siloxane formed as a byproduct, the residual oil was dried under reduced pressure to give **3y** (1.12 g, 97%) (a mixture of two isomers; 36:64): ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.37 (d, J = 7.3 H, 3 H, CH_3(major); average ^3J (^{117,119}Sn, ^{1}H) = 220.7 Hz), 1.43 (d, J = 7.3 Hz, 3 H, CH_3(minor); average ^3J (^{117,119}Sn, ^{1}H) = 219.6 Hz), 1.56-1.90 (m, 3 H), 1.95-2.13 (m, 1 H), 2.20-2.61 (m, 4 H), 2.67-2.78 (m, 1 H, C*H*CH_3(minor)), 2.77-2.90 (m, 1 H), 3.03-3.20 (m, 1 H, C*H*CH_3(major); average ^2J (^{117,119}Sn, ^{1}H) = 254.2 Hz). Anal. Calcd for $C_8H_{13}OSnCl_3$: C, 27.43; H, 3.74. Found: C, 27.16; H, 3.65. To the solution of **3y** in $CDCl_3$ was added 1 equiv of pyridine at 20 °C. ^{1}H NMR analysis of the reaction mixture showed almost exclusive formation of (*E*)-ethylidenecylohexanone (>98%). We estimated the *E*/*Z* ratio of product to be 98/2 by integration of the vinyl protons; the chemical shift of *E* form is 6.92 and that of *Z* form is 5.49.

Acknowledgment. Support of this work by a Grant-in-Aid from the Ministry of Education, Science and Culture of Japan is gratefully acknowledged. Thanks are given to the Instrumental Analysis Center, Faculty of Engineering, Osaka University for assistance in obtaining MS, HRMS, 600-MHz NMR, and elemental analyses. We thank Shin-Etsu Chem. Co. Ltd. for a gift of trimethylchlorosilane.

Registry No. **1a**, 137518-38-8; **1b**, 137518-39-9; **1c**, 42161-97-7; **1d**, 101653-02-5; **1e**, 38858-75-2; **1f**, 38858-73-0; **1g**, 54781-38-3; **1h**, 137518-40-2; **1i**, 56011-29-1; **1j**, 38858-74-1; **1k**, 127375-76-2; **1l**, 99957-05-8; (*E*)-**1m**, 50629-63-5; (*Z*)-**1m**, 50629-49-7; **1n**, 50338-50-6; **1o**, 38858-76-3; **1p**, 50338-48-2; **1q**, 50338-49-3; **1r**, 59454-27-2; **1s**, 137518-41-3; **1t**, 137518-42-4; **1u**, 137518-43-5; **1v**, 101653-03-6; **1w**, 137518-44-6; **3a** (CC entry), 137518-67-3; **3a** (stannane entry), 137518-48-0; **3a'** (CC entry), 137518-68-4; **3a'** (stannane entry), 137518-49-1; **3b** (CC entry), 137518-69-5; **3b** (stannane entry), 137518-50-4; **3b'** (CC entry), 137518-70-8; **3b'** (stannane entry), 137518-51-5; **3c** (CC entry), 137518-71-9; **3c** (stannane entry), 137518-52-6; **3d** (CC entry), 101653-12-7; **3d** (stannane entry), 101653-05-8; **3d'** (CC entry), 137518-72-0; **3d'** (stannane entry), 137518-53-7; **3e** (CC entry), 101653-11-6; **3e** (stannane entry), 101653-04-7; **3e'** (CC entry), 137518-73-1; **3e'** (stannane entry), 137518-54-8; **3e''** (CC entry), 137518-85-5; **3e''** (stannane entry), 137518-47-9; **3e'''**, 97782-58-6; **3f** (CC entry, 137518-74-2; **3f** (stannane entry), 137518-55-9; **3g** (CC entry), 101653-13-8; **3g** (stannane entry), 101653-06-9; **3h'** (CC entry), 137518-75-3; **3h'** (stannane entry), 137518-56-0; **3i** (CC entry), 101653-14-9; **3i** (stannane entry), 101653-07-0; **3j** (CC entry), 137518-76-4; **3j** (stannane entry), 137518-57-1; **3k** (CC entry), 137518-77-5; **3k** (stannane entry), 137518-58-2; **3l** (CC entry), 137518-78-6; **3l** (stannane entry), 137518-59-3; **3m** (CC entry), 101653-15-0; **3m** (stannane entry), 101653-08-1; **3n** (CC entry), 101653-16-1; **3n** (stannane entry), 101653-09-2; **3o** (CC entry), 137518-79-7; **3o** (stannane entry), 137518-60-6; **3p** (CC entry), 101653-17-2; **3p** (stannane entry), 101653-10-5; **3** (CC entry), 101653-18-3; **3q** (stannane entry), 101670-94-4; **3r** (CC entry), 137518-80-0; **3r** (stannane entry), 137518-61-7; **3s** (CC entry), 137518-81-1; **3s** (stannane entry), 137518-62-8; **3t** (CC entry), 137518-82-2; **3t** (stannane entry), 137518-63-9; **3u** (CC entry), 137518-83-3; **3u** (stannane entry), 137518-64-0; **3v** (CC entry), 101653-19-4; **3v** (stannane entry), 137518-65-1; **3w** (CC entry), 137518-84-4; **3w** (stannane entry), 137518-66-2; **3x** (CC entry), 123992-97-2; **3x** (stannane entry), 59586-09-3; **3y** (CC entry), 137518-86-6; **3y** (stannane entry), 137518-46-8; **4a**, 24415-26-7; **4b**, 21509-95-5; **4c**, 59819-62-4; **4d**, 1606-47-9; **4e**, 2177-30-2; **4f**, 768-03-6; **4g**, 62672-77-9; **4i**, 769-60-8; **4j**, 3045-98-5; **4k**, 137518-37-7; **4l**, 57089-67-5; **4m**, 42858-50-4; **4o**, 13203-73-1; **4p**, 3045-99-6; **4q**, 3045-71-4; **4r**, 3045-76-9; **4s**, 30457-88-6; **4t**, 4125-23-9; **4u**, 4417-80-5; **4v**, 22414-69-3; (*E*)-**4y**, 7417-55-2; **5**, 137518-34-4; **6**, 137518-35-5; **7**, 137518-36-6; **8**, 100539-22-8; **9**, 137518-45-7; **14**, 137540-36-4; $SnCl_4$, 7646-78-8; *n*-$BuSnCl_3$, 1118-46-3; $HSnCl_3$, 20265-43-4; $CH_3COCH{=}CH_2$, 78-94-4.

Supplementary Material Available: ^{1}H or ^{13}C NMR spectra of new compounds for which elemental analyses were not obtained (14 pages). Ordering information is given on any current masthead page.

Pinacol Homocoupling of (*S*)-2-[*N*-(Benzyloxycarbonyl)amino] Aldehydes by $[V_2Cl_3(THF)_6]_2[Zn_2Cl_6]$. Synthesis of C_2-Symmetric (1*S*,2*R*,3*R*,4*S*)-1,4-Diamino 2,3-Diols

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Six (*S*)-2-[*N*-(benzyloxycarbonyl)amino] aldehydes **3a-f** were homocoupled by $[V_2Cl_3(THF)_6]_2[Zn_2Cl_6]$ (**1**) to give C_2-symmetric (1*S*,2*R*,3*R*,4*S*)-1,4-bis[*N*-(benzyloxycarbonyl)amino] 2,3-diols **4a-f** in good yield. High-yield conversions of the diols to bisoxazolidinones (sodium hydride, tetrahydrofuran) and to the deprotected (1*S*,2*R*,3*R*,4*S*)-1,4-diamino 2,3-diol dihydrochloride salts (10% Pd/C, formic acid, HCl in ether) were performed.

Multidentate, chiral, C_2-symmetric ligands are well-known for their ability to impart asymmetry to transition and main-group elements.[1] Among such molecules, C_2-symmetric diols,[2] diamines,[3] and diphosphines[4] have found the most frequent applications, especially in the area of asymmetric catalysis. Many of these ligands have been derived from naturally occurring C_2-symmetric molecules which are available in optically pure form (e.g., tartaric acid).[1] However, the small number of such chiral pre-

(1) (a) For a review on C_2-symmetric molecules see: Whitesell, J. K. *Chem. Rev.* **1989**, *89*, 1581. (b) Several C_2-symmetric 1,4-diamino 2,3-diols have been previously prepared from tartaric acid via multistep procedures, see; Seebach, D.; Kalinowski, H.; Bastani, B.; Crass, G.; Daum, H.; Dorr, H.; DuPreez, N. P.; Ehrig, V.; Langer, W.; Nussler, C.; Oei, H.; Schmidt, M. *Helv. Chim. Acta* **1977**, *60*, 301.

(2) For recent applications of C_2-symmetric diol ligands in metal-mediated asymmetric synthesis see: (a) Johnson, R. A.; Sharpless, K. B. *Compr. Org. Synth.* **1990**, *7*, Chapter 3.2. (b) Mikami, K.; Terada, M.; Nakai, T. *J. Am. Chem. Soc.* **1989**, *111*, 1940. (c) Roush, W. R.; Hoong, L. K.; Palmer, M. A. J.; Straub, J. A.; Palkowitz, A. D. *J. Org. Chem.* **1990**, *55*, 4117 and references cited therein. (d) Schmidt, B.; Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 99 and references therein.

(3) For recent applications of C_2-symmetric diamine ligands in asymmetric synthesis see: (a) Corey, E. J.; Kim, S. S. *Tetrahedron Lett.* **1990**, *31*, 3715. (b) Zhang, W.; Loebach, J. L.; Wilson, S. R.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1990**, *112*, 2801. (c) Corey, E. J.; Yu, CM.; Kim, S. S. *Ibid* **1989**, *111*, 5495. (d) Corey, E. J.; Imwinkelried, R.; Pikul, s.; Xiang, Y. B. *Ibid.* **1989**, *111*, 5493. (e) Corey, E. J.; Jardin, P. S.; Virgil, S.; Yuen, P.-W.; Conell, R. D. *Ibid.* **1989**, *111*, 9243 and references cited therein. (f) Tomioka, K.; Makajima, M.; Iitaka, Y.; Koga, K. *Tetrahedron Lett.* **1988**, *29*, 573 and references cited therein.

(4) For recent applications of C_2-symmetric diphosphine ligands in metal-mediated asymmetric synthesis see: Burk, M. J.; Feaster, J. E.; Harlow, R. L. *Organometallics* **1990**, *9*, 2653 and references cited therein.

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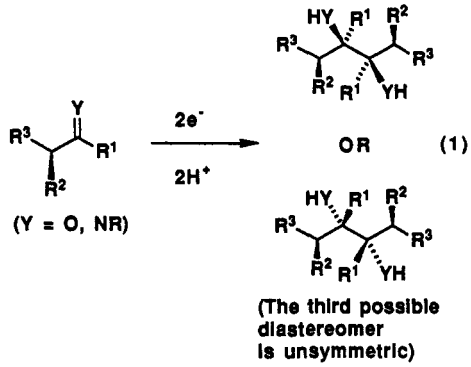
cursors is a serious limitation. Alternatively, many chiral, C_2-symmetric ligands have been obtained by resolution of racemic compounds, a step(s), that is not trivial in many instances. One potentially powerful approach to the synthesis of C_2-symmetric diols and diamines involves the stereoselective coupling of chiral, optically pure, carbonyls or imines, respectively (eq 1).[5]

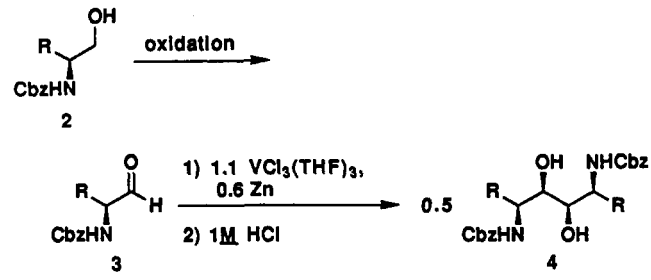


We have recently reported several stereoselective pinacol cross-coupling reactions using the readily available vanadium(II) reagent $[V_2Cl_3(THF)_6]_2[Zn_2Cl_6]$ (1).[6] The cross-coupling reactions require one aldehyde which is capable of forming a bidentate chelate with vanadium (a chelating aldehyde). The high stereoselectivity of the cross-coupling reactions led us to speculate that chelating aldehydes might also homocouple in a stereoselective fashion leading to C_2-symmetric diols.[7] Nonracemic, (S)-2-[N-(benzyloxycarbonyl)amino] aldehydes (N-Cbz-2-amino aldehydes) 3 were chosen for our initial homocoupling studies because both enantiomers are available in many instances and because these aldehydes undergo little or no racemization in cross-coupling reactions.[6c] The expected products from these reactions would be C_2-symmetric 1,4-diamino 2,3-diols.[1b] Not only would these constitute a potentially useful class of C_2-symmetric ligands,[1b] but they have also spurred interest as promising HIV protease inhibitors.[8] Herein, we report that several (S)-N-Cbz-2-amino aldehydes are homocoupled by 1 to give (1S,2R,3R,4S)-1,4-bis[N-(benzyloxycarbonyl)amino] 2,3-diols 4 with high diastereoselectivity and in good yield.[9]

Results

The N-Cbz-2-amino aldehydes 3 were prepared by oxidation the corresponding (S)-2-[N-(benzyloxycarbonyl)-amino] alcohols (N-Cbz-2-amino alcohols) 2 (Table I). The procedure of Luly and co-workers[10] (oxalyl chloride, dimethyl sulfoxide, triethylamine) was adapted to oxidize alcohols 2a–d to afford aldehydes 3a–d in 95–105% mass recovery (procedure A, Table I). As evidenced by TLC, the aldehydes prepared by this procedure were free of starting alcohol. The procedure of Hamada and coworkers[11] (pyridine sulfur trioxide, dimethyl sulfoxide, triethylamine) was used to oxidize alcohols 2e and 2f which contain functional groups that are often not stable to the former conditions. Aldehydes 3e and 3f were obtained in 40–50% mass recovery. Modification of the Hamada procedure by substitution of saturated aqueous sodium chloride for ice–water as the quenching solution (procedure B) improved mass recoveries to 90–100%, and is recommended. As evidenced by TLC, the aldehydes obtained by the modified Hamada procedure were contaminated by small quantities of the starting alcohols, despite the use of excess oxidant. Longer reaction times were found to not improve conversion of the alcohols and were subsequently avoided to minimize racemization of the product aldehydes. All the N-Cbz-2-amino aldehydes prepared by either procedure A or B were used in homocoupling reactions without further purification.

Table I. Preparation and Homocoupling of (S)-N-Cbz-2-amino Aldehydes



entry	R	oxidation procedure[a]	yield[b] (%)
a	*i*-Pr	A	89
b	*i*-Bu	A	61
c	CH_2Ph	A	76
d	$(CH_2)_4NHCbz$	A	75
e	$(CH_2)_2SCH_3$	B	67
f	CH_2-(3-indolyl)	B	41

[a] Procedure A: 1.5 $(COCl)_2$, 2.0 $(CH_3)_2SO$, 4.0 NEt_3, CH_2Cl_2, −63 °C. Procedure B: 3.0 SO_3·Py, 3.0 NEt_3, excess $(CH_3)_2SO$, saturated NaCl quench. [b] Isolated yield calculated from amino alcohol 2.

Pinacol homocoupling reactions of the N-Cbz-2-amino aldehydes were performed using the vanadium(II) reagent, $[V_2Cl_3(THF)_6]_2[Zn_2Cl_6]$ (1), prepared in situ via the reduction of $VCl_3(THF)_3$[12] by zinc powder in dichloromethane. Generation of this reagent is most rapid at high concentrations, and hence preparation of 1 was performed at approximately 0.6 M $VCl_3(THF)_3$ in dichloromethane. The aldehydes were dissolved in dichloromethane and added to a slight excess of 1, giving homogeneous brown solutions which were stirred for 3 h. Workup of the reactions with 10% sodium tartrate, which gives separable phases for pinacol cross-coupling reactions involving 3,[6c] gave problematic emulsions for the homocoupling reactions. However, changing to 1 M HCl gave easily separated aqueous and organic phases and is recommended. During the workup procedure, a few of the desired (1S,2R,3R,4S)-1,4-bis[N-(benzyloxycarbonyl)amino] 2,3-diols 4c,d,f precipitated from the dichloromethane layer requiring the addition of tetrahydrofuran to give separable

(5) (a) Touboul, E.; Dana, G. *Tetrahedron* **1975**, *31*, 1925. (b) Paquette, L. A.; Itoh, I.; Farnham, W. B. *J. Am. Chem. Soc.* **1975**, *97*, 7280. (c) Mundy, B. P.; Srinivasa, R.; Kim, Y.; Dolph, T. *J. Org. Chem.* **1982**, *47*, 1657. (d) Mundy, B. P.; Bruss, D. R.; Kim, Y.; Larsen, R. D.; Warnet, R. J. *Tetrahedron Lett.* **1985**, *26*, 3927. (e) Pradhan, S. K.; Thakker, K. R. *Ibid.* **1987**, *28*, 1813. (f) Pierrot, M.; Pons, J.-M.; Santelli, M. *Ibid.* **1988**, *29*, 5925.

(6) (a) Freudenberger, J. H.; Konradi, A. W.; Pedersen, S. F. *J. Am. Chem. Soc.* **1989**, *111*, 8014. (b) Takahara, P. M.; Freudenberger, J. H.; Konradi, A. W.; Pedersen, S. F. *Tetrahedron Lett.* **1989**, *30*, 7177. (c) Konradi, A. W.; Pedersen, S. F. *J. Org. Chem.* **1990**, *55*, 4506. (d) Park, J.; Pedersen, S. F. *Ibid.* **1990**, *55*, 5924. (e) Raw, A. S.; Pedersen, S. F. *Ibid.* **1991**, *56*, 830.

(7) Achiral 3-formylpropanamides are homocoupled in a stereoselective manner (15:1 threo–erythro). Freudenberger, J. H.; Pedersen, S. F. Unpublished results.

(8) Kempf, D. J.; Norbeck, D. W.; Codacovi, L. M.; Wang, X. C.; Kohlbrenner, W. E.; Wideburg, N. E.; Paul, D. A.; Knigge, M. F.; Vasavanonda, S.; Craig-Kennard, A.; Saldivar, A.; Rosenbrook, W., Jr.; Clement, J. J.; Plattner, J. J.; Erickson, J. *J. Med. Chem.* **1990**, *33*, 2687.

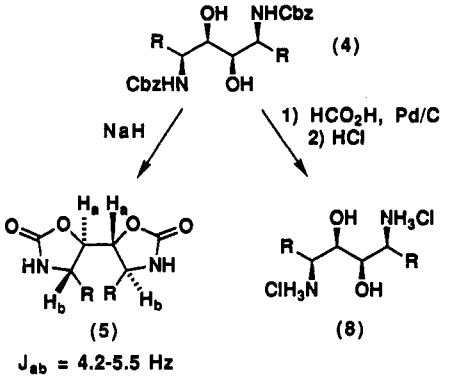
(9) Preliminary results of this chemistry were described at the 199th National Meeting of the American Chemical Society, Boston, MA, April 22–27, 1990; American Chemical Society: Washington, DC, 1990; ORGN 409.

(10) Luly, J. R.; Dellaria, J. J.; Soderquist, J. L.; Yi, Nwe *J. Org. Chem.* **1987**, *52*, 1487.

(11) Hamada, Y.; Shioiri, T. *Chem. Pharm. Bull.* **1982**, *30*, 1921.

(12) Manzer, L. E. *Inorg. Synth.* **1982**, *21*, 135.

Scheme I



homogeneous phases. Following separation, washing, and drying of the organic layers, evaporation of the volatiles gave crude diols 4 in 80–100% mass recoveries, calculated from the corresponding *N*-Cbz-2-amino alcohols.

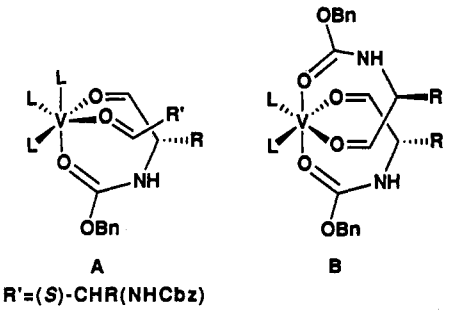
$^{13}C\{^1H\}$ NMR spectra of the crude diols 4 in $(CD_3)_2SO$ were recorded at 98 °C. At this temperature, interconversion of the cis and trans rotamers of the *N*-Cbz groups is rapid, giving NMR spectra not complicated by hindered rotation. The high-temperature NMR spectra revealed that all of the homocoupling reactions gave mainly one C_2-symmetric diol. Two crude products **4a,d** were contaminated by traces (<5%) of the corresponding starting aldehydes **3a,d**. In two other cases, the crude products **4e,f** contained significant amounts (10–20%) of the corresponding *N*-Cbz-2-amino alcohol **2e,f**. The latter result is consistent with the fact that unreacted starting alcohol was detected by TLC (vide supra) of the aldehydes **3e,f** prepared by procedure B. Two crude products **4c,f** show small quantities (ca. 10%) of unidentified compounds, possibly diastereomers of the principal C_2-symmetric diols. Production of diastereomers may arise from either imperfect stereoselectivity during the coupling reaction or the coupling of *N*-Cbz-2-amino aldehydes that were partially racemized during preparation. Five of the diols **4b–f** are solids, permitting purification by recrystallization to give good yields of analytically pure material. Product **4a** is an oil, and thus was purified by chromatography.

Confirmation of the relative stereochemistry in the C_2-symmetric products was accomplished as illustrated in Scheme I. Aliquots of the purified diols 4 were treated with 2.0 equiv of sodium hydride in tetrahydrofuran, giving after an aqueous quench mixtures of the corresponding bisoxazolidinones 5 and benzyl alcohol in 95–100% mass recovery (Scheme I). ^1H NMR spectra of the crude products revealed the central methyne protons (H_a) of the bisoxazolidinones to be doublets with coupling constants (J_{ab}) in the range of 4.2–5.5 Hz (Scheme I). The magnitudes of J_{ab} are consistent with trans-substituted oxazolidinones.[13] Hence, the all-syn stereochemistry of the diols was established. Two bisoxazolidinones **5a,e** were purified in good yield by recrystallization.

We hypothesized that the optical purity of the six purified diols **4a–f** could be determined by analysis of the NMR spectra of the corresponding C_2-symmetric Mosher diesters. However, reactions of **4a–f** with excess Mosher chloride in the presence of 4-(dimethylamino)pyridine (DMAP) and triethylamine gave the corresponding Mosher monoesters, and only traces of the Mosher diesters, even after prolonged reaction times. Given the risk of preferential diesterification of one of the enantiomers of **4a–f** under these conditions, we did not assess the optical purity

(13) Rich, D. H.; Sun, E. T. O. *J. Med. Chem.* **1980**, *23*, 27.

Scheme II



of **4a–f** from the NMR spectra of the Mosher monoesters. Furthermore, the presence of two Cbz groups in each of the Mosher monoesters requires the recording of ^1H and ^{19}F NMR spectra at high temperature to prevent complication of the NMR spectra by hindered rotation. Thus, we turned our attention to preparing the C_2-symmetric Mosher diimides **6** and **7** via acylation of both NH functions of the bisoxazolidinones **5a–f** with Mosher chloride. Reactions of crude samples of **5a–f** (contaminated by 2 equiv of benzyl alcohol, a byproduct from reaction of **4a–f** with NaH) with excess (*S*)-Mosher chloride in the presence of DMAP and triethylamine cleanly gave the corresponding (*R*)-Mosher diimides **6a–f** and the Mosher ester of benzyl alcohol. The analogous (*S*)-Mosher diimides **7a–f** were prepared using (*R*)-Mosher chloride under identical conditions. The ^{19}F NMR resonances of the (*R*)- and (*S*)-Mosher diimides overlap for each pair of diastereomers, making ^{19}F NMR spectroscopy unsuitable for determination of optical purity in this instance. However, the ^1H NMR spectra of the Mosher diimide diastereomers have resonances that are well separated and show that each Mosher diimide diastereomer is not contaminated by its counterpart. Thus, the optical purity of the crude bisoxazolidinones **5a–f**, obtained by reaction of the purified diols **4a–f** with NaH, has been conclusively demonstrated.

Catalytic transfer hydrogenolysis of the *N*-Cbz groups of two diols **4b,c** was explored as a means of generating the unprotected (1*S*,2*R*,3*R*,4*S*)-1,4-diamino 2,3-diols (Scheme I). Either ammonium formate or formic acid, in the presence of catalytic amounts of 10% palladium on carbon in methanol, rapidly cleaved the *N*-Cbz groups, giving the (1*S*,2*R*,3*R*,4*S*)-1,4-diamino 2,3-diol dihydroformate salts. The use of formic acid instead of ammonium formate was found to be superior, because treatment of the filtered reaction mixtures with dry HCl in diethyl ether then gave solutions of the (1*S*,2*R*,3*R*,4*S*)-1,4-diamino 2,3-diol dihydrochlorides **8b,c** free of ammonium chloride. Addition of diethyl ether to solutions prepared in this manner precipitated the desired dihydrochloride salts **8b,c** in 94–97% yields.

Discussion

Stereoselective pinacol coupling of aldehydes requires efficient selection of the faces of the two reacting carbonyl groups. The high diastereofacial selectivity of homocoupling of *N*-Cbz-2-amino aldehydes by 1 may be established by the reaction of the aldehydes in either of two possible modes of coordination on vanadium. As we have proposed for cross-coupling of *N*-Cbz-2-amino aldehydes, homocoupling may involve one chelating aldehyde and one nonchelating aldehyde (Scheme II, structure A). In this model, diastereofacial selection results from coordination of the nonchelating aldehyde on the less-hindered side of the chelating aldehyde and orientation of the side chain (R′) of the nonchelating aldehyde away from the chelate ring. Based on this model, the stereochemical directing

properties of the chelating aldehyde will dictate the outcome of this reaction, regardless of conformational considerations associated with the nonchelating aldehyde. Another possibility is that homocoupling may involve two chelating aldehydes (Scheme II, structure B). In this model, diastereofacial selection is set by approach of the less hindered faces of two chelates. It must be stressed that neither the ligands on vanadium nor the extent of aldehyde reduction has been established for any intermediates involved in couplings of aldehydes by solutions of 1. Either monomeric or dimeric vanadium complexes may be involved, as may either ketyl radicals or genuine organometallic species. Work aimed at addressing these points is currently in progress in our laboratories.

In summary, a readily available vanadium(II) reagent (1) is capable of promoting the stereoselective homocoupling of nonracemic *N*-Cbz-2-amino aldehydes leading to C_2-symmetric, 1,4-diamino 2,3-diols. Conversion of these materials into bisoxazolidinones or dihydrochloride salts is easily accomplished in high yields. The diols obtained from these coupling reactions have considerable potential as C_2-symmetric ligands. Furthermore, one can envision using this methodology for the synthesis of enantiomerically pure, chiral frameworks for applications in organic synthesis.

Experimental Section

General. Melting points are uncorrected. ^{1}H NMR spectra were recorded at 400 MHz. ^{1}H NMR chemical shifts are reported in ppm relative to the solvent resonance: $(CD_3)_2SO$, δ 2.49; CD_3CN, δ 1.93; CD_3OD, δ 3.30. ^{1}H NMR coupling constants are reported in Hz. $^{13}C\{^1H\}$ NMR spectra were recorded at 100 MHz. $^{13}C\{^1H\}$ NMR chemical shifts are reported in ppm relative to the solvent resonance: $(CD_3)_2SO$, δ 39.5; CD_3CN, δ 1.30; CD_3OD, δ 49.0. Fast atom bombardment mass spectra (FABMS) were performed using either glycerol (G), thioglycerol/glycerol (TG/G) or 3-nitrobenzyl alcohol (NBA) as matrix.

2-Amino alcohols were purchased from commercial sources and used as received. The *N*-Cbz-2-amino alcohols were prepared by standard methods (K_2CO_3, H_2O, Cbz-chloride).[14]

(*S*)-2-[*N*-(Benzyloxycarbonyl)amino] Aldehydes 3a–d. Procedure A. Adapted from the procedure of Luly et al.[10] To a stirred solution of 1.31 mL (15.0 mmol) of oxalyl chloride in 30 mL of CH_2Cl_2 at −63 °C (dry ice/$CHCl_3$) was added a solution of 1.42 mL (20.0 mmol) of DMSO in 30 mL of CH_2Cl_2 over 10 min. Immediately following, a solution of 10.0 mmol (*S*)-2-[*N*-(benzyloxycarbonyl)amino] alcohol **2a–d** in 40 mL of CH_2Cl_2 was added over 10 min, resulting in a cloudy solution which was stirred for 20 min. Then, 5.58 mL (40.0 mmol) of triethylamine was added over 5 min, generating first a clear solution and then a precipitate after stirring for 20 min at −63 °C. At this point, TLC of the reaction showed no starting material. Following removal of the cooling bath, 40 mL of 20% saturated $KHSO_4$ and 115 mL of hexanes were added, and the resulting mixture was stirred vigorously while warming, generating two phases. The layers were separated, and the aqueous phase was extracted with 115 mL of Et_2O. The combined organic layers were washed with saturated $NaHCO_3$ (40 mL × 2), H_2O (40 mL × 3), and saturated NaCl (40 mL × 2), and then dried over $MgSO_4$, filtered, and evaporated in vacuo at or below room temperature, giving a white solid or a clear oil. After the residual solvent was removed by drying in vacuo (0.5 Torr for 15 min), the desired aldehyde was obtained in 95–105% mass recovery and was used immediately without purification. ^{1}H NMR spectra of the crude aldehydes are consistent with the formulated structures.

(*S*)-2-[*N*-(Benzyloxycarbonyl)amino] Aldehydes 3e–f. Procedure B. Adapted from the procedure of Hamada et al.[11] To a stirred solution of 10.0 mmol of (*S*)-2-[*N*-(benzyloxycarbonyl)amino] alcohol **2e,f** and 4.18 mL (30.0 mmol) of triethylamine in 30 mL of anhydrous DMSO was added a solution of 4.77 g (30 mmol) of sulfur trioxide pyridine complex in 30 mL of anhydrous DMSO over 7 min. The reaction vessel was maintained at 20 °C by immersion in a water bath. Following stirring for 1 h, the reaction solution was poured into 325 mL of saturated NaCl precooled to 0 °C, and the mixture was extracted with Et_2O (160 mL × 3). The combined organic layers were washed with 5% citric acid (110 mL), H_2O (110 mL × 2), saturated $NaHCO_3$ (110 mL), and saturated NaCl (110 mL), and then dried over $MgSO_4$, filtered, and evaporated in vacuo at or below room temperature, giving a clear oil. After being dried in vacuo (0.5 Torr for 15 min) to remove residual solvent, the desired aldehyde **3e,f** was obtained in 90–100% mass recovery and was used immeditely without purification. ^{1}H NMR spectra of the crude aldehydes were consistent with the formulated structures. TLC of the products obtained by this procedure typically showed some starting alcohol.

(1*S*,2*R*,3*R*,4*S*)-1,4-Bis[*N*-(benzyloxycarbonyl)amino] 2,3-Diols 4a–f. Under N_2, 392 mg (6.0 mmol) of Zn powder was added to a solution of 4.11 g (11.0 mmol) of $VCl_3(THF)_3$[12] in 25 mL of CH_2Cl_2, causing after stirring for 20 min a color change from red to green. A solution of 10.0 mmol of (*S*)-2-[*N*-(benzyloxycarbonyl)amino] aldehyde **3a–f** in 25 mL of CH_2Cl_2 was added, causing a color change from green to brown. After being stirred for 3 h, the reaction solution was opened to air and poured into 50 mL of 1 M HCl. The two phases were stirred together for 12 h giving a nearly colorless CH_2Cl_2 layer and a blue aqueous layer. In three instances (**4c,d,f**) the coupling product precipitated from the CH_2Cl_2 layer, requiring the addition of CH_2Cl_2 and THF to dissolve all solids. The organic and aqueous layers were separated and the aqueous layer was extracted with 50 mL of CH_2Cl_2. The combined organic layers were washed with 10 mL of saturated $NaHCO_3$ and 10 mL of saturated NaCl, and then dried with $MgSO_4$, filtered, and evaporated to give diamino diols **4a–f** in 80–100% mass recovery, calculated from the amino alcohols **2a–f**. A 150-mg aliquot of the crude product was saved for analysis by high-temperature NMR spectroscopy, and the remainder was purified by recrystallization or chromatography. The yield of each purified product is adjusted to reflect the portion of crude product saved for analysis by NMR spectroscopy.

(3*S*,4*R*,5*R*,6*S*)-3,6-Bis[*N*-(benzyloxycarbonyl)amino]-2,7-dimethyl-4,5-octanediol (4a). Extracted with CH_2Cl_2 and purified by flash chromatography on silica gel using a gradient of 30–50% (v/v) ethyl acetate in hexanes to give 2.10 g (89%) of a colorless foam: ^{1}H NMR ($(CD_3)_2SO$, 98 °C) δ 7.35–7.26 (m, 5 H), 6.00 (bs, 1 H), 5.07 (d, J = 12.8, 1 H), 5.01 (d, J = 12.8, 1 H), 3.62 (bs, 1 H), 3.47 (s, 1 H), 3.44 (d, J = 9.5, 1 H), 1.82–1.75 (m, 1 H), 0.84 (d, J = 6.8, 3 H), 0.81 (d, J = 6.7, 3 H); ^{13}C NMR ($(CD_3)_2SO$, 22 °C) δ 156.2, 137.5, 128.3, 127.6, 127.4, 70.3, 65.0, 56.8, 29.5, 19.7, 19.3; FABMS (NBA) m/z 495 ([M + Na]$^+$, 100), 473 (MH$^+$, 40), 429 (37), 339 (78), 321 (11); $[\alpha]^{20}_D$ −20.5° (c 0.0160, MeOH). Anal. Calcd for $C_{26}H_{36}N_2O_6$: C, 66.08; H, 7.68; N, 5.93. Found: C, 66.04; H, 7.75; N, 5.93.

(4*S*,5*R*,6*R*,7*S*)-4,7-Bis[*N*-(benzyloxycarbonyl)amino]-2,9-dimethyl-5,6-decanediol (4b). Extracted with CH_2Cl_2 and recrystallized from ethyl acetate and hexanes to give in two crops 1.53 g (61%) of a white solid: mp 134–135 °C; ^{1}H NMR ($(CD_3)_2SO$, 98 °C) δ 7.34–7.26 (m, 5 H), 6.06 (bs, 1 H), 5.08 (d, J = 12.7, 1 H), 4.99 (d, J = 12.7, 1 H), 3.87–3.82 (m, 1 H), 3.62 (bs, 1 H), 3.29 (s, 1 H), 1.61–1.53 (m, 1 H), 1.43 (ddd, J = 5.6, 9.0, 13.8, 1 H), 1.24 (ddd, J = 5.1, 8.0, 13.3, 1 H), 0.853 (d, J = 6.6, 3 H), 0.850 (d, J = 6.5, 3 H); ^{13}C NMR ($(CD_3)_2SO$, 22 °C) δ 156.0, 137.6, 128.3, 127.6, 127.4, 72.9, 65.0, 49.6, 41.5, 24.2, 23.3, 21.9; FABMS (NBA) m/z 523 ([M + Na]$^+$, 22), 501 (MH$^+$, 79), 457 (100), 367 (82), 349 (22); $[\alpha]^{20}_D$ −2.4° (c 0.0116, MeOH). Anal. Calcd for $C_{28}H_{40}N_2O_6$: C, 67.18; H, 8.05; N, 5.60. Found: C, 67.32; H, 8.08; N, 5.51.

(2*S*,3*R*,4*R*,5*S*)-2,5-Bis[*N*-(benzyloxycarbonyl)amino]-1,6-diphenyl-3,4-hexanediol (4c). Precipitated during workup, extracted with CH_2Cl_2 and THF, and recrystallized from THF and hexanes to give in two crops 2.16 g (76%) of a white solid: mp 219.5–220 °C; ^{1}H NMR ($(CD_3)_2SO$, 98 °C) δ 7.32–7.11 (m, 10 H), 6.18 (bs, 1 H), 4.95 (d, J = 12.8, 1 H), 4.90 (d, J = 12.8, 1 H), 4.20 (bs, 1 H), 4.10 (q, J = 7.8, 1 H), 3.40 (s, 1 H), 2.91 (bs, 1 H), 2.75 (d, J = 6.3, 2 H); ^{13}C NMR ($(CD_3)_2SO$, 22 °C) δ 155.8, 139.3, 137.5, 129.2, 128.2, 127.8, 127.5, 127.2, 125.7, 72.7, 64.8, 52.9, 38.3; FABMS (NBA) m/z 569 (MH$^+$, 73), 525 (58), 435 (33), 307 (51), 289 (100), 277 (53); $[\alpha]^{20}_D$ −12.8° (c 0.0137, THF). Anal. Calcd

(14) Bergmann, M.; Zervas, L. *Ber.* **1932**, *65*, 1192.

for $C_{34}H_{36}N_2O_6$: C, 71.81; H, 6.38; N, 4.93. Found: C, 71.93; H, 6.51; N, 4.72.

(5*S*,6*R*,7*R*,8*S*)-1,5,8,12-Tetrakis[*N*-(benzyloxycarbonyl)amino]-6,7-dodecanediol (4d). Precipitated during workup, extracted with CH_2Cl_2 and THF, and recrystallized from ethyl acetate and hexanes to give in one crop 3.32 g (83%) of a white solid: mp 145–146.5 °C; ^{1}H NMR ($(CD_3)_2SO$, 98 °C) δ 7.33–7.27 (m, 10 H), 6.62 (bs, 1 H), 6.10 (bs, 1 H), 5.06 (d, *J* = 12.8, 1 H), 5.03 (s, 2 H) 5.02 (d, *J* = 12.8, 1 H), 4.04 (bs, 1 H), 3.74–3.70 (m, 1 H), 3.33 (bs, 1 H), 3.01 (d, *J* = 7.0, 1 H), 2.98 (d, *J* = 7.0, 1 H), 2.91 (bs, 1 H), 1.49–1.39 (m, 4 H), 1.31–1.23 (m, 2 H); ^{13}C NMR ($(CD_3)_2SO$, 22 °C) δ 156.13, 156.06, 137.5, 137.3, 128.33, 128.27, 127.7, 127.6, 127.5, 72.3, 65.1, 65.0, 51.6, 40.3, 31.6, 29.3, 22.9; FABMS (TG/G) *m/z* 821 ([M + Na]$^+$, 9), 799 (MH$^+$, 22), 755 (40), 665 (100), 647 (16); $[\alpha]^{20}_D$ −4.8° (*c* 0.0128, THF). Anal. Calcd for $C_{44}H_{54}N_4O_{10}$: C, 66.15; H, 6.81; N, 7.01. Found: C, 66.47; H, 6.80; N, 6.76.

(3*S*,4*R*,5*R*,6*S*)-3,6-Bis[*N*-(benzyloxycarbonyl)amino]-1,8-bis(methylthio)-4,5-octanediol (4e). Extracted with CH_2Cl_2 and recrystallized from ethyl acetate and hexanes to give in one crop 2.04 g (76%) of a white solid: mp 136–137 °C; ^{1}H NMR ($(CD_3)_2SO$, 98 °C) δ 7.35–7.28 (m, 5 H), 6.28 (bd, *J* = 6.5, 1 H), 5.07 (d, *J* = 12.7, 1 H), 5.02 (d, *J* = 12.7, 1 H), 4.17 (bs, 1 H), (q, *J* = 7.4, 1 H), 3.38 (s, 1 H), 2.92 (bs, 1 H), 2.46–2.35 (m, 2 H), 2.01 (s, 3 H), 1.77 (d, *J* = 7.0, 1 H), 1.73 (d, *J* = 7.6, 1 H); ^{13}C NMR ($(CD_3)_2SO$, 22 °C) δ 156.2, 137.4, 128.3, 127.7, 127.5, 71.7, 65.1, 51.6, 31.6, 30.1, 14.7; FABMS (NBA) *m/z* 559 ([M + Na]$^+$, 93), 537 (MH$^+$, 100); $[\alpha]^{20}_D$ +1.4° (*c* 0.0130, THF). Anal. Calcd for $C_{26}H_{36}N_2O_6S_2$: C, 58.18; H, 6.76; N, 5.22. Found: C, 58.41; H, 6.72; N, 5.06.

(2*S*,3*R*,4*R*,5*S*)-2,5-Bis[*N*-(benzyloxycarbonyl)amino]-1,6-di(3-indolyl)-3,4-hexanediol (4f). Precipitated during workup, extracted with CH_2Cl_2 and THF, and recrystallized from ethyl acetate and hexanes to give in two crops 1.32 g (41%) of a white solid: mp 201–203 °C; ^{1}H NMR ($(CD_3)_2SO$, 98 °C) δ 9.45 (s, 1 H), 7.54 (d, *J* = 7.8, 1 H), 7.31–7.19 (m, 6 H), 7.04–7.00 (m, 2 H), 6.91 (t, *J* = 7.1, 1 H), 6.11 (bs, 1 H), 4.88 (d, *J* = 12.8, 1 H), 4.84 (d, *J* = 12.8, 1 H), 4.13–4.05 (m, 1 H), 3.56 (s, 1 H), 3.31 (bs, 2 H), 2.91 (dd, *J* = 14.6, 6.3, 1 H), 2.85 (dd, *J* = 14.6, 8.0, 1 H); ^{13}C NMR ($(CD_3)_2SO$, 22 °C) δ 155.9, 137.4, 136.1, 128.2, 127.7, 127.5, 127.3, 123.1, 120.6, 118.7, 118.0, 111.6, 111.0, 72.6, 64.8, 52.4, 27.9; FABMS (TG/G) *m/z* 559 ([M + Na]$^+$, 10), 647 (MH$^+$, 19), 603 (53), 513 (47); $[\alpha]^{20}_D$ −17.7° (*c* 0.0149, THF). Anal. Calcd for $C_{38}H_{38}N_4O_6$: C, 70.57; H, 5.92; N, 8.66. Found: C, 70.43; H, 5.88; N, 8.45.

Bisoxazolidinones 5a–f. To a stirred solution of 0.60 mmol of (1*S*,2*R*,3*R*,4*S*)-1,4-bis[*N*-(benzyloxycarbonyl)amino] 2,3-diol **4a–f** in 7 mL of THF was added 48 mg (1.20 mmol) of NaH (60% dispersion in mineral oil), causing immediate evolution of gas. After being stirred for 12 h, the solution was treated with 7 mL of saturated NH_4Cl, giving two phases and a precipitate after 5 min of stirring. The THF layer was separated, and the aqueous layer was sequentially extracted with 10 mL of THF and 10 mL of CH_2Cl_2. The combined organic phases were washed with 5 mL of saturated NaCl, dried with $MgSO_4$, filtered, and evaporated to give a mixture of the bisoxazolidinone **5a–f** and benzyl alcohol in 95–100% mass recovery. A 10-mg aliquot of the crude product was saved for analysis by ^{1}H NMR spectroscopy. Two bisoxazolidinones **5a,e** were purified by recrystallization.

(3*S*,4*R*,5*R*,6*S*)-3,4:5,6-Di-*N*,*O*-carbonyl-3,6-diamino-2,7-dimethyl-4,5-octanediol (5a). Recrystallized from ethyl acetate to give in one crop 124 mg (81%) of colorless prisms: mp 258–259 °C; ^{1}H NMR (CD_3CN, 22 °C) δ 6.13 (bs, 1 H), 4.27 (d, *J* = 4.1, 1 H), 3.52 (t, *J* = 4.3, 1 H), 1.74 (octet, *J* = 6.2, 1 H), 0.89 (d, *J* = 6.8, 6 H); ^{13}C NMR (CD_3CN, 22 °C) δ 158.8, 80.0, 59.9, 33.1, 17.8, 17.2; FABMS (NBA) *m/z* 257 (MH$^+$, 73); $[\alpha]^{20}_D$ −145.8° (*c* 0.0055, THF). Anal. Calcd for $C_{12}H_{20}N_2O_4$: C, 56.23; H, 7.86; N, 10.93. Found: C, 56.43; H, 7.67; N, 10.73.

(3*S*,4*R*,5*R*,6*S*)-3,4:5,6-Di-*N*,*O*-carbonyl-3,6-diamino-1,8-bis(methylthio)-4,5-octanediol (5e). Recrystallized from ethyl acetate and hexanes to give in one crop 159 mg (83%) of colorless prisms: mp 117 °C; ^{1}H NMR (CD_3CN, 22 °C) δ 6.22 (bs, 1 H), 4.34 (d, *J* = 4.7, 1 H), 3.84 (q, *J* = 5.2, 1 H), 2.59–2.46 (m, 2 H), 2.07 (s, 3 H), 1.90–1.80 (m, 2 H); ^{13}C NMR (CD_3CN, 22 °C) δ 158.5, 80.9, 53.7, 35.2, 30.0, 15.2; FABMS (NBA) *m/z* 321 (MH$^+$, 45); $[\alpha]^{20}_D$ −157.7° (*c* 0.0111, THF). Anal. Calcd for $C_{12}H_{20}N_2O_4S_2$: C, 44.98; H, 6.29; N, 8.74. Found: C, 45.17; H, 6.13; N, 8.67.

***N*,*N*′-Bis[(*R*)-methoxy(trifluoromethyl)phenylacetyl] Bisoxazolidinones 6a–f.** To a mixture of 0.053 mmol of crude bisoxazolidinone **5a–f** (prepared from purified diols **4a–f**) and 0.11 mmol of benzyl alcohol (byproduct from the preparation of **5a–f**) were added 1.0 mL of dry CH_2Cl_2, 32 mg (0.26 mmol) of 4-(dimethylamino)pyridine, 74 μL (54 mg, 0.53 mmol) of triethylamine, and 49 μL (67 mg, 0.26 mmol) of (*S*)-methoxy(trifluoromethyl)phenylacetyl chloride, giving a yellow solution after brief stirring. The reaction solution was allowed to stand for 16 h, at which point 10 mL of Et_2O was added, giving a suspension which was washed with 5% citric acid (4 mL), saturated $NaHCO_3$ (4 mL), and saturated NaCl (4 mL). The resulting homogeneous organic layer was dried by passing through a plug of $MgSO_4$ in a pipette and the volatiles were evaporated giving a residue consisting of the *N*,*N*′-bis[(*R*)-methoxy(trifluoromethyl)phenylacetyl] bisoxazolidinone **6a–f** and benzyl (*R*)-methoxy(trifluoromethyl)phenylacetate. The residue was analyzed directy by ^{1}H NMR spectroscopy. The analogous *N*,*N*′-bis[(*S*)-methoxy(trifluoromethyl)phenylacetyl] bisoxazolidinone **7a–f** was prepared in the same manner using (*R*)-methoxy(trifluoromethyl)-phenylacetyl chloride. Copies of the ^{1}H NMR spectra are provided as supplementary material.

(1*S*,2*R*,3*R*,4*S*)-1,4-Diamino 2,3-Diol Dihydrochlorides 8b,c. To a suspension of 0.528 mmol of (1*S*,2*R*,3*R*,4*S*)-1,4-bis[*N*-(benzyloxycarbonyl)amino] 2,3-diol **4b,c** in 10 mL of MeOH were added 60 mg of 10% palladium on carbon and 199 μL (5.28 mmol) of 95% formic acid. After being stirred for 6 h, the mixture was filtered through Celite and rinsed with 5 mL of MeOH. To the filtrate were added 2.00 mL of a saturated solution of HCl gas in Et_2O and 3 mL of toluene. The resulting solution was evaporated in vacuo, giving a white solid. The product was redissolved in MeOH and precipitated by addition of Et_2O, giving a white solid which was isolated by filtration and dried under high vacuum.

(4*S*,5*R*,6*R*,7*S*)-4,7-Diamino-2,9-dimethyl-5,6-decanediol Dihydrochloride (8b). 151 mg (94%) of a white solid: mp 270 °C dec; ^{1}H NMR (CD_3OD, 22 °C) δ 3.88 (d, *J* = 2.0, 1 H), 3.45 (td, *J* = 6.9, 1.6, 1 H), 1.75 (sept, *J* = 6.5, 1 H), 1.58 (dd, *J* = 7.0, 14.3, 1 H), 1.51 (dd, *J* = 7.2, 14.3, 1 H), 1.00 (d, *J* = 6.5, 3 H), 0.99 (d, *J* = 6.5, 3 H); ^{13}C NMR (CD_3OD, 22 °C) δ 72.2, 54.0, 40.4, 25.2, 23.0, 22.4; FABMS (G) *m/z* 233 ([M − 2HCl]H$^+$, 100); $[\alpha]^{20}_D$ −11.8° (*c* 0.0140, MeOH).

(2*S*,3*R*,4*R*,5*S*)-2,5-Diamino-1,6-diphenyl-3,4-hexanediol Dihydrochloride (8c). 191 mg (97%) of a white solid: mp 245 °C dec; ^{1}H NMR (CD_3OD, 22 °C) δ 7.35–7.26 (m, 5 H), 3.80 (bs, 1 H), 3.64 (t, *J* = 7.1, 1 H), 3.00 (dd, *J* = 14.0, 7.7, 1 H), 2.92 (dd, *J* = 14.0, 7.2, 1 H); ^{13}C NMR (CD_3OD, 22 °C) δ 136.7, 130.5, 130.1, 128.5, 71.2, 57.0, 37.2; FABMS (TG/G) *m/z* 301 ([M − 2HCl]H$^+$, 100); $[\alpha]^{20}_D$ −3.6° (*c* 0.0113, MeOH).

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Supplementary Material Available: ^{1}H NMR spectra of crude Mosher diimides **6** and **7** (37 pages). Ordering information is given on any current masthead page.