaminopimelic acid product was ascertained by comparing the ^{19}F NMR spectrum of the bis-N-acylated (+)-α-methoxy-α-(trifluoromethyl)-phenylacetamide (**19–21**) with that of an authentic mixture

(15) (a) Barton, D. H. R.; McCombie, S. W. *J. Chem. Soc., Perkin Trans. 1* **1975**, 1574. (b) Barton, D. H. R.; Subramanian, R. *J. Chem. Soc., Perkin Trans. 1*, **1977**, 1718.

(16) (a) Hemmi, K.; Takeno, H.; Okada, S.; Nakaguchi, O.; Kitaura, Y.; Hashimoto, M. *J. Am. Chem. Soc.* **1981**, *103*, 7026. (b) Berges, D. A.; DeWolf, W. E.; Dunn, G. L.; Grappel, S. F.; Newman, D. J.; Taggart, J. J.; Gilvarg, C. *J. Med. Chem.* **1986**, *29*, 89.

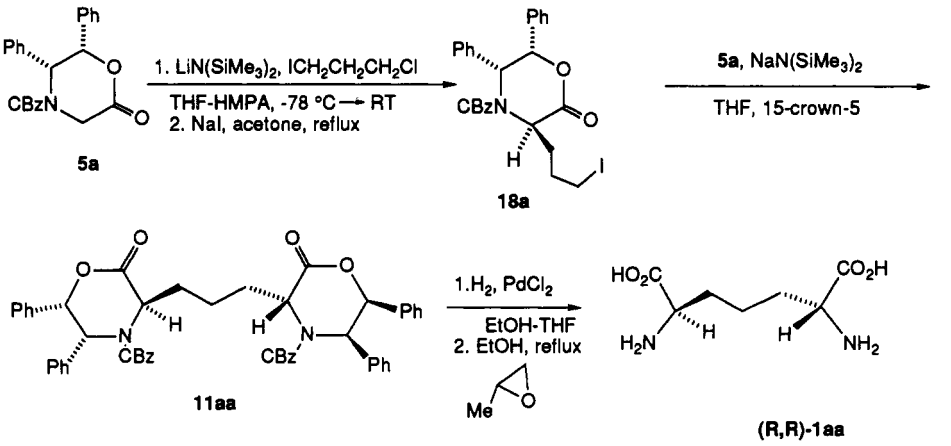
(17) Nutt, R. F.; Strachan, R. G.; Veber, D. F.; Holly, F. W. *J. Org. Chem.* **1980**, *45*, 3078.

Scheme II



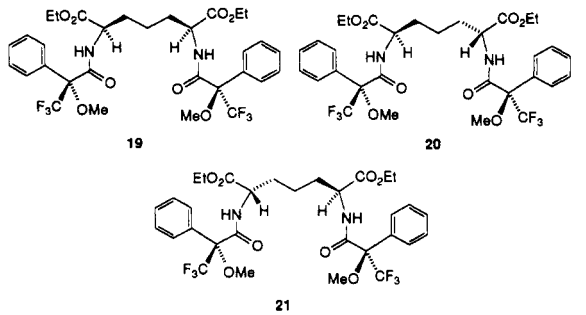
5d, 12d, 13d, 5a, 8a, 14da, 15da, 16da, (S,R)-17da

Scheme III



5a, 18a, 11aa, (R,R)-1aa

of (+)-α-methoxy-α-(trifluoromethyl)phenylacetamides obtained from a commercially available mixture consisting of (*S,S*)-, (*R,R*)-, and (*S,R*)-diaminopimelic acids (Figure 1). The optical purity of each isomer was >98% ee.

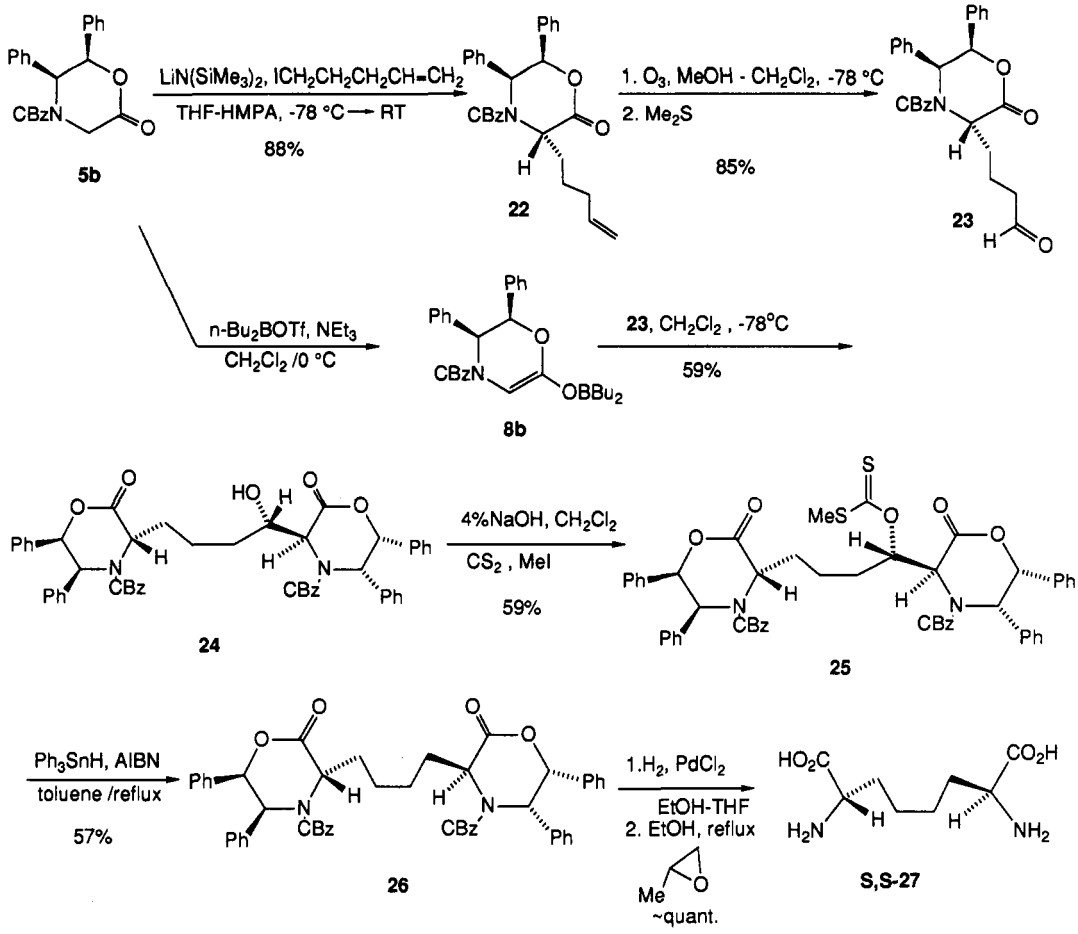


19, 20, 21

Application of the same basic protocol to higher homologs of DAP can be readily envisioned. For example, α,α′-diaminosuberic acid (**27**, Scheme IV) has been used as a nonreducible analog of cystine. Previous stereodefined syntheses of this amino acid have relied on Kolbe electrolytic coupling of glutamic acid derivatives. As shown in Scheme IV, enolate alkylation of **5b** with 1-iodo-4-pentene furnished **22** in high yield (88%). Ozonolysis and aldol coupling of the resulting aldehyde **23** with enol borane **8b** provided **24** in good yield. Radical deoxygenation and reductive cleavage furnished (*S,S*)-2,7-diaminosuberic acid (**27**) in high optical purity. Application of this general approach to the synthesis of functionalized suberic acid derivatives is currently being pursued in these laboratories.

In summary, an asymmetric and stereochemically unambiguous construction of diaminopimelic acid and related

Scheme IV



5b 22 23 8b 24 25 26 S,S-27

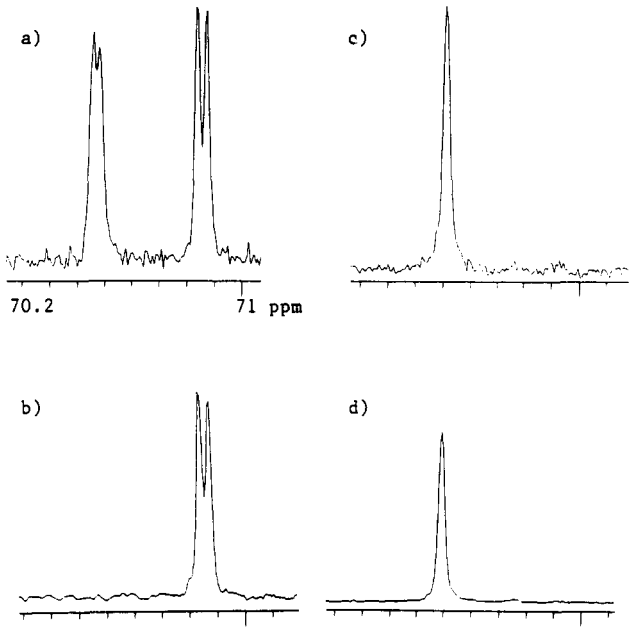


Figure 1.

systems has been developed.[18] The availability of both optical antipodes of the glycinate templates renders this chemistry adaptable to preparing all possible diastereoisomers of substances based on the DAP skeleton in optically pure form. Efforts to extend this methodology to construct other functionalized DAP systems and selected peptides of these substances, particularly those with potential antimicrobial activity, are being pursued in these laboratories and will be reported on in due course.

(18) We thank Prof. John C. Vederas for communicating his results in the area of DAP synthesis prior to publication.

Experimental Section

General Information. Visualization of TLC was achieved with ultraviolet light, I_2 developing chamber, and/or heating of TLC plates submerged in a 5% solution of phosphomolybdic acid in 95% ethanol. Preparative chromatography was performed by the following methods. Column chromatography was performed using Merck silica gel grade 60, 230–400 mesh, 60 Å. Radical chromatography was done on 1-, 2-, and 4-mm silica gel plates using E. Merck silica gel 60 PF-254 containing gypsum on a Harrison Research Chromatotron Model 7924. Reagents and solvents were commercial grade and were used as supplied with the following exceptions. Tetrahydrofuran was freshly distilled from solution benzophenone ketyl. Dry methylene chloride and carbon tetrachloride were obtained by distillation over CaH_2. DMF and HMPA were dried over activated 4-Å molecular sieves. The amino acids furnished crude from the hydrogenation were always obtained in greater than the theoretical amount due to a certain fraction of HCl salt resulting from the $PdCl_2$ catalyst. TBAHS is tetrabutylammonium hydrogen sulfate (97%, Aldrich). TMS is tetramethylsilane.

Determination of Optical Purity, General Procedure. The amino acid (5–10 mg) were converted into the corresponding ester hydrochloride salts as follows: The diaminopimelic acids were refluxed for 2 h in EtOH containing 5 equiv of oxalyl chloride. All the resulting reaction mixtures were cooled, concentrated, and dried in vacuo. The amino ester hydrochloride salts were treated with (±)- or (+)-α-methoxy-α-(trifluoromethyl)phenylacetyl chloride (1.2 equiv) in THF in the presence of excess propylene oxide at 50 °C. After 1 h, the solvent was evaporated and the residue was dried in vacuo. The crude Mosher amides were analyzed by ^1H and ^{19}F NMR spectroscopy and compared to spectra of authentic diastereomeric mixture of Mosher amides

prepared by the same protocol from the corresponding commercial, stereoisomeric mixture of DAP isomers (Sigma Chemical Co.).

(3*R*,5*R*,6*S*)-4-(Benzyloxycarbonyl)-5,6-diphenyl-3-(2'-oxoethyl)-2,3,5,6-tetrahydro-4*H*-1,4-oxazin-2-one (7a). Ozone was bubbled through a solution of **6a** (2.40 g, 0.187 mol, 1.0 equiv) in MeOH–CH_2Cl_2 (200 mL, 1:1) until the solution turned blue (ca. 15 min) at −78 °C. Nitrogen gas was then passed through the reaction mixture to remove excess O_3 until the solution become colorless, and then the solution was allowed to warm to room temperature. The resulting solution was quenched with excess dimethyl sulfide. After 12 h the reaction mixture was concentrated and separated by column chromatography on silica gel (eluted with hexane–CH_2Cl_2–EtOAc, 5:4:1) to afford 1.90 g (79%) of 7 as a white solid: ^{1}H NMR (200 MHz, 393 K, DMSO-d_6 vs TMS) δ 2.42 (2 H, q, J = 7.0 Hz), 2.68 (2 H, t, J = 6.7 Hz), 4.84 (1 H, t, J = 7.1 Hz), 4.97 (2 H, s), 5.26 (1 H, d, J = 2.9 Hz), 6.25 (1 H, d, J = 2.9 Hz), 6.53 (1 H, s), 6.57 (1 H, s), 7.02–7.33 (13 H, m), 9.70 (1 H, s); IR (NaCl, CH_2Cl_2) 2725, 1745, 1702 cm^{-1}; mp 148–149 °C (recryst hexane–CH_2Cl_2–EtOAc; 5:4:1); $[\alpha]^{25}_D$ = +42.5° (*c* 0.50, CH_2Cl_2). Combustion analytical data obtained in the antipodal series **7b**.

Aldol Adduct 9aa. To a stirred solution of **5a** (388 mg, 1.00 mmol, 1.0 equiv) in CH_2Cl_2 (10 mL) was added di-*n*-butyl boron triflate (2.0 mL, 2.00 mmol, 2.0 equiv of a 1 M solution in CH_2Cl_2) followed by the addition of Et_3N (421 μL, 2.0 mmol, 3.0 equiv) at −5 °C. After 15 min the reaction mixture was cooled to −78 °C, and a CH_2Cl_2 (5 mL) solution of aldehyde **7a** (664 mg, 1.5 mmol, 1.5 equiv) was added. After 1 h the reaction mixture was quenched with phosphate buffer solution (0.025 M, pH = 7) and poured into water. The aqueous layer was extracted three times with CH_2Cl_2. The combined organic solution was dried over anhydrous Na_2SO_4, filtered, concentrated, and separated by column chromatography on silica gel (eluted with hexane–CH_2Cl_2–EtOAc, 5:4:1) to afford 460 mg (55%) of **9aa** as a white solid: ^{1}H NMR (200 MHz, DMSO-d_6, 393 K vs TMS) δ 1.91–2.02 (2 H, m), 2.32–2.38 (2 H, m), 4.27 (1 H, m), 4.91 (2 H, s), 4.99 (2 H, s), 4.85–5.06 (2 H, m), 5.25 (1 H, d, J = 2.9 Hz), 5.30 (1 H, d, J = 2.9 Hz), 5.67 (1 H, br, D_2O exchange), 6.23 (1 H, d, J = 1.9 Hz), 6.51 (1 H, d, J = 3.1 Hz), 6.58 (2 H, s), 6.61 (2 H, s), 7.00–7.30 (26 H, m); IR (NaCl, CH_2Cl_2) 3545, 1747, 1738, 1700 cm^{-1}; mp 231–4 °C (recryst hexane–CH_2Cl_2–EtOAc, 5:4:1); $[\alpha]^{25}_D$ = +19.1° (*c* 0.48, CH_2Cl_2). Anal. Calcd for $C_{51}H_{46}N_2O_9$: C, 73.72; H, 5.58; N, 3.37. Found: C, 73.61; H, 5.59; N, 3.21.

Xanthate Ester 10aa. To a stirred solution of **9aa** (420 mg, 0.505 mmol, 1.0 equiv) in CH_2Cl_2 (200 mL) containing CS_2 (30 mL) and MeI (2 mL) was added 4% aqueous NaOH solution (50 mL) and TBAHS (5 mg). The reaction mixture was cooled to 0 °C, and excess MeI was added. The reaction mixture was stirred for 5 h at 0–15 °C. The organic layer was separated, and the aqueous phase was extracted twice with CH_2Cl_2. The combined organic extracts were washed with water and saturated aqueous NaCl and dried over anhydrous Na_2SO_4. The residue was purified by column chromatography on silica gel (eluted with hexane–CH_2Cl_2–EtOAc, 5:4:1) to yield 340 mg (73%) of product **10aa** as a greenish oil and 30 mg of unreacted **9aa** as a white solid: ^{1}H NMR (200 MHz, DMSO-d_6, 393 K vs TMS) δ 2.11 (4 H, m), 2.63 (3 H, s), 4.88 (1 H, t, J = 7.2 Hz), 4.94 (3 H, s), 5.02 (2 H, s), 5.03 (2 H, s), 5.28 (1 H, d, J = 3.0 Hz), 5.33 (1 H, d, J = 3.0 Hz), 5.33 (1 H, d, J = 2.0 Hz), 6.25 (1 H, d, J = 2.6 Hz), 6.54 (1 H, d, J = 3.1 Hz), 6.61 (2 H, s), 6.64 (2 H, s), 6.95–7.25 (26 H, m); IR (NaCl, CH_2Cl_2) 3033, 1757, 1706, 1229 cm^{-1}; $[\alpha]^{25}_D$ = −16.0 (*c* 0.5, CH_2Cl_2). Combustion analytical data obtained in the antipodal series **10bb**.

Reduction Product 11aa. To a solution of **10aa** (340 mg, 0.38 mmol, 1.0 equiv) in toluene (15 mL) was added AIBN (6 mg, 0.038 mmol, 0.1 equiv) follow by the addition of triphenyltin hydride (296 mg, 0.76 mmol, 2.0 equiv). The resulting solution was brought to reflux temperature. After 1 h the toluene was evaporated, and the residue was separated by column chromatography on silica gel (eluted with hexane–CH_2Cl_2–EtOAc, 5:4:1) to afford 226 mg (73.0%) of **11aa** as a white solid. Combustion analytical data obtained in the antipodal series **11bb**: ^{1}H NMR (200 MHz, DMSO-d_6, 393 K vs TMS) δ 1.73–1.83 (2 H, m), 2.19–2.29 (4 H, m), 4.91 (2 H, t, J = 6.7 Hz), 4.95 (2 H, s), 4.98 (2 H, s), 5.29 (2 H, d, J = 2.9 Hz), 6.21 (2 H, d, J = 2.9 Hz), 6.57 (2 H, s), 6.61 (12 H, s), 6.99–7.25 (26 H, m); IR (NaCl, CH_2Cl_2) 1749, 1706 cm^{-1}; mp 284–8 °C (recryst EtOAc); $[\alpha]^{25}_D$ = +36.7° (*c* 0.54, CH_2Cl_2).

(2*R*,6*R*)-2,6-Diaminopimelic Acid [(*R*,*R*)-1a]. To a solution of **11aa** (76 mg, 0.093 mmol, 1.0 equiv) in CH_2Cl_2–EtOH (8 mL, 5:2) was added palladium chloride (50 mg, 0.028 mmol, 2.0 equiv). The reaction vessel was charged with H_2 gas and the mixture was hydrogenated at 60 psi for 48 h. The mixture was then purged with nitrogen and filtered to remove the catalyst. The filtrate was concentrated and dried in vacuo. The crude product was dissolved in dry EtOH (2 mL) and heated to reflux. To this refluxing solution was added excess propylene oxide, and stirring was continued for 30 min at reflux. The white precipitate was filtered to give 18 mg (100%) of product as a white solid: $[\alpha]^{25}_D$ = −20.0° (*c* 0.50, H_2O); ^{1}H NMR (270 MHz, D_2O vs DSS) δ 1.40 (2 H, m), 1.85 (4 H, m), 3.72 (2 H, m).

(3*S*,5*S*,6*R*)-4-(Benzyloxycarbonyl)-5,6-diphenyl-3-(2'-oxoethyl)-2,3,5,6-tetrahydro-4*H*-1,4-oxazin-2-one (7b). Ozone was bubbled through a solution of **6b** (740 mg, 1.68 mmol, 1.0 equiv) in MeOH–CH_2Cl_2 (200 mL, 1:1) until the solution turned blue (ca. 15 min) at −78 °C. Nitrogen gas was passed through the reaction mixture to remove excess O_3 until the solution became colorless, and then the solution was allowed to warm up to room temperature. The resulting solution was quenched with excess dimethyl sulfide. After 12 h the reaction mixture was concentrated and separated by column chromatography on silica gel (eluted with hexane CH_2Cl_2–EtOAc, 5:4:1) to afford 622 mg (84%) of **7b** as a white solid: mp 144–145 °C (recryst hexane–CH_2Cl_2–EtOAc); ^{1}H NMR (200 MHz, DMSO-d_6, 393 K vs TMS) δ 2.42 (2 H, q, J = 7.7 Hz), 2.71 (2 H, t, J = 6.9 Hz), 4.86 (1 H, t, J = 7.3 Hz), 4.98 (2 H, s), 5.27 (1 H, d, J = 2.9 Hz), 6.24 (1 H, d, J = 2.9 Hz), 6.54 (1 H, s), 6.58 (1 H, s), 6.95–7.31 (13 H, m), 9.71 (1 H, s); IR (NaCl, CH_2Cl_2) 2732, 1752, 1700 cm^{-1}; $[\alpha]^{25}_D$ = −37.3° (*c* 0.67, CH_2Cl_2). Anal. Calcd for $C_{27}H_{25}NO_5$: C, 73.12; H, 5.68; N, 3.16. Found: C, 72.87; H, 5.87, N, 3.18.

Aldol Adducts 9bb. To a stirred solution of **5b** (170 mg, 0.43 mmol, 1.0 equiv) in CH_2Cl_2 (5 mL) was added di-*n*-butyl boron triflate (860 μL, 0.86 mmol, 2.90 equiv, 1 M solution in CH_2Cl_2) followed by the addition of Et_3N (181 μL, 1.29 mmol, 3.0 equiv) at −5 °C. After 15 min the reaction mixture was cooled to −78 °C and a 5 mL CH_2Cl_2 solution of aldehyde **7b** (290 mg, 0.65 mmol, 1.5 equiv) was added. After 1 h the reaction mixture was quenched with phosphate buffer solution (0.025 M, pH = 7) and poured into water. The aqueous layer was extracted three times with CH_2Cl_2. The combined organic extracts were dried over anhydrous Na_2SO_4, filtered, concentrated, and separated by column chromatography on silica gel (eluted with hexane–CH_2Cl_2–EtOAc, 5:4:1) to afford 220 mg of **9bb** (62%) as a white solid: ^{1}H NMR (200 MHz, DMSO-d_6, 393 K vs TMS) δ 1.87–2.00 (2 H, m), 2.26–2.37 (2 H, m), 4.26 (1 H, m), 4.92 (2 H, s), 4.97 (2 H, s), 4.89–5.07 (2 H, m), 5.26 (1 H, d, J = 2.8 Hz), 5.31 (1 H, d, J = 2.8 Hz), 5.66 (1 H, br, D_2O exchange), 6.24 (1 H, d, J = 1.8 Hz), 6.51 (1 H, d, J = 2.9 Hz), 6.59 (2 H, s), 6.62 (2 H, s), 7.02–7.31 (26 H, m); IR (NaCl, CH_2Cl_2) 3528, 1734, 1702 cm^{-1}; mp 244–7 °C (recryst hexane–CH_2Cl_2–EtOAc); $[\alpha]^{25}_D$ = −20.3 (*c* 0.5, $CHCl_3$).

Xanthate Ester 10bb. To a stirred solution of **9bb** (200 mg, 0.24 mmol, 1.0 equiv) in CH_2Cl_2 (100 mL) containing CS_2 (15 mL) was added 4% aqueous NaOH solution (15 mL) and TBAHS (5 mg). After being stirred for 5 h at room temperature, the reaction mixture was cooled down to 0 °C and excess MeI was added. The reaction mixture was then stirred for 1 h at 0 °C. The organic layer was separated, and the aqueous phase was extracted twice with CH_2Cl_2. The combined organic extracts were washed with water and saturated NaCl solution and dried over anhydrous Na_2SO_4. The residue was purified by column chromatography on silica gel (eluted with hexane–CH_2Cl_2–EtOAc, 5:4:1) to yield 177 mg of product **10bb** (82%) as a white solid: ^{1}H NMR (200 MHz, DMSO-d_6, 393 K vs TMS) δ 2.22–2.41 (4 H, m), 2.64 (3 H, s), 4.88 (3 H, m), 4.99 (4 H, s), 5.22 (1 H, d, J = 3.2 Hz), 5.30 (1 H, d, J = 2.8 Hz), 5.38 (1 H, d, J = 2.8 Hz), 6.01 (1 H, d, J = 2.8 Hz), 6.59 (2 H, s), 6.62 (2 H, s), 6.95–7.25 (26 H, m); IR (NaCl, CH_2Cl_2) 3033, 1759, 1703, 1229 cm^{-1}; mp 95–105 °C (recryst hexane–CH_2Cl_2–EtOAc); $[\alpha]^{25}_D$ = +16.0° (*c* 0.62, $CHCl_3$). Anal. Calcd for $C_{53}H_{48}N_2O_9S_2$: C, 69.11; H, 5.25; N, 3.04; S, 6.96. Found: C, 68.89; H, 5.47; N, 3.13; S, 6.76.

Reduction Product 11bb. To a solution of **10bb** (500 mg, 0.55 mmol, 1.0 equiv) in toluene (20 mL) was added AIBN (6 mg, 0.038 mmol, 0.1 equiv) followed by addition of triphenyltin hydride (436 mg, 1.11 mmol, 2.0 equiv). The resulting solution was brought

to reflux temperature. After 1 h the toluene was evaporated off the residue was separated by column chromatography on silica gel (eluted with hexane–CH_2Cl_2–EtOAc, 5:4:1) to afford 280 mg (62%) of **11bb** as a white solid: ^{1}H NMR (200 MHz, 393 K, DMSO-d_6 vs TMS) δ 1.71–1.79 (2 H, m), 2.23–2.30 (4 H, m), 4.89 (2 H, m), 4.92 (2 H, s), 4.98 (2 H, s), 5.29 (2 H, d, J = 2.5 Hz), 6.24 (2 H, d, J = 2.5 Hz), 6.57 (2 H, s), 6.60 (2 H, s), 7.00–7.25 (26 H, m); IR (NaCl, CH_2Cl_2) 1748, 1701 cm^{-1}; mp 270 °C (recryst, EtOAc); $[\alpha]^{25}_D$ = −36.8° (c 0.5, CH_2Cl_2). Anal. Calcd for $C_{51}H_{46}N_2O_8$: C, 75.16; H, 5.69; N, 3.44. Found: C, 75.31; H, 5.88; N, 3.39.

(2*S*,6*S*)-2,6-Diaminopimelic Acid [(*S*,*S*)-1bb]. To a solution of **11bb** (100 mg, 0.12 mmol, 1.0 equiv) in CH_2Cl_2–EtOH (8 mL, 5:2) was added $PdCl_2$ (60 mg, 0.028 mmol, 3.0 equiv). The reaction vessel was charged with hydrogen, and the mixture was hydrogenated at 60 psi for 48 h. The mixture was then purged with nitrogen and filtered to remove the catalyst. The filtrate was concentrated and dried in vacuo. The crude product was dissolved in dried EtOH (2 mL) and heated to reflux. To this refluxing solution was added excess propylene oxide, and stirring was continued for 30 min at reflux. The white precipitate was filtered to give 19 mg (100%) of product (*S*,*S*)-**1bb** as a white solid: $[\alpha]^{25}_D$ = +20.0° (c 0.506, H_2O); $[\alpha]^{25}_D$ = +44.5 (c 0.95, 1 N HCl) [lit.[3i] $[\alpha]^{25}_D$ = +45° (c 1, 1 N HCl)]; ^{1}H NMR (270 MHZ, D_2O vs DSS) δ 1.40 (2 H, m), 1.85 (4 H, m), 3.72 (2 H, m).

Aldol Adducts 14db. To a stirred solution of **5b** (630 mg, 1.60 mmol, 1.0 equiv) in CH_2Cl_2 (10 mL) was added di-*n*-butyl boron triflate (2.4 mL, 2.40 mmol, 2.0 equiv, 1 M solution in CH_2Cl_2) followed by the addition of Et_3N (670 μL, 4.8 mmol, 3.0 equiv) at −5 °C. After 15 min the reaction mixture was cooled to −78 °C, and a CH_2Cl_2 (5 mL) solution of aldehyde **13d** (1000 mg, 2.4 mmol, 1.5 equiv) was added. After 1 h the reaction mixture was quenched with phosphate buffer solution (0.025 M, pH = 7) and poured into water. The aqueous layer was extracted three times with CH_2Cl_2. The combined organic extracts were dried over anhydrous Na_2SO_4, filtered, concentrated, and separated by column chromatography on silica gel eluted with hexane–CH_2Cl_2–EtOAc (5:4:1) to afford 728 mg (61%) of **14db** as a white solid: ^{1}H NMR (200 MHz, 393 K, DMSO-d_6 vs TMS) δ 1.18 (9 H, s), 1.86–1.97 (2 H, m), 2.17–1.33 (2 H, m), 4.21–4.32 (1 H, m), 4.81–5.08 (4 H, m), 5.18 (1 H, d, J = 2.8 Hz), 5.25 (1 H, d, J = 2.9 Hz), 5.75 (1 H, br, D_2O exchange), 6.19 (1 H, d, J = 1.3 Hz), 6.52 (1 H, d, J = 3.1 Hz), 6.57 (2 H, s), 6.61 (2 H, s), 6.97–7.34 (21 H, m); IR (NaCl, CH_2Cl_2) 3523, 1757, 1701 cm^{-1}; mp 223–5 °C (recyst hexane–CH_2Cl_2–EtOAc); $[\alpha]^{25}_D$ = −22.5° (c 0.32, CH_2Cl_2). Anal. Calcd for $C_{48}H_{48}N_2O_9$: C, 72.41; H, 6.06; N, 3.51. Found: C, 72.19; H, 6.04; N, 3.47.

Xanthate Ester 15db. To a stirred solution of **14db** (728 mg, 0.91 mmol, 1.0 equiv) and methyl iodide (2 mL) in CH_2Cl_2 (100 mL) and CS_2 (15 mL) were added 4% aqueous NaOH solution (15 mL) and TBAHS (5 mg). The reaction mixture was stirred for 5 h at 0–15 °C. The organic layer was separated, and the aqueous phase was extracted twice with CH_2Cl_2. The combined organic extracts were washed with water and saturated aqueous NaCl and then dried over anhydrous Na_2SO_4. The residue was purified by column chromatography on silica gel, eluted with hexane–CH_2Cl_2–EtOAc (5:4:1) to yield 606 mg (74%) of product **15db** as a white solid: ^{1}H NMR (300 MHz, 393 K, DMSO-d_6 vs TMS) δ 1.21 (9 H, s), 2.27 (4 H, m), 2.65 (3 H, s), 4.83–5.02 (5 H, m), 5.19 (1 H, d, J = 2.8 Hz), 5.22 (1 H, d, J = 3.1 Hz), 5.38 (1 H, d, J = 2.4 Hz), 6.01 (1 H, d, J = 3.1 Hz), 6.61 (2 H, s), 6.64 (2 H, s), 6.97–7.26 (21 H, m); IR (NaCl, CH_2Cl_2) 3019, 2976, 1759, 1704, 1229 cm^{-1}; mp 191–7 °C (recyst hexane–CH_2Cl_2–EtOAc); $[\alpha]^{25}_D$ = +31.0° (c 0.42, CH_2Cl_2).

Reduction Product 16db. To a solution of **15db** (570 mg, 0.64 mmol, 1.0 equiv) in toluene (20 mL) was added AIBN (6 mg, 0.9038 mmol, 0.1 equiv) followed by the addition of triphenyltin hydride (740 mg, 1.89 mmol, 2.0 equiv). The resulting solution was brought to reflux. After 1 h in the toluene was evaporated off and the residue was separated by column chromatography on silica gel eluted with hexane–CH_2Cl_2–EtOAc (5:4:1) to afford 410 mg (79%) **16db** as a white solid: ^{1}H NMR (200 MHz, 393 K, DMSO-d_6 vs TMS) 1.18 (9 H, s), 1.72–1.85 (2 H, m), 2.18–2.29 (4 H, m), 4.86–5.02 (4 H, m), 5.16 (1 H, d, J = 2.9 Hz), 5.30 (1 H, d, J = 2.9 Hz), 6.19 (1 H, d, J = 2.7 Hz), 6.26 (1 H, d, J = 3.00 Hz), 6.56 (2 H, s), 6.60 (2 H, s), 7.04–7.25 (21 H, m); IR (NaCl, CH_2Cl_2) 1749, 1703 cm^{-1}; mp 214–6 °C (recryst EtOAc); $[\alpha]^{25}_D$ = =43.4° (c 0.5, CH_2Cl_2). Anal. Calcd for $C_{48}H_{48}N_2O_8$: C, 73.82; H, 6.20; N, 3.59; Found: C, 73.90; H, 6.14; N, 3.58.

(3*S*,5*S*,6*R*)-4-(*tert*-Butyloxycarbonyl)-5,6-diphenyl-3-(3′-butenyl)-2,3,5,6-tetrahydro-4*H*-1,4-oxazin-2-one (12d). To a stirred solution of **5d** (7.06 g, 20 mmol, 1.0 equiv) and 4-iodobutene (18.2 g, 100 mmol, 5 equiv) in THF (150 mL) and HMPA (15 mL) was added lithium bis(trimethylsilyl)amide (30 mL, 30 mmol, 1.5 equiv, 1.0 M in methylene chloride) dropwise via syringe at −78 °C. After 10 min the dry ice bath was removed. After an additional 1 h, the reaction mixture was poured into ethyl acetate. The organic layer was washed with water and brine, dried over anhydrous Na_2SO_4, filtered, concentrated, and separated by column chromatography on silica gel (eluted with hexane–ethyl acetate, 3:2) to afford 4.75 g (58.4%) of **12d** as a white solid. The antipode was similarly obtained from **5c** in 56% yield: ^{1}H NMR (200 MHz, 393 K, DMSO-d_6 vs TMS) δ 1.17 (9 H, s), 2.11–2.39 (4 H, m), 4.80 (1 H, t, J = 6.8 Hz), 5.01–5.24 (2 H, m), 5.14 (1 H, d, J = 2.9 Hz), 5.81–6.00 (1 H, m), 6.18 (1 H, d, J = 3.2 Hz), 6.54 (1 H, d, J = 1.9 Hz), 6.58 (1 H, d, J = 1.4 Hz), 7.00–7.38 (8 H, m); IR (NaCl, CH_2Cl_2) 2978, 1747, 1703 cm^{-1}; mp 158–160 °C (recryst hexane–CH_2Cl_2–EtOAc); $[\alpha]^{25}_D$ = −56.7 (c 0.54, CH_2Cl_2). Anal. Calcd for $C_{25}H_{29}NO_4$: C, 76.46; H, 6.42; N, 3.09. Found: C, 76.49; H, 6.59; N, 3.09.

(3*S*,5*S*,6*R*)-4-(*tert*-Butyloxycarbonyl)-5,6-diphenyl-3-(2′-oxoethyl)-2,3,5,6-tetrahydro-4*H*-1,4-oxazin-2-one (13d). Ozone was bubbled through a solution of **12d** (1.52 g, 3.68 mmol, 1.0 equiv) and $NaHCO_3$ (100 mg) in MeOH–CH_2Cl_2 (100 mL, 1:1) until the solution turned blue (ca. 15 min) at −78 °C. Nitrogen gas was then passed through the reaction mixture to remove excess O_3 until the solution become colorless, and then the solution was allowed to warm up to room temperature. The resulting solution was quenched with excess dimethyl sulfide. After 12 h the reaction mixture was concentrated and separated by column chromatography on silica gel (eluted with hexane–CH_2Cl_2–EtOAc, 5:4:1) to afford 1.32 g (88%) of **13d** as a white solid. The antipode was similarly obtained in 90% yield: ^{1}H NMR (200 MHz, 393 K, DMSO-d_6 vs TMS) δ 1.17 (9 H, s), 2.39 (2 H, m), 2.69 (2 H, m), 4.83 (1 H, t, J = 6.5 Hz), 5.14 (1 H, d, J = 2.5 Hz), 6.20 (1 H, d, J = 2.6 Hz), 6.55 (1 H, s), 6.59 (1 H, s) 7.04–7.24 (8 H, m), 9.75 (1 H, s); IR (NaCl, CH_2Cl_2) 2720, 1757, 1699 cm^{-1}; mp 170–4 °C; $[\alpha]^{25}_D$ = −45.7° (c 0.83, CH_2Cl_2). Anal. Calcd for $C_{25}H_{27}NO_5$: C, 70.39; H, 6.65; N, 3.42. Found: C, 70.38; H, 6.71; N, 3.43.

Aldol Adducts 14da. To a stirred solution of **5a** (949 mg, 2.44 mmol, 1.0 equiv) in CH_2Cl_2 (20 mL) was added di-*n*-butyl boron triflate (3.66 mL, 3.66 mmol, 1.5 equiv of a 1 M solution in CH_2Cl_2) followed by the addition of Et_3N (1026 μL, 7.32 mmol, 3.0 equiv) at −5 °C. After 15 min the reaction mixture was cooled to −78 °C and a CH_2Cl_2 (10 mL) solution of aldehyde **13d** (1.5 g, 3.67 mmol, 1.5 equiv) was added. After 1 h the reaction mixture was quenched with phosphate buffer solution (0.025 M, pH = 7) and poured into water. The aqueous layer was extracted three times with CH_2Cl_2. The combined organic extracts were dried over anhydrous Na_2SO_4, filtered, concentrated, and separated by column chromatography on silica gel (eluted with hexane–CH_2Cl_2–EtOAc, 5:4:1) to afford 1.63 g (56%) of **14da** as a white solid: ^{1}H NMR (200 MHz, 393 K, DMSO-d_6 vs TMS) δ 1.21 (9 H, s), 1.76–1.85 (2 H, m), 2.20–2.32 (2 H, m), 4.24–4.26 (1 H, m), 4.84–5.04 (2 H, m), 4.92 (2 H, s), 5.19 (1 H, d, J = 2.5 Hz), 5.25 (1 H, d, J = 2.7 Hz), 5.65 (1 H, br, D_2O exchange), 6.19 (1 H, d, J = 2.5 Hz), 6.51 (1 H, d, J = 2.9 Hz), 6.58 (2 H, s), 6.62 (2 H, s), 6.97–7.34 (21 H, m); IR (NaCl, CH_2Cl_2) 3421, 1752, 1701, 1663 cm^{-1}; mp 204–211 °C (recryst hexane–CH_2Cl_2–EtOAc); $[\alpha]^{25}_D$ = +15.2° (c 0.67, CH_2Cl_2). Anal. Calcd for $C_{48}H_{48}N_2O_9$: C, 72.41; H, 6.06; N, 3.51. Found: C, 72.21; H, 6.19; N, 3.26.

Xanthate Ester 15da. To a stirred solution of **14da** (1.50 g, 1.88 mmol, 1.0 equiv) in CH_2Cl_2 (100 mL) containing CS_2 (30 mL) were added 4% aqueous NaOH solution (30 mL) and TBAHS (20 ng). After being stirred for 5 h at room temperature, the reaction mixture was cooled to 0 °C, and excess MeI was added. The reaction mixture was then stirred for 1 h at 0 °C. The organic layer was separated, and the aqueous phase was extracted twice with CH_2Cl_2. The combined organic extracts were washed with water and saturated aqueous NaCl and dried over anhydrous Na_2SO_4. The residue was purified on column chromatography on silica gel (eluted with hexane–CH_2Cl_2–EtOAc, 5:4:1) to yield

1.178 g (71%) of product **15da** as a white solid: ^{1}H NMR (200 MHz, 393 K, DMSO-d_6 vs TMS) δ 1.20 (9 H, s), 2.19–2.39 (4 H, m), 2.62 (3 H, s), 4.85–5.04 (4 H, m), 5.17 (1 H, t, J = 3.4 Hz), 5.25 (1 H, d, J = 2.4 Hz), 5.42 (1 H, d, J = 4.1 Hz), 6.02 (1 H, d, J = 3.1 Hz), 6.17 (1 H, d, J = 2.7 Hz), 6.51–6.64 (4 H, m), 6.97–7.26 (21 H, m); IR (NaCl, CH_2Cl_2) 1748, 1700 cm^{-1}; mp 21–220 °C (recryst hexane–CH_2Cl_2–EtOAc); $[\alpha]^{25}_D$ = +32.6° (c 0.50, CH_2Cl_2). Anal. Calcd for $C_{50}H_{50}N_2O_9S_2$: C, 67.70; H, 5.63; N, 3.16; S, 7.23. Found: C, 67.81; H, 5.63; N, 3.15; S, 7.42.

Reduction Product 16da. To a solution of **15da** (1131 mg, 1.29 mmol, 1.0 equiv) in toluene (50 mL) was added AIBN (20 mg) followed by the addition of triphenyltin hydride (1000 mg, 2.58 mmol, 2.0 equiv). The resulting solution was brought to reflux temperature. After 1 h the toluene was evaporated off and the residue was separated by column chromatography on silica gel (eluted with hexane–CH_2Cl_2–EtOAc, 5:4:1) to afford 841 mg (83%) of **16da** as a white solid: ^{1}H NMR (200 MHz, 393 K, DMSO-d_6 vs TMS) δ 1.15 (9 H, s), 1.75 (2 H, m), 2.25 (4 H, m), 4.20–4.92 (2 H, m), 4.97 (2 H, s), 5.16 (1 H, d, J = 2.5 Hz), 5.29 (1 H, d, J = 2.7 Hz), 6.18 (1 H, d, J = 2.7 Hz), 6.23 (1 H, d, J = 2.7 Hz), 6.56 (2 H, s), 6.59 (2 H, s), 6.96–7.23 (21 H, m); IR (NaCl, CH_2Cl_2) 1750, 1699 cm^{-1}; mp 225–7 °C (recryst hexane–CH_2Cl_2–EtOAc); $[\alpha]^{25}_D$ = +1.7 (c 0.6, CH_2Cl_2). Anal. Calcd for $C_{48}H_{48}N_2O_8$: C, 73.82; H, 6.20; N, 3.59. Found: C, 74.00; H, 6.21; N, 3.42.

Mono-*N*-Boc-DAP (17da). To a mixture of **16da** (81 mg, 0.1 mmol, 1.0 equiv), absolute, EtOH (300 μL), and THF (4 mL) in liquid ammonia (30 mL, distilled from Li at −33 °C) was added Li (28 mg, 4 mmol, 40 equiv). The resulting blue solution was stirred for 30 min at −33 °C and then was quenched with NH_4Cl. The mixture was allowed to warm. After the NH_3 was evaporated, the residue was diluted with water (2 mL) and was carefully acidified with 1 N HCl to pH of 5. The aqueous solution was extracted with EtOAc, and was then concentrated to dryness. The resulting white precipitates was triturated in absolute EtOH (2 mL), the precipitates were filtered out, and the filtrate was concentrated and recrystallized in THF to yield 20 mg (72%) of product as a white solid: ^{1}H NMR (270 MHz, 393 K, D_2O vs DSS) δ 1.30 (9 H, s), 1.50–1.58 (2 H, m), 1.61–1.85 (4 H, m), 3.64 (1 H, t, J = 6.2 Hz), 3.76 (1 H, m); IR (NaCl, CH_2Cl_2) 3422, 1638, 1404 cm^{-1}; mp 264 °C dec (recryst THF); $[\alpha]^{25}_D$ = +2.2° (c 0.45, H_2O); mass spectrum (FAB) m/z 313 (M + 1) for $C_{12}H_{21}N_2NaO_6$.

(3*S*,5*S*,6*R*)-4-(Benzyloxycarbonyl)-5,6-diphenyl-3-(4′-pentenyl)-2,3,5,6-tetrahydro-4*H*-1,4-oxazin-2-one (22). To a stirred solution of **5b** (1.94 g, 5 mmol, 1.0 equiv) and 5-iodopentene (4.90 g, 25 mmol, 5.0 equiv) in warm THF and HMPA was added lithium bis(trimethylsilyl)amide (5.5 mL, 5.5 equiv, 1.0 M in CH_2Cl_2) dropwise via syringe at −78 °C. After 10 min the dry ice bath was removed. After an additional 1 h, the reaction mixture was poured into ethyl acetate. The organic layer was washed with water and brine, dried over anhydrous Na_2SO_4, filtered, concentrated, and separated by column chromatography on silica gel (eluted with hexane–ethyl acetate, 3:2) to afford 2.00 g (87.7%) of **22** as a white solid: ^{1}H NMR (200 MHz, 393 K, DMSO-d_6 vs TMS) δ 1.55–1.63 (2 H, m), 2.07–2.19 (4 H, m), 4.81 (1 H, t, J = 7.2 Hz), 4.97 (2 H, s), 4.94–5.06 (2 H, m), 5.27 (1 H, d, J = 2.9 Hz), 5.72–5.93 (1 H, m), 6.19 (1 H, d, J = 3.0 Hz), 6.55 (1 H, s), 6.58 (1 H, s), 7.03–7.32 (13 H, m); IR (NaCl, CH_2Cl_2) 1750, 1705, 1454, 1401 cm^{-1}; mp 153–4 °C (recryst hexane–CH_2Cl_2–EtOAc); $[\alpha]^{25}_D$ = −20.0° (c 0.5, CH_2Cl_2). Anal. Calcd for $C_{29}H_{29}NO_4$: C, 73.67; H, 7.33; N, 3.44. Found: C, 73.81; H, 7.33; N, 3.44.

(3*S*,5*S*,6*R*)-4-(Benzyloxycarbonyl)-5,6-diphenyl-3-(4′-oxobutyl)-2,3,5,6-tetrahydro-4*H*-1,4-oxazin-2-one (23). Ozone was bubbled through a solution of **22** (2.00 g, 4.49 mmol, 1.0 equiv) and $NaHCO_3$ (100 mg) in MeOH–CH_2Cl_2 (100 mL, 1:1) until the solution turned blue (ca. 15 min) at −78 °C. Nitrogen gas was then passed through the reaction mixture to remove excess O_3 until the solution became colorless, and then the solution was allowed to warm up to room temperature. The resulting solution was quenched with excess dimethyl sulfide. After 12 h the reaction mixture was concentrated and separated by column chromatography on silica gel (eluted with hexane–CH_2Cl_2–EtOAc, 5:4:1) to afford 1.71 g (85%) of **23** as a white solid: ^{1}H NMR (200 MHz, 393 K, DMSO-d_6 vs TMS) δ 1.72–1.821 (2 H, m), 2.09–2.21 (2 H, m), 2.51–2.62 (2 H, m), 4.81 (1 H, t, J = 7.3 Hz), 4.98 (2 H, s), 5.26 (1 H, d, J = 3.0 Hz), 6.19 (1 H, d, J = 3.1 Hz), 6.55 (1 H, s), 6.58 (1 H, s), 7.02–7.25 (13 H, m), 9.68 (1 H, s); IR (NaCl, CH_2Cl_2) 2722, 1755, 1703 cm^{-1}; mp 162–5 °C (recryst hexane–CH_2Cl_2–EtOAc); $[\alpha]^{25}_D$ = −26.8° (c 0.5, CH_2Cl_2). Anal. Calcd for $C_{29}H_{27}NO_5$: C, 73.50; H, 5.95; N, 3.06. Found: C, 73.36; H, 6.14; N, 3.06. **Aldol Adduct 24.** To a stirred solution of **5b** (155 mg, 0.40 mmol, 1.0 equiv) in CH_2Cl_2 (4 mL) was added dibutyl boron triflate (800 μL, 0.80 mmol, 2.0 equiv of a 1 M solution in CH_2Cl_2) followed by the addition of Et_3N (168 μL, 1.2 mmol, 3.0 equiv) at −5 °C. After 15 min the reaction mixture was cooled to −78 °C, and CH_2Cl_2 (5 mL) solution of aldehyde **23** (260 mg, 0.57 mmol, 1.5 equiv) was added. After 1 h the reaction mixture was quenched with phosphate buffer solution (0.025 M, pH = 7) and poured into water. The aqueous layer was extracted three times with CH_2Cl_2. The combined organic extracts were dried over anhydrous Na_2SO_4, filtered, concentrated, and separated by column chromatography on silica gel (eluted with hexane–CH_2Cl_2–EtOAc, 5:4:1) to afford 200 mg (59%) of **32** as a white solid: ^{1}H NMR (200 MHz, 393 K, DMSO-d_6 vs TMS) δ 1.62–1.89 (4 H, m), 2.13–2.27 (2 H, m), 4.16–4.21 (1 H, m), 4.88 (H, t, J = 8.8 Hz), 4.95, 5.10 (3 H, m), 5.02 (2 H, s), 5.25 (H, d, J = 3.0 Hz), 5.28 (H, d, J = 2.9 Hz), 5.57 (H, br, D_2O exchange), 6.25 (1 H, d, J = 2.4 Hz), 6.52 (1 H, d, J = 2.8 Hz), 6.55 (2 H, s), 6.58 (2 H, s), 6.95–7.26 (26 H, m); IR (NaCl, CH_2Cl_2) 3526, 1752, 1734, 1699 cm^{-1}; mp 186–9 °C (recryst hexane–CH_2Cl_2–EtOAc); $[\alpha]^{25}_D$ = −20.8° (c 0.26, CH_2Cl_2). Anal. Calcd for $C_{52}H_{48}N_2O_9$: C, 73.91; H, 5.73; N, 3.32. Found: C, 73.78; H, 5.92; N, 3.26.

Xanthate Ester 25. To a stirred solution of **24** (98 mg, 0.12 mmol, 1.0 equiv) in CH_2Cl_2 (10 mL) and CS_2 (5 mL) were added 4% aqueous NaOH solution (2 mL) and TBAHS (1 mg). After being stirred for 5 h at room temperature, the reaction mixture was cooled to 0 °C and excess MeI was added. The reaction mixture was then stirred for 1 h at 0 °C. The organic layer was separated, and the aqueous phase was extracted twice with CH_2Cl_2. The combined organic extracts were washed with water and saturated aqueous NaCl and dried over Na_2SO_4. The residue was purified by column chromatography on silica gel (eluted with hexane–CH_2Cl_2–EtOAc, 5:4:1) to yield 62 mg (58.6%) of product (**25**) as a white solid: ^{1}H NMR (200 MHz, 393 K, DMSO-d_6 vs TMS) δ 1.63–1.82 (2 H, m), 2.05–2.29 (4 H, m), 2.61 (3 H, s), 4.84–5.04 (4 H, m), 4.88 (H, t), 5.00 (2 H, s), 5.21 (1 H, d, J = 2.8 Hz), 5.29 (1 H, d, J = 2.5 Hz), 5.96 (1 H, d, J = 3.5 Hz), 6.20 (1 H, d, J = 3.0 Hz), 6.56–6.64 (4 H, m), 6.94–7.35 (26 H, m); IR (NaCl, CH_2Cl_2) 1744, 1703, 1281, 1229, 1195 cm^{-1}; mp 234–6 °C (recryst hexane–CH_2Cl_2–EtOAc); $[\alpha]^{25}_D$ = −5.6° (c 0.43, CH_2Cl_2). Anal. Calcd for $C_{54}H_{50}N_2O_9S_2$: C, 69.36; H, 5.39; N, 3.00; S, 6.86. Found: C, 69.04; H, 5.44; N, 2.86; S, 6.67.

Reduction Product 26. To a solution of **25** (96 mg, 0.105 mmol, 1.0 equiv) in toluene (20 mL) was added AIBN (2 mg, 0.0 mmol, 0.1 equiv) followed by the addition of triphenyltin hydride (412 mg, 1.05 mmol, 10 equiv). The resulting solution was brought to reflux temperature. After 1 h the toluene was evaporated, and the residue was separated by column chromatography on silica gel (eluted with hexane–CH_2Cl_2–EtOAc, 5:4:1) to afford 50 mg (57%) of **26** as a white solid: ^{1}H NMR (200 MHz, 393 K, DMSO-d_6 vs TMS) δ 1.609 (4 H, m), 2.14 (4 H, m), 4.80 (2 H, t, J = 7.3 Hz), 4.97 (2 H, s), 4.99 (2 H, s), 5.27 (2 H, d, J = 6.3 Hz), 6.22 (2 H, d, J = 2.8 Hz), 6.55 (2 H, s), 6.59 (2 H, s), 6.95–7.78 (26 H, m); IR (NaCl, CH_2Cl_2) 1749, 1700 cm^{-1}; mp 291–9 °C (recryst, EtOAc); $[\alpha]^{25}_D$ = −31.9° (c 0.26 $CHCl_3$). Anal. Calcd for $C_{52}H_{48}N_2O_8$: C, 75.34; H, 5.84; N, 3.38. Found: C, 75.12; H, 6.00; N, 3.17.

(*S*,*S*)-2,7-Diaminosuberic Acid [(*S*,*S*)-27]. To a solution of **26** (23 mg, 0.028 mmol, 1.0 equiv) in CH_2Cl_2–EtOH (8 mL, 5:2) was added $PdCl_2$ (10 mg, 0.056 mmol, 2.0 equiv). The reaction vessel was charged with H_2, and the mixture was hydrogenated at 60 psi for 48 h. The mixture was then purged with nitrogen, and filtered to remove the catalyst. The filtrate was concentrated and dried in vacuo. The crude product was dissolved in dry EtOH (2 mL) and heated to reflux. To this refluxing solution was added excess propylene oxide, and the mixture was stirred for 30 min at reflux. The white precipitate was filtered to give 6 mg (100%) of product (**27**) as a white solid: ^{1}H NMR (270 MHz, D_2O vs DSS) δ 1.41 (4 H, m), 1.90 (4 H, m), 3.95 (2 H, m); $[\alpha]^{25}_D$ = +24.8° (c 0.25, H_2O).

Representative Procedure for Preparing 18. To a stirred solution of **5b** (388 mg, 1.0 mmol, 1.0 equiv) and 15-crown-5 ether

(600 μL, 3.0 mmol, 3.0 equiv) in THF (12 mL) was added sodium bis(trimethylsilyl)amide (1.5 mL, 3 equiv, 1.0 M in methylene chloride) dropwise via syringe at −78 °C. After 10 min, 3-chloro-1-iodopropane (322 μL, 3.0 mmol, 3.0 equiv) was added. After an additional 2 h, the reaction mixture was poured into ethyl acetate. The organic layer was washed with water and brine, dried over anhydrous Na_2SO_4, filtered, concentrated, and separated by column chromatography on silica gel (eluted with hexane–CH_2Cl_2–EtOAc, 5:4:1) to afford 240 mg (51.6%) of the 3′-chloride as a white solid. This material was used directly for the Finkelstein reaction without further purification: ^{1}H NMR (270 MHz, $CDCl_3$ vs TMS) δ 2.00–2.40 (4 H, m), 3.60 (2 H, t, J = 6.8 Hz), 4.85–5.30 (3 H, m), 5.98 (1 H, d, J = 2.8 Hz), 6.55 (1 H, d, J = 3.1 Hz), 6.95 (2 H, s), 7.00–7.40 (13 H, m).

The 3′-chloride (330 mg, 0.71 mmol, 1.0 equiv) and NaI (1.06 g, 7.1 mmol, 10 equiv) in acetone (15 mL) were stirred overnight at reflux temperature. After the solvent was evaporated, the resulting residue was dissolved in ethyl acetate (50 mL), washed with brine, and dried over Na_2SO_4. The residue was purified by column chromatography on silica gel (eluted with hexane–CH_2Cl_2–EtOAc, 5:4:1) to yield 350 mg (89%) of **18b** as a white solid: ^{1}H NMR (200 MHz, DMSO-d_6 vs TMS) δ 1.90 (2 H, m), 2.23 (2 H, m), 3.30 (2 H, t, J = 7.3 Hz), 4.85–5.35 (3 H, m), 6.27 (1 H, d, J = 3.0 Hz), 6.52 (2 H, s), 6.70 (1 H, d, J = 3.3 Hz), 7.00–7.45 (13 H, m); IR (NaCl, CH_2Cl_2) 1754, 1704, 1245, 1207, 699 cm^{-1}; mp 167–169 °C (recryst hexane–EtOAc, 5:1); $[\alpha]^{25}_D$ = =26.4 (c 0.5, CH_2Cl_2). The antipode (**18a**) was similarly obtained from **5a** in 45% yield (two steps); mp 168–71 °C (recryst hexane/EtOAc, 5:1); $[\alpha]^{25}_D$ = +25.6° (c 0.5, CH_2Cl_2).

Represenative Enolate Alkylation of 5 To Produce 11/16. To a stirred solution of **5a** (146 mg, 0.38 mmol, 1.5 equiv) in HMPA/THF (7 mL, 1:6) was added sodium bis(trimethylsilyl)amide (375 μL, 1.5 equiv, 1.0 M in CH_2Cl_2) dropwise via syringe at −78 °C. After 10 min a solution of **18a** (140 mg, 0.25 mmol, 1.0 equiv) was added. After an additional 2 h, the reaction mixture was allowed to warm to room temperature, quenched by phosphate buffer solution (pH of 7), extracted with methylene chloride, washed with water and brine, dried over anhydrous Na_2SO_4, filtered, concentrated, and recrystallized in ethyl acetate to afford 62 mg (20%) of **11aa** as a white solid. This material was identical to that obtained above from the reduction of **10aa**.

Note Added in Proof. A recent paper describing the synthesis of differentially protected *meso*-2,6-diaminopimelic acid has appeared: Jurgens, A. R. *Tetrahedron Lett.* **1992**, *33*, 4727.

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Supplementary Material Available: Detailed procedure and spectral data for the Mosher amides **19**, **20**, and **21** (1 page). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

Asymmetric [1,3]-Dipolar Cycloaddition Reactions: Synthesis of Highly Substituted Proline Derivatives

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The asymmetric [1,3]-dipolar cycloaddition reactions of azomethine ylides derived from (5*R*,6*S*)-2,3,5,6-tetrahydro-5,6-diphenyl-1,4-oxazin-2-one with various aldehydes and dimethyl maleate is described. The reactions prove to be highly endo-selective, installing three contiguous stereogenic centers in the newly formed five-membered ring with essentially complete stereochemical control. In the case of aldehydes higher than formaldehyde, a fourth stereogenic center is created; in most cases, poor stereoselectivity is observed at this center; the diastereomers formed in these cases can be separated by chromatography and separately converted into the amino acids. The bicyclic dipolar adducts can be cleaved with either catalytic hydrogenolysis or hydrolytic ring opening, esterification, and lead tetraacetate removal of the chiral auxiliary.

The [1,3]-dipolar cycloaddition reaction of azomethine ylides has become a powerful method for constructing pyrrolidine ring systems.[1] A large array of important natural alkaloids possess highly substituted pyrrolidine ring systems. Several natural products have been synthesized by utilization of the [1,3]-dipolar ring-forming reaction as a key step.[2] Recent attention in this area has focused on devising methods to directly provide optically active [1,3]-dipolar cycloaddition products from azo-

Table I. Dipolar Adducts 4

entry	aldehyde (R)	yield (% 4)	diastereomer ratio
1	formaldehyde	71 **4a**	
2	propionaldehyde	32 **4b**	1.33:1
3	isobutyraldehyde	52 **4c**	1:0
4	benzaldehyde	70 **4d**	1.7:1
5	*p*-anisaldehyde	71 **4e**	1:1
6	*p*-nitrobenzaldehyde	71 **4f**	1:1
7	2-furaldehyde	61 **4g**	1:1

(1) (a) For a review, see: Lown, W. J. In *1,3-Dipolar Cycloaddition Chemistry*; Padwa, A., Ed.; Wiley: New York, 1984; Vol. 1. See also: (b) Padwa, A.; Dean, D. C.; Zhi, L. *J. Am. Chem. Soc.* **1989**, *111*, 6451. (c) Tufariello, J. J. *Acc. Chem. Res.* **1979**, *12*, 396. (d) Vedejs, E.; Grissom, J. W. *J. Org. Chem.* **1988**, *53*, 1876. (e) Vedejs, E.; Martinez, G. R. *J. Am. Chem. Soc.* **1980**, *102*, 7993. (f) Joucla, M.; Mortier, J. *Tetrahedron Lett.* **1987**, *28*, 2973. (g) Vedejs, E.; Grissom, J. W. *J. Am. Chem. Soc.* **1988**, *110*, 3238. (h) Chastanet, J.; Roussi, G. *J. Org. Chem.* **1988**, *53*, 3808. (i) Imai, N.; Nemoto, M.; Terao, Y.; Achiwa, K.; Sekiya, M. *Chem. Pharm. Bull.* **1986**, *34*, 1078. (j) Imai, N.; Terao, Y.; Achiwa, K. *Chem. Pharm. Bull.* **1987**, *35*, 2085. (k) Grigg, R.; Kemp, J.; Warnock, W. J. *J. Chem. Soc., Perkin Trans. 1* **1987**, 2275. (l) Martin, S. F.; Cheavens, T. H. *Tetrahedron Lett.* **1989**, *30*, 7017. (m) Barr, D. A.; Grigg, R.; Sridharan, V. *Tetrahedron Lett.* **1989**, *30*, 4727. (n) Burns, B.; Coates, B.; Neeson, S.; Stevenson, P. J. *Tetrahedron Lett.* **1990**, *31*, 4351. (o) Tsuge, O.; Kanemasa, S.; Ohe, M.; Takenaka, S. *Chem. Lett.* **1986**, 973. (p) Joucla, M.; Mortier, J.; Hamelin, J. *Tetrahedron Lett.* **1985**, *26*, 277. (q) Padwa, A.; Dent, W.; Nimmesgern, H.; Venkatramanan, M. K.; Wong, G. S. K. *Chem. Ber.* **1986**, *119*, 813. (r) Husinec, S.; Savic, V.; Porter, A. E. A. *Tetrahedron Lett.* **1988**, *29*, 6649. (s) Grigg, R.; Surendrakumar, S.; Thianpatanagul, S.; Vipond, D. *J. Chem. Soc., Chem. Commun.* **1987**, 47. (t) Tsuge, O.; Kanemasa, S.; Yoshioka, M. *J. Org. Chem.* **1988**, *53*, 1384.

(2) For examples, see: (a) Kraus, G. A.; Nagy, J. O. *Tetrahedron* **1985**, *41*, 3537. (b) DeShong, P.; Kell, D. A. *Tetrahedron Lett.* **1986**, *27*, 3979. (c) Wang, C.-L. J. Ripka, W. C.; Confalone, P. N. *Tetrahedron Lett.* **1984**, *25*, 4613. (d) Confalone, P. N.; Earl, R. A. *Tetrahedron Lett.* **1986**, *27*, 2695. (e) Garner, P.; Ho, W. B.; Shin, H. *J. Am. Chem. Soc.* **1992**, *114*, 2767 and earlier references cited therein. (f) Pearson, W. H. In *Studies in Natural Products Chemistry*; Atta-ur-Rahman, Ed.; Elsevier: New York, Vol. 1, pp 323–358.

0022-3263/92/1957-6527$03.00/0