Synthesis of Nitrogen-Containing Macrocycles with Reductive Intramolecular Coupling of Aromatic Diimines[1]

Naoki Kise,* Hideaki Oike, Eiichi Okazaki, Masami Yoshimoto, and Tatsuya Shono†

Division of Synthetic Chemistry and Biological Chemistry, Graduate School of Engineering, Kyoto University, Yoshida, Sakyo, Kyoto 606-01, Japan

Received January 31, 1995®

Reductive intramolecular coupling of aromatic diimines is an effective method for the synthesis of a variety of nitrogen-containing macrocycles. 1,4-Diazacrown ethers **3** were effectively synthesized by intramolecular coupling of bis(imino ethers) **9** promoted by electroreduction (method A) or chemical reduction with zinc powder (method B) in the presence of methanesulfonic acid. In spite of the formation of macrocycles, the yields of **3** were relatively high. This can be explained by the formation of proton-bridged intermediates **14**, in which intramolecular hydrogen bonds are formed between hydrogen and oxygen atoms of diiminium salts. Method B was more effective in the formation of 1,4-diaza-12-crown-4 derivatives **3** ($n = 1$) due to the template effect of Zn^{2+}. Optically active macrocyclic bislactones **4** were synthesized stereoselectively by reductive intramolecular coupling of bis(imino esters) **20** with zinc powder (method B). The high stereoselectivity is explained by considering proton-bridged intermediate **23**. The resultant compounds **4** were transformed to optically active 1,2-diarylethylenediamines **7**. Various sizes of macrocyclic bislactams **5** were synthesized by reductive intramolecular coupling of bis(imino amides) **26** with zinc powder (method B). Reduction of **5** gave the corresponding macrocyclic polyamines **6**.

Nitrogen-containing macrocycles, such as diazacrown ethers[2,3] and cyclams,[4] are compounds of growing interest due to their unique complexation properties relative to those of most crown ethers. The synthesis of these compounds has usually been achieved by acylation of diamines with diacid chlorides followed by reduction of the resultant diamides or by alkylation of diamines with dihalides, though both methods require conditions of high dilution and the yields are not always satisfactory.[5,6] Recently, we reported the stereoselective synthesis of piperazines **2** with electroreductive coupling of aromatic diimines **1** in the presence of methanesulfonic acid (MsOH) (eq 1).[7] In this paper, we report that intramolecular coupling of aromatic diimines is an effective method for the synthesis of a variety of nitrogen-containing macrocycles. We found that reduction with zinc powder can be employed instead of electroreduction. Various sizes of 1,4-diazacrown ethers **3**, macrocyclic bislactones **4**, and bislactams **5** were effectively synthesized by electroreduction or chemical reduction with zinc from bis(imino ethers), bis(imino esters), and bis(imino amides), respectively. Reduction of the bislactams **5** afforded the corresponding macrocyclic polyamines **6**. These nitrogen-containing macrocycles **3**–**6** are very attractive as new host molecules in host-guest chemistry, especially in transition metal coordination chemistry. These compounds are also interesting as starting materials for the synthesis of new types of cryptands and nitrogen-pivot lariat ethers.

(1)

Furthermore, we found that the reductive coupling of optically active bis(imino esters) proceeded stereoselectively, and the resultant compounds **4** were transformed to optically active 1,2-diarylethylenediamines **7**. Although derivatives of optically active 1,2-diphenylethylenediamine (**7a**) have been extensively used as chiral ligands for enantioselective syntheses,[8] optically active

† Present address: Reseach Institute for Science and Technology, Kinki University, Kowakae, Higashi-Osaka, 577, Japan.

® Abstract published in *Advance ACS Abstracts,* June 1, 1995.

(1) Preliminary reports: Shono, T.; Kise, N.; Okazaki, E. *Tetrahedron Lett.* **1992**, *33*, 3347. Shono, T.; Kise, N.; Oike, H.; Yoshimoto, M.; Okazaki, E. *Tetrahedron Lett.* **1992**, *33*, 5559.

(2) For reviews, see: (a) Izatt, R. M.; Bradshaw, J. S.; Nielsen, S. A.; Lamb, J. D.; Christensen, J. J.; Sen, D. *Chem. Rev.* **1985**, *85*, 271. (b) Sutherland, I. O. *Chem. Soc. Rev.* **1986**, *15*, 63. (c) Gokel, G. W. *Chem. Soc. Rev.* **1992**, *21*, 39.

(3) For recent reports of modified azacrown ethers, see: (a) Bradshaw, J. S.; Krakowiak, K. E.; An, H.; Izatt, R. M. *Tetrahedron* **1990**, *46*, 1163. (b) Zinic, M.; Frkanec, L.; Skaric, V.; Trafton, J.; Gokel, G. W. *J. Chem. Soc., Chem. Commun.* **1990**, 1726. (c) Tsukube, H.; Iwachido, T.; Shimotani, T.; Dando, T.; Zenki, M. *Bull. Chem. Soc. Jpn.* **1993**, *66*, 2440. (d) Muñoz, S.; Mallén, J.; Nakano, A.; Chen, Z.; Gay, I.; Echegoyen, L.; Gokel, G. W. *J. Am. Chem. Soc.* **1993**, *115*, 1705. (e) De Vries, E. F. J.; Steenwinkel, P.; Brussee, J.; Kruse, C. G.; Van der Gen, A. *J. Org. Chem.* **1993**, *58*, 4315. (f) Tsukube, H.; Uenishi, J.; Higaki, H.; Kikkawa, K.; Tanaka, T.; Wakabayashi, S.; Oae, S. *J. Org. Chem.* **1993**, *58*, 4389. Other references cited therein.

(4) For recent reports of modified cyclams, see: (a) Kinneary, J. F.; Wagler, T. R.; Burrows, C. J. *Tetrahedron Lett.* **1988**, *29*, 877. (b) Wagler, T. R.; Fang, Y.; Burrows, C. J. *J. Org. Chem.* **1989**, *54*, 1584. (c) Cox, J. P. L.; Craig, A. S.; Helps, I. M.; Jankowski, Parker, D.; Eaton, M. A. W.; Millican, A. T.; Millar, K.; Beeley, N. R. A.; Boyce, B. A. *J. Chem. Soc., Perkin Trans. 1* **1990**, 2567. (d) Krakowiak, K. E.; Bradshaw, J. S.; Izatt, R. M. *J. Org. Chem.* **1990**, *55*, 3364. (e) Kimura, E.; Koike, T.; Shiota, T.; Yoichi, I. *Inorg. Chem.* **1990**, *29*, 4621. (f) Bencini, A.; Burguete, M. I.; García-España, E.; Luis, S. V.; Miravet, J. F.; Soriano, C. *J. Org. Chem.* **1993**, *58*, 4749. Other references cited therein.

(5) For a review, see: Bradshaw, J. S.; Krakowiak, K. E.; Zamecka-Krakowiak, D. J. *Chem. Rev.* **1989**, *89*, 929.

(6) Bradshaw, J. S.; Krakowiak, K. E.; Izatt, R. M.; Zamecka-Krakowiak, D. J. *Tetrahedron Lett.* **1990**, *31*, 1077 and references cited herein.

(7) Shono, T.; Kise, N.; Shirakawa, E.; Matsumoto, H.; Okazaki, E. *J. Org. Chem.* **1991**, *56*, 3063.

(8) For recent reports, see: (a) Corey, E. J.; Imwinkelried, R.; Pikul, S.; Xiang, Y. B. *J. Am. Chem. Soc.* **1989**, *111*, 5493. (b) Corey, E. J.; Yu, C.-M.; Lee, D.-H. *J. Am. Chem. Soc.* **1990**, *112*, 878. (c) Corey, E. J.; Kim, S. S. *J. Am. Chem. Soc.* **1990**, *112*, 4976. (d) Corey, E. J.; Lee, D.-H. *J. Am. Chem. Soc.* **1991**, *113*, 4076. (e) Ahn, K. H.; Yoo, D. J.; Kim, J. S. *Tetrahedron Lett.* **1992**, *33*, 6661.

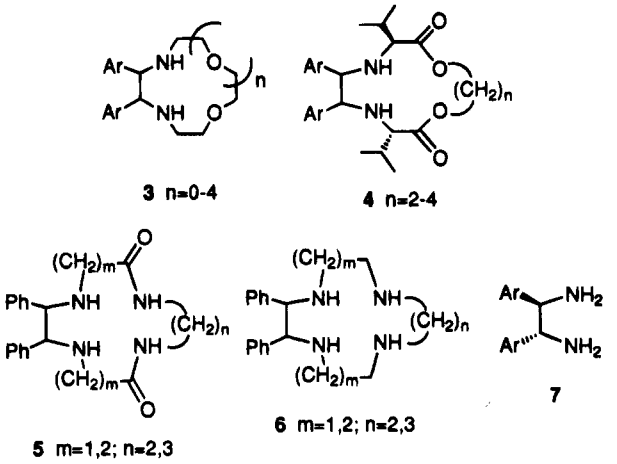
0022-3263/95/1960-3980$09.00/0

Table 1. Reductive Intramolecular Coupling of Aromatic Diimines 1 to Piperazines 2

run	1	Ar	R^1	R^2	R^3	method	2	% yield[a]
1	**1a**	C_5H_5	H	H	H	A	**2a**	95
2						B		95
3	**1b**	*o*-HOC_6H_4	H	H	H	A	**2b**	40
4						B		82
5	**1c**	*p*-$Me_2NC_6H_4$	H	H	H	A	**2c**	50
6						B		99
7	**1d**	C_6H_5	H	CO_2Me[b]	H	A	**2d**	0
8						B		60
9	**1e**	C_6H_5	H	-$(CH_2)_4$-[c]		A	**2e**	59
10						B		95
11	**1f**	C_6H_5	Me	H	H	A	**2f**	20
12						B		99

[a] Isolated yields. Each product was obtained as a single stereoisomer (racemic except for **2e**). [b] Prepared from racemic methyl 2,3-diaminopropionate. [c] Prepared from (1*R*,2*R*)-diaminocyclohexane.

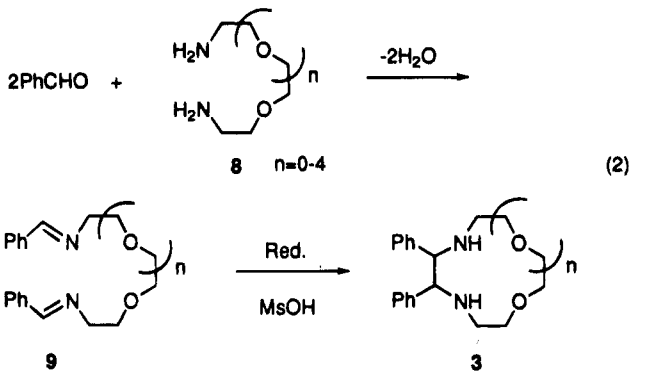
7a has been prepared by optical resolution of *dl*-**7a**[8a,9] or transformation from optically active 1,2-diphenylethane-1,2-diol.[10]



Results and Discussion

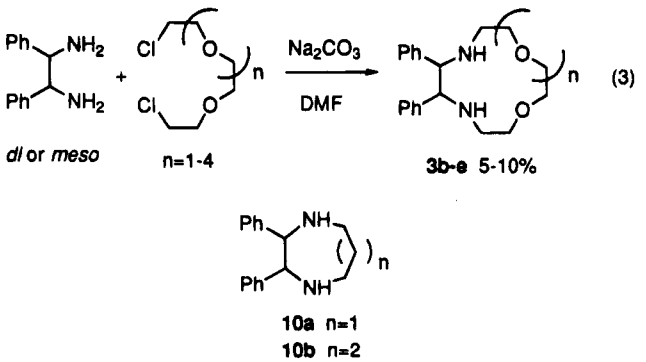
Reductive Coupling of Aromatic Diimines 1 with Zinc. We have reported that *trans*-2,3-diarylpiperazines were synthesized stereoselectively by electroreduction of aromatic diimines in the presence of MsOH (method A) (eq 1).[7] The same transformation was also achieved by chemical reduction with zinc powder (method B). A comparison of these methods is presented in Table 1. Method B gave better results in the reaction of substituted dialdimines **1b**–**e** (runs 3–10) and diketimine **1f** (runs 11 and 12) than method A. In particular, although the electroreduction of the diimine possessing an ester group (**1d**) resulted in the formation of a complex mixture (run 7), the reduction with zinc afforded trisubstituted piperazine **2d** stereospecifically (run 8).

Synthesis of 1,4-Diazacrown Ethers 3 by Reductive Intramolecular Coupling of Bis(imino ethers) 9. 1,4-Diazacrown ethers **3** were effectively synthesized by intramolecular coupling of bis(imino ethers) **9** promoted by electroreduction (method A) or chemical reduction with zinc powder (method B) (eq 2). Bis(imino ethers) **9a**–**e** (n = 0–4) were prepared quantitatively from benzaldehyde and the corresponding bis(amino ethers) **8** by refluxing in benzene for 1 h. The reductive coupling of **9** was carried out in the presence of MsOH. A variety of 1,4-diazacrown ethers **3a**–**e** were synthesized as shown in Table 2. The reaction conditions were surveyed using **9b** (runs 5–11), and it was found that the yields and stereoselectivities were affected by reaction temperature and solvent. Lowering the reaction temperature produced better results with method B. Using a less polar solvent was also more effective, as evidenced by the fact that mixed solvent DMF–THF (1:1) gave better results than DMF. The diiminium salt of **9b** and MsOH was, however, sparingly soluble in THF alone. The best result (90% yield) was obtained when the reduction of **9b** was carried out with method B at −50°C in DMF–THF (1:1) (run 11). Although both methods showed similar results in the synthesis of **3a**, **3d**, and **3e**, method B gave better yields and *trans* diastereoselectivities than did method A in the synthesis of **3b** and **3c**.



Other conditions for the reduction of **9b** were also investigated (Table 3). Other metals instead of Zn such as Mg (run 2), Sn, and Pb resulted in lower yields. The presence of a strong protic acid was essential to promote the intramolecular coupling. Trifluoroacetic acid (run 3) was as effective as MsOH, whereas acetic acid and Lewis acids such as $AlBr_3$ (run 4) and $BF_3{\cdot}Et_2O$ were less effective. The reduction with Mg–$TiCl_4$ (run 5) and SmI_2 (run 6) in THF gave poor results.

The stereoconfigurations of each isomer of **3b**–**e** were confirmed by their comparison with the authentic samples prepared from *dl*- or *meso*-1,2-diphenylethylenediamine (**7a**) by the usual alkylation (eq 3).[11] The product **3a** was obtained as a single stereoisomer and assigned to be *trans* by the correlation of its ^1H NMR spectrum with that of **10**.[7]



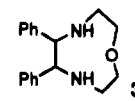
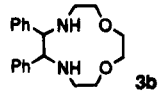
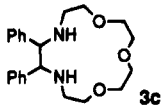
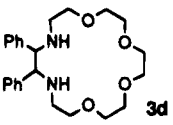
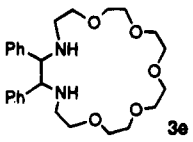
Method B was also found to be highly effective for the reductive coupling of bis(imino ethers) prepared from

(9) (a) Williams, O. F.; Bailar, J. C., Jr. *J. Am. Chem. Soc.* **1959**, *81*, 4464. (b) Saigo, K.; Kubota, N.; Takebayashi, S.; Hasegawa, M. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 931.

(10) (a) Pini, D.; Iuliano, A.; Rosini, C.; Salvadori, P. *Synthesis* **1990**, 1023. (b) Lohray, B. B.; Ahuja, J. R. *J. Chem. Soc., Chem. Commun.* **1991**, 95.

(11) Maeda, H.; Furuyoshi, S.; Nakatsuji, Y.; Okahara, M. *Bull. Chem. Soc. Jpn.* **1983**, *56*, 3073.

Table 2. Reductive Intramolecular Coupling of Bis(imino ethers) 9a–e to 1,4-Diazacrown Ethers 3a–e

run	9	method	temp.	solvent	3	% yield [a]	*trans*:*cis* [b]
1	9a	A	25°C	DMF	 3a	40	~100: 0
2		A	25°C	DMF-THF(1:1)		49	~100: 0
3		B	25°C	DMF		49	~100: 0
4		B	-50°C	DMF-THF(1:1)		43	~100: 0
5	9b	A	25°C	DMF	 3b	57	55:45
6		A	25°C	DMF-THF(1:1)		75	65:35
7		A	-20°C	DMF-THF(1:1)		68	60:40
8		B	25°C	DMF		78	80:20
9		B	-50°C	DMF		85	85:15
10		B	25°C	DMF-THF(1:1)		85	80:20
11		B	-50°C	DMF-THF(1:1)		90	90:10
12	9c	A	25°C	DMF	 3c	60	50:50
13		A	25°C	DMF-THF(1:1)		72	60:40
14		B	25°C	DMF		74	65:35
15		B	-50°C	DMF-THF(1:1)		85	75:25
16	9d	A	25°C	DMF	 3d	67	50:50
17		A	25°C	DMF-THF(1:1)		73	50:50
18		B	25°C	DMF		72	65:35
19		B	-50°C	DMF-THF(1:1)		77	65:35
20	9e	A	25°C	DMF	 3e	56	40:60
21		A	25°C	DMF-THF(1:1)		62	45:55
22		B	25°C	DMF		55	60:40
23		B	-50°C	DMF-THF(1:1)		65	60:40

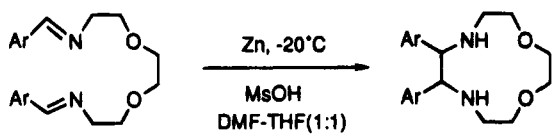
[a] Isolated yields. [b] Determined by ^{1}H NMR or separation with column chromatography.

Table 3. Reductive Intramolecular Coupling of 9b to 3b

run	reagent	solvent	temp (°C)	% yield of **3b**[a]	*trans*:cis[b]
1	Zn–MsOH	DMF–THF (1:1)	25	85	80:20
2	Mg–MsOH	DMF–THF (1:1)	25	50	50:50
3	Zn–TFA	DMF–THF (1:1)	25	80	80:20
4	Zn–$AlBr_3$	THF	25	36	65:35
5	Mg–$TiCl_4$	THF	25	44	85:15
6	SmI_2	THF	reflux	20	15:85

[a] Isolated yields. [b] Determined by ^{1}H NMR.

Table 4. Synthesis of 1,4-Diaza-12-crown-4 Derivatives 3f–l



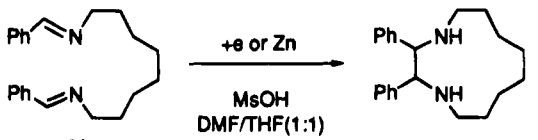
9f-l **3f-l**

run	9	Ar	3	% yield[a]	*trans*:cis[b]
1	**9f**	*p*-$MeOC_6H_4$	**3f**	86	90:10
2	**9g**	*p*-ClC_6H_4	**3g**	86	85:15
3	**9h**	*p*-$MeO_2CC_6H_4$	**3h**	52	50:50
4	**9l**	2-furyl	**3i**	70	95:5
5	**9j**	*o*-$MeOC_6H_4$	**3j**	75	55:45
6	**9k**	*m*-$MeOC_6H_4$	**3k**	90	87:13
7	**9l**	1-naphthyl	**3l**	17 (25)[c]	100:0

[a] Isolated yields. [b] Determined by ^{1}H NMR. [c] The yield obtained by method A.

aromatic aldehydes other than benzaldehyde, as shown in Table 4. Methoxy and chloro groups at the *p*-position on the aromatic ring did not inhibit the intramolecular coupling (runs 1,2), while a methoxycarbonyl group brought about a decrease in the yield and stereoselectivity (run 3). A methoxy group at the *o*-position caused a decrease in the stereoselectivity (run 5). Bis(1-naphthyl imine) **9l** gave the product **3l** as a single stereoisomer, though the yield was low probably due to steric hindrance (run 7). The stereoconfigurations of **3f–l** were determined by comparison of their ^{1}H NMR spectra with those of **3b**.

Although ring closing reactions leading to the formation of macrocycles are not always easily achieved, the macrocyclic products **3** were formed in relatively high yields by the reductive intramolecular coupling of **9** as shown above. This result is attributed to not only the oxygen atoms in the ether linkage but also the protons on the nitrogen atoms in the diprotonated **9**, since the reduction of the alkane analog **11** corresponding to ether **9a** and the *N,N'*-dimethyldiiminium salt of **9a** (**13**) gave poor results under the same reduction conditions (eqs 4 and 5).

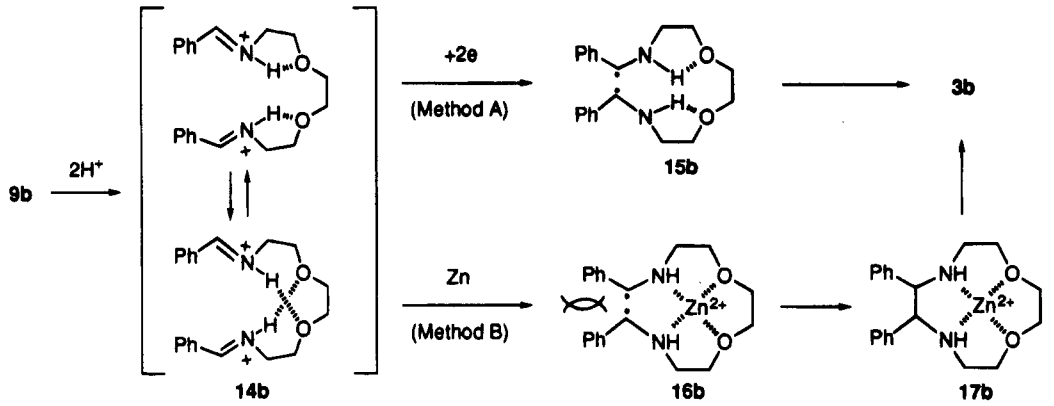


11 **12** <15% *trans*:*cis*=2:1 (4)

13 (5)

Thus, it seems reasonable that the interaction between the hydrogen and oxygen atoms in diprotonated **9** (**14**) forces the two iminium moieties closer and therefore assists the intramolecular coupling of the biradical species **15** or **16** that is generated by donation of two electrons to **14** (Scheme 1). It is also reasonable that the

Scheme 1



hydrogen bonding is effective at the biradical stage (**15**). The presence of the intramolecular hydrogen bonds in **14** is suggested by ^{1}H NMR analysis. The addition of DME to the iminium salt of *N*-benzylidenemethylamine and MsOH causes an upfield shift of the NH proton due to the intermolecular hydrogen bond, although the shift was very small. On the other hand, the addition of DME to **14b** (n = 1) did not affect the chemical shift of the NH protons. The effects of reaction temperature, solvent, and a substituent on the aryl group are shown in Tables 2 and 4 and support the important role of the proton-bridged intermediate **14**.

The fact that method B gave better results in the formation of **3b** (n = 1) than method A can be explained by the template effect[12] of Zn^{2+}. Thus, complex **16b** is formed with the transfer of two electrons to **14b** from Zn. The formation of **16b** makes the intramolecular coupling of two radical centers easier than the coupling in **15b**, and the product (**17b**) is more stable than **3b**. The high *trans* diastereoselectivity in the formation of **3b** is due to the repulsion between the two phenyl groups in **16b**. Since the diameter of the hole in 12-crown-4 is close to the ionic diameter of Zn^{2+} (1.48 Å),[13] the template effect of Zn^{2+} is most conspicuous in the formation of the 1,4-diaza-12-crown-4 derivative (**3b**) and decreases by increasing the ring size of **3** (n = 1−3). As expected, the template effect of Zn^{2+} was negligible in the formation of the 1,4-diaza-9-crown-3 derivative (**3a**, n = 0). The template effect of Zn^{2+} is also supported by the results of ^{13}C NMR binding studies for **3** with Zn^{2+}. The ^{13}C NMR spectrum of *trans*-**3b** was affected by the addition of Zn^{2+} more significantly than that of *trans*-**3c**, and the addition of Li^+ to *trans*-**3b** caused only modest changes to its ^{13}C NMR spectrum. These results show the strong interaction between *trans*-**3b** and Zn^{2+}.

Synthesis of Optically Active Nitrogen-Containing Macrocyclic Bislactones 4 by Reductive Intramolecular Coupling of Bis(imino esters) 20. The bis(imino esters) **20** (n = 1−3) were synthesized from aromatic aldehydes and the bis(amino esters) **19** by stirring at room temperature for 6 h in a solution of CH_2Cl_2 containing $MgSO_4$. Bis(amino esters) **19** were prepared by the esterification with DCC in THF of (*S*)-*N*-methoxycarbonylvaline and diols, followed by *N*-deprotection of **18** with HBr/AcOH. Bis(imino esters) **20** were obtained in 60−90% overall yields (Scheme 2).

Scheme 2

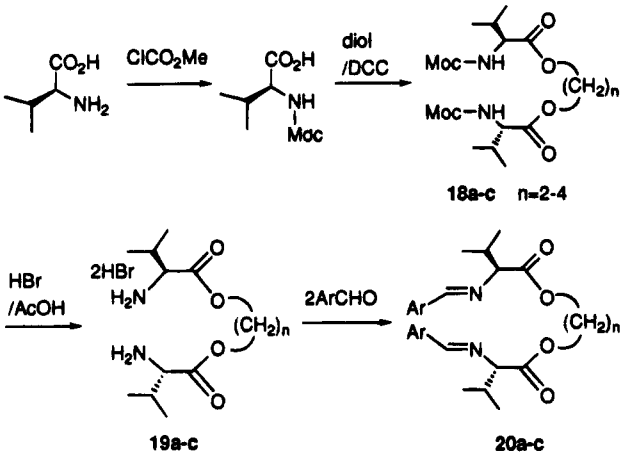
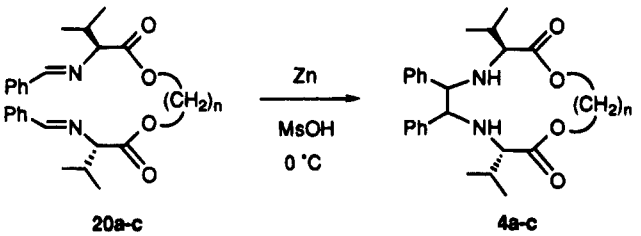


Table 5. Reductive Coupling of Bis(imino esters) 20a−c to Macrocyclic Bislactones 4a−c



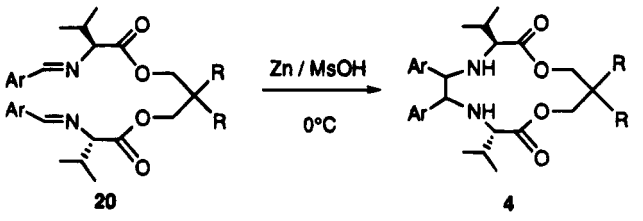
run	20	n	solv	4	yield (%)[a]	(*R*,*R*):(*R*,*S*):(*S*,*S*)[b]
1	**20a**	2	THF	**4a**	53	78:22:0
2			DMF		52	43:57:0
3	**20b**	3	THF	**4b**	68	91:9:0
4			THF[c]		56	92:8:0
5			DMF		44	43:57:0
6			CH_3CN		31	82:18:0
7	**20c**	4	THF	**4c**	47	70:30:0
8			DMF		47	25:75:0

[a] Isolated yields. [b] Determined by ^{1}H NMR spectra. [c] At −30 °C.

The results of the intramolecular coupling of **20a−c** using zinc powder (method B) are summarized in Table 5. Macrocyclic bislactones **4a−c** were obtained efficiently in all cases. The stereoselectivity in the coupling of **20** was influenced by the length of the carbon chain, though (*R*,*R*)-**4** was generally the main isomer and (*S*,*S*)-**4** was not formed at all. As a solvent, THF gave good results (runs 1, 3, and 7), while more polar solvents such as DMF and acetonitrile gave low selectivities (runs 2, 5, 6, and 8). Lowering the temperature scarcely influenced the selectivity (run 4). The best selectivity (91%) and yield

(12) (a) Taylor, L. T.; Vergez, S. C.; Busch, D. H. *J. Am. Chem. Soc.* **1966**, *88*, 3170. (b) Greene, R. N. *Tetrahedron Lett.* **1972**, 1793.
(13) (a) Pedersen, C. J. *J. Am. Chem. Soc.* **1967**, *89*, 7017. (b) Pedersen, C. J. *J. Am. Chem. Soc.* **1970**, *92*, 386.

Table 6. Reductive Coupling of Bis(imino esters) 20 to Macrocyclic Bislactones 4

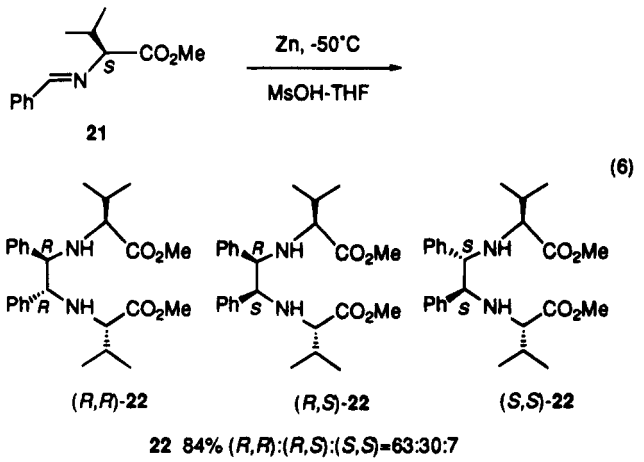


20 4

run	20	Ar	R	solv	4	yield (%)[a]	(*R*,*R*):(*R*,*S*):(*S*,*S*)[b]
1	**20b**	Ph	H	THF	**4b**	68	91:9:0
2	**20d**	*p*-ClC_6H_4	H	THF	**4d**	63	89:11:0
3	**20e**	*p*-$MeOC_6H_4$	H	THF	**4e**	68	97:3:0
4	**20f**	*p*-NCC_6H_4	H	THF	**4f**	59	72:28:0
5	**20g**	*o*-HOC_6H_4	H	THF–DMF (5:1)[c]	**4g**	39	60:40:0
6	**20h**	2-furyl	H	THF–DMF (5:1)[c]	**4h**	26	56:44:0
7	**20i**	Ph	Me	THF	**4i**	56	87:13:0
8	**20j**	*o*-HOC_6H_4	Me	THF	**4j**	39	>99:1:0
9	**20k**	2-furyl	Me	THF	**4k**	35	>99:1:0

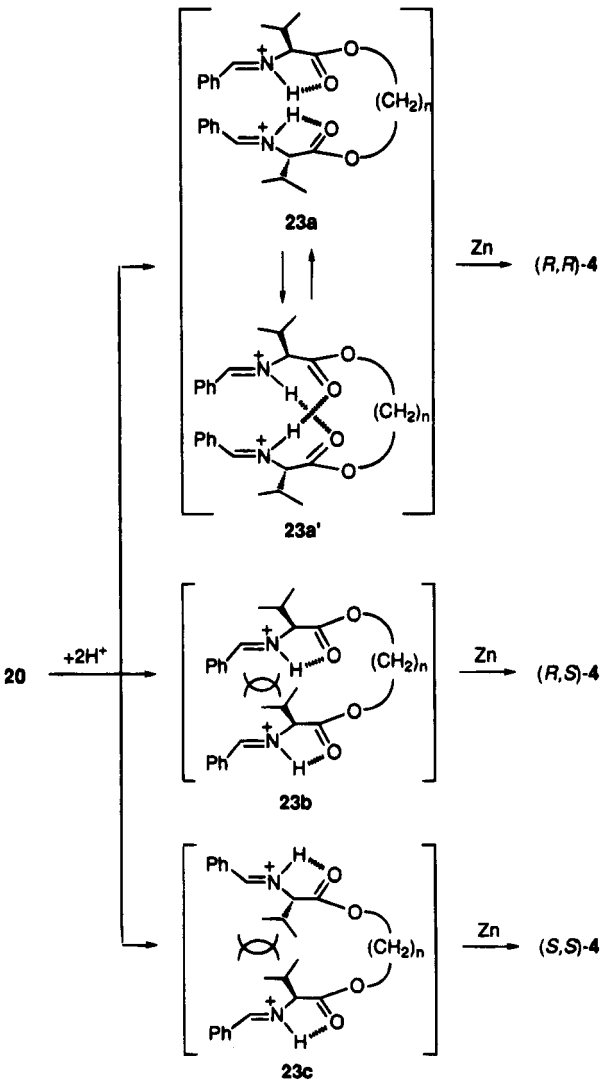
[a] Isolated yields. [b] Determined by ^1H NMR. [c] Iminium salts were insoluble in THF.

(68%) were obtained in the case of $n = 3$ (run 3). The electroreduction of **20** using method A gave a complex mixture. The high selectivity of the intramolecular coupling of **20b** was in contrast to the low selectivity of the intermolecular coupling of optically active imino ester **21** to dimer **22** (eq 6). The absolute stereoconfigurations of the newly formed stereogenic centers in compounds **4a–c** and **22** were determined by their transformation to 1,2-diphenylethylenediamine (**7a**), as described below.



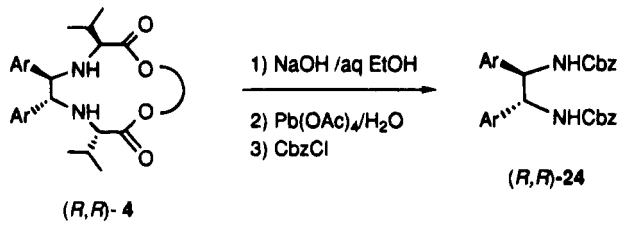
The results obtained with other bis(imino esters) are summarized in Table 6. Macrocyclic bislactones **4b,d–f,i** were obtained in good yields (runs 1–4 and 7). The stereoconfigurations of **4d–f,i** were assigned by the correlation of their ^1H NMR spectra with those of **4b**. The stereoselectivity was influenced by the electronic character of the substituent on the aromatic ring. Namely, an electron-donating substituent gave high selectivity (runs 3, 8, and 9) while an electron-withdrawing one produced a decrease in the stereoselectivity (run 4). When the aryl group was *o*-hydroxyphenyl (runs 5 and 8) or 2-furyl (runs 6 and 9), the yield was low. The use of a mixed solvent THF:DMF = 5:1 resulted in low selectivities (runs 5 and 6), but the diiminium salts of **20g** (Ar = *o*-HOC_6H_4) and **20h** (Ar = 2-furyl) were sparingly soluble in THF. Since diiminium salts of similar compounds **20j** and **20k** were soluble in THF, their reduction was achieved with high stereoselectivity (runs 8 and 9).

Scheme 3



The high stereoselectivity in the coupling of **20** is explained by the steric interaction of isopropyl groups in the diprotonated intermediate **23** (Scheme 3). The proton-bridged intermediate **23** is suggested by ^1H NMR analysis, as described above. An upfield shift of the NH proton resonance of PhCH=NMe·MsOH was observed by the addition of methyl acetate due to the formation of

Table 7. Transformation of (*R,R*)-4 to (1*R*,2*R*)-Diarylethylenediamines



4	Ar	24	yield (%)[a]
4a	Ph	**24a**	70
4b	Ph	**24a**	73
4c	Ph	**24a**	68
4d	*p*-ClC_6H_4	**24d**	73
4e	*p*-$MeOC_6H_4$	**24e**	71
4f	*p*-NCC_6H_4	**24f**	57
4k	2-furyl	**24k**	30

[a] Isolated yield.

an intermolecular hydrogen bond between the NH proton and the carbonyl oxygen atom of methyl acetate, while no upfield shift of the signal due to the NH protons of **23** ($n = 3$) was observed. Three types of intermediates (**23a**, **23b**, and **23c**) may be envisioned for the intramolecular coupling. Among them, steric crowding is maximal in **23c**, which leads to (*S,S*)-**4**, and minimal in **23a**, which yields (*R,R*)-**4**. On the other hand, the steric crowding is also influenced by the chain length between the two ester moieties. Thus, when n is 2, it increases even in the case of **23a**, while when n is 4, it decreases even in the case of **23b**. Hence, the best selectivity was obtained when n was 3. The fact that the proton-bridged intermediate **23** is important in governing the stereoselectivity is also supported by the observed effect of the substituent on the *p*-position of the aryl group as shown in Table 6. Namely, electron-donating substituents gave high selectivities, while the selectivity decreased when the substituents were electron-withdrawing.

Conversion of Optically Active Macrocyclic Bislactones (*R,R*)-4 into (1*R*,2*R*)-Diarylethylenediamines 7. Optically active macrocyclic bislactones (*R,R*)-**4a–c** and (*R,R*)-**22** were converted into (1*R*,2*R*)-diphenylethylenediamine (**7a**) by their hydrolysis followed by oxidation with $Pb(OAc)_4$. On the other hand, (*R,S*)-**4a–c** and (*R,S*)-**22** gave *meso*-**7a** by the same method. Other macrocyclic bislactones (*R,R*)-**4d–f,m** were also transformed into the corresponding (1*R*,2*R*)-diarylethylenediamines **7** in reasonable yields (Table 7). In order to simplify the purification, the diamines (*R,R*)-**7** were isolated as bis(benzyl carbamates) (*R,R*)-**24**.

Synthesis of Nitrogen-Containing Macrocyclic Bislactams 5 by Reductive Intramolecular Coupling of Bis(imino amides) 26. The starting bis(imino amides) **26** were prepared from bis(*N*-(methoxycarbonyl)-amino amides) **25**[14] (Scheme 4). The reductive intramolecular coupling of bis(imino amide) **26a–d** was achieved by reduction with zinc powder in DMF in the presence of MsOH. The results are shown in Table 8. The 12- to 15-membered bislactams **5a–d** were obtained in moderate yields. The stereoselectivity was influenced by the ring size of **5**. The *meso* selectivity increased with decreasing ring size; however, the reason for this unusual selectivity is not yet clear. Lowering the temperature

(14) Waglar, T. R.; Fang, Y.; Burrows, C. J. *J. Org. Chem.* **1989**, *54*, 1584.

Scheme 4

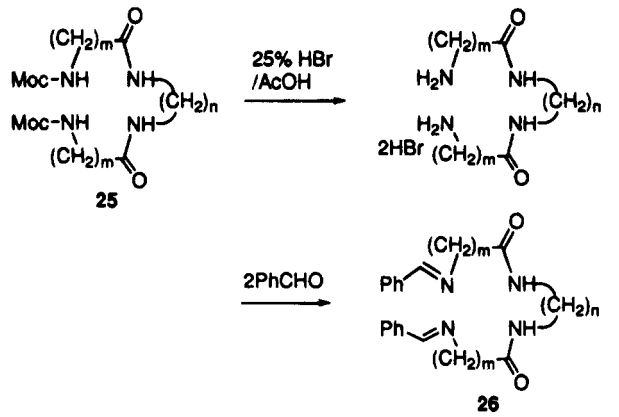
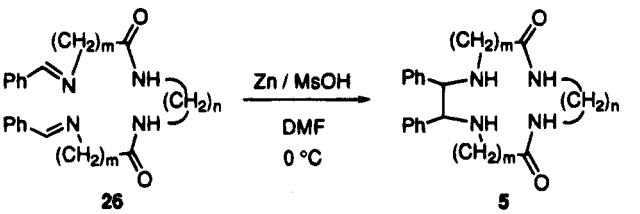


Table 8. Reductive Coupling of Bis(imino amides) 26a–d to Macrocyclic Bislactams 5a–d

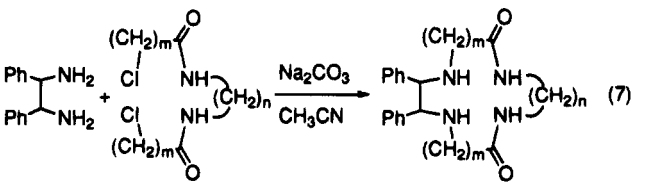


run	26	*m*	*n*	5	yield (%)[a]	trans:cis[b]
1	**26a**	1	2	**5a**	41	14:86
2	**26b**	1	3	**5b**	47	35:65
3	**26c**	2	2	**5c**	67	40:60
4					84[c]	42:58
5	**26d**	2	3	**5d**	58	63:37

[a] Isolated yields. [b] Determined by ^1H NMR spectra. [c] Reaction was carried out at −30 °C.

increased the yield of **5c**, but the stereoselectivity was not improved (run 4).

The stereoconfigurations of macrocyclic bislactams **5a–d** were confirmed by their comparison with authentic samples prepared from *dl*- or *meso*-1,2-diphenylethylenediamine by cyclization with bis(α-chloro amides) or bis(β-chloro amides) (eq 7).[6] The yields of **5** were very low when these methods were utilized.

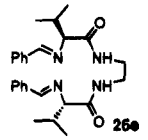
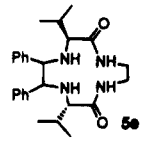
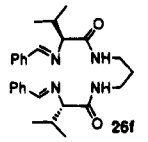
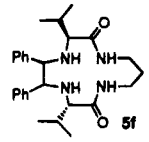
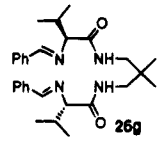
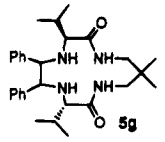


(7)

The reductive coupling of optically active bis(imino amides) **26e–g** was examined, and the results are shown in Table 9. Each of the optically active bislactams **5e–g** was obtained as a mixture of two diastereomers in moderate yield. ^1H and ^{13}C NMR analyses show that one of the isomers is asymmetrical and the other one is symmetrical. Therefore, the former is assigned to be the (*R,S*)-isomer and the latter the (*R,R*) isomer, since it is reasonable that the intramolecular coupling of **26e–g** is similar to that of chiral bis(imino esters) **20** previously described. The low stereoselectivities were probably due to the use of DMF as a solvent, but the diiminium salts of **26** were completely insoluble in THF.

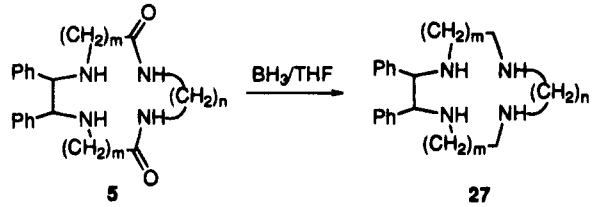
Reduction of Macrocyclic Bislactams to Macrocyclic Tetraamines. Macrocyclic bislactams **5a–d**

Table 9. Synthesis of Optically Active Macrocyclic Bislactams 5e–g

26	5	yield (%)[a]	(R,R):(R,S):(S,S)[b]
 26e	 5e	55	45 : 55 : 0
 26f	 5f	61	51 : 49 : 0
 26g	 5g	43	47 : 53 : 0

[a] Isolated yields. [b] Determined by ^{1}H NMR.

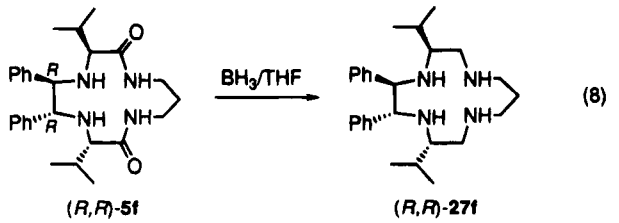
Table 10. Reduction of Macrocyclic Bislactams 5 to Cyclams 27



5	m	n	27	yield (%)[a]
5a	1	2	27a	67
5b	1	3	27b	72
5c	2	2	27c	88
5d	2	3	27d	79

[a] Isolated yields.

were easily reduced using an excess of BH_3/THF in refluxing THF for 20 h.[6] After treatment with 6 M HCl and aqueous NaOH, the corresponding macrocyclic tetraamines (cyclams) **27a–d** were obtained in good yields (Table 10). Optically active bislactam (*R,R*)-**5f** was transformed to tetraamine (*R,R*)-**27f** by the same method (eq 8).



(8)

(*R,R*)-5f (*R,R*)-27f

Experimental Section

Diimines 1 and 9 were prepared quantitatively (^{1}H NMR analysis) by reflux of the corresponding aromatic aldehyde (2 equiv) and diamine (1 equiv) in benzene for 30 min and were subjected to the following reaction without further purification. Diamino ethers were prepared by Gabriel synthesis.[15]

1a: ^{1}H NMR ($CDCl_3$) δ 3.98 (s, 4H), 7.35–7.45 (m, 6 H), 7.68–7.80 (m, 4 H), 8.30 (s, 2 H).

1b: ^{1}H NMR ($CDCl_3$) δ 3.96 (s, 4 H), 6.85–7.00 (m, 4 H), 7.23–7.35 (m, 6 H), 8.38 (s, 2 H).

(15) Dietrich, B.; Lehn, J. M.; Sauvage, J. P.; Blanzat, J. *Tetrahedron* **1973**, *29*, 1629.

1c: ^{1}H NMR ($CDCl_3$) δ 3.00 (s, 12 H), 3.87 (s, 4 H), 6.68 (d, 4 H, J = 9.0 Hz), 7.58 (d, 4 H, J = 9.0 Hz) 8.16 (s, 2 H).

1d: ^{1}H NMR ($CDCl_3$) δ 3.78 (s, 3 H), 3.88–3.98 (m, 1 H), 4.30–4.51 (m, 1 H), 7.32–7.75 (m, 10 H), 8.28 (s, 1 H), 8.31 (s, 1 H).

1e: ^{1}H NMR ($CDCl_3$) δ 1.70–2.05 (m, 8 H), 3.34–3.48 (m, 2 H), 7.28–7.33 (m, 6 H), 7.55–7.62 (m, 4 H), 8.21 (s, 2 H).

1f: ^{1}H NMR ($CDCl_3$) δ 2.61 (s, 6 H), 3.93 (s, 4 H), 7.35–7.43 (m, 6 H), 7.75–7.80 (m, 4 H).

9a: ^{1}H NMR ($CDCl_3$) δ 3.80 (s, 8 H), 7.37–7.44 (m, 6 H), 7.74–7.82 (m, 2 H), 8.27 (s, 1 H).

9b: ^{1}H NMR ($CDCl_3$) δ 3.63 (s, 4 H), 3.77 (s, 8 H), 7.37–7.44 (m, 6 H), 7.70–7.78 (m, 4 H), 8.28 (s, 2 H).

9c: ^{1}H NMR ($CDCl_3$) δ 3.60 (s, 8 H), 3.78 (s, 8 H), 7.37–7.44 (m, 6 H), 7.70–7.78 (m, 4 H), 8.30 (s, 2 H).

9d: ^{1}H NMR ($CDCl_3$) δ 3.57 (s, 4 H), 3.57–3.68 (m, 8 H), 3.79 (s, 8 H), 7.37–7.46 (m, 6 H), 7.70–7.78 (m, 4 H), 8.24 (s, 2 H).

9e: ^{1}H NMR ($CDCl_3$) δ 3.57–3.63 (m, 16 H), 3.80 (s, 8 H), 7.36–7.43 (m, 6 H), 7.70–7.78 (m, 4 H), 8.31 (s, 2 H).

9f: ^{1}H NMR ($CDCl_3$) δ 3.63 (s, 4 H), 3.75 (s, 8 H), 3.84 (s, 6 H), 6.88–6.97 (m, 4 H), 7.63–7.72 (m, 4 H), 8.21 (s, 2 H).

9g: ^{1}H NMR ($CDCl_3$) δ 3.62 (s, 4 H), 3.75 (s, 8 H), 7.32–7.43 (m, 4 H), 7.61–7.72 (m, 4 H), 8.23 (s, 2 H).

9h: ^{1}H NMR ($CDCl_3$) δ 3.63 (s, 4 H), 3.79 (s, 8 H), 3.93 (s, 6 H), 7.79 (d, 4 H, J = 8.5 Hz), 8.07 (d, 4 H, J = 8.5 Hz), 8.32 (s, 2 H).

9i: ^{1}H NMR ($CDCl_3$) δ 3.62 (s, 4 H), 3.76 (s, 8 H), 6.47 (dd, 2 H, J = 3.4, 1.8 Hz), 6.75 (d, 2 H, J = 3.4 Hz), 7.51 (d, 2 H, J = 1.8 Hz), 8.10 (s, 2 H).

9j: ^{1}H NMR ($CDCl_3$) δ 3.65 (s, 4 H), 3.78 (s, 8 H), 3.86 (s, 6 H), 6.87–7.01 (m, 4 H), 7.37 (dt, 2 H, J = 8.2, 1.8 Hz), 7.93 (dd, 2 H, J = 7.7, 1.8 Hz), 8.73 (s, 2 H).

9k: ^{1}H NMR ($CDCl_3$) δ 3.62 (s, 4 H), 3.76 (s, 6 H), 3.83 (s, 8 H), 6.93–7.02 (m, 2 H), 7.20–7.38 (m, 6 H), 8.24 (s, 2 H).

9l: ^{1}H NMR ($CDCl_3$) δ 3.69 (s, 4 H), 3.86 (s, 8 H), 7.44–7.63 (m, 6 H), 7.82–7.94 (m, 6 H), 8.80–8.87 (m, 2 H), 8.92 (s, 2 H).

General Procedure for Reductive Intramolecular Coupling of Diimines with Zinc. To a solution of a diimine (2 mmol) in THF (40 mL) was added MsOH (1.9 g, 20 mmol) and zinc powder (1.3 g, 20 mmol) at −50 °C under nitrogen, and the suspension was stirred for 12 h at this temperature. After addition of saturated aqueous $NaHCO_3$ (50 mL), the solution was filtered off. The filtrate was extracted with CH_2Cl_2, and the organic layer was dried over $MgSO_4$ and concentrated. The product was isolated by column chromatography on basic alumina (activity III, hexane–EtOAc).

Electroreductive coupling of diimines was carried out according to a previously reported method.[7] Physical data of **2a,b,e,f** are shown in the previous report.[7]

2c: R_f = 0.25 (hexane–EtOAc, 2:1); mp 258 °C; IR (KBr) 3700–3200, 1620, 1540, 800 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.98 (br s, 2 H), 3.10 (s, 4 H), 3.61 (s, 2 H), 6.51 (d, 4 H, J = 8.8 Hz), 6.98 (d, 4 H, J = 8.8 Hz); ^{13}C NMR ($CDCl_3$) δ 40.91 (q), 47.55 (t), 67.63 (d), 112.59 (d), 129.20 (d), 130.70 (s), 150.18 (s). Anal. Calcd for $C_{20}H_{28}N_4$: C, 74.03; H, 8.70; N, 17.27. Found: C, 74.21; H, 8.74; N, 17.10.

2d: R_f = 0.55 (hexane–EtOAc, 2:1); IR (neat) 3700–3200, 1725, 770, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.02 (t, 1 H, J = 10.6 Hz), 3.47 (dd, 1 H, J = 3.2, 10.6 Hz), 3.64 (d, 1 H, J = 9.2 Hz), 3.70 (s, 3 H), 3.76 (d, 1 H, J = 9.2 Hz), 3.78–3.87 (m, 1 H), 6.98–7.18 (m, 10 H); ^{13}C NMR ($CDCl_3$) δ 49.00 (t), 52.35 (q), 58.83 (d), 67.75 (d), 67.96 (d), 127.39 (d), 127.82 (d), 127.91 (d), 128.27 (d), 128.39 (d), 128.53 (d), 128.75 (d), 128.93 (d), 141.05 (s), 141.18 (s), 172.33 (s). Anal. Calcd for $C_{18}H_{20}N_2O_2$: C, 72.95; H, 6.80; N, 9.45. Found: C, 72.87; H, 6.74; N, 9.35.

***trans*-3a**: R_f = 0.65 (hexane–EtOAc, 1:1); mp 95–96 °C; IR (KBr) 3500–3100, 1600,1480, 775, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.05 (br s, 2 H), 2.91 (ddd, 2 H, J = 15.0, 9.8, 2.7 Hz), 3.19 (dt, 2 H, J = 15.0, 2.7 Hz), 3.65 (ddd, 2 H, J = 12.2, 9.8, 2.7 Hz), 4.13 (dt, 2 H, J = 12.3, 2.7 Hz), 4.34 (s, 2 H); ^{13}C NMR ($CDCl_3$) δ 48.82 (t), 66.30 (d), 76.16 (t), 126.60 (d), 127.40 (d), 127.91 (d), 141.42 (s). Anal. Calcd for $C_{18}H_{22}N_2O$: C, 76.56; H, 7.85; N, 9.92. Found: C, 76.63; H, 7.86; N, 9.85.

***trans*-3b**: R_f = 0.3 (hexane–EtOAc, 1:1); mp 105–106 °C; IR (KBr) 3600–3100, 765, 695 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.50 (br s, 2 H), 2.75 (t, 4 H, J = 5.5 Hz), 3.50–3.73 (m, 4 H), 3.58 (s, 2 H), 3.78–4.03 (m, 4 H), 7.00–7.20 (m, 10 H); ^{13}C NMR ($CDCl_3$) δ 48.06 (t), 69.68 (d), 69.89 (t), 127.18 (d), 128.42 (d), 142.94 (s). Anal. Calcd for $C_{20}H_{26}N_2O_2$: C, 73.59; H, 8.03; N, 8.58. Found: C, 73.61; H, 8.08; N, 8.50.

***cis*-3b**: R_f = 0.2 (hexane–EtOAc, 1:2); mp 73–74 °C; IR (KBr) 3600–3100, 800, 775, 695 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.00 (br s, 2 H), 2.82–2.90 (m, 4 H), 3.58–3.82 (m, 8 H), 4.02 (s, 2 H), 6.87–6.97 (m, 4 H), 7.10–7.20 (m, 6 H); ^{13}C NMR ($CDCl_3$) δ 46.73 (t), 66.14 (d), 69.67 (t), 70.84 (t), 127.08 (d), 127.97 (d), 128.64 (d), 141.20 (s). Anal. Calcd for $C_{20}H_{26}N_2O_2$: C, 73.59; H, 8.03; N, 8.58. Found: C, 73.68; H, 8.05; N, 8.47.

***trans*-3c**: R_f = 0.25 (hexane–EtOAc, 1:1); mp 87–88 °C; IR (KBr) 3600–3100, 780, 760, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.32 (br s, 2 H), 2.50–2.70 (m, 4 H), 3.47–3.59 (m, 2 H), 3.64 (s, 2 H), 3.62–3.80 (m, 10 H), 6.90–7.17 (m, 10 H); ^{13}C NMR ($CDCl_3$) δ 46.45 (t), 69.38 (d), 69.82 (t), 69.95 (t), 70.55 (t), 127.14 (d), 128.20 (d), 128.56 (d), 142.03 (s). Anal. Calcd for $C_{22}H_{30}N_2O_3$: C, 71.32; H, 8.16; N, 7.56. Found: C, 71.23; H, 8.12; N, 7.41.

***cis*-3c**: R_f = 0.5 (hexane–EtOAc, 1:1); IR (neat) 3600–3100, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.30 (br s, 2 H), 2.50–2.66 (m, 2 H), 2.70–2.82 (m, 2 H), 3.42–3.53 (m, 2 H), 3.63–3.70 (m, 10 H), 4.09 (s, 2 H), 6.88–7.00 (m, 4 H), 7.08–7.20 (m, 6 H); ^{13}C NMR ($CDCl_3$) δ 46.44 (t), 67.05 (d), 69.15 (t), 70.18 (t), 70.39 (t), 127.19 (d), 127.84 (d), 129.13 (d), 140.14 (s). Anal. Calcd for $C_{22}H_{30}N_2O_3$: C, 71.32; H, 8.16; N, 7.56. Found: C, 71.48; H, 8.25; N, 7.29.

3d (*trans*:*cis* = 65:35): R_f = 0.3 (hexane–EtOAc, 1:1); IR (neat) 3600–3150, 755, 695 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.52–2.68 (m, 4 H), 2.75 (br s, 2H), 3.40–3.80 (m, 17.3 H), 4.04 (s, 0.7 H), 6.92–7.28 (m, 10 H); ^{13}C NMR ($CDCl_3$) δ (*trans*) 46.98 (t), 69.50 (d), 70.53 (t), 70.60 (t), 70.86 (t), 71.01 (t), 127.28 (d), 128.33 (d), 128.59 (d), 142.01 (s); (*cis*) 46.87 (t), 67.90 (d), 70.57 (t), 70.79 (t), 71.07 (t), 71.20 (t), 127.21 (d), 127.94 (d), 129.10 (d), 140.51 (s). Anal. Calcd for $C_{24}H_{34}N_2O_4$: C, 69.54; H, 8.27; N, 6.76. Found: C, 69.68; H, 8.36; N, 6.55.

***trans*-3e**: R_f = 0.15 (hexane–EtOAc, 1:5); IR (neat) 3600–3100, 760, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.23 (br s, 2 H), 2.58 (t, 4 H, J = 5.1 Hz), 3.43–3.57 (m, 2 H), 3.58–3.80 (m, 18 H), 3.76 (s, 2 H), 6.95–7.13 (m, 10 H); ^{13}C NMR ($CDCl_3$) δ 47.44 (t), 69.86 (d), 71.17 (t), 71.20 (t), 71.32 (t), 71.42 (t), 71.54 (t), 127.73 (d), 128.38 (d), 128.65 (d), 142.17 (s). Anal. Calcd for $C_{26}H_{38}N_2O_5$: C, 68.10; H, 8.35; N, 6.11. Found: C, 68.39; H, 8.48; N, 6.01.

***cis*-3e**: R_f = 0.45 (hexane–EtOAc, 1:5); IR (neat) 3700–3100, 750, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.45 (br s, 2 H), 2.50–2.72 (m, 4 H), 3.40–3.55 (m, 2 H), 3.55–3.83 (m, 18 H), 3.99 (s, 2 H), 7.00–7.23 (m, 10 H); ^{13}C NMR ($CDCl_3$) δ 47.25 (t), 68.00 (d), 71.02 (t), 71.20 (t), 71.32 (t), 71.49 (t), 127.36 (d), 128.14 (d), 129.05 (d), 140.90 (s). Anal. Calcd for $C_{26}H_{38}N_2O_5$: C, 68.10; H, 8.35; N, 6.11. Found: C, 68.32; H, 8.43; N, 5.97.

***trans*-3f**: R_f = 0.2 (hexane–EtOAc, 1:5); mp 106–107 °C; IR (KBr) 3400–3150, 1680, 1610, 1515, 825 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.65 (br s, 2 H), 2.73 (t, 4 H, J = 5.1 Hz), 3.50 (s, 2 H), 3.50–3.68 (m, 4 H), 3.72 (s, 6 H), 3.77–3.97 (m, 4 H), 6.67 (d, 4 H, J = 8.6 Hz), 6.97 (d, 4 H, J = 8.6 Hz); ^{13}C NMR ($CDCl_3$) δ 47.41 (t), 54.78 (q), 68.59 (d), 69.07 (t), 69.36 (t), 113.18 (d), 128.75 (d), 134.69 (s), 158.20 (s). Anal. Calcd for $C_{22}H_{30}N_2O_2$: C, 68.37; H, 7.82; N, 7.25. Found: C, 68.41; H, 7.83; N, 7.18.

***cis*-3f**: R_f = 0.25 (hexane–EtOAc, 1:2); IR (neat) 3400–3100, 1610, 1510, 825, 725 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.50 (br s, 2 H), 2.75–2.92 (m, 4 H), 3.68–3.82 (m, 8 H), 3.75 (s, 6 H), 3.93 (s, 2 H), 6.69 (d, 4 H, J = 8.8 Hz), 6.85 (d, 4 H, J = 8.8 Hz); ^{13}C NMR ($CDCl_3$) δ 46.24 (t), 54.98 (q), 65.09 (d), 69.14 (t), 70.26 (t), 112.85 (d), 129.27 (d), 132.91 (s), 158.42 (s). Anal. Calcd for $C_{22}H_{30}N_2O_2$: C, 68.37; H, 7.82; N, 7.25. Found: C, 68.17; H, 7.88; N, 7.05.

***trans*-3g**: R_f = 0.15 (hexane–EtOAc, 2:1); mp 120–121 °C; IR (KBr) 3500–3200, 1485, 900, 820, 725 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.60 (br s, 2 H), 2.72 (t, 4 H, J = 5.1 Hz), 3.51 (s, 2 H), 3.50–3.73 (m, 4 H), 3.77–4.00 (m, 4 H), 6.93–7.02 (m, 4 H), 7.08–7.16 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 47.05 (t), 68.27 (d), 68.83 (t), 68.85 (t), 127.86 (d), 128.86 (d), 132.00 (s), 140.48 (s). Anal. Calcd for $C_{20}H_{24}N_2O_2Cl_2$: C, 60.76; H, 6.12; N, 7.09; Cl, 17.94. Found: C, 60.78; H, 6.10; N, 7.13; Cl, 17.86.

***cis*-3g**: R_f = 0.5 (hexane–EtOAc, 2:1); IR (neat) 3550–3150, 1485, 910, 825, 730 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.60 (br s, 2 H), 2.75–2.90 (m, 4 H), 3.60–3.73 (m, 8 H), 3.95 (s, 2 H), 6.83–6.90 (m, 4 H), 7.10–7.18 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 46.17 (t), 65.32 (d), 69.21 (t), 70.47 (t), 127.77 (d), 129.59 (d), 132.47 (s), 139.06 (s). Anal. Calcd for $C_{20}H_{24}N_2O_2Cl_2$: C, 60.76; H, 6.12; N, 7.09; Cl, 17.94. Found: C, 60.93; H, 6.17; N, 6.98; Cl, 17.72.

***trans*-3h**: R_f = 0.2 (hexane–EtOAc, 1:2); mp 134–135 °C; IR (KBr) 3600–5150, 1720, 1610, 770, 705 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.65 (br s, 2 H), 2.74 (t, 4 H, J = 4.4 Hz), 3.50–3.87 (m, 4 H), 3.64 (s, 2 H), 3.86 (s, 6 H), 3.89–3.98 (m, 4 H), 7.07–7.14 (m, 4 H), 7.75–7.83 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 47.43 (t), 51.70 (q), 69.03 (d), 69.11 (t), 127.74 (d), 128.72 (s), 129.34 (d), 147.39 (s), 166.90 (s). Anal. Calcd for $C_{24}H_{30}N_2O_6$: C, 65.14; H, 6.83; N, 6.33. Found: C, 65.19; H, 6.85; N, 6.27.

***cis*-3h**: R_f = 0.5 (hexane–EtOAc, 1:1); IR (neat) 3500–3200, 1720, 1605, 905, 770, 725, 710 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.45 (br s, 2 H), 2.80–2.90 (m, 4 H), 3.60–3.83 (m, 8 H), 3.88 (s, 6 H), 4.10 (s, 2 H), 6.98 (d, 4 H, J = 8.4 Hz), 7.81 (d, 4 H, J = 8.4 Hz); ^{13}C NMR ($CDCl_3$) δ 46.00 (t), 51.63 (q), 65.57 (d), 68.98 (t), 70.24 (t), 127.96 (d), 128.46 (s), 128.75 (d), 145.79 (s), 167.01 (s). Anal. Calcd for $C_{24}H_{30}N_2O_6$: C, 65.14; H, 6.83; N, 6.33. Found: C, 65.27; H, 6.93; N, 6.15.

***trans*-3i**: R_f = 0.15 (hexane–EtOAc, 1:5); mp 86–87 °C; IR (KBr) 3600–3050, 800, 780, 725 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.70 (br s, 2 H), 2.65–2.88 (m, 4 H), 3.53–3.82 (m, 8 H), 4.00 (s, 6 H), 5.97–6.02 (m, 4 H), 6.16–6.21 (m, 4 H), 7.27 (s, 4 H); ^{13}C NMR ($CDCl_3$) δ 45.98 (t), 58.55 (d), 69.14 (t), 69.60 (t), 106.96 (d), 109.75 (d), 141.49 (d), 154.67 (s). Anal. Calcd for $C_{16}H_{22}N_2O_4$: C, 62.73; H, 7.24; N, 9.14. Found: C, 62.77; H, 7.28; N, 9.05.

***trans*-3j**: R_f = 0.15 (hexane–EtOAc, 1:5); mp 116–117 °C; IR (KBr) 3500–3150, 1600, 1585, 910, 745, 725 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.65–2.85 (m, 4 H), 3.10 (br s, 2 H), 3.40–3.95 (m, 10 H), 3.55 (s, 6 H), 6.45-7.40 (m, 8 H); ^{13}C NMR ($CDCl_3$) δ 46.90 (t), 54.84 (q), 57.0–63.0 (d), 69.32 (t), 69.55 (t), 109.87 (d), 119.86 (d), 127.20 (d), 128.65 (d), 130.65 (s), 157.80 (s). Anal. Calcd for $C_{22}H_{30}N_2O_2$: C, 68.37; H, 7.82; N, 7.25. Found: C, 68.44; H, 7.85; N, 7.11.

***cis*-3j**: R_f = 0.2 (hexane–EtOAc, 1:2); mp 104–105 °C; IR (KBr) 3400–3150, 1595, 1485, 745 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.40 (br s, 2 H), 2.78–3.00 (m, 4 H), 3.45 (s, 6 H), 3.57–3.80 (m, 8 H), 4.62 (s, 2 H), 6.65 (dd, 2 H, J = 8.2, 1.1 Hz), 6.78 (dt, 2 H, J = 1.1, 7.5 Hz), 6.97 (dd, 2 H, J = 7.5, 1.8 Hz), 7.09 (ddd, 2 H, J = 8.2, 7.5, 1.8 Hz); ^{13}C NMR ($CDCl_3$) δ 46.03 (t), 54.80 (q), 55.63 (d), 68.89 (t), 69.94 (t), 109.36 (d), 119.80 (d), 127.09 (d), 127.63 (d), 129.62 (s), 157.29 (s). Anal. Calcd for $C_{22}H_{30}N_2O_2$: C, 68.37; H, 7.82; N, 7.25. Found: C, 68.35; H, 7.80; N, 7.21.

***trans*-3k**: R_f = 0.2 (hexane–EtOAc, 1:5); IR (neat) 3400–3150, 1595, 1580, 900, 875, 780, 755, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.70 (br s, 2 H), 2.77 (t, 4 H, J = 5.0 Hz), 3.50–3.77 (m, 5 H), 3.68 (s, 6 H), 3.78–4.00 (m, 5 H), 6.61–6.70 (m, 6 H), 7.00–7.10 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 47.56 (t), 54.83 (q), 69.14 (t), 69.34 (d and t), 112.12 (d), 113.29 (d), 120.28 (d), 128.83 (d), 144.12 (s), 159.33 (s). Anal. Calcd for $C_{22}H_{30}N_2O_2$: C, 68.37; H, 7.82; N, 7.25. Found: C, 68.48; H, 7.92; N, 7.04.

***cis*-3k**: R_f = 0.25 (hexane–EtOAc, 1:2); IR (neat) 3400–3150, 1590, 780, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.45 (br s, 2 H), 2.82–2.92 (m, 4 H), 3.60–3.80 (m, 8 H), 3.63 (s, 6 H), 4.02 (s, 2 H), 6.42–6.48 (m, 2 H), 6.45–6.62 (m, 2 H), 6.66–6.74 (m, 2 H), 7.08 (t, 2 H, J = 7.8 Hz); ^{13}C NMR ($CDCl_3$) δ 46.33 (t), 55.02 (q), 65.62 (d), 69.26 (t), 70.33 (t), 112.71 (d), 113.45 (d), 120.67 (d), 128.54 (d), 142.46 (s), 159.18 (s). Anal. Calcd for $C_{22}H_{30}N_2O_2$: C, 68.37; H, 7.82; N, 7.25. Found: C, 68.51; H, 7.96; N, 7.07.

***trans*-3l**: R_f = 0.25 (hexane–EtOAc, 2:1); mp 143–144 °C; IR (KBr) 3600–3100, 780 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.65 (br s, 2 H), 2.92–3.16 (m, 4 H), 3.60–3.90 (m, 8 H), 5.14 (s, 2 H), 7.00–7.22 (m, 6 H), 7.24–7.50 (m, 4 H), 7.54 (d, 2 H, J = 8.4

Hz), 7.71 (d, 2 H, J = 8.0 Hz); ^{13}C NMR ($CDCl_3$) δ 46.58 (t), 58.69 (d), 69.35 (t), 70.63 (t), 122.28 (d), 124.68 (d), 124.97 (d), 125.19 (d), 127.01 (d), 128.57 (d), 132.22 (s), 133.20 (s), 136.44 (s). Anal. Calcd for $C_{28}H_{30}N_2O_2$: C, 78.84; H, 7.09; N, 6.57. Found: C, 78.80; H, 7.14; N, 6.53.

Preparation of 18. A mixture of 5.3 g (0.03 mol) of *N*-(methoxycarbonyl)-(*S*)-valine and 6.4 g (0.031 mol) of DCC in 60 mL of THF was stirred at 0 °C for 15 min. Ethylene glycol (0.84 mL, 0.015 mol) was added dropwise to the mixture at 0 °C. The reaction mixture was stirred at room temperature for 18 h. A white precipitate (1,3-dicyclohexylurea) was filtered off, and the filtrate was evaporated under reduced pressure. The residue was chromatographed on silica gel (hexane–EtOAc) to give 4.5 g (80%) of **18a** as an oil: R_f = 0.55 (hexane–EtOAc, 1:1); IR (neat) 3400, 1715 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.91 (d, 6 H, J = 7.0 Hz), 0.98 (d, 6 H, J = 7.0 Hz), 2.10–2.24 (m, 2 H), 3.70 (s, 6 H), 4.29 (dd, 2 H, J = 5.0, 10 Hz), 4.37 (s, 4 H), 5.32 (d, 2 H, J = 10 Hz); ^{13}C NMR ($CDCl_3$) δ 17.24 (q), 18.74 (q), 30.91 (d), 52.28 (q), 58.92 (d), 62.50 (t), 157.11 (s), 172.19 (s). Anal. Calcd for $C_{16}H_{28}N_2O_8$: C, 51.06; H, 7.50; N, 7.44. Found: C, 50.96; H, 7.41; N, 7.33.

18b: *N*-(methoxycarbonyl)-(*S*)-valine (5.3 g, 0.03 mol) was treated with DCC (6.4 g, 0.031 mol) and 1,3-propanediol (1.1 g, 0.014 mol) to yield **18b** (5.6 g, 99%) as an oil; R_f = 0.5 (hexane–EtOAc, 1:1); IR (neat) 3400, 1725 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.90 (d, 6 H, J = 6.9 Hz), 0.97 (d, 6 H, J = 6.9 Hz), 1,96–2.24 (m, 4 H), 3.69 (s, 6 H), 4.20–4.34 (m, 6 H), 5.35 (d, 2 H, J = 10 Hz); ^{13}C NMR ($CDCl_3$) δ 17.26 (q), 18.79 (q), 27.67 (t), 31.01 (d), 52.30 (q), 58.95 (d), 61.49 (t), 157.21 (s), 172.42 (s). Anal. Calcd for $C_{17}H_{30}N_2O_8$: C, 52.30; H, 7.74; N, 7.17. Found: C, 52.39; H, 7.80; N, 7.05.

18c: *N*-(methoxycarbonyl)-(*S*)-valine (5.3 g, 0.03 mol) was treated with DCC (6.4 g, 0.031 mol) and 1,4-butanediol (1.3 g, 0.015 mol) to yield **18c** (4.3 g, 74%) as an oil; R_f = 0.6 (hexane–EtOAc, 1:1); IR (neat) 3400, 1720 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.90 (d, 6 H, J = 6.9 Hz), 0.98 (d, 6 H, J = 6.9 Hz), 1.70–1.78 (m, 4 H), 2.06–2.22 (m, 2 H), 3.69 (s, 6 H), 4.14–4.32 (m, 6 H), 5.24 (d, 2 H, J = 8.6 Hz); ^{13}C NMR ($CDCl_3$) δ 17.20 (q), 18.69 (q), 24.92 (t), 30.95 (d), 52.16 (q), 58.89 (d), 64.41 (t), 157.09 (s), 172.40 (s). Anal. Calcd for $C_{18}H_{32}N_2O_8$: C, 53.45; H, 7.97; N, 6.93. Found: C, 53.68; H, 8.08; N, 6.72.

18d: *N*-(methoxycarbonyl)-(*S*)-valine (5.3 g, 0.03 mol) was treated with DCC (6.4 g, 0.031 mol) and 2,2-dimethyl-1,3-propanediol (1.5 g, 0.015 mol) to yield **18d** (4.8 g, 76%) as a white solid; mp 130 °C; R_f = 0.35 (hexane–EtOAc, 2/1); IR (KBr) 3355, 1720, 1540 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.89 (d, 6 H, J = 6.7 Hz), 0.98 (d, 6 H, J = 6.7 Hz), 0.99 (s, 6 H), 2.10–2.24 (m, 2 H), 3.69 (s, 6 H), 3.95 (s, 4 H), 4.30 (dd, 2 H, J = 4.4, 9.1 Hz), 5.25 (d, 2 H, J = 9.1 Hz); ^{13}C NMR ($CDCl_3$) δ 17.23 (q), 18.83 (q), 21.54 (q), 31.00 (d), 34.49 (s), 52.27 (q), 58.99 (d), 69.71 (t), 157.14 (s), 172.27 (s). Anal. Calcd for $C_{19}H_{34}N_2O_8$: C, 54.53; H, 8.19; N, 6.69. Found: C, 54.69; H, 8.14; N, 6.57.

Preparation of Bis(imino esters) 20a–k. The preparation of **20a** is described as a typical example. To a 25% HBr/AcOH solution (20 mL) was added **18a** (4.5 g, 0.012 mol), and the mixture was stirred at room temperature for 24 h. The mixture was concentrated under reduced pressure to give a crude product of **19a**·2HBr. A suspension of crude **19a**·2HBr, triethylamine (5 mL, 0.036 mol), magnesium sulfate (ca. 2 g), and benzaldehyde (3 g, 0.028 mol) in dichloromethane (60 mL) was stirred at room temperature for 6 h. The reaction mixture was filtered. Saturated $NaHCO_3$ (*ca.* 60 mL) was added to the filtrate, and the solution was extracted with dichloromethane. The organic layers were combined, dried ($MgSO_4$), filtered, and concentrated. The residue was chromatographed on basic alumina (Et_2O) to give 4.66 g (89% from **18a**) of **20a** as an oil; R_f = 0.55 (hexane–EtOAc, 5:1); IR (neat) 1725, 1640, 750, 685 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.92 (d, 6 H, J = 6.7 Hz), 0.94 (d, 6 H, J = 6.8 Hz), 2.28–2.46 (m, 2 H), 3.65 (d, 2 H, J = 7.1 Hz), 4.40 (s, 4 H), 7.36–7.46 (m, 6 H), 7.76–7.84 (m, 4 H), 8.21 (s, 2 H); ^{13}C NMR($CDCl_3$) δ 18.35 (q), 19.22 (q), 31.45 (d), 62.23 (t), 79.94 (d), 128.69 (d), 131.19 (d), 135.80 (s), 163.57 (d), 171.91 (s). Anal. Calcd for $C_{26}H_{32}N_2O_4$: C, 71.53; H, 7.39; N, 6.42. Found: C, 71.38; H, 7.24; N, 6.18.

20b was prepared from benzaldehyde and **18b** (88% yield from **18b**): R_f = 0.55 (hexane–EtOAc, 5:1); IR (neat) 1735, 1645, 755, 695 cm^{-1}; ^{1}H NMR($CDCl_3$) δ 0.92 (d, 6 H, J = 5.9 Hz), 0.95 (d, 6 H, J = 6.4 Hz), 1.94–2.12 (m, 2 H), 2.26–2.48 (m, 2 H), 3.65 (d, 2 H, J = 7.3 Hz), 4.14–4.34 (m, 4 H), 7.34–7.38 (m, 6 H), 7.74–7.86 (m, 4 H), 8.24 (s, 2 H); ^{13}C NMR ($CDCl_3$) δ 18.40 (q), 19.28 (q), 27.72 (t), 31.47 (d), 61.09 (t), 80.24 (d), 128.69 (d), 131.17 (d), 135.82 (s), 163.54 (d), 172.10 (s). Anal. Calcd for $C_{27}H_{34}N_2O_4$: C, 71.97; H, 7.61; N, 6.22. Found: C, 71.80; H, 7.52; N, 6.09.

20c was prepared from benzaldehyde and **18c** (90% yield from **18c**): R_f = 0.4 (hexane–EtOAc, 5:1); IR (neat) 1730, 1640, 755, 690 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.93 (d, 6 H, J = 6.5 Hz), 0.96 (d, 6 H, J = 6.5 Hz), 1.68–1.80 (m, 4 H), 2.28–2.48 (m, 2 H), 3.64 (d, 2 H, J = 7.3 Hz), 4.12–4.26 (m, 4 H), 7.38–7.46 (m, 6 H), 7.76–7.86 (m, 4 H), 8.24 (s, 2 H); ^{13}C NMR($CDCl_3$) δ 18.43 (q), 19.29 (q), 25.08 (t), 31.43 (d), 64.15 (t), 80.35 (d), 128.89 (d), 131.15 (d), 135.83 (s), 163.44 (d), 172.17 (s). Anal. Calcd for $C_{28}H_{36}N_2O_4$: C, 72.39; H, 7.81; N, 6.03. Found: C, 72.22; H, 7.75; N, 5.92.

20d was prepared from *p*-chlorobenzaldehyde and **18b** (93% yield from **18b**): R_f = 0.45 (hexane–EtOAc, 5:1); IR (neat) 1740, 1645, 830 cm^{-1}; ^{1}H NMR ($CDCl_3$); δ 0.92 (d, 6 H, J = 6.5 Hz), 0.95 (d, 6 H, J = 6.2 Hz), 1.96–2.02 (m, 2 H), 2.26–2.46 (m, 2 H), 3.65 (d, 2 H, J = 7.3 Hz), 4.18–4.32 (m, 4 H), 7.34–7.44 (m, 4 H), 7.70–7.76 (m, 4 H), 8.20 (s, 2 H); ^{13}C NMR ($CDCl_3$) δ 18.30 (q), 19.20 (q), 27.58 (t), 31.43 (d), 61.01 (t), 79.99 (d), 128.90 (d), 129.82 (d), 134.14 (s), 137.13 (s), 162.13 (d), 171.89 (s). Anal. Calcd for $C_{27}H_{32}N_2O_4Cl_2$: C, 62.43; H, 6.21; N, 5.39: Cl, 13.65. Found: C, 62.54; H, 6.30; N, 5.37: Cl, 13.38.

20e was prepared from *p*-anisaldehyde and **18b** (99% yield from **18b**): R_f = 0.2 (hexane–EtOAc, 5:1); IR (neat) 1740, 1640, 1605, 835 cm^{-1}; ^{1}H NMR($CDCl_3$) δ 0.92 (d, 6 H, J = 6.6 Hz), 0.95 (d, 6 H, J = 6.6 Hz), 1.96–2.12 (m, 2 H), 2.26–2.46 (m, 2 H), 3.60 (d, 2 H, J = 7.4 Hz), 3.83 (s, 6 H), 4.18–4.30 (m, 4 H), 6.88–6.96 (m, 4 H), 7.70–7.78 (m, 4 H), 8.17(s, 2 H); ^{13}C NMR ($CDCl_3$) δ 18.36 (q), 19.20 (q), 27.59 (t), 31.36 (d), 55.15 (q), 60.94 (t), 80.20 (d), 113.87 (d), 128.65 (s), 130.23 (d), 162.02 (s), 162.69 (d), 172.25 (s). Anal. Calcd for $C_{29}H_{38}N_2O_6$: C, 68.21; H, 7.50; N, 5.49. Found: C, 68.28; H, 7.54; N, 5.27.

20f was prepared from *p*-cyanobenzaldehyde and **18b** (90% yield from **18b**): R_f = 0.5 (hexane–EtOAc, 2:1); IR (neat) 2230, 1730, 1640, 835 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.93 (d, 6 H, J = 6.7 Hz), 0.96 (d, 6 H, J = 6.8 Hz), 1.98–2.12 (m, 2 H), 2.28–2.50 (m, 2 H), 3.73 (d, 2 H, J = 7.0 Hz), 4.20–4.32 (m, 4 H), 7.68–7.78 (m, 4 H), 7.88–7.96 (m, 4 H), 8.28 (s, 2 H); ^{13}C NMR ($CDCl_3$) δ 18.22 (q), 19.17 (q), 27.53 (t), 31.50 (d), 61.06 (t), 79.81 (d), 114.27 (s), 118.46 (s), 129.01 (d), 132.47 (d), 139.38 (s), 161.62 (d), 171.52 (s). Anal. Calcd for $C_{29}H_{32}N_4O_4$: C, 69.58; H, 6.44; N, 11.19. Found: C, 69.39; H, 6.26; N, 11.03.

20g was prepared from salicylaldehyde and **18b** (84% yield from **18b**): R_f = 0.7 (hexane–EtOAc, 2:1); IR (KBr) 1735, 1630, 765 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.96 (d, 12 H, J = 6.9 Hz), 1.96–2.10 (m, 2 H), 2.16–2.46 (m, 2 H), 3.72 (d, 2 H, J = 6.1 Hz), 4.20–4.28 (m, 4 H), 6.84–7.02 (m, 4 H), 7.24–7.38 (m, 4 H), 8.30 (s, 2 H); ^{13}C NMR ($CDCl_3$) δ 17.92 (q), 19.17 (q), 27.67 (t), 31.69 (d), 61.25 (t), 77.80 (d), 117.23 (d), 118.57 (s), 118.79 (d), 131.85 (d), 132.94 (d), 161.34 (s), 166.86 (d), 171.17 (s). Anal. Calcd for $C_{27}H_{34}N_2O_6$: C, 67.20; H, 7.10; N, 5.80. Found: C, 67.36; H, 7.20; N, 5.59.

20h was prepared from 2-furaldehyde and **18b** (90% yield from **18b**): R_f = 0.15 (hexane–EtOAc, 5:1); IR (neat) 1730, 1645, 760 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.92 (d, 6 H, J = 7.2 Hz), 0.95 (d, 6 H, J = 6.7 Hz), 1.96–2.12 (m, 2 H), 2.28–2.50 (m, 2 H), 3.57 (d, 2 H, J = 7.7 Hz), 4.23 (t, 4 H, J = 6.3 Hz), 6.49 (dd, 2 H, J = 1.7, 3.4 Hz), 6.85 (d, 2 H, J = 3.4 Hz), 7.54 (d, 2 H, J = 1.7 Hz), 8.06 (s, 2 H); ^{13}C NMR ($CDCl_3$) δ 18.40 (q), 19.10 (q), 27.50 (t), 31.23 (d), 61.07 (t), 80.42 (d), 111.69 (d), 115.31 (d), 145.24 (d), 150.99 (s), 151.75 (d), 171.63 (s). Anal. Calcd for $C_{23}H_{30}N_2O_6$: C, 64.17; H, 7.02; N, 6.51. Found: C, 64.24; H, 7.11; N, 6.45.

20i was prepared from benzaldehyde and **18d** (96% yield from **18d**): mp 105 °C; R_f = 0.6 (hexane–EtOAc, 5:1); IR (KBr) 1730, 1640, 750, 690 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.93 (d, 6 H, J = 6.7 Hz), 0.94 (d, 6 H, J = 6.8 Hz), 0.97 (s, 6 H), 2.26–2.48 (m, 2 H), 3.66 (d, 2 H, J = 7.0 Hz), 3.95 (d, 2 H, J = 15.3 Hz), 4.00 (d, 2 H, J = 15.3 Hz), 7.34–7.46 (m, 6 H), 7.74–7.84 (m,

4 H), 8.22 (s, 2 H); ^{13}C NMR ($CDCl_3$) δ 18.42 (q), 19.35 (q), 21.60 (q), 31.46 (d), 34.66 (s), 69.25 (t), 80.11 (d), 128.68 (d), 131.15 (d), 135.92 (s), 163.36 (d), 172.03 (s). Anal. Calcd for $C_{29}H_{38}N_2O_4$: C, 72.77; H, 8.00; N, 5.85. Found: C, 72.86; H, 8.03; N, 5.73.

20j was prepared from salicylaldehyde and **18d** (99% yield from **18d**): mp 114 °C; R_f = 0.5 (hexane−EtOAc, 5:1); IR (KBr) 1740, 1630, 765 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.95 (d, 6 H, J = 6.8 Hz), 0.96 (d, 6 H, J = 6.8 Hz), 0.99 (s, 6 H), 2.24−2.44 (m, 2 H), 3.73 (d, 2 H, J = 5.9 Hz), 3.97 (s, 4 H), 6.84−7.02 (m, 4 H), 7.24−7.38 (m, 4 H), 8.26 (s, 2 H); ^{13}C NMR ($CDCl_3$) δ 17.95 (q), 19.21 (q), 21.62 (q), 31.78 (d), 34.62 (s), 69.56 (t), 78.03 (d), 117.27 (d), 118.58 (s), 118.78 (d), 132.93 (d), 161.39 (s), 166,78 (d), 170.10 (s). Anal. Calcd for $C_{29}H_{38}N_2O_6$: C, 68.21; H, 7.50; N, 5.49. Found: C, 68.26; H, 7.58; N, 5.43.

20k was prepared from 2-furaldehyde and **18d** (97% yield from **18d**): R_f = 0.3 (hexane−EtOAc, 5:1); IR (KBr) 1730, 1635, 750 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.92 (d, 6 H, J = 6.7 Hz), 0.95 (d, 6 H, J = 7.6 Hz), 0.97 (s, 6 H), 2.28−2.48 (m, 2 H), 3.59 (d, 2 H, J = 7.4 Hz), 3.93 (d, 2 H, J = 16.9 Hz), 3.99 (d, 2 H, J = 16.9 Hz), 6.46−6.50 (m. 2 H), 6.84−6.86 (m, 2 H), 7.52−7.54 (m, 2 H), 8.06 (s, 2 H); ^{13}C NMR ($CDCl_3$) δ 18.39 (q), 19.11 (q), 21.40 (q), 31.12 (d), 34.44 (s), 69.12 (t), 79.99 (d), 111.65 (d), 114.93 (d), 145.12 (d), 151.12 (s), 151.78 (d), 171.44 (s). Anal. Calcd for $C_{25}H_{34}N_2O_6$: C, 65.48; H, 7.47; N, 6.11. Found: C, 65.34; H, 7.43; N, 6.03.

Reductive intramolecular coupling of bis(imino esters) 20 with zinc was carried out by the same method as described above. The products **4** were isolated by column chromatography on silica gel (hexane−EtOAc).

***(R,R)*-4a**: mp 148 °C (recrystallized from hexane−EtOAc); R_f = 0.5 (hexane−EtOAc, 5:1); $[\alpha]^{20}_D$ −204 (c 1.00, $CHCl_3$); IR (KBr) 3380, 1740, 1720, 705 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.88 (d, 6 H, J = 7.1 Hz), 0.91 (d, 6 H, J = 6.9 Hz), 1.65−1.90 (br s, 2 H), 1.70−1.96 (m, 2 H), 2.87 (d, 2 H, J = 8.0 Hz), 3.74 (s, 2 H), 4.43−4.72 (m, 4 H), 6.80−6.90 (m, 4 H), 7.04−7.20 (m, 6 H); ^{13}C NMR ($CDCl_3$) δ 18.92 (q), 19.17 (q), 31.07 (d), 61.39 (t), 67.83 (d), 68.55 (d), 127.01 (d), 127.40 (d), 128.46 (d), 139.60 (s), 175.62 (s). Anal. Calcd for $C_{26}H_{34}N_2O_4$: C, 71.21; H, 7.81; N,6.39. Found: C, 70.97; H, 7.89; N, 6.38.

***(R,S)*-4a** (could not be purified): R_f = 0.5 (hexane−EtOAc, 5:1); ^{1}H NMR ($CDCl_3$) δ 0.60−0.98 (m, 12 H), 1.80−2.06 (m, 1 H), 1.80−2.20 (br s, 2 H), 2.14−2.42 (m, 1 H), 2.71 (d, 1 H, J = 8.0 Hz), 3.15 (d, 1 H, J = 10.0 Hz), 3.67 (d, 1 H, J = 2.0 Hz), 3.88 (d, 1 H, J = 2.0 Hz), 3.82−3.87 (m, 1 H), 4,42−4.68 (m, 2 H), 5.14−5.30 (m, 1 H), 6.74−6.86 (m, 4 H), 7.04−7.20 (m, 6 H).

***(R,R)*-4b**: mp 103 °C (recrystallized from hexane-EtOAc); R_f = 0.4 (hexane−EtOAc, 5:1); $[\alpha]^{20}_D$ −145 (c 0.96, $CHCl_3$); IR (KBr) 3400, 1715, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.82 (d, 6 H, J = 6.8 Hz), 0.83 (d, 6 H, 6.8 Hz), 1.74−1.98 (m, 2 H), 1.86−2.04 (br s, 2 H), 2.14−2.28 (m, 2 H), 2.95 (d, 2 H, J = 6.4 Hz), 3.73 (s, 2 H), 4.20−4.34 (m, 2 H), 4.48−4.62 (m, 2 H), 6.86−6.96 (m, 4 H), 7.00−7.14 (m, 6 H); ^{13}C NMR ($CDCl_3$) δ 18.37 (q), 19.06 (q), 27.50 (t), 31.65 (d), 63.49 (t), 67.80 (d), 69.12 (d), 126.97 (d), 127.48 (d), 128,61 (d), 140.33 (s), 174.94 (s). Anal. Calcd for $C_{27}H_{36}N_2O_4$: C, 71.65; H, 8.02; N, 6.19. Found: C, 71.36; H, 7.96; N, 6.08,.

***(R,S)*-4b**: mp 156 °C (recrystallized from hexane-EtOAc); R_f = 0.5 (hexane−EtOAc, 5:1); $[\alpha]^{20}_D$ −101 (c 1.09, $CHCl_3$); IR (KBr) 3350, 1740, 1720, 720, 710 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.71−0.91 (m, 12 H), 1.80−2.26 (m, 6 H), 2.96 (d, 1 H, J = 7.2 Hz), 3.16 (d, 1 H, J = 8.9 Hz), 3.84 (d, 1 H, J = 3.2 Hz), 4.01 (d, 1 H, J = 3.2 Hz), 4.16−4.62 (m, 4 H), 6.80−6.90 (m, 4 H), 7.08−7.20 (m, 6 H); ^{13}C NMR ($CDCl_3$) δ 18.64 (q), 18.73 (q), 19.13 (q), 19.28 (q), 27.17 (t), 28.22 (d), 31.98 (d), 62.74 (t), 64.91 (d), 66.34 (d), 67.00 (d), 126.84 (d), 127.45 (d), 127.77 (d), 128.61 (d), 139.63 (s), 141.05 (s), 173.52 (s), 175.34 (s). Anal. Calcd for $C_{27}H_{36}N_2O_4$: C, 71.65; H, 8.02; N, 6.19. Found: C, 71.66; H, 7.94; N, 6.18.

***(R,R)*-4c**: mp 142 °C (recrystallized from hexane−EtOAc); R_f = 0.4 (hexane−EtOAc, 5:1); $[\alpha]^{20}_D$ −169 (c 1.76, $CHCl_3$); IR (KBr) 3350, 1730, 735, 705 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.78 (d, 6 H, J = 6.8 Hz), 0.85 (d, 6 H, J = 6.7 Hz), 1.68−2.06 (m, 8 H), 2.80 (d, 2 H, J = 7.3 Hz), 3.70 (s, 2 H), 3.82−4.00 (m, 2 H), 4.72−4.84 (m, 2 H), 6.82−6.92 (m, 4 H), 7.04−7.20 (m, 6 H); ^{13}C NMR ($CDCl_3$) δ 18.68 (q), 18.98 (q), 27.10 (t), 31.28 (d), 62.96 (t), 66.95 (d), 68.30 (d), 127.17 (d), 127.31 (d), 128.89 (d), 139.16 (s), 174.17 (s). Anal. Calcd for $C_{28}H_{38}N_2O_4$: C, 72.07; H, 8.21; N, 6.00. Found: C, 72.20; H, 8.22; N, 6.01.

***(R,S)*-4c**: mp 181 °C (recrystallized from hexane-EtOAc); R_f = 0.5 (hexane−EtOAc, 5:1); IR (KBr) 3350, 1730, 705 cm^{-1}; $[\alpha]^{20}_D$ −111 (c 2.34, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.81 (d, 6 H, J = 6.6 Hz), 0.89 (d, 6 H, J = 6.7 Hz), 1.78−2.10 (m, 6 H), 2.12−2.36 (br s, 2 H), 2.73 (d, 1 H, J = 7.4 Hz), 3.19 (d, 1 H, J = 7.0 Hz), 3.97 (d, 1 H, J = 4.4 Hz), 4.17 (d, 1 H, J = 4.4 Hz), 4.14−4.26 (m, 2 H), 4.42−4.58 (m, 2 H), 6.88−7.00 (m, 4 H), 7.08−7.20 (m, 6 H); ^{13}C NMR ($CDCl_3$) δ 18.11 (q), 18.61 (q), 18.80 (q), 19.23 (q), 25.39(t), 26.59 (t), 29.52 (d), 31.30 (d), 63.21 (d), 63.37 (t), 64.03 (d), 64.73 (d), 65.30 (d), 127.09 (d), 127.19 (d), 127.30 (d), 127.70 (d), 128.28 (d), 129.41 (d), 137.89 (s), 140.72 (s), 173.01 (s), 175.56 (s). Anal. Calcd for $C_{28}H_{38}N_2O_4$: C, 72.07; H, 8.21; N, 6.00. Found: C, 71.99; H, 8.21; N, 6.05.

***(R,R)*-4d**: mp 128 °C (recrystallized from hexane-EtOAc); R_f = 0.3 (hexane−EtOAc, 5:1); $[\alpha]^{20}_D$ −189 (c 1.05, $CHCl_3$); IR (KBr) 3400, 1720, 835 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.82 (d, 6 H, J = 6.6 Hz), 0.84 (d, 6 H, J = 6.8 Hz), 1.76−1.96 (m, 4 H), 2.14−2.28 (m, 2 H), 2.88 (d, 2 H, J = 6.5 Hz), 3.71 (s, 2 H), 4.18−4.32 (m, 2 H), 4.50−4.64 (m, 2 H), 6.80−6.90 (m, 4 H), 7.06−7.16 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 18.26 (q), 19.17 (q), 27.57 (t), 31.59 (d), 63.79 (t), 67.60 (d), 68.11 (d), 127.81 (d), 129.92 (d), 132.98 (s), 138.22 (s), 174.90 (s). Anal. Calcd for $C_{27}H_{34}N_2O_4Cl_2$: C, 62.19; H, 6.57; N, 5.37; Cl, 13.60. Found: C, 62.04; H, 6.60; N, 5.15; Cl, 13.55.

***(R,S)*-4d** (could not be purified): R_f = 0.45 (hexane-EtOAc, 5:1); IR (KBr) 3350, 1730, 735 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.68−0.96 (m, 12 H) 1.70−2.24 (m, 6 H), 2.86 (d, 1 H, J = 7.0 Hz), 3.13 (d, 1 H, J = 9.3 Hz), 3.76 (d, 1 H, J = 3.4 Hz), 3.97 (d, 1 H, J = 3.4 Hz), 4.16−4.62 (m, 4 H), 6.76−6.86 (m, 4 H), 7.08−7.20 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 18.73 (q), 19.13 (q), 19.32 (q), 27.10 (t), 27.83 (d), 31.90 (d), 61.68 (d), 62.69 (t), 64.99 (d), 65.36 (d), 66.88 (d), 127.81 (d), 128.14 (d), 129.19 (d), 129.81 (d), 132.86 (s), 137.94 (s), 139.27 (s), 173.37 (s), 175.30 (s).

***(R,R)*-4e**: mp 75 °C (recrystallized from EtOH); R_f = 0.6 (hexane-EtOAc, 2:1); $[\alpha]^{20}_D$ −159 (c 1.01, $CHCl_3$); IR (KBr) 3400, 1725, 845 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.81 (d, 6 H, J = 6.7 Hz), 0.83 (d, 6 H, J = 6.8 Hz), 1.74−1.94 (m, 4 H), 2.14−2.26 (m, 2 H), 2.92 (d, 2 H, J = 6.6 Hz), 3.67 (s, 2 H), 3.74 (s, 6 H), 4.18−4.32 (m, 2 H), 4.48−4.62 (m, 2 H), 6.60−6.70 (m, 4 H), 6.76−6.86 (m, 4 H); ^{13}C NMR($CDCl_3$) δ 18.33 (q), 19.10 (q), 27.50 (t), 31.54 (d), 54.94 (q), 63.57 (t), 67.55 (d), 68.19 (d), 112.71 (d), 128.67 (d), 132.25 (s), 158.60 (s), 175.20 (s). Anal. Calcd for $C_{29}H_{40}N_2O_6$: C, 67.95; H,7.87; N, 5.46. Found: C, 67.90; H, 7.98; N, 5.40.

***(R,S)*-4e** (could not be purified): R_f = 0.7 (hexane-EtOAc, 2:1); IR (neat) 3350, 1730, 1520, 735 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.70−0.94 (m, 12 H), 1.76−2.26 (m, 6 H), 2.92 (d, 1 H, J = 6.9 Hz), 3.14 (d, 1 H, J = 8.8 Hz), 3.76 (s, 3 H), 3.77 (s, 3 H), 3.74 (d, 1 H, J = 3.6 Hz), 3.91 (d, 1 H, J = 3.6 Hz), 4.16−4.60 (m, 4 H), 6.64−6.86 (m, 8 H); ^{13}C NMR ($CDCl_3$) δ 18.69 (q), 18.79 (q), 19.13 (q), 19.34 (q), 27.17 (t), 28.16 (d), 31.90 (d), 54.98 (q), 62.29 (d), 62.78 (t), 64.87 (d), 65.73 (d), 66.89 (d), 112.74 (d), 113.07 (d), 128.97 (d), 129.73 (d), 131.78 (s), 133.27 (s), 158.49 (s), 173.62 (s), 175.45 (s).

***(R,R)*-4f**: mp 193 °C (recrystallized from hexane-EtOAc); R_f = 0.35 (hexane−EtOAc, 2:1); $[\alpha]^{20}_D$ −221 (c 1.02, $CHCl_3$); IR (KBr) 3370, 2230, 1720, 835 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.84 (d, 6 H, J = 6.8 Hz), 0.86 (d, 6 H, J = 6.8 Hz), 1.78−2.00 (m, 4 H), 2.18−2.30 (m, 2 H), 2.85 (d, 2 H, J = 6.3 Hz), 3.84 (s, 2 H), 4.20−4.36 (m, 2 H), 4.50−4.66 (m, 2 H), 6.98−7.08 (m, 4 H), 7.38−7.48 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 18.26 (q), 19.17 (q), 27.55 (t), 31.65 (d), 63.93 (t), 67.69 (d), 68.40 (d), 111.40 (s), 118.75 (s), 129.12 (d), 131.63 (d), 144.84 (s), 174.51 (s). Anal. Calcd for $C_{28}H_{34}N_4O_4$: C, 69.30; H, 6.82; N, 11.15. Found: C, 69.40; H, 6.89; N, 11.18.

***(R,S)*-4f**: mp 120 °C (recrystallized from hexane-EtOAc); R_f = 0.5 (hexane−EtOAc, 2:1); $[\alpha]^{20}_D$ −186 (c 1.30, $CHCl_3$); IR (KBr) 3380, 2250, 1740, 925, 745 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.64−0.96 (m, 12 H), 1.80−2.24 (m, 6 H), 2.82 (d, 1 H, J = 6.9 Hz), 3.13 (d, 1 H, J = 9.1 Hz), 3.85 (d, 1 H, J = 3.6 Hz), 4.13 (d, 1 H, J = 3.6 Hz), 4.12−4.74 (m, 4 H), 6.90−6.98 (m, 2 H), 7.02−7.10 (m, 2 H), 7.42−7.52 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ

18.55 (q), 18.96 (q), 19.16 (q), 26.89 (t), 27.54 (d), 31.77 (d), 61.58 (d), 62.47 (t), 62.58 (t), 64.89 (d), 65.39 (d), 66.89 (d), 110.96 (s), 111.10 (s), 118.62 (s), 118.72 (s), 128.32 (d), 128.83 (d), 131.49 (d), 131.89 (d), 144.54 (s), 146.08 (s), 173.08 (s), 175.09 (s). Anal. Calcd for $C_{29}H_{34}N_4O_4$: C, 69.30; H, 6.82; N, 11.15. Found: C, 69.43; H, 6.85; N, 11.07.

(*R,R*)- and (*R,S*)-4g (60:40 mixture): R_f = 0.4 (hexane–EtOAc, 2:1); IR (KBr) 3360, 3500–2100 (broad), 1730, 755 cm^{-1}; ^1H NMR ($CDCl_3$) (*R,R*) δ 0.91 (d, 6 H, J = 6.8 Hz), 0.93 (d, 6 H, J = 6.8 Hz), 1.94–2.28 (m, 6 H), 3.25 (d, 2 H, J = 5.1 Hz), 3.93 (s, 2 H), 4.08–4.20 (m, 2 H), 4.72–4.84 (m, 2 H), 6.60–7.20 (m, 8 H), (*R,S*) δ 0.80–1.02 (m, 12 H), 1.94–2.28 (m, 6 H), 3.14 (d, 1 H, J = 6.7 Hz), 3.36 (d, 1 H, J = 8.8 Hz), 3.83 (d, 1 H, J = 3.7 Hz), 4.12–4.44 (m, 5 H), 6.60–7.20 (m, 8 H); ^{13}C NMR ($CDCl_3$) δ 18.15 (q), 18.62 (q), 18.75 (q), 26.86 (t), 26.99 (d), 27.81 (t), 31.32 (d), 61.18 (d), 62.41 (t), 62.56 (t), 64.66 (t), 64.80 (d), 66.70 (d), 66.88 (d), 67.72 (d), 116.66 (d), 117.23 (d), 118.96 (d), 119.27 (d), 119.51 (d), 120.75 (s), 121.87 (s), 122.41 (s), 128.80 (d), 128.97 (d), 129.30 (d), 129.51 (d), 129.63 (d), 156.24 (s), 157.25 (s), 157.36 (s), 172.25 (s), 172.84 (s), 174.55 (s). Anal. Calcd for $C_{27}H_{36}N_2O_6$: C, 66.92; H, 7.49; N, 5.78. Found: C, 67.08; H, 7.54; N, 5.56.

(*R,R*) and (*R,S*)-4h (56:44 mixture): R_f = 0.3 (hexane–EtOAc, 5:1); IR (KBr) 3370, 1720, 730 cm^{-1}; ^1H NMR($CDCl_3$) (*R,R*) δ 0.78 (d, 12 H, J = 6.7 Hz), 1.74–1.96 (m, 2 H), 2.00–2.20 (m, 4 H), 2.99 (d, 2 H, J = 6.6 Hz), 3.83 (s, 2 H), 4.12–4.88 (m, 4 H), 5.86–5.90 (m, 2 H), 6.07–6.11 (m, 2 H), 7.16–7.24 (m, 2 H), (*R,S*) δ 0.74–0.88 (m, 12 H), 1.80–2.20 (m, 6 H), 3.05 (d, 1 H, J = 7.1 Hz), 3.14 (d, 1 H, J = 6.5 Hz), 3.98 (d, 1 H, J = 3.0 Hz), 4.12–4.50 (m, 5 H), 5.88–5.92 (m, 1 H), 5.96–5.99 (m, 1 H), 6.12–6.19 (m, 2 H), 7.20–7.23 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 17.93 (q), 18.09 (q), 18.37 (q), 18.73 (q), 18.84 (q), 19.06 (q), 27.08 (t), 27.26 (t), 30.30 (d), 31.40 (d), 32.26 (d), 57.28 (d), 61.13 (d), 61.53 (d), 63.06 (t), 63.50 (t), 64.25 (d), 67.65 (d), 67.83 (d), 106.41 (d), 107.10 (d), 107.90 (d), 109.87 (d), 110.06 (d), 141.42 (d), 141.61 (d), 154.05 (s), 155.00 (s), 173.52 (s), 174.47 (s), 174.57 (s). Anal. Calcd for $C_{23}H_{32}N_2O_6$: C, 63.87; H, 7.46; N, 6.48. Found: C, 63.76; H, 7.39; N, 6.33.

(*R,R*)-4i: mp 148 °C (recrystallized from hexane-EtOAc); R_f = 0.4 (hexane–EtOAc, 10/1); $[\alpha]^{20}_D$ −117 (*c* 1.00, $CHCl_3$); IR (KBr) 3400, 1725, 1710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.76 (d, 6 H, J = 6.7 Hz), 0.82 (d, 6 H, J = 6.7 Hz), 1.09 (s, 6 H), 1.80–1.92 (m, 2 H), 1.92–2.00 (br s, 2 H), 2.85 (d, 2 H, J = 8.0 Hz), 3.63 (s, 2 H), 3.94 (d, 2 H, J = 10.8 Hz), 4.17 (d, 2 H, J = 10.8 Hz), 6.90–6.98 (m, 4 H), 7.02–7.08 (m, 6 H); ^{13}C NMR ($CDCl_3$) δ 18.54 (q), 18.99 (q), 22.55 (q), 31.18 (d), 34.13 (s), 68.72 (d), 69.34 (d), 70.32 (t), 126.81(d), 127.56 (d), 128.37 (d), 140.96 (s), 174.84 (s). Anal. Calcd for $C_{29}H_{40}N_2O_4$: C, 72.47; H, 8.39; N, 5.83. Found: C, 72.27; H, 8.23; N, 5.86.

(*R,S*)-4i: mp 110 °C (recrystallized from hexane-EtOAc); R_f = 0.5 (hexane–EtOAc, 10:1); $[\alpha]^{20}_D$ −75 (*c* 0.72, $CHCl_3$); IR (KBr) 3340, 1720, 905, 730 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.70–0.92 (m, 12 H), 1.07 (s, 3 H), 1.12 (s, 3 H), 1.52–2.10 (m, 4 H), 2.88 (d, 1 H, J = 7.4 Hz), 3.13 (d, 1 H, J = 9.3 Hz), 3.64 (d, 1 H, J = 11.1 Hz), 3.71 (d, 1 H, J = 3.3 Hz), 3.85 (d, 1 H, J = 11.1 Hz), 3.98 (d, 1 H, J = 3.3 Hz), 4.08 (d, 1 H, J = 11.1 Hz), 4.65 (d, 1 H, J = 11.1 Hz), 6.76–6.84 (m, 2 H), 6.94–7.00 (m, 2 H), 7.06–7.24 (m, 6 H); ^{13}C NMR ($CDCl_3$) δ 18.77 (q), 18.88 (q), 19.17 (q), 19.27 (q), 22.33 (q), 22.91 (q), 27.98 (d), 31.47 (s), 33.94 (d), 61.80 (d), 64.74 (d), 66.42 (d), 67.14 (d), 70.16 (t), 70.78 (t), 126.73 (d), 126.87 (d), 127.36 (d), 127.84 (d), 128.50 (d), 139.37 (s), 141.67 (s), 173.70 (s), 176.17 (s). Anal. Calcd for $C_{29}H_{40}N_2O_4$: C, 72.47; H, 8.39; N, 5.83. Found: C, 72.36; H, 8.28; N, 5.91.

(*R,R*)-4j: R_f = 0.2 (hexane–EtOAc, 5:1); $[\alpha]^{20}_D$ −29 (*c* 0.50, $CHCl_3$); IR (KBr) 3350, 1740, 760 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.91 (d, 12 H, J = 6.9 Hz), 1.12 (s, 6 H), 1.90–2.10 (m, 2 H), 3.19 (d, 2 H, J = 5.9 Hz), 3.92 (d, 2 H, J = 11.3 Hz), 3.96 (s, 4 H), 4.35 (d, 2 H, J = 11.3 Hz), 6.55–6.80 (m, 6 H), 7.00–7.12 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 18.33 (q), 18.78 (q), 22.46 (q), 31.27 (d), 34.51 (s), 67.67 (d), 68.47 (d), 71.60 (t), 116.67 (d), 119.23 (d), 121.53 (s), 129.33 (d), 129.66 (d), 156.84 (s), 172.80 (s). Anal. Calcd for $C_{29}H_{40}N_2O_6$: C, 67.95; H, 7.86; N, 5.46. Found: C, 67.88; H, 7.84; N, 5.39.

(*R,R*)-4k: mp 155 °C (recrystallized from hexane-EtOAc); R_f = 0.5 (hexane–EtOAc, 5:1); $[\alpha]^{20}_D$ −69 (*c* 1.01, $CHCl_3$); IR (KBr) 3380, 1735, 750 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.82 (d, 6 H, J = 6.4 Hz), 0.85 (d, 6 H, J = 6.7 Hz), 1.06 (s, 6 H), 1.72–1.92 (m, 2 H), 2.06–2.14 (br s, 2 H), 2.90 (d, 2 H, J = 8.1 Hz), 3.81 (s, 2 H), 3.94 (d, 2 H, J = 10.9 Hz), 4.06 (d, 2 H, J = 10.9 Hz), 5.94–6.00 (m, 2 H), 6.12–6.18 (m, 2 H), 7.22–7.26 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 18.37 (q), 18.93 (q), 22.53 (q), 31.07 (d), 34.06 (s), 61.50 (d), 68.72 (d), 70.24 (t), 107.08 (d), 109.85 (d), 141.67 (d), 154.01 (s), 174.64 (s). Anal. Calcd for $C_{25}H_{36}N_2O_6$: C, 65.20; H, 7.88; N, 6.08. Found: C, 64.94; H, 7.95; N, 6.04.

(*R,R*)-22: mp 95 °C (recrystallized from hexane-EtOAc); R_f = 0.6 (hexane–EtOAc, 5:1); $[\alpha]^{20}_D$ −109 (*c* 1.00, $CHCl_3$); IR (KBr) 3355, 3320, 1740, 1715, 800, 770, 750, 705, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.90 (d, 6 H, J = 6.8 Hz), 0.96 (d, 6 H, J = 6.8 Hz), 1.43–1.79 (br s, 2 H), 1.81–2.07 (m, 2 H), 2.84 (d, 2 H, J = 5.7 Hz), 3.50 (s, 2 H), 3.65 (s, 6 H), 6.97–7.14 (m, 10 H); ^{13}C NMR ($CDCl_3$) δ 17.41 (q), 18.53 (q), 30.68 (d), 50.50 (q), 63.88 (d), 66.86 (d), 126.17 (d), 126.95 (d), 127.68 (d), 140.36 (s), 175.29 (s). Anal. Calcd for $C_{26}H_{36}N_2O_4$: C, 70.88; H, 8.24; N, 6.36. Found: C, 70.80; H, 8.45; N, 6.40.

(*R,S*)-22 (could not be purified): R_f = 0.4 (hexane-EtOAc, 5:1); ^1H NMR ($CDCl_3$) δ 0.65–0.81 (m, 12 H), 1.60–1.82 (m, 2 H), 2.69 (d, 1 H, J = 6.4 Hz), 2.88 (d, 1 H, J = 6.9 Hz), 3.43 (s, 3 H), 3.60 (s, 3 H), 3.57 (d, 1 H, J = 7.3 Hz), 3.75 (d, 1 H, J = 7.3 Hz), 7.19–7.25 (m, 10 H).

(*S,S*)-22 (could not be purified): R_f = 0.4 (hexane-EtOAc, 5:1); ^1H NMR ($CDCl_3$) δ 0.95 (d, 6 H, J = 6.4 Hz), 1.04 (d, 6 H, J = 6.4 Hz), 1.86–2.06 (m, 2 H), 2.96 (d, 2 H, J = 5.8 Hz), 3.25 (s, 6 H), 3.66 (s, 2 H), 6.93–7.08 (m, 10 H).

Typical Transformation of 4 to 7 (24). To a solution of (*R,R*)-**4b** (130 mg, 0.29 mmol) in EtOH (10 mL) was added NaOH (25 mg, 0.63 mmol) dissolved in 1 mL of H_2O, and the mixture was stirred at 40 °C for 4 h. The solvent was removed under reduced pressure. To the residue was added water (15 mL), and then $Pb(OAc)_4$ (280 mg, 0.63 mmol) was added at 0 °C. The mixture was stirred at 0 °C for 2 h. After the pH was adjusted to 1 or 2 by addition of 1 M HCl, the mixture was stirred at room temperature for 6 h. The reaction mixture was washed three times with CH_2Cl_2. To the aqueous solution was added 2 M NaOH (30 mL), and the solution was extracted three times with CH_2Cl_2. The organic layers were combined, dried ($MgSO_4$), filtered, and concentrated to give 50 mg of the crude diamine. The comparison of its ^1H NMR spectrum and optical rotation with reported data[9,10] showed that the crude diamine was (*R,R*)-diphenylethylenediamine (**7a**): $[\alpha]^{25}_D$ +102 (*c* 1.0, MeOH) [lit.[9] $[\alpha]^{25}_D$ +106.5 (*c* 1.06, MeOH)]; ^1H NMR ($CDCl_3$) δ 1.63 (brs 4 H), 4.10 (s, 2 H), 7.20–7.34 (m, 10 H). By the same procedure, (*R,S*)-**4b** was transformed to *meso*-**7a**: ^1H NMR ($CDCl_3$) δ 1.63 (brs, 4 H), 4.02 (s, 2 H), 7.28–7.42 (m, 10 H).

To a mixture of the crude (*R,R*)-**7a** (50 mg) and K_2CO_3 (30 mg) in CH_2Cl_2 (5 mL) was added benzyl chloroformate (0.09 mL, 0.63 mmol) at 0 °C, and the suspension was stirred at room temperature for 2 h. Saturated $NaHCO_3$ (15 mL) was added, and the solution was extracted three times with CH_2Cl_2. The organic layers were combined, dried ($MgSO_4$), filtered, and concentrated. Recrystallization of the residue from EtOH gave (*R,R*)-**24a** (102 mg, 73%). Its optical rotation was in accordance with that of the authentic sample.

(*R,R*)-24a: mp 188 °C; $[\alpha]^{20}_D$ −10.2 (*c* 1.03, $CHCl_3$); IR (KBr) 3360, 3040, 1690, 1535, 755, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.97 (d, 2 H, J = 4.8 Hz), 5.05 (s, 4 H), 5.82–5.98 (br s, 2 H), 6.98–7.12 (m, 4 H), 7.12–7.24 (m, 6 H), 7.24–7.38 (m, 10 H); ^{13}C NMR ($CDCl_3$) δ 61.20 (d), 67.35 (t), 127.89 (d), 128.34 (d), 128.36 (d), 129.01 (d), 136.76 (s), 139.20 (s), 157.28 (s). Anal. Calcd for $C_{30}H_{28}N_2O_4$: C, 74.98; H, 5.87; N, 5.83. Found: C, 74.80; H, 5.86; N, 5.84.

(*R,R*)-24d: mp 215 °C (recrystallized from EtOH); $[\alpha]^{20}_D$ +12.9 (*c* 1.10, $CHCl_3$); IR (KBr) 3330, 1680, 1535 cm^{-1}; ^1H NMR ($CDCl_3$); δ 4.90 (d, 2 H, J = 4.7 Hz), 5.03 (s, 4 H), 5.86–6.00 (br s, 2 H), 6.88–7.02 (m, 4 H), 7.14–7.22 (m, 4 H), 7.22–7.36 (m, 10 H); ^{13}C NMR ($CDCl_3$) δ 60.11 (d), 67.18 (t), 128.21 (d), 128.38 (d), 128.65 (d), 128.96 (d), 133.96 (s), 136.09 (s), 137.19 (s), 156.79 (s). Anal. Calcd for $C_{30}H_{26}N_2O_4Cl_2$: C,

65.58; H, 4.77; N, 5.10; Cl, 12.90. Found: C, 65.46; H, 4.71; N, 4.92; Cl, 12.67.

***(R,R)*-24e**: mp 214 °C (recrystallized from EtOH); $[\alpha]^{20}_D$ −18.1 (*c* 0.47, $CHCl_3$); IR (KBr) 3350, 1690, 1525, 845 cm^{-1}; ^1H NMR($CDCl_3$) δ 3.74 (s, 6 H), 4.88 (d, 2 H, *J* = 5.3 Hz), 5.07 (s, 4 H), 5.62−5.76 (br s, 2 H), 6.68−6.78 (m, 4 H), 6.92−7.04 (m, 4 H), 7.24−7.36 (m, 10 H); ^{13}C NMR ($CDCl_3$) δ 55.08 (q), 60.16 (d), 66.89 (t), 113.90 (d), 128.20 (d), 128.62 (d), 131.12 (s), 136.43 (s), 156.83 (s), 159.12 (s). Anal. Calcd for $C_{32}H_{32}N_2O_6$: C, 71.10; H, 5.97; N, 5.18. Found: C, 70.83; H, 5.93; N, 5.23.

***(R,R)*-24f**: mp 176 °C (recrystallized from EtOH); $[\alpha]^{20}_D$ +38.9 (*c* 0.35, $CHCl_3$); IR (KBr) 3350, 2260, 1690, 1540 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.98 (br s, 2 H), 5.06 (s, 4 H), 5.88 (brs, 2 H), 7.08−7.22 (m, 4 H), 7.24−7.42 (m, 10 H), 7.44−7.58 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 60.08 (d), 67.48 (t), 112.24 (s), 118.24 (s), 128.04 (d), 128.25 (d), 128.62 (d), 128.74 (d), 132.64 (d), 135.82 (s), 143.61 (s), 156.67 (s). Anal. Calcd for $C_{32}H_{26}N_4O_4$: C, 72.44; H, 4.94; N, 10.56. Found: C, 72.50; H, 5.05; N, 10.39.

***(R,R)*-24k**: mp 174 °C (recrystallized from EtOH); $[\alpha]^{20}_D$ −50.4 (*c* 0.50, $CHCl_3$); IR (KBr) 3320, 3040, 1680, 1520, 735 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.09 (s, 4 H), 5.22−5.30 (m, 2 H), 5.60−5.70 (br s, 2 H), 6.06−6.08 (m, 2 H), 6.20−6.24 (m, 2 H), 7.26−7.36 (m, 12 H); ^{13}C NMR ($CDCl_3$) δ 52.33 (d), 67.05 (t), 107.76 (d), 110.34 (d), 128.15 (d), 128.27 (d), 128.62 (d), 136.33 (s), 142.43 (d), 150.88 (s), 156.41 (s). Anal. Calcd for $C_{26}H_{24}N_2O_6$: C, 67.82; H, 5.25; N, 6.08. Found: C, 67.52; H, 5.14; N, 6.02.

Bis(imino amides) 26 were prepared from **25a**[14] and benzaldehyde by the same method as for the preparation of **20**. The products were isolated by recrystallization from EtOH or column chromatography on basic alumina.

26a was prepared from **25a** (40%). **26a**: mp 150 °C (recrystallized from EtOH); R_f = 0.7 (CH_2Cl_2−MeOH, 20:1); IR (KBr) 3270, 3080, 1650, 1540, 1250, 755, 690 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.50−3.60 (m, 4 H), 4,25 (s, 4 H), 7.30−7.50 (m, 8 H), 7.74−7.86 (m, 4 H), 8.26 (s, 2 H); ^{13}C NMR ($CDCl_3$) δ 39.04 (t), 62.61 (t), 128.50 (d), 128.87 (d), 131.57 (d), 135.49 (s), 163.91 (d), 171.34 (s). Anal. Calcd for $C_{20}H_{22}N_4O_2$: C, 68.55; H, 6.33; N, 15.99. Found: C, 68.52; H, 6.29; N, 15.85.

26b was prepared from **25b** (46%). **26b**: R_f = 0.5 (CH_2Cl_2−MeOH, 20:1); IR (KBr) 3300, 1640, 1520, 760, 690 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.70−1.84 (m, 2 H), 3.36−3.50 (m, 4 H), 4.27 (s, 4 H), 7.34−7.50 (m, 8 H), 7.78−7.84 (m, 4 H), 8.29 (s, 2 H); ^{13}C NMR ($CDCl_3$) δ 29.72 (t), 35.94 (t), 62.72 (t), 128.48 (d), 128.83 (d), 131.49 (d), 135.55 (s), 163.74 (d), 170.90 (s). Anal. Calcd for $C_{20}H_{22}N_4O_2$: C, 69.21; H, 6.64; N, 15.37. Found: C, 69.15; H, 6.60; N, 15.18.

26c was prepared from **25c** (42%). **26c**: mp 177 °C (recrystallized from EtOH); R_f = 0.65 (CH_2Cl_2−MeOH, 20:1); IR (KBr) 3270, 3060, 2830, 1625, 1540, 745, 685 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.50 (t, 4 H, *J* = 6.3 Hz), 3.32−3.42 (m, 4 H), 3.82 (t, 4 H, *J* = 6.3 Hz), 7.07 (br s, 2 H), 7.36−7.48 (m, 6 H), 7.64−7.74 (m, 4 H), 8.27 (s, 2 H); ^{13}C NMR($CDCl_3$) δ 37.51 (t), 39.58 (t), 56.99 (t), 128.21 (d), 128.83 (d), 131.12 (d), 135.83 (s), 162.44 (d), 172.94 (s). Anal. Calcd for $C_{22}H_{26}N_4O_2$: C, 69.82; H, 6.92; N, 14.80. Found: C, 69.72; H, 6.88; N, 14.71.

26d was prepared from **25d** (48%). **26d**: mp 127 °C (recrystallized from EtOH); R_f = 0.65 (CH_2Cl_2−MeOH, 20:1); IR (KBr) 3290, 1635, 1545, 750, 690 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.40−1.60 (m, 2 H), 2.57 (t, 4 H, *J* = 6.3 Hz), 3.14−3.26 (m, 4 H), 3.88 (t, 4 H, *J* = 6.3 Hz), 6.95 (t, 2 H, *J* = 5.9 Hz), 7.36−7.46 (m, 6 H), 7.66−7.76 (m, 4 H), 8.31 (s, 2 H); ^{13}C NMR ($CDCl_3$) δ 29.58 (t), 35.62 (t), 37.74 (t), 57.19 (t), 128.24 (d), 128.78 (d), 131.05 (d), 135.89 (s), 162.50 (d), 172.46 (s). Anal. Calcd for $C_{23}H_{28}N_4O_2$: C, 70.38; H, 7.19; N, 14.27. Found: C, 70.27; H, 7.23; N, 14.15.

26e was prepared from **25e** (57%). **26e**: mp 125 °C (recrystallized from EtOH); R_f = 0.45 (hexane−EtOAc, 1:1); IR (KBr) 3320, 1660, 1520, 765, 745, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.89 (d, 6 H, *J* = 7.0 Hz), 0.95 (d, 6 H, *J* = 7.0 Hz), 2.28−2.42 (m, 2 H), 3.40−3.58 (m, 4 H), 3.59 (d, 2 H, *J* = 4.0 Hz), 7.18 (br s, 2 H), 7.44−7.52 (m, 6 H), 7.78−7.84 (m, 4 H), 8.06 (s, 2 H); ^{13}C NMR ($CDCl_3$) δ 17.12 (q), 19.26 (q), 32.60 (d), 38.86 (t), 78.88 (d), 128.54 (d), 128.71 (d), 131.27 (d), 135.56 (s), 162.42 (d), 173.59 (s). Anal. Calcd for $C_{26}H_{34}N_4O_2$: C, 71.86; H, 7.89; N, 12.89. Found: C, 71.72; H, 7.87; N, 12.66.

26f was prepared from **25f** as an oil (93%). **26f**: R_f = 0.4 (hexane−EtOAc, 1:1); IR (neat) 3350, 1660, 1510, 1450, 755, 730, 690 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.93 (d, 6 H, *J* = 7.2 Hz), 0.96 (d, 6 H, *J* = 7.1 Hz), 1.66−1.80 (m, 2 H), 2.28−2.46 (m, 2 H), 3.20−3.50 (m, 4 H), 3.63 (d, 2 H, *J* = 4.3 Hz), 7.16 (t, 2 H, *J* = 6.2 Hz), 7.42−7.48 (m, 6 H), 7.80−7.88 (m, 4 H), 8.15 (s, 2 H); ^{13}C NMR ($CDCl_3$) δ 17.24 (q), 19.38 (q), 30.01 (t), 32.67 (d), 35.73 (t), 79.22 (d), 128.65 (d), 128.79 (d), 131.28 (d), 135.77 (s), 162.35 (d), 173.31 (s). Anal. Calcd for $C_{27}H_{36}N_4O_2$: C, 72.29; H, 8.09; N, 12.49. Found: C, 72.08; H, 8.16; N, 12.36.

26g was obtained from **25g** as an oil (54%). **26g**: R_f = 0.65 (hexane−EtOAc, 1:1); IR (neat) 3340, 1650, 1510, 1450, 755, 690 cm^{-1}; ^1H NMR($CDCl_3$) δ 0.88 (s, 6 H), 0.96 (d, 6 H, *J* = 6.9 Hz), 0.98 (d, 6 H, *J* = 6.9 Hz), 2.26−2.44 (m, 2 H), 3.09 (d, 4 H, *J* = 6.9 Hz), 3.64 (d, 2 H, *J* = 4.7 Hz), 7.36−7.44 (m, 8 H), 7.84−7.92 (m, 4 H), 8.17 (s, 2 H); ^{13}C NMR ($CDCl_3$) δ 17.64 (q), 19.42 (q), 23.35 (q), 32.68 (d), 36.31 (s), 45.40 (t), 79.60 (d), 128.74 (d), 131.19 (d), 135.85 (s), 162.14 (d), 173.49 (s). Anal. Calcd for $C_{29}H_{40}N_4O_2$: C, 73.07; H, 8.46; N, 11.75. Found: C, 72.94; H, 8.50; N, 11.61.

Reductive intramolecular coupling of bis(imino amides) 26 with zinc was carried out by the same method as described above. The products **5** were isolated by column chromatography on silica gel (hexane−EtOAc) or basic alumina (CH_2Cl_2/MeOH).

***meso*-5a**: mp 243 °C (recrystallized from EtOH); R_f = 0.45 (alumina, CH_2Cl_2−MeOH, 20:1); IR (KBr) 3300, 1640, 1530, 700 cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 2.60−3.00 (m, 6 H), 3.32−3.52 (m, 2 H), 3.64−3.82 (m, 2 H), 3.83 (s, 2 H), 6.84−6.94 (m, 4 H), 7.12−7.22 (m, 6 H), 7.90 (br s, 2H); ^{13}C NMR(Me_2SO-d_6) δ 37.00 (t), 51.87 (t), 68.35 (d), 126.82 (d), 127.40 (d), 128.29 (d), 140.15 (s), 172.60 (s). Anal. Calcd for $C_{20}H_{24}N_4O_2$: C, 68.16; H, 6.86; N, 15.90. Found: C, 68.26; H, 6.91; N, 15.74.

***dl*-5a** (could not be purified): R_f = 0.44 (alumina, CH_2Cl_2−MeOH, 20:1); ^1H NMR (Me_2SO-d_6) δ 2.70−3.02 (m, 4 H), 3.10−3.68 (m, 6 H), 4.04 (s, 2 H), 6.92−7.04 (m, 4 H), 7.04-7.16 (m, 6 H), 7.90 (br s, 2 H); ^{13}C NMR(Me_2SO-d_6) δ 37.13 (t), 50.11 (t), 63.45 (d), 126.65 (d), 127.33 (d), 128.86 (d), 140.46 (s), 172.67 (s).

***dl*- and *meso*-5b** (35:65 mixture): R_f = 0.5 (alumina, CH_2Cl_2−MeOH, 20:1); IR (KBr) 3300, 1630, 1520, 1450, 680 cm^{-1}; ^1H NMR ($CDCl_3$) (*dl*) δ 1.86−2.04 (m, 4 H), 3.16−3.32 (m, 2 H), 3.18 (d, 2 H, *J* = 17.4 Hz), 3.48 (d, 2 H, *J* = 17.4 Hz), 3.73 (s, 2 H), 3.84−4.00 (m, 2 H), 6.88−6.94 (m, 4 H), 7.06−7.18 (m, 6 H), 8.18 (br s, 2 H); (*meso*) δ 1.74−2.10 (m, 4 H), 3.06 (d, 2 H, *J* = 17.9 Hz), 3.14−3.30 (m, 2 H), 3.53 (d, 2 H, *J* = 17.9 Hz), 3.89 (s, 2 H), 3.84−4.00 (m, 2 H), 6.86−6.96 (m, 4 H), 7.22−7.32 (m, 6 H), 8.08 (br s, 2 H); ^{13}C NMR ($CDCl_3$) (*dl*) δ 27.94 (t), 39.41 (t), 52.09 (t), 71.10 (d), 127.39 (d), 127.55 (d), 128.45 (d), 140.95 (s), 171.96 (s); (*meso*) δ 28.56 (t), 39.45 (t), 50.51 (t), 67.18 (d), 128.04 (d), 128.36 (d), 138.44 (s), 171.70 (s). Anal. Calcd for $C_{21}H_{26}N_4O_2$: C, 68.83; H, 7.15; N, 15.29. Found: C, 68.70; H, 7.07; N, 15.02.

***dl*- and *meso*-5c** (40:60 mixture): R_f = 0.35 (alumina, CH_2Cl_2−MeOH, 20:1); IR (KBr) 3320, 1635, 1540, 1450, 700 cm^{-1}; ^1H NMR ($CDCl_3$) (*dl*) δ 2.00−2.50 (m, 6 H), 2.68−2.80 (m, 4 H), 3.34−3.50 (m, 2 H), 3.59 (s, 2 H), 3.64-3.80 (m, 2 H), 6.94−7.02 (m, 4 H), 7.08−7.20 (m, 6 H), 7.34 (br s, 2 H); (*meso*) δ 1.75 (br s, 2 H), 2.22−2.54 (m, 4 H), 2.76−2.96 (m, 4 H), 3.36−3.72 (m, 4 H), 4.00 (s, 2 H), 6.74−6.84 (m, 4 H), 7.16−7.24 (m, 6 H), 8.26−8.36 (br s, 2 H); ^{13}C NMR ($CDCl_3$) (*dl*) δ 36.89 (t), 38.93 (t), 43.31 (t), 69.00 (d), 127.48 (d), 127.81 (d), 128.35 (d), 140.00 (s), 173.37 (s); (*meso*) δ 36.20 (t), 38.90 (t), 43.04 (t), 66.15 (d), 127.60 (d), 127.96 (d), 128.46 (d), 138.47 (s), 173.34 (s). Anal. Calcd for $C_{22}H_{28}N_4O_2$: C, 69.45; H, 7.42; N, 14,72. Found: C, 69.45; H, 7.48; N, 14.56.

***dl*- and *meso*-5d** (63:37 mixture): R_f = 0.35 (alumina, CH_2Cl_2−MeOH, 20:1); IR (KBr) 3290, 1635, 1540, 705 cm^{-1}; ^1H NMR ($CDCl_3$) (*dl*) δ 1.80−1.96 (m, 2 H), 2.22−2.46 (m, 4 H), 2.58−2.76 (m, 4 H), 2.92 (br s, 2 H), 3.34−3.66 (m, 4 H), 3.62 (s, 2 H), 6.90−7.00 (m, 4 H), 7.04−7.16 (m, 6 H), 7.56 (t, 2 H, *J* = 5.5 Hz); (*meso*) δ 1.80−2.12 (m, 2 H), 2.22−2.58 (m, 6 H), 2.76−2.98 (m, 4 H), 3.40−3.60 (m, 4 H), 3.97 (s, 2 H), 6.76−6.86 (m, 4 H), 7.20−7.28 (m, 6 H), 8.08 (br s, 2 H); ^{13}C NMR

($CDCl_3$) (*dl*) δ 26.67 (t), 36.40 (t), 43.33 (t), 69.10 (d), 127.23 (d), 127.75 (d), 128.17 (d), 140.37 (s), 173.67 (s); (*meso*) δ 27.58 (t), 36.94 (t), 66.77 (d), 43.23 (t), 127.37 (d), 127.77 (d), 127.96 (d), 138.44 (s), 173.28 (s). Anal. Calcd for $C_{23}H_{30}N_4O_2$: C, 70.02; H, 7.66; N, 14.20. Found: C, 69.89; H, 7.53; N, 14.07.

***(R,R)*- and *(R,S)*-5e** (45:55 mixture): R_f = 0.35 (silica gel, hexane–EtOAc, 1:5); IR (KBr) 3320, 1660, 1645, 1540, 705 cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 0.54–0.92 (m), 1.60–1.94 (m), 2.10–2.56 (m), 2.74–2.90 (m), 3.10–3.50 (m), 3.62-4.10 (m), 6.64–6.72 (m), 6.84–6.92 (m), 7.04–7.24 (m), 7.31 (br s), 8.05 (br s); ^{13}C NMR (Me_2SO-d_6); δ 18.98 (q), 19.12 (q), 19.33 (q), 19.96 (q), 24.87 (d), 30.10 (d), 30.58 (d), 37.36 (t), 38.68 (t), 60.13 (d), 60.97 (d), 63.99 (d), 66.21 (d), 66.83 (d), 68.97 (d), 126.24 (d), 126.42 (d), 126.67 (d), 127.08 (d), 127.22 (d), 127.36 (d), 127.77 (d), 127.88 (d), 128.23 (d), 140.29 (s), 140.98 (s), 142.07 (s), 173.64 (s), 174.24 (s), 175.00 (s). Anal. Calcd for $C_{26}H_{36}N_4O_2$: C, 71.53; H, 8.31; N, 12.83. Found: C, 71.58; H, 8.36; N, 12.65.

***(R,R)*-5f**: mp 179 °C (recrystallized from hexane–EtOAc); R_f = 0.25 (silica gel, hexane–EtOAc, 1:5); $[\alpha]^{20}_D$ −127 (*c* 1.00, $CHCl_3$); IR (KBr) 3320, 1660, 1520, 1470, 735, 710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.75 (d, 6 H, *J* = 6.9 Hz), 0.86 (d, 6 H, *J* = 7.0 Hz), 1.64–1.70 (br s, 2 H), 1.88–1.98 (m, 2 H), 2.02–2.18 (m, 2 H), 3.07 (d, 2 H, *J* = 4.3 Hz), 3.16–3.30 (m, 2 H), 3.74 (s, 2 H), 3.86–4.00 (m, 2 H), 6.86–6.92 (m, 4 H), 7.06–7.14 (m, 6 H), 7.99 (br s, 2 H); ^{13}C NMR ($CDCl_3$) δ 16.91 (q), 19.37 (q), 28.26 (t), 31.07 (d), 39.23 (t), 67.57 (d), 70.23 (d), 127.34 (d), 127.56 (d), 128.17 (d), 140.44 (s), 173.96 (s). Anal. Calcd for $C_{27}H_{38}N_4O_2$: C, 71.97; H, 8.50; N,12.43. Found: C, 71.70; H, 8.33; N, 12.44.

***(R,S)*-5f**: mp 182 °C (recrystallized from hexane–EtOAc); R_f = 0.35 (silica gel, hexane-EtOAc, 1:5); $[\alpha]^{20}_D$ −135 (*c* 1.22, $CHCl_3$); IR (KBr) 3320, 1635, 1525, 1450, 705 cm^{-1}; ^1H NMR ($CDCl_3$) 0.72–0.94 (m, 12 H), 1.60–1.78 (br s, 2 H), 1.82–2.20 (m, 4 H), 2.98 (d, 1 H, *J* = 5.4 Hz), 3.24 (d, 1 H, *J* = 4.8 Hz), 3.20–3.40 (m, 2 H), 3.66–4.00 (m, 2 H), 3.88 (d, 1 H, *J* = 2.5 Hz), 4.18 (d, 1 H, *J* = 2.5 Hz), 6.70–6.76 (m, 2 H), 6.92–6.98 (m, 2 H), 7.16–7.30 (m, 6 H), 7.43 (brs, 1 H), 7.93 (br s, 1 H); ^{13}C NMR ($CDCl_3$) δ 17.71 (q), 17.78 (q), 19.13 (q), 19.48 (q), 28.91 (t), 29.79 (d), 31.69 (d), 39.07 (t), 39.33 (t), 63.82 (d), 65.68 (d), 70.45 (d), 70.79 (d), 127.38 (d), 127.69 (d), 127.99 (d), 128.21 (d), 128.94 (d), 137.85 (s), 140.62 (s), 174.01 (s), 174.91 (s). Anal. Calcd for $C_{27}H_{38}N_4O_2$: C, 71.97; H, 8.50; N,12.43. Found: C, 71.75; H, 8.72; N, 12.26.

***(R,R)*-5g**: mp 176 °C (recrystallized from hexane–toluene); R_f = 0.55 (silica gel, hexane–EtOAc, 1:2); $[\alpha]^{20}_D$ −104 (*c* 1.05, $CHCl_3$); IR (KBr) 3305, 1640, 1500, 1455, 690 cm^{-1}; ^1H NMR ($CDCl_3$) 0.75 (d, 6 H, *J* = 6.9 Hz), 0.86 (d, 6 H, *J* = 7.0 Hz), 1.13 (s, 6 H), 1.58–1.80 (br s, 2 H), 2.00–2.20 (m, 2 H), 2.82 (dd, 2 H, *J* = 2.5, 13.8 Hz), 3.12 (d, 2 H, *J* = 4.4 Hz), 3.75 (s, 2 H), 3.85 (dd, 2 H, *J* = 10.3, 13.8 Hz), 6.86–6.94 (m, 4 H), 7.02–7.10 (m, 6 H), 8.07 (br s, 2 H); ^{13}C NMR ($CDCl_3$) δ 17.08 (q), 19.42 (q), 24.04 (q), 31.29 (d), 34.82 (s), 49.19 (t), 67.97 (d), 70.75 (d), 127.41 (d), 127.63 (d), 128.29 (d), 141.05 (s), 174.00 (s). Anal. Calcd for $C_{29}H_{42}N_4O_2$: C, 72.77; H, 8.84; N, 11.70. Found: C, 72.70; H, 8.75; N, 11.53.

***(R,S)*-5g**: mp 217 °C (recrystallized from hexane–EtOAc); R_f = 0.72 (silica gel, hexane–EtOAc, 1:2); $[\alpha]^{20}_D$ −126 (*c* 1.25, $CHCl_3$); IR (KBr) 3340, 1640, 1525, 1460, 705 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.68–0.90 (m, 12 H), 1.05 (s, 3 H), 1.06 (s, 3 H), 1.72–2.28 (m, 4 H), 2.94–3.14 (m, 2 H), 3.20–3.34 (m, 2 H), 3.38–3.54 (m, 2 H), 3.86 (d, 1 H, *J* = 2.4 Hz), 4.26 (d, 1 H, *J* = 2.4 Hz), 6.74–6.82 (m, 2 H), 6.96–7.06 (m, 2 H), 7.14–7.30 (m, 6 H), 7.39 (br s, 1 H), 8.19 (br s, 1 H); ^{13}C NMR ($CDCl_3$) δ 17.49 (q), 17.75 (q), 19.17 (q), 19.42 (q), 23.85 (q), 24.63 (q), 29.83 (d), 32.20 (d), 34.86 (s), 49.59 (t), 63.01 (d), 65.93 (d), 70.38 (d), 70.85 (d), 127.19 (d), 127.30 (d), 127.74 (d), 128.07 (d), 129.01 (d), 137.41 (s), 141.03 (s), 174.18 (s), 175.16 (s). Anal. Calcd for $C_{29}H_{42}N_4O_2$: C, 72.77; H, 8.84; N,11.70. Found: C, 72.57; H, 9.13; N, 11.60.

Reduction of 5 to 27. A 1 M BH_3/THF solution (1.2 mL, 1.2 mmol) was added dropwise to a cooled (0 °C) solution of **5** (0.11 mmol) in THF (15 mL). After addition was complete, the solution was allowed to warm to room temperature for 1 h followed by heating to reflux for an additional 18 h. The resulting reaction was quenched by dropwise addition of H_2O (1 mL). The solvent was removed *in vacuo*, and 6 M HCl (10 mL) was added to the residue and heated to reflux for 1 h. After cooling, 2 M NaOH (30 mL) was added, and the solution was extracted with CH_2Cl_2. The organic layers were combined, dried ($MgSO_4$), filtered, and concentrated. The macrocyclic tetraamine **27** was isolated by column chromatography on basic alumina (activity II, CH_2Cl_2–MeOH).

***meso*-27a**: R_f = 0.4 (CH_2Cl_2–MeOH, 20:1); IR (neat) 3280, 1460, 735, 705 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.40 (br s, 4 H), 2.79 (s, 12 H), 4.03 (s, 2 H), 6.82–6.88 (m, 4 H), 7.10–7.18 (m, 6 H); ^{13}C NMR ($CDCl_3$) δ 44.83 (t), 46.01 (t), 46.10 (t), 63.51 (d), 126.79 (d), 127.70 (d), 128.00 (d), 140.44 (s). Anal. Calcd for $C_{20}H_{28}N_4$: C, 74.03; H, 8.70. Found: C, 74.12; H, 8.79.

***meso*-27b**: R_f = 0.45 (CH_2Cl_2–MeOH, 20:1); IR (neat) 3280, 1450, 1115, 730, 695 cm^{-1}; ^1H NMR($CDCl_3$) δ 1.60–1.90 (m, 2 H), 2.46 (br s, 4 H), 2.64–3.03 (m, 12 H), 3.97 (s, 2 H), 6.80-6.90 (m, 4 H), 7.10–7.20 (m, 6 H); ^{13}C NMR ($CDCl_3$) δ 28.89 (t), 46.29 (t), 49.12 (t), 50.81 (t), 65.58 (d), 126.71 (d), 127.63 (d), 128.13 (d), 140.58 (s). Anal. Calcd for $C_{21}H_{30}N_4$: C, 74.52; H, 8.93. Found: C, 74.62; H, 8.95.

***dl*-27c**: mp 192 °C; R_f = 0.2 (CH_2Cl_2–MeOH, 20:1); IR (KBr) 3220, 1460, 1110, 950, 780, 695 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.56–1.78 (m, 4 H), 2.38–3.10 (m, 16 H), 3.57 (s, 2 H), 6.90–7.02 (m, 4 H), 7.02–7.14 (m, 6 H); ^{13}C NMR ($CDCl_3$) δ 29.32 (t), 49.24 (t), 49,81 (t), 51.45 (t), 70.30 (d), 126.57 (d), 127.67 (d), 127.84 (d), 141.39 (s). Anal. Calcd for $C_{22}H_{32}N_4$: C, 74.96; H, 9.15. Found: C, 75.03; H, 9.18.

***meso*-27c**: mp 150–152 °C; R_f = 0.3 (CH_2Cl_2–MeOH, 20:1); IR (KBr) 3400, 3310, 3275, 3185, 1601, 865, 775, 745, 695 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.58–1.82 (m, 4 H), 2.48–2.94 (m, 16 H), 3.96 (s, 2 H), 6.70–6.82 (m, 4 H), 7.12–7.28 (m, 6 H); ^{13}C NMR ($CDCl_3$) δ 29.03 (t), 48.08 (t), 49.88 (t), 51.19 (t), 67.87 (d), 126.58 (d), 127.59 (d), 127.93 (d), 139.32 (s). Anal. Calcd for $C_{22}H_{32}N_4$: C, 74.96; H, 9.15. Found: C, 75.12; H, 9.21.

***dl*- and *meso*-27d**: R_f = 0.35 (CH_2Cl_2–MeOH, 20:1); IR (neat) 3280, 1450, 1120, 755, 730, 695 cm^{-1}; ^1H NMR ($CDCl_3$) (*dl*) δ 1.50–1.88 (m, 6 H), 2.34–2.90 (m, 16 H), 3.60 (s, 2 H), 7.00–7.16 (m, 10 H), (*meso*) δ 1.58–1.90 (m, 6 H), 2.34–2.90 (m, 16 H), 3.93 (s, 2 H), 6.78–6.86 (m, 4 H), 7.12–7.22 (m, 6 H); ^{13}C NMR ($CDCl_3$) δ 28.70 (t), 29.68 (t), 47.89 (t), 48.61 (t), 50.47 (t), 51.22 (t), 52.02 (t), 68.03 (d), 69.83 (d), 126.61 (d), 127.55 (d), 127.81 (d), 128.10 (d), 140.11 (s), 141.99 (s). Anal. Calcd for $C_{23}H_{34}N_4$: C, 75.37; H, 9.35. Found: C, 75.43; H, 9.36.

***(R,R)*-27f**: R_f = 0.45 (alumina, CH_2Cl_2–MeOH = 20:1); $[\alpha]^{20}_D$ +12 (*c* 1.3, $CHCl_3$); IR (neat) 3300, 2980, 1470, 1125, 920, 770, 740, 710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.46 (d, 6 H, *J* = 6.7 Hz), 0.70 (d, 6 H, *J* = 7.0 Hz), 1.40–1.60 (m, 2 H), 1.68–1.80 (m, 2 H), 2.30–3.00 (m, 14 H), 3.42 (s, 2 H), 6.88–7.02 (m, 10 H); ^{13}C NMR ($CDCl_3$) δ 15.45 (q), 19.79 (q), 28.43 (t), 28.74 (d), 48.87 (t), 51.30 (t), 65.21 (d), 70.81 (d), 125.10 (d), 127.52 (d), 127.96 (d), 144.30 (s). Anal. Calcd for $C_{27}H_{42}N_4$: C, 76.72; H, 10.02; N,13.26. Found: C, 76.86; H, 10.09; N, 13.04.

Supplementary Material Available: ^1H NMR spectra of **14b** and PhCH=NMe·MsOH in the presence of DME, ^1H NMR spectra of **23** (*n* = 3) and PhCH=NMe·MsOH in the presence of methyl acetate, and ^{13}C NMR spectra of *trans*-**3b** and *trans*-**3c** in the presence of $Zn(OTf)_2$ (7 pages). This material is contained in 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.

JO950190+