Macrocyclic Amides Consisting of Helical Chiral 1,12-Dimethylbenzo[*c*]phenanthrene-5,8-dicarboxylate

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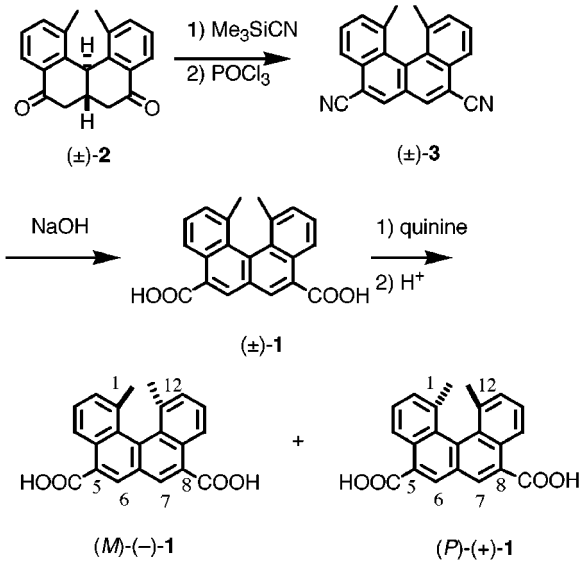
Helical chiral 1,12-dimethylbenzo[*c*]phenanthrene-5,8-dicarboxylic acid was synthesized and resolved in multigram quantities. The absolute configuration was determined by X-ray analysis of the bis(camphorsultamamide) derivative. A series of optically active macrocyclic amides consisting of the chiral unit and a dianiline spacer were synthesized by one-pot procedures, and their structures were compared by spectroscopy and X-ray crystallography. One of the cycloamides exhibited catalytic activity in the asymmetric addition of diethylzinc to aromatic aldehydes. *N*-Alkylated derivatives were also synthesized, which possessed folded structures distinct from those of the parent cyclic amides.

The chirality of helicenes has long been known in the field of organic chemistry.[1] Although the chirality due to the helical π-electron system is expected to exhibit interesting properties, its behavior is not well-understood compared to tetrahedral chirality and axis chirality.[2,3] This is largely due to the unavailability of such compounds. Although a variety of optically active helicenes have been synthesized, generally the methods were not suitable for large scale preparation. An exception is the work of Katz, who developed the Diels−Alder method for the synthesis of helicenes.[4] 1,12-Dimethylbenzo[*c*]phenanthrene, first synthesized and resolved by Newman,[5] is a configurationally stable helicene with a minimal number of benzene rings. We developed a preparative method for optically pure 1,12-dimethylbenzo[*c*]phenanthrene-5,8-dicarboxylic acid (**1**) in multigram quantities.[6,7] The synthesis, structure, and properties of a series of macrocyclic amides containing the C_2-symmetric chiral unit is described here.

Synthesis of racemic 1,12-dimethylbenzo[*c*]phenanthrene-5,8-dicarboxylic acid (±)-**1** started from a known

Scheme 1



diketone (±)-**2** prepared by Newman (Scheme 1).[5] Compound **2** itself possessed molecular chirality as indicated by chiral HPLC analysis: The enantiomers were separable by Daicel Chiralcel OD. Although we previously assigned cis stereochemistry to **2** based on the results of molecular modeling,[6] recently a trans configuration was determined by X-ray analysis.[8] The diketone (±)-**2** was converted to 1,12-dimethylbenzo[*c*]phenanthrene-5,8-dinitrile, (±)-**3**, by cyanation[9] and dehydration with concomitant dehydrogenation. Then, (±)-**3** was hydrolyzed to dicarboxylic acid (±)-**1** in 58% yield from (±)-**2**. Optical resolution was examined by forming diastereomeric salts with 2 equiv of amines such as cinchonidine, cinchonine, brucine, and quinine. It was found that recrystallization of the quinine salt from chloroform−methanol gave one diastereomer, which was converted to (+)-**1** on acidification. The mother liquid was concentrated, and the residue was washed with hot methanol. Acidification gave the antipode (−)-**1**. The optical puri-

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(1) Reviews: Martin, R. H. *Angew. Chem., Int. Ed. Engl.* **1974**, *13*, 649. Osuga, H.; Suzuki, H. *J. Synth. Org. Chem., Jpn.* **1994**, *52*, 1020. For some recent examples: Nakazaki, M.; Yamamoto, K.; Maeda, M. *J. Org. Chem.* **1981**, *46*, 1985. Sudhakar, A.; Katz, T. J. *J. Am. Chem. Soc.* **1986**, *108*, 179. Pereira, D. E.; Neelima, Leonard, N. J. *Tetrahedron* **1990**, *46*, 5895. Osuga, H.; Suzuki, H.; Tanaka, K. *Bull. Chem. Soc. Jpn.* **1997**, *70*, 891. Also see references therein.

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(3) Hassine, B. B.; Gorsane, M.; Pecher, J.; Martin, R. H. *Bull. Soc. Chim. Belg.* **1985**, *94*, 597. Hassine, B. B.; Gorsane, M.; Geerts-Evrard, F.; Pecher, J.; Martin, R. H.; Castelet, D. *Bull. Soc. Chim. Belg.* **1986**, *95*, 557.

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(5) Newman, M. S.; Wolf, M. *J. Am. Chem. Soc.* **1952**, *74*, 3225. Newman, M. S.; Wise, R. M. *J. Am. Chem. Soc.* **1956**, *78*, 450.

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(7) Chemistry of optically active hexahelicene-7, 7′-dicarboxylate. Balan, A.; Gottlieb, H. E. *J. Chem. Soc., Perkin Trans. I* **1981**, 350. Kim, Y. H.; Balan, A.; Tishbee, A.; Gil-Av, E. *J. Chem. Soc., Chem. Commun.* **1982**, 1336.

(8) Cheung, J.; Field, L. D.; Hambley, T. W.; Sternhell, S. *J. Org. Chem.* **1997**, *62*, 62.

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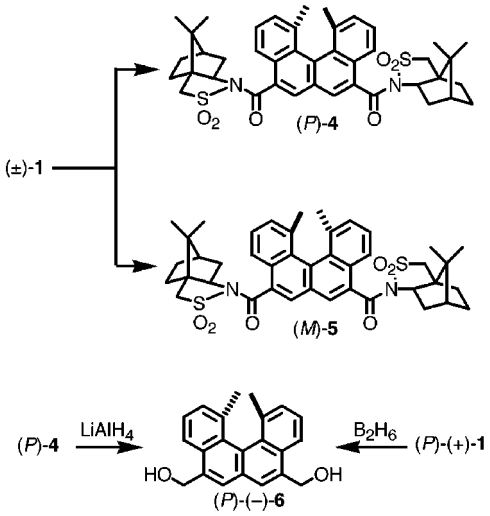
Scheme 2



ties of **1** were determined to be more than 98% by chiral HPLC (Daicel Chiralcel OD) analysis of the dimethyl esters. These procedures provided (−)-**1** and (+)-**1** in multigram quantities.

To determine the absolute configuration, (±)-**1** was treated with *d*-(−)-camphorsultam[10] giving **4** and **5** (Scheme 2), which were separated by silica gel chromatography. X-ray crystallographic analysis of **4**, a chromatographically polar diastereomer, revealed (*P*)-configuration at the helicene moiety (Figure 1). The helical structure of the benzo[*c*]phenanthrene moiety is indicated by the dihedral angles between the condensed benzene rings: 161°, 163°, and 168° for the AB (angle C(1)−C(12c)−C(4a)−C(5)), BC (angle C(12c)−C(12b)−C(6a)−C(7)), and CD rings (angle C(12b)−C(12a)−C(8a)−C(9)), respectively. The chiral auxiliary of (*P*)-**4** was removed by reduction with lithium aluminum hydride giving diol (*P*)-**6**, to which (+)-**1** was correlated by borane reduction. Here, the absolute configuration, (+)-(*P*)-**1** and (−)-(*M*)-**1**, was determined unambiguously. The circular dichroism (CD) and UV spectra of the dimethyl ester of (*P*)-**1** are shown in Figure 2. It was recently found that the helical chirality of **1** could be recognized by polysaccharides such as cyclodextrins in water.[11]

The diacid **1** can be envisaged as a chiral derivative of 1,3-benzenedicarboxylate or 2,7-naphthalenedicarboxylate (Figure 3). Since such partial structures are included in many organic compounds, we investigated the substitution of the aromatic moiety with **1**, which converts achiral aromatic compounds to chiral compounds. Hunter and Vögtle prepared cyclic amides containing catenanes by the condensation of 1,3-benzenedicarboxylic acid with dianiline spacer **7**.[12] Substitution of the dicarboxylate

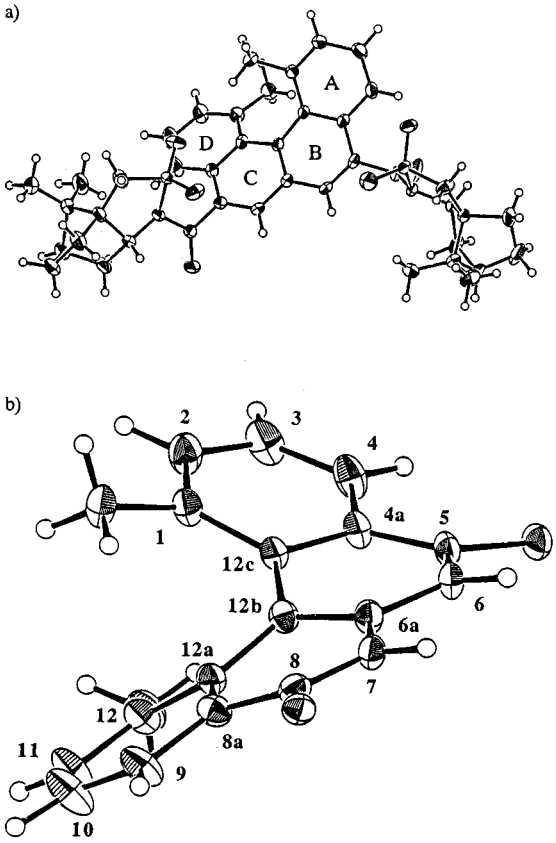


Figure 1. ORTEP drawings of (*P*)-**4** (a) and the partial structure of the benzo[*c*]phenanthrene moiety (b).

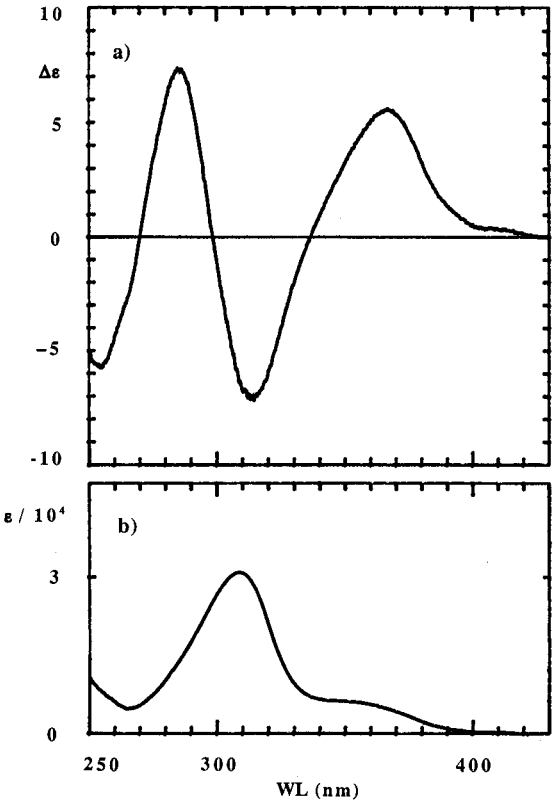


Figure 2. CD and UV spectra of (*P*)-**1** dimethyl ester in $CHCl_3$ at the concentration of 3.3×10^{-2} mM.

moiety with **1** was expected to give optically active versions of the compounds. The synthesis and spectro-

(10) Harada, N.; Soutome, T.; Nehira, T.; Uda, H.; Oi, S.; Okamura, A.; Miyano, S. *J. Am. Chem. Soc.* **1993**, *115*, 7547. Harada, N.; Soutome, T.; Murai, S.; Uda, H. *Tetrahedron: Asymmetry* **1993**, *4*, 1755.

(11) Kano, K.; Negi, S.; Takaoka, R.; Kamo, H.; Kitae, T.; Yamaguchi, M.; Okubo, H.; Hirama, M. *Chem. Lett.* **1997**, 715. Kano, K.; Negi, S.; Kamo, H.; Kitae, T.; Yamaguchi, M.; Okubo, H.; Hirama, M. *Chem. Lett.* **1998**, 151.

(12) Hunter, C. A. *J. Am. Chem. Soc.* **1992**, *114*, 5303. Adams, H.; Carver, F. J.; Hunter, C. A. *J. Chem. Soc., Chem. Commun.* **1995**, 809. Vögtle, F.; Meier, S.; Hoss, R. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 1619. Ottens-Hildebrandt, S.; Nieger, M.; Rissannen, K.; Rouvinen, J.; Meier, S.; Harder, G.; Vögtle, F. *J. Chem. Soc., Chem. Commun.* **1995**, 777. Jäger, R.; Vögtle, F. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 930.

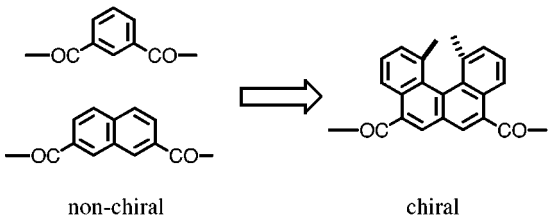
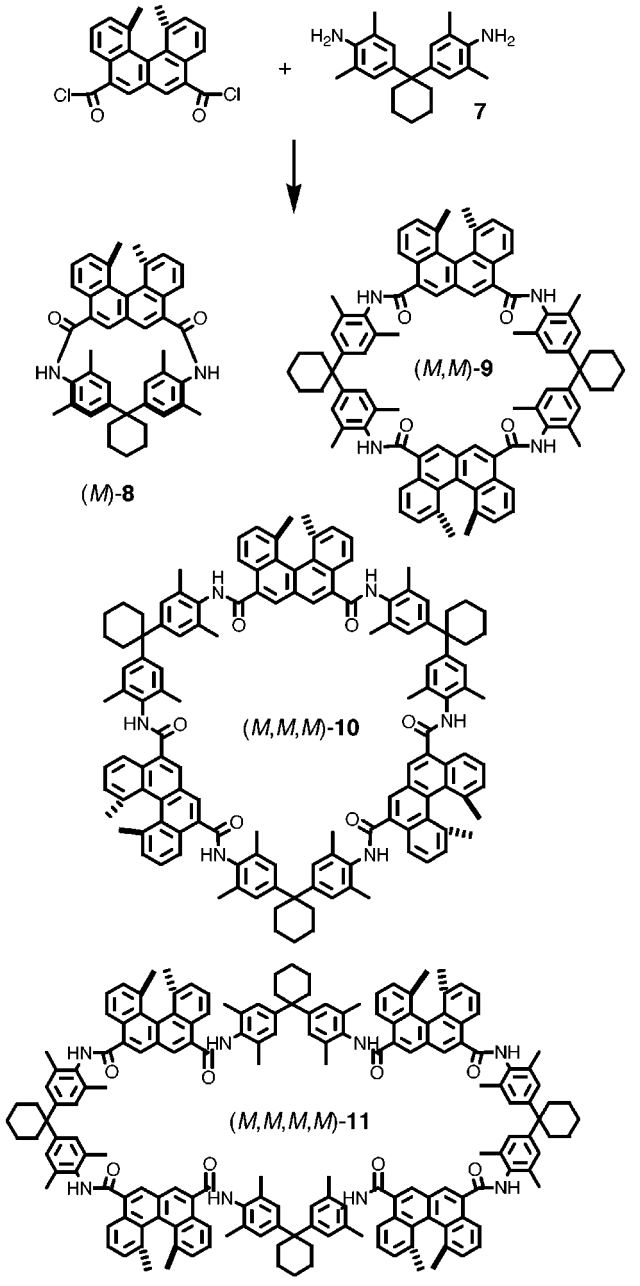


Figure 3. 1,12-Dimethylbenzo[*c*]phenanthrene as chiral *m*-phenylene and 2,7-naphthylene unit.

Scheme 3



scopic properties of the optically active macrocyclic amides are described below.

(*M*)-**1** was converted to diacid chloride by treatment with refluxing thionyl chloride, which was then reacted with an equimolar amount of **7** in 1% pyridine−methylene chloride at room temperature for 1 day under highly diluted conditions (3 mM) (Scheme 3). Oligomers were separated by preparative recycling gel permeation chromatography (GPC) to give [2+2]cycloamide (*M,M*)-**9**, [3+3]cycloamide (*M,M,M*)-**10**, and [4+4]cycloamide (*M,M,M,M*)-**11** in 24%, 23%, and 19% yields, respectively. Using (*P*)-**1** in place of (*M*)-**1**, the enantiomeric macrocyclic amides (*P,P*)-**9**, (*P,P,P*)-**10**, and (*P,P,P,P*)-**11** were synthesized. Here, we define, for example, [3+3]cycloamide as a macrocyclic amide consisting of three molecules of **1** and three molecules of **7**. The GPC method was effective for the separation of these compounds. This method has the additional advantage of allowing the molecular size to be estimated from the retention time. The combined yield of the three macrocyclic amides exceeded 60%. However, no catenane could be isolated. As Hunter and Vögtle pointed out, hydrogen bonding between the 1,3-benzenedicarbamoyl moiety and carbonyl oxygen of the acid chloride might be essential for catenane formation.[12] In the present case, the two carbonyl groups of **1** were separated by two benzene rings, which might have prevented such interactions.

In regard to the base, use of 1% pyridine in methylene chloride was essential for effective cyclization. Et_3N gave an intractable mixture. Hindered base *i*-Pr_2NEt gave better results than Et_3N, although the yield was still lower than with pyridine. The concentration of the base was also critical, and no reaction took place in 10% pyridine or in pyridine solvent. Since addition of methanol to these mixtures gave the methyl ester of (*M*)-**1** in quantitative yields, it was concluded that excess pyridine inhibited amide formation. In the presence of pyridine and not Et_3N or *i*-Pr_2NEt, ^1H NMR absorption of the amide proton of (*M,M,M*)-**10** shifted downfield in $CDCl_3$. Such interactions might be the origin of the above pyridine effect. Notably, 4,4′-bipyridine considerably changed the chemical shifts of (*M,M,M*)-**10** in $CDCl_3$. The complexation phenomena, however, appeared to be rather complex, and the association constant could not be obtained by assuming a 1:1 complex.

The cyclic structures of the three macrocyclic amides **9**, **10**, and **11** were confirmed from the simple NMR spectra. All the three compounds exhibited four benzo[*c*]phenanthrene aromatic protons and one aniline aromatic proton. The molecular compositions of the cycloamides were determined by FAB-MS and/or by vapor pressure osmometry (VPO) at 5 mM, where the aggregation was not significant (vide infra). ^1H NMR ($CDCl_3$) chemical shifts of the amide protons of (*M,M,M*)-**10** and (*M,M,M,M*)-**11** occurred downfield as the concentration increased (Figure 4). In contrast, 4-H and 6-H of benzo[*c*]phenanthrene shifted upfield. Since no concentration dependence was observed in DMSO-d_6, aggregation via hydrogen bonding probably took place in the nonpolar solvent. Binding constants of approximately 30 and 10 were obtained for (*M,M,M*)-**10** and (*M,M,M,M*)-**11**, respectively.[13] In contrast, the ^1H NMR ($CDCl_3$) spectra of (*M,M*)-**9** showed very slight concentration dependence. The same trends were observed by IR spectroscopy.[14] While (*M,M,M*)-**10** and (*M,M,M,M*)-**11** exhibited hydrogen bonded NH at approximately 3300 cm^{-1} at the concentration of ca. 10 mM, this absorption was very weak with (*M,M*)-**9**. The UV spectra of the three cycloamides (*P,P*)-**9**, (*P,P,P*)-**10**, and (*P,P,P,P*)-**11** were very similar except for the level of absorbance (Figure 5). The

(13) Horman, I.; Dreux, B. *Helv. Chim. Acta* **1984**, *67*, 754.
(14) Bellamy, L. J. *The Infra-red Spectra of Complex Molecules*; Chapman and Hall: London, 1975; Chapter 12, p 231.

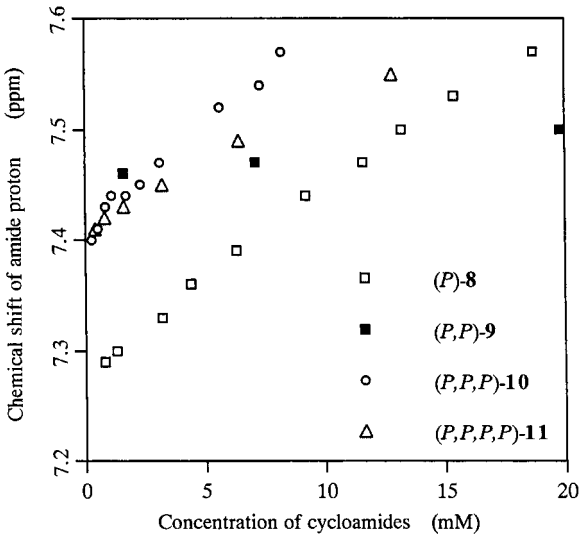


Figure 4. Concentration dependence of amide proton chemical shifts by ^{1}H NMR in $CDCl_3$.

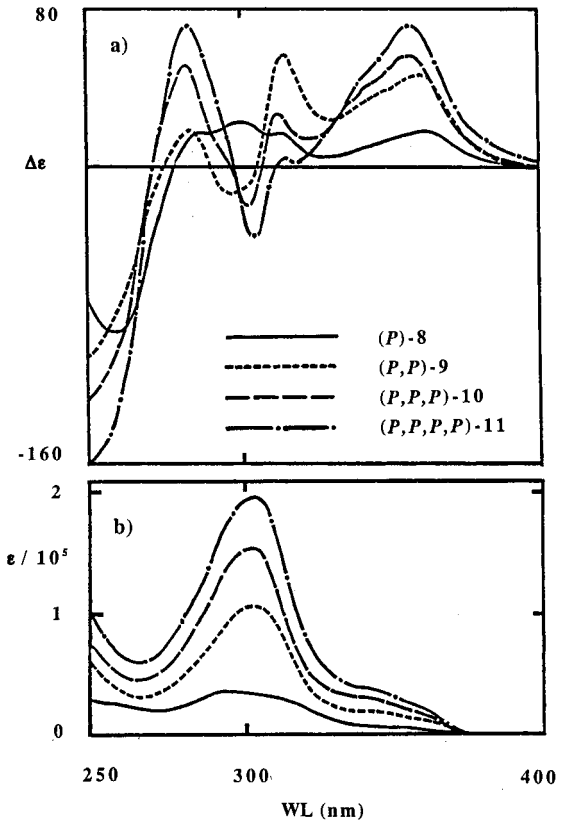


Figure 5. CD and UV spectra of (*P*)-**8**, (*P*,*P*)-**9**, (*P*,*P*,*P*)-**10**, and (*P*,*P*,*P*,*P*)-**11** in $CHCl_3$ at the concentration of 1.4×10^{-2}, 1.1×10^{-2}, 8.5×10^{-3}, and 4.5×10^{-3} mM.

positive Cotton effect of the cycloamides observed by CD at 280 and 360 nm was ascribed to the helicene structure (cf. Figure 2). The Cotton effect at 310 nm was characteristic of (*P*,*P*)-**9** and decreased as the ring size increased.

When (*M*)-**1** was reacted with **7** in refluxing $ClCH_2$-CH_2Cl (1 mM) in the presence of Et_3N, [1+1]cycloamide (*M*)-(+)-**8** and (*M*,*M*)-(−)-**9** were obtained in 29% and 16% yield, respectively (Scheme 3). A higher reaction temperature gave macrocyclic amides of smaller ring sizes. The amide (*M*)-**8** also aggregated as indicated by the

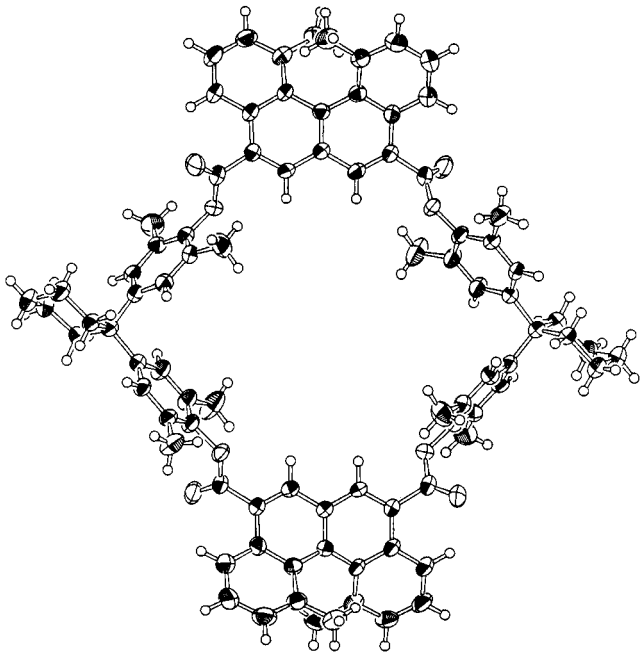


Figure 6. ORTEP drawings of (*P*,*P*)-**9**.

concentration dependence in ^{1}H NMR (Figure 4). A binding constant of approximately 10 was obtained.[13] The ^{1}H NMR spectra of (*M*)-**8** differed considerably from those of other cycloamides: two sets of aromatic protons (δ 6.02 and 6.51) and methyl protons (δ 1.92 and 2.06) appeared at aniline moiety and did not coalesce up to 80 °C. Rotation of the aniline ring was restricted, and the activation energy was estimated to be more than 17 kcal/mol. The amide carbonyl appeared at 1651 cm^{-1} on IR ($CHCl_3$), while higher homologues absorbed at ca. 1670 cm^{-1}. The absorption of free N−H at 3374 cm^{-1} also differed from the absorption of higher cycloamides at ca. 3414 cm^{-1}. These observations may be ascribed to the *s-cis* structure of the secondary amide moiety. The CD spectra of **8** also differed considerably from those of other cycloamides (Figure 5).

Racemates (±)-**8**, (±)-**9**, (±)-**10**, and (±)-**11** were prepared by mixing equal amounts of the enantiomers. ^{1}H NMR ($CDCl_3$) spectra of the optically active and racemic macrocyclic amides were identical at the same concentrations. This suggested the presence of certain chiral recognition in the aggregation of cycloamides: for example, the self-aggregation of (*P*)-**8** probably is stronger than the aggregation between (*P*)-**8** and (*M*)-**8**.

The structure of (*P*,*P*)-**9** was confirmed by X-ray analysis. It contained 10 ethanol molecules per (*P*,*P*)-**9** molecule (Figure 6). (*P*,*P*)-**9** displays a highly symmetrical "planar and open" structure which is consistent with the simple ^{1}H NMR spectra. The diameter of the cavity was estimated to be 0.6 nm. The entire amide moiety possesses an *s-trans* structure, and the aniline ring stands perpendicular to the amide plane. It may be reasonably assumed that **10** and **11** possess related planar structures with larger cavities.

N-Alkyl derivatives of macrocyclic amides were synthesized (Scheme 4). (*P*)-Cycloamides were treated with sodium hydride in THF followed by treatment with excess methyl iodide or benzyl bromide at room temperature, and *N*-methylated or *N*-benzylated products were ob-

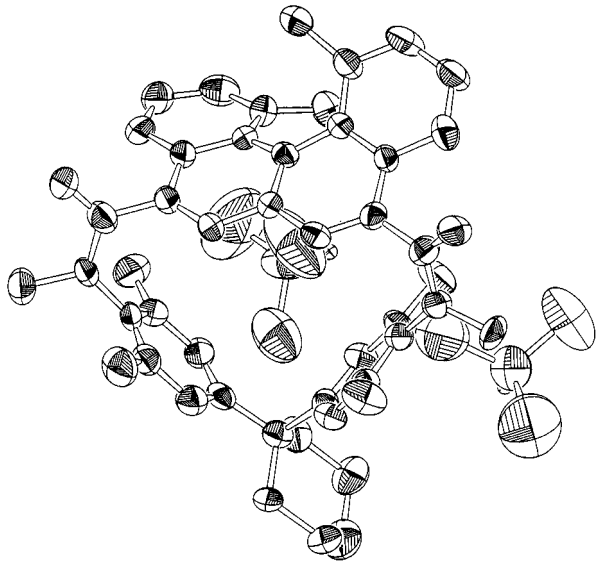
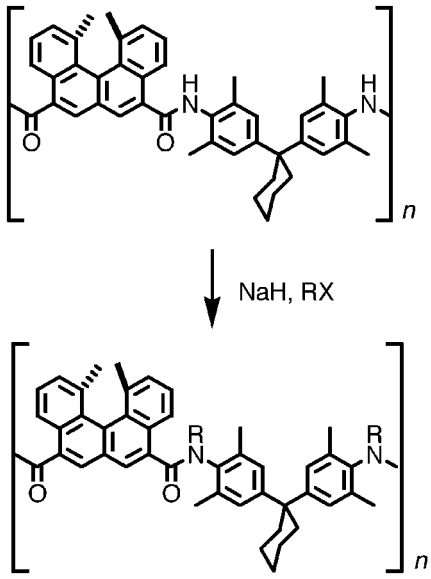


Figure 7. ORTEP drawings of (*P*)-*N*,*N*′-dimethyl[1+1]cycloamide. Protons were omitted for clarity.

Scheme 4



n = 1, 2, 3, 4

	n = 1	2	3	4
R = Me	100%	73%	87%	82%
R = CH_2Ph	100%	62%		

tained in good yields. As many as eight reaction sites of (*P*,*P*,*P*,*P*)-**11** were effectively methylated by this method.

The ^{1}H NMR spectrum of (*P*)-*N*,*N*′-dimethyl[1+1]-cycloamide was similar to that of (*P*)-**8** except for the presence of *N*-methyl protons in the former, indicative of the similar conformation of the both compounds. X-ray analysis of (*P*)-*N*,*N*′-dimethyl[1+1]cycloamide was conducted (Figure 7). The crystal contained two chloroform molecules per cycloamide molecule. Both amides were fixed in a *s-cis* conformation. Restricted rotation of the aniline ring was apparent from the structure.

The ^{1}H NMR ($CDCl_3$) spectra of (*P*,*P*)-*N*,*N*′,*N*″,*N*‴-tetrabenzyl[2+2]cycloamide (Figure 8b) was considerably complicated compared to those of (*P*,*P*)-**9** (Figure 8a). The

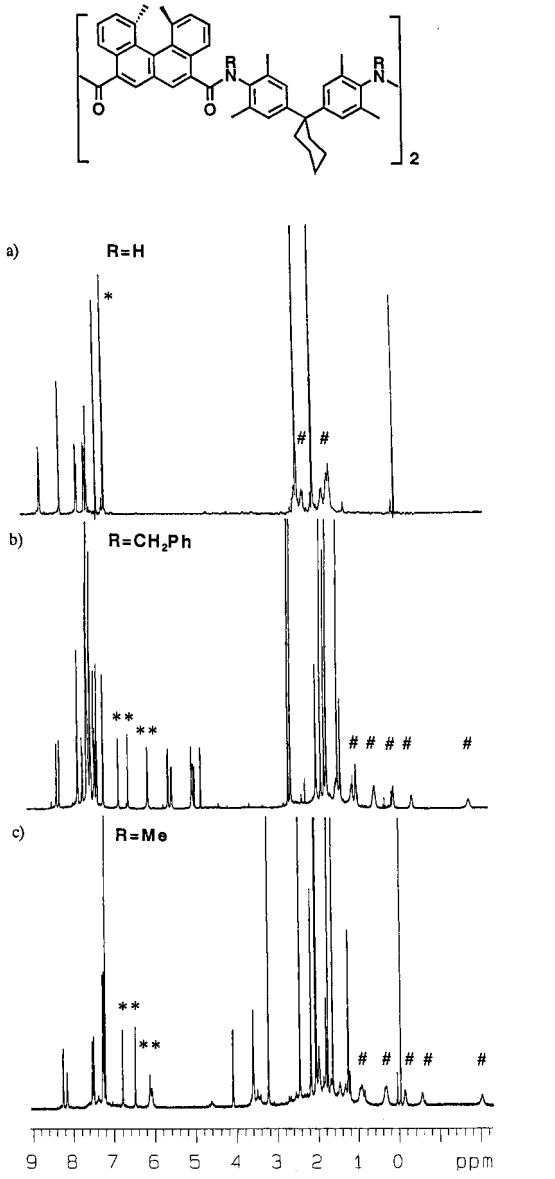


Figure 8. ^{1}H NMR ($CDCl_3$) spectra of (*P*,*P*)-[2+2]cycloamide (a), (*P*,*P*)-*N*,*N*′,*N*″,*N*‴-tetrabenzyl[2+2]cycloamide (b), and (*P*,*P*)-*N*,*N*′,*N*″,*N*‴-tetramethyl[2+2]cycloamide (c) at 6 mM. Aniline protons are shown by * and cyclohexyl protons by #.

presence of four aniline methyl proton peaks, two benzo[*c*]phenanthrene methyl proton peaks, and four aniline ring proton peaks (indicated by *) of tetrabenzyl[2+2]-cycloamide demonstrated the reduced symmetry of the structure in solution, where the molecular motions may be restricted. Notably, considerable proportion of cyclohexyl protons were shifted upfield, to δ −2. Since such a shift was also observed in the *N*-methyl derivative (Figure 8c), it is thought to be due to the shielding effect of benzo[*c*]phenanthrene and not of the benzyl group.

The ^{1}H NMR assignments of (*P*,*P*)-*N*,*N*′,*N*″,*N*‴-tetrabenzyl[2+2]cycloamide are shown in Figure 9, which were obtained by NMR spectroscopy using NOE. While NOE was observed between the methyl A at δ 1.92 and benzo[*c*]phenanthrene 1,12-methyl protons, methyl B at δ 1.74 showed NOE with 6,7-aromatic protons. The amide moiety existing between these arenes probably possess an *s-cis* configuration. The preference of *N*-

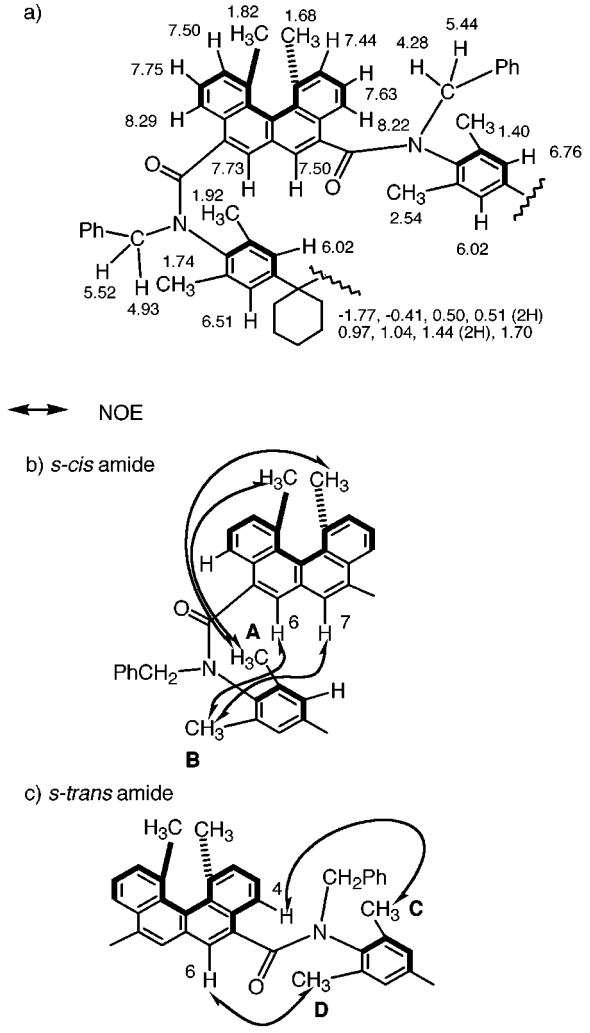


Figure 9. ^{1}H NMR assignments of (*P*,*P*)-*N*,*N*′,*N*″,*N*‴-tetrabenzyl[2+2]cycloamide (a). Selected NOEs are shown (b and c).

methylbenzanilide to possess an *s-cis* structure is known.[15] The aniline methyl C at δ 1.40 showed NOE with 4-H of the benzo[*c*]phenanthrene, while the methyl D at δ 2.54 showed NOE with 6-H. A *s-trans* configuration is likely for this amide moiety. NOEs were observed between several cyclohexyl protons and benzo[*c*]phenanthrene protons.

The ^{1}H NMR spectra of the *N*-methyl derivative were more complicated, and many other broad peaks appeared in addition to those observed for the *N*-benzyl derivative. Apparently, the *N*-methyl derivative was a mixture of conformers. By silica gel chromatography, (*P*,*P*)-*N*,*N*′,*N*″,*N*‴-tetramethyl[2+2]cycloamide was separable into two parts. They were stable at 0 °C in solution, although equilibrated at room temperature. The ^{1}H NMR spectra of the polar fraction was similar to the *N*-benzyl derivative (Figure 8c), while the less polar fraction appeared to be a mixture of several conformers. ^{1}H NMR spectra of the *N*-alkylated derivatives of [3+3]cycloamides and [4+4]cycloamides, which could also be mixtures of conformers, were extremely complex.

The structures of *N*-alkylated derivatives differed considerably from those of N−H compounds. Since a crystal suitable for X-ray analysis was not obtained, a calculation method was employed to clarify the structure. The structure of *N*,*N*′,*N*″,*N*‴-tetramethyl[2+2]cycloamide determined by Amber[16] (Figure 10) is consistent with that determined by NMR studies (Figure 9), and the Amber method was demonstrated to be reliable in the present system. The *N*-alkylated cycloamides appear to possess "folded" rather than "open" structures. *N*-Alkylation dramatically changed the structures of the cyclic amides.

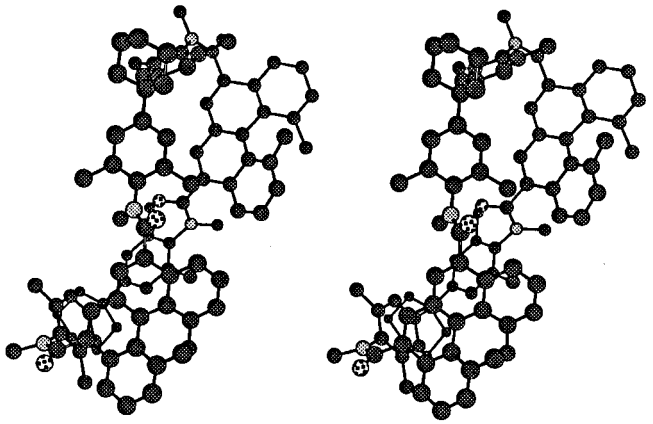


Figure 10. Structure of (*P*,*P*)-*N*,*N*′,*N*″,*N*‴-tetramethyl[2+2]-cycloamide obtained by Amber calculations (stereoview).

The most stable conformations of *N*,*N*′,*N*″,*N*‴,*N*⁗,*N*⁗⁗-hexamethyl[3+3]cycloamide and *N*,*N*′,*N*″,*N*‴,*N*⁗,*N*⁗⁗,*N*⁗⁗⁗,*N*⁗⁗⁗⁗-octamethyl[4+4]cycloamide were predicted by the calculations, which showed rather complex folded structures (Figure 11). The former possessed six *s-cis* amides, and the latter six *s-cis* and two *s-trans* amides.

Various applications of these optically active cyclic amides are conceivable. Their use in asymmetric catalysis was briefly examined as an example. The asymmetric addition reaction of diethylzinc to aldehydes was catalyzed by compounds such as amino alcohols, binaphthols, sulfoneamides, etc.[17] The cycloamide (*P*,*P*)-**9** also catalyzed the asymmetric reaction (Table 1). Lithiation of the cyclic amide with butyllithium and use of THF solvent were essential for the asymmetric induction. Other derivatives, for example, (*P*)-**8**, (*P*,*P*,*P*)-**10**, and (*P*,*P*,*P*,*P*)-**11**, gave racemic alcohols in the reaction of benzaldehyde. All the adducts derived from aromatic aldehydes possessed an (*R*)-configuration, and as high as 50% ee was attained in the reaction with β-naphthaldehyde. Although the asymmetric induction is modest, asymmetric catalysis by the novel cyclic amide may be interesting.

A helical chiral dicarboxylic acid, 1,12-dimethylbenzo[*c*]phenanthrenedicarboxylic acid, was prepared in multigram quantities, and optically active macrocyclic amides containing the chiral unit were synthesized. While the secondary amides possessed an open structure with a cavity, the *N*-alkylated derivatives possessed a folded structure. Studies on the properties of the cycloamides

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(16) The calculation was conducted using Amber* (McDonald, D. Q.; Still, W. C. *Tetrahedron Lett.* **1992**, *33*, 7743) contained in the MacroModel Ver 6.0. Mohamadi, F.; Richards, N. G. J.; Guida, W. C.; Liskamp, R.; Lipton, M.; Caulsfield, C.; Chang, G.; Hendrickson, T.; Still, W. C. *J. Comput. Chem.* **1990**, *11*, 440.

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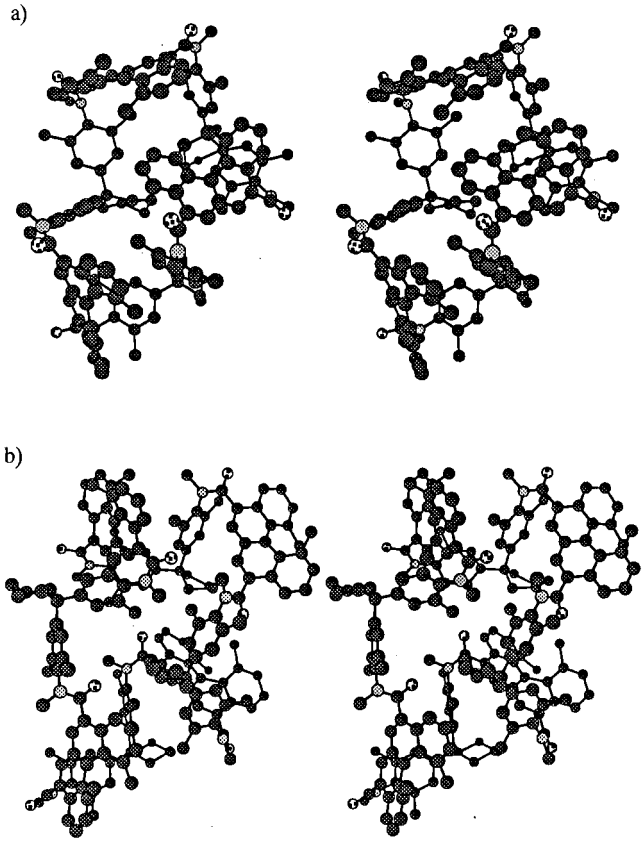
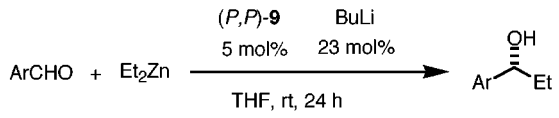


Figure 11. Structures of (*P,P,P*)-*N,N′,N″,N‴,N,⁗N⁗⁗*-hexamethyl[3+3]cycloamide (a) and (*P,P,P,P*)-*N,N′,N″,N‴,N,⁗,N⁗⁗,N⁗⁗⁗,N⁗⁗⁗⁗*-octamethyl[4+4]cycloamide (b) obtained by Amber calculations (stereoview).

Table 1. Asymmetric Addition of Diethylzinc to Aromatic Aldehydes Catalyzed by (*P,P*)-9



R	yield/%	ee/%	configuration
Ph	76	33	*R*
	66	31	*S*[a]
p-$MeOC_6H_4$	88	27	*R*
p-MeC_6H_4	73	28	*R*
p-ClC_6H_4	81	31	*R*
α-naphthyl	51	40	*R*
β-naphthyl	59	50	*R*

[a] (*M,M*)-**9** was used.

are now underway. For example, some of the cycloamides were found to form LB films.[18]

Experimental Section

(±)-1,12-Dimethylbenzo[*c*]phenanthrene-5,8-dinitrile, (±)-3. Under an argon atmosphere, trimethylsilylnitrile (9.00 mL, 64.1 mmol) was added to a solution of diketone (±)-**2**[5] (7.45 g, 25.7 mmol) and zinc iodide (0.2 g) in dry benzene (10 mL). After stirring for 27 h at room temperature, pyridine (40 mL) and phosphoryl chloride (12.0 mL, 130 mmol) were added, and the reaction mixture was heated at reflux for 17 h. After cooling, the contents were poured into ice-cold 2 M hydrochloric acid, and the organic materials were extracted with methylene chloride. The organic layer was washed with water and brine and dried over $MgSO_4$. The solvents were evaporated under a reduced pressure, and crude (±)-**3** (9.40 g) thus obtained was used in the next reaction without further purification. An analytical sample was obtained by recrystallizing 3 times from benzene: mp >300 °C (benzene). Elemental analysis. Calcd for $C_{22}H_{14}N_2$: C, 86.25; H, 4.61; N, 9.14%. Found: C, 86.00; H, 4.69; N, 9.16%. MS (EI, 70 eV) *m/z* 307 (M^+ + H, 27%), 306 (M^+, 100), 291 (M^+ − Me, 95), 276 (M^+ − 2Me, 34). HRMS (EI, 70 eV) calcd for $C_{22}H_{14}N_2$: 306.1157. Found: 306.1149. UV−vis (CH_2Cl_2) λ_{max} (ϵ) 308 nm (5.4×10^4). IR (KBr) 2220 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ 1.92 (6 H, s), 7.59 (2 H, d, J = 7.2 Hz), 7.83 (2 H, dd, J = 7.2, 7.5 Hz), 8.29 (2 H, s), 8.34 (2 H, d, J = 7.5 Hz). ^{13}C NMR (50 MHz, $CDCl_3$) δ 23.0, 110.6, 117.3, 123.0, 128.8, 129.2, 130.2, 130.7, 131.1, 131.2, 132.0, 137.8.

(±)-1,12-Dimethylbenzo[*c*]phenanthrene-5,8-dicarboxylic acid, (±)-1. Dinitrile (±)-**3** (9.40 g, 30.7 mmol) and sodium hydroxide (4.30 g, 10.8 mmol) were suspended in ethylene glycol (43 mL), and the mixture was stirred at 185−195 °C for 21 h. Ammonia evolved vigorously upon heating. After cooled, the reaction mixture was poured into water and extracted with ether−benzene. The alkaline aqueous solution was acidified with 2 M hydrochloric acid and filtered to give crude (±)-**1** (6.73 g). Recrystallization from benzene−methanol gave yellow powder of (±)-**1** (5.12 g, 58% from (±)-**2**): mp > 300 °C (benzene−methanol). MS (EI, 70 eV) *m/z* 344 (M^+, 100%), 311 (M^+ − Me − OH_2, 13), 239 (M^+ − 2COOH − Me, 20). HRMS (EI, 70 eV) calcd for $C_{22}H_{16}O_4$: 344.1049. Found: 344.1046. Calcd for $C_{22}H_{16}O_4$: C, 76.73; H, 4.68%. Found: C, 76.68; H, 4.79%. UV−vis (MeOH) λ_{max} (ϵ) 341 (9.8×10^3), 312 nm (2.3×10^4). IR (KBr) 3650−3100, 1684 cm^{-1}. ^1H NMR (600 MHz, CD_3OD) δ 1.85 (6 H, s), 7.39 (2 H, d, J = 7.0 Hz), 7.71 (2 H, dd, J = 7.1, 8.4 Hz), 8.58 (2 H, s), 8.87 (2 H, d, J = 8.2 Hz). ^{13}C NMR (150 MHz, CD_3OD) δ 24.0, 124.6, 128.7, 129.1, 130.0, 130.3, 131.2, 132.0, 132.2, 132.5, 137.7, 170.8.

Bis(*d*-camphorsultam)amide of 1, (*P*)-4 and (*M*)-5. Under an argon atmosphere, sodium hydride (60% oil suspension, 1.10 g, 27.5 mmol) was added to a dry benzene (20 mL) solution of *d*-(−)-camphorsultam (4.40 g, 20.5 mmol) in flask A. The mixture was stirred for 2 h at room temperature. In flask B, a mixture of (±)-**1** (2.96 g, 8.61 mmol) and thionyl chloride (20 mL) were refluxed for 4 h. After the mixture was cooled, excess thionyl chloride was removed under a reduced pressure. The crude diacid chloride in flask B was diluted with dry benzene (40 mL) and was added to the flask A. After stirring for 37 h at room temperature water was added, and organic materials were extracted with ethyl acetate. The extracts were washed with water and brine and dried over $MgSO_4$. After removing the solvents, silica gel chromatographic separation (ethyl acetate:dichloromethane:hexane = 1:4:4) gave polar isomer (*P*)-**4** (0.66 g, 10%) and less polar isomer (*M*)-**5** (1.28 g, 20%). Analytical samples were obtained by recrystallization from ethyl acetate. (*P*)-**4**: mp >300 °C (ethyl acetate). $[\alpha]^{25}_D$ −69.1 (*c* 1.05, $CHCl_3$). HRMS (EI, 70 eV) calcd for $C_{42}H_{46}N_2O_6S_2$: 738.2798. Found: 738.2793. Calcd for $C_{42}H_{46}N_2O_6S_2$: C, 68.27; H, 6.27; N, 3.79; S, 8.68%. Found: C, 67.68; H, 6.31; N, 3.85; S, 8.76%. UV−vis ($CHCl_3$) λ_{max} (ϵ) 341 (9.4×10^3), 313 nm (2.3×10^4). IR (KBr) 1680 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 1.00 (6 H, s), 1.30−1.37 (2 H, m), 1.38 (6 H, s), 1.43−1.48 (2 H, m), 1.85−1.90 (6 H, m), 1.91 (6 H, s), 1.92−1.99 (2 H, m), 2.18−2.27 (2 H, m), 3.40 (2 H, d, J = 14.0 Hz), 3.46 (2 H, d, J = 13.5 Hz), 4.15−4.20 (2 H, m), 7.44 (2 H, d, J = 7.0 Hz), 7.63 (2 H, dd, J = 7.0, 8.0 Hz), 8.00 (2 H, s), 8.14 (2 H, d, J = 8.0 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 19.9, 21.4, 23.5, 26.4, 33.2, 38.5, 45.1, 47.9, 48.4, 53.2, 65.8, 122.6, 127.3, 127.6, 128.5, 128.9, 129.4, 130.3, 130.9 (overlapped), 137.2, 168.5. (*M*)-**5**: mp >300 °C (ethyl acetate). $[\alpha]^{25}_D$ −209 (*c* 0.906, $CHCl_3$). HRMS (EI, 70 eV) calcd for $C_{42}H_{46}N_2O_6S_2$: 738.2798. Found: 738.2800. UV−vis ($CHCl_3$) λ_{max} (ϵ) 341 (1.1×10^4), 314 nm (2.3×10^4). IR (KBr) 1680 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 0.88 (6 H, s), 1.26−1.34 (2 H, m), 1.39 (6 H, s), 1.40−1.46 (2 H, m), 1.82−1.96 (8 H, m), 1.92 (6 H, s), 2.06−2.15 (2 H, m), 3.44 (2 H, d, J = 13.5 Hz), 3.51 (2 H, d, J = 13.5 Hz), 4.21−4.26 (2 H, m), 7.43 (2 H,

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d, J = 7.0 Hz), 7.62 (2 H, dd, J = 7.0, 8.0 Hz), 8.04 (2 H, d, J = 8.0 Hz), 8.09 (2 H, s). ^{13}C NMR (125 MHz, $CDCl_3$) δ 19.9, 21.3, 23.3, 26.4, 33.1, 38.4, 45.0, 47.8, 48.4, 53.2, 65.6, 122.5, 127.5, 127.9, 128.3, 129.4, 129.9, 130.1, 131.0, 131.0, 137.0, 169.1.

Optical resolution of 1. Methanol solution of (±)-**1** (70 g, 0.2 mol) and methanol solution of (−)-quinine (130 g, 0.4 mol) were mixed at room temperature, and the solvent was evaporated under a reduced pressure. The residue was recrystallized from chloroform−methanol. The crystals obtained were heated in refluxing chloroform−methanol (1:1, 300−400 mL) for 30 min and filtered while hot. The washing was repeated three times. To the resulted salt was added 4 M hydrochloric acid (300−400 mL), and the suspension was sonicated for 10 min. Then the powder was filtered and dried. These neutralizing procedures were repeated 3 times, and the product was finally dried at 80 °C overnight giving (*P*)-**1** (21 g, 30%, >99% ee). $[\alpha]^{23}_D$ +313 (*c* 0.690, MeOH). The mother liquid obtained by the recrystallization was concentrated, and the crystals were treated three times with hot methanol as mentioned above. Neutralization with 4 M hydrochloric acid as above gave (*M*)-**1** (20 g, 29%, 99% ee). $[\alpha]^{23}_D$ −332 (*c* 0.120, MeOH). The optical purities were determined by chiral HPLC analysis (Daicel, Chiral OD) of dimethyl esters, which were obtained by diazomethane treatment in ether at 0 °C. Dimethyl ester of (*P*)-**1**: mp 242−243 °C (ethyl acetate−hexane). $[\alpha]^{23}_D$ +313 (*c* 0.133 $CHCl_3$). MS (EI, 70 eV) *m*/*z* 372 (M^+, 100%), 341 (M^+ − OMe, 11), 239 (M^+ − Me − 2COOMe, 8). HRMS (EI, 70 eV) calcd for $C_{22}H_{20}O_4$: 372.1362. Found 372.1369. UV−vis ($CHCl_3$) λ_{max} (ϵ) 314 nm (3.2×10^4). IR (KBr) ν 1717 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.88 (6 H, s), 4.07 (6 H, s), 7.44 (2 H, d, J = 6.9 Hz), 7.68 (2 H, dd, J = 6.9, 8.3 Hz), 8.51 (2 H, s), 8.84 (2 H, d, J = 8.3 Hz). ^{13}C NMR (150 MHz, $CDCl_3$) δ 23.4, 52.4, 123.1, 127.0, 127.8, 128.8, 129.1, 129.8, 130.6, 131.3, 131.3, 136.8, 167.7. Dimethyl ester of (*M*)-**1**: $[\alpha]_D^{23}$ −310 (*c* 0.668 $CHCl_3$).

(*P*)-1,12-Dimethylbenzo[*c*]phenanthrene-5,8-dimethanol, (*P*)-6, from (*P*)-4. Under an argon atmosphere, to a solution of (*P*)-**4** (397 mg, 0.537 mmol) in dry tetrahydrofuran (3 mL) was added lithium aluminum hydride (69 mg, 1.83 mmol). The mixture was stirred for 10 h at room temperature. Then, ethanol, water, and 2 M hydrochloric acid were added successively, and organic materials were extracted with ethyl acetate. The organic layer was washed with water and brine and dried over $MgSO_4$. After removing the solvents under a reduced pressure, silica gel chromatography gave (*P*)-**6** (160 mg, 90%): mp 261−264 °C ($CHCl_3$−MeOH). $[\alpha]_D^{27}$ −186 (*c* 0.190 $CHCl_3$−MeOH). Calcd for $C_{22}H_{20}O_2$: C, 83.52; H, 6.37%. Found: C, 83.23; H, 6.51%. MS (EI, 70 eV) *m*/*z* 316 (M^+, 100%), 299 (M^+ − OH, 3), 285 (M^+ − CH_2OH, 2), 239 (M^+ − Me − $2CH_2OH$, 9). HRMS (EI, 70 eV) calcd for $C_{22}H_{20}O_2$: 316.1463. Found: 316.1465. UV−vis (MeOH) λ_{max} (ϵ) 333 (8.4×10^3), 303 nm (1.4×10^4). IR (KBr) 3286 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$−CD_3OD) δ 1.66 (6 H, s), 4.32 (2 H, s), 4.96 (2 H, d, J = 13.3 Hz), 5.03 (2 H, d, J = 13.2 Hz), 7.14 (2 H, d, J = 7.0 Hz), 7.33 (2 H, dd, J = 7.0, 8.0 Hz), 7.61 (2 H, s), 7.84 (2 H, d, J = 8.1 Hz). ^{13}C NMR (150 MHz, $CDCl_3$−CD_3OD) δ 22.7, 62.0, 120.2, 123.6, 124.7, 125.3, 127.6, 129.9, 131.2, 131.2, 135.2, 136.2. Similar procedures converted (*M*)-**5** to (*M*)-**6** (88%). $[\alpha]_D^{26}$ +182 (*c* 0.098, $CHCl_3$−MeOH).

(*P*)-6 from (+)-1. Under an argon atmosphere, to a solution of (+)-**1** (24 mg, 0.069 mmol) in dry tetrahydrofuran (1 mL) was added 1 M borane tetrahydrofuran solution (0.18 mL, 0.18 mmol). After the mixture was stirred at room temperature for 15 h aqueous saturated ammonium chloride was added, and the mixture was stirred vigorously for 30 min. Organic materials were then extracted with ethyl acetate. The organic layer was washed with water and brine and was dried over $MgSO_4$. The solvents were evaporated under a reduced pressure, and (*P*)-**6** (18 mg, 81%) was obtained by silica gel chromatography.

Cycloamides, (*M*,*M*)-9, (*M*,*M*,*M*)-10, and (*M*,*M*,*M*,*M*)-11. Under an argon atmosphere, (*M*)-**1** (200 mg, 0.58 mmol) in thionyl chloride (6 mL) was heated at reflux for 2 h. After removing excess thionyl chloride under a reduced pressure, a trace amount of thionyl chloride was removed by repeated addition of dry dichloromethane and evaporation in vacuo. The diacid chloride was then diluted with dry dichloromethane (300 mL) and pyridine (1 mL), to which **7**[12] (187 mg, 0.58 mmol) in dichloromethane (5 mL) was added at room temperature over 2 h. The mixture was stirred at the temperature for 48 h. After removing insoluble materials by filtration, the filtrate was washed with aqueous saturated potassium hydrogen sulfate, water, and brine and dried over $MgSO_4$. The solvents were evaporated under a reduced pressure, and the residue was chromatographed by recycling GPC giving (*M*,*M*)-**9** (90 mg, 24%), (*M*,*M*,*M*)-**10** (86 mg, 23%), and (*M*,*M*,*M*,*M*)-**11** (69 mg, 19%). (*M*,*M*)-**9**: mp >300 °C (CH_2Cl_2−MeOH−acetone). $[\alpha]^{26}_D$ −179 (*c* 0.332 $CHCl_3$). MS (FAB, NBA) *m*/*z* 1261 (M^+ + 1). UV−vis ($CHCl_3$) λ_{max} (ϵ) 303 nm (9.9×10^4). IR (KBr) 3286, 1671 cm^{-1}. IR ($CHCl_3$, 57.1 mM) 3416, 3308, 1673 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$−CD_3OD, 24 mM) δ 1.52−1.78 (12 H, m), 1.98 (12 H, s), 2.18−2.35 (8 H, m), 2.36 (24 H, s), 7.06 (8 H, s), 7.47 (4 H, s), 7.53 (4 H, d, J = 7.0 Hz), 7.73 (4 H, dd, J = 7.0, 7.7 Hz), 8.13 (4 H, s), 8.61 (4 H, d, J = 7.7 Hz). ^{13}C NMR (150 MHz, $CDCl_3$−CD_3OD, 24 mM) δ 18.5, 22.8, 22.8, 26.1, 36.3, 45.5, 122.8, 125.6, 127.0, 127.3, 128.9, 129.0, 129.1, 130.2, 131.1, 131.3, 133.1, 134.5, 136.8, 148.2, 168.2. (*M*,*M*,*M*)-**10**: mp >300 °C (CH_2Cl_2−MeOH−hexane). $[\alpha]^{27}_D$ −147 (*c* 0.230 $CHCl_3$). UV−vis ($CHCl_3$) λ_{max} (ϵ) 302 nm (1.5×10^5). IR (KBr) 3244, 1661 cm^{-1}. IR ($CHCl_3$, 17.2 mM) 3412, 3296, 1667 cm^{-1}. MS (FAB, NBA) *m*/*e* 1892 (M^+ + 2). VPO ($CHCl_3$, 35 °C, 5.3 mM) 1840 ± 100 g mol^{-1} (benzil as standard). ^{1}H NMR (600 MHz, $CDCl_3$−CD_3OD, 9.5 mM) δ 1.47−1.68 (18 H, m), 1.95 (18 H, s), 2.24−2.42 (12 H, m), 2.43 (36 H, s), 7.14 (12 H, s), 7.44 (6 H, s), 7.50 (6 H, d, J = 7.2 Hz), 7.68 (6 H, dd, J = 7.2, 8.0 Hz), 8.10 (6 H, s), 8.45 (6 H, d, J = 8.0 Hz). ^{1}H NMR (200 MHz, $CDCl_3$, 0.3 mM) δ 7.40 (1 H, s, NH), 8.13 (1 H, s, benzo[*c*]phenanthrene H-6). ^{1}H NMR (200 MHz, $CDCl_3$, 26 mM) δ 7.64 (1 H, s, NH), 7.96 (1 H, s, benzo[*c*]phenanthrene H-6). ^{13}C NMR (150 MHz, $CDCl_3$−CD_3OD, 9.5 mM) δ 18.8, 22.7, 23.0, 26.1, 36.7, 45.2, 122.6, 124.0, 126.8, 127.2, 128.2, 129.1, 129.3, 129.8, 130.9, 131.1, 133.9, 135.0, 136.8, 147.7, 168.7. (*M*,*M*,*M*,*M*)-**11**: mp >300 °C ($CHCl_3$−hexane). $[\alpha]^{26}_D$ −178 (*c* 0.220, $CHCl_3$). MS (FAB, NBA) *m*/*e* 2523 (M^+ + 3). VPO ($CHCl_3$, 35 °C, 4 mM) 2440 ± 120 g mol^{-1} (benzil as standard). UV−vis ($CHCl_3$) λ_{max} (ϵ) 303 nm (2.4×10^5). IR (KBr) 3278, 1655 cm^{-1}. IR ($CHCl_3$, 4.17 mM) 3414, 2938, 1667 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$−CD_3OD, 3.9 mM) δ 1.63−1.83 (24 H, m), 2.08 (24 H, s), 2.44−2.55 (16 H, m), 2.60 (48 H, s), 7.30 (16 H, s), 7.65 (8 H, d, J = 7.1 Hz), 7.84 (8 H, dd, J = 7.1, 8.8 Hz), 8.34 (8 H, s), 8.56 (8 H, d, J = 8.1 Hz). ^{13}C NMR (150 MHz, $CDCl_3$−CD_3OD, 3.9 mM) δ 18.5, 22.5, 22.8, 26.0, 36.5, 44.9, 122.4, 124.0, 126.7, 127.0, 128.0, 129.0, 129.3, 129.7, 130.8, 131.0, 133.8, 134.9, 136.7, 147.5, 169.0. Similar treatment of (*P*)-**1** gave (*P*,*P*)-**9**, (*P*,*P*,*P*)-**10**, and (*P*,*P*,*P*,*P*)-**11**. (*P*,*P*)-**9**: mp >300 °C (CH_2Cl_2−MeOH−acetone). $[\alpha]^{27}_D$ +179 (*c* 0.698, $CHCl_3$). (*P*,*P*,*P*)-**10**: mp >300 °C (CH_2Cl_2−MeOH−acetone). $[\alpha]^{27}_D$ +131 (*c* 0.206 $CHCl_3$). (*P*,*P*,*P*,*P*)-**11**: mp >300 °C ($CHCl_3$−hexane). $[\alpha]^{21}_D$ +187 (*c* 0.114, $CHCl_3$).

(*M*)-[1+1]Cycloamide, (*M*)-8. A mixture of (*M*)-**1** (74 mg, 0.22 mmol) and thionyl chloride (2 mL) was refluxed for 3 h. After the mixture was cooled to room temperature, thionyl chloride was removed as above. Under an argon atmosphere the residue was dissolved in dry 1,2-dichloroethane (200 mL) and triethylamine (1 mL). Then a solution of **7** (67 mg, 0.21 mmol) in 1,2-dichloroethane (10 mL) was added dropwise at reflux over 1 h. After refluxing for 13 h, the reaction mixture was cooled and filtered. The solution was washed with 2 M hydrochloric acid, water, and brine. After the mixture was dried over $MgSO_4$, the solvents were evaporated. Separation by GPC gave (*M*)-**8** (38 mg, 29%), which was accompanied by (*M*,*M*)-**9** (21 mg, 16%). Mp >300 °C (benzene−MeOH). $[\alpha]^{27}_D$ +35.3 (*c* 0.774, $CHCl_3$). UV−vis ($CHCl_3$) λ_{max} (ϵ) 296 nm (3.4

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$\times 10^4$). IR (KBr) 3234, 1655 cm^{-1}. IR ($CHCl_3$, 34.7 mM) 3374, 3186, 1651 cm^{-1}. HRMS (EI, 70 eV) calcd for $C_{22}H_{20}O_2$: 630.3247. Found: 630.3246. ^1H NMR (600 MHz, $CDCl_3$, 32 mM) δ 1.45−1.63 (6 H, m), 1.80 (6 H, s), 1.91 (6 H, s), 2.06 (6 H, s), 2.24−2.39 (4 H, m), 6.37 (2 H, s), 6.78 (2 H, s), 6.98 (2 H, s), 7.41 (2 H, d, J = 7.0 Hz), 7.64 (2 H, dd, J = 7.0, 8.2 Hz), 7.73 (2 H, s), 8.51 (2 H, d, J = 8.2 Hz). ^{13}C NMR (150 MHz, $CDCl_3$, 32 mM) δ 18.6, 19.1, 22.8, 23.3, 26.3, 33.0, 45.1, 123.5, 124.6, 124.9, 125.9, 126.9, 127.3, 127.6, 128.6, 128.9, 129.9, 131.0, 132.5, 134.4, 136.8, 170.0. A similar treatment of (*P*)-**1** gave (*P*)-**8** (30%), which was accompanied by (*P,P*)-**9** (14%). Mp >300 °C (benzene−MeOH). $[\alpha]_D^{26}$ −32.2 (*c* 0.534, $CHCl_3$).

(*P*)-*N,N′*-Dimethyl[1+1]cycloamide. Under an argon atmosphere, to an ice cooled solution of (*P*)-**8** (7.5 mg, 0.012 mmol) in tetrahydrofuran (2 mL) was added NaH (60% oil suspension, 1.5 mg, 0.038 mmol) and methyl iodide (3.0 μL, 0.048 mmol) successively. The mixture was vigorously stirred for 23 h at room temperature and was added to 2 M hydrochloric acid. The organic materials were extracted with chloroform, and the extracts were washed with water and brine. After the solution was dried over $MgSO_4$, the solvents were removed in vacuo, and the crude product was purified by silica gel chromatography (n-hexane−ethyl acetate) giving the product (7.8 mg, 100%). Mp >300 °C (ethyl acetate−n-hexane). $[\alpha]^{27}_D$ −16.4 (*c* 0.675 $CHCl_3$). MS (EI, 70 eV) *m/z* 658 (M^+, 100%), 643 (M^+ − Me, 2). UV−vis ($CHCl_3$) λ_{max} (ϵ) 290 nm (2.2×10^4), 303 nm (2.6×10^4). IR (KBr) 2926, 2860, 1642 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$) δ 1.53−1.60 (6 H, m), 1.74 (6 H, s), 1.95 (6 H, s), 2.00 (6 H, s), 2.20−2.35 (4 H, m), 3.52 (6 H, s), 6.32 (2 H, s), 6.83 (2 H, s), 6.96 (2 H, s), 7.35 (2 H, d, J = 7.0 Hz), 7.57 (2 H, dd, J = 7.1, 8.3 Hz), 8.30 (2 H, d, J = 8.2 Hz). ^{13}C NMR (150 MHz, $CDCl_3$) δ 18.4, 18.7, 22.8, 23.3, 26.3, 29.7, 33.4, 36.2, 44.8, 123.7, 123.8, 125.3, 126.0, 126.3, 127.7, 128.2, 130.0, 130.9, 131.0, 135.1, 135.3, 136.6, 138.6, 148.8, 168.8.

(*P,P*)-*N,N′,N″,N‴*-Tetramethyl[2+2]cycloamide. Mp >300 °C (ethyl acetate−hexane). $[\alpha]^{27}_D$ +80.7 (*c* 0.205 $CHCl_3$). MS (FAB, NBA) *m/e* 1316 (M^+ + 2). UV−vis ($CHCl_3$) λ_{max} (ϵ) 308 nm (5.0×10^4). IR (KBr) 2936,1647 cm^{-1}. The conformers were separated by silica gel column chromatography (n-hexane−ethyl acetate) below −10 °C and one major conformer was isolated. ^1H NMR (600 MHz, $CDCl_3$, −30 °C) δ −2.05 to −1.95 (2 H, m), −0.60 to −0.50 (2 H, m), −0.20 to −0.10 (2 H, m), 0.25−0.45 (4 H, m), 0.85−1.00 (4 H, m), 1.30−1.40 (2 H, m), 1.45−1.55 (2 H, m), 1.63 (6 H, s), 1.60−1.70 (2 H, m), 1.75 (6 H, s), 1.97 (6 H, brs), 2.03 (6 H, s), 2.17 (6 H, s), 2.45 (6 H, s), 3.23 (6 H, s), 3.60 (6 H, brs), 6.12 (2 H, brs), 6.16 (2 H, brs), 6.52 (2 H, s), 6.83 (2 H, s), 7.29 (2 H, s), 7.31 (2 H, d, J = 7.5 Hz), 7.32 (2 H, s), 7.33 (2 H, d, J = 7.5 Hz), 7.54 (2 H, dd, J = 7.5, 8.3 Hz), 7.58 (2 H, dd, J = 7.5, 8.0 Hz), 8.22 (brd, J = 8.0 Hz), 8.32 (2 H, d, J = 8.3 Hz). ^{13}C NMR (150 MHz, $CDCl_3$, −30 °C) δ 17.9, 18.6, 18.7, 19.6, 22.7 (two carbons), 23.1, 24.0, 25.0, 36.0 (two carbons), 37.3, 39.7, 46.0, 122.4, 122.6, 123.5, 124.4, 126.1 (two carbons), 126.3, 126.6, 127.2, 127.5, 128.2, 128.5, 128.5, 128.6 (two carbons), 129.9, 130.1, 131.2, 131.3, 131.9, 133.6, 134.8, 134.9, 135.4, 136.0, 137.1, 138.4, 140.4, 170.8, 170.9. Two aniline carbons at N-*C* were not detected.

(*P,P,P*)-*N,N′,N″,N‴,N⁗,N⁗′*-Hexamethyl[3+3]-cycloamide. Mp >300 °C (ethyl acetate−n-hexane). $[\alpha]^{27}_D$ +74.9 (*c* 1.58, $CHCl_3$). Calcd for $C_{138}H_{138}O_6N_6 \cdot 8H_2O$: C, 78.16; H, 7.32; N, 3.96%. Found: C, 78.32; H, 7.22; N, 3.86%. Found: C, 77.37; H, 6.97; N, 3.72%. Found: C, 77.79; H, 6.97; N, 3.95%. Found: C, 78.11; H, 7.26; N, 4.18%. The analytical sample was prepared by precipitating from ethyl acetate by adding hexane and dried at 80 °C/1 mmHg for 1 day. MS (FAB, NBA) *m/z* 1977 (M^+ + 3). UV−vis ($CHCl_3$) λ_{max} (ϵ) 303 nm (7.8×10^4). IR (KBr) 2928, 1651 cm^{-1}.

(*P,P,P,P*)-*N,N′,N″,N‴,N⁗,N⁗′,N⁗″,N⁗‴*-Octamethyl-[4+4]cycloamide. Mp >300 °C (ethyl acetate−n-hexane). $[\alpha]^{27}_D$ +69 (*c* 0.21, $CHCl_3$). Calcd for $C_{184}H_{184}O_8N_8 \cdot 13H_2O$: C, 77.01; H, 7.38; N, 3.90%. Found: C, 76.49; H, 7.12; N, 3.69%. Found: C, 76.91; H, 7.17; N, 3.64%. Found: C, 77.44; H, 7.19; N, 4.04%. The analytical sample was prepared by precipitating from ethyl acetate by adding hexane and dried at 80 °C/1 mmHg for 1 day. MS (FAB, NBA) *m/z* 2634 (M^+ + 2). UV−vis ($CHCl_3$) λ_{max} (ϵ) 306 nm (1.1×10^5). IR (KBr) 2930, 2860, 1647 cm^{-1}.

(*P*)-*N,N′*-Dibenzyl[1+1]cycloamide. Under an argon atmosphere, to an ice cooled solution of (*P*)-**8** (7.5 mg, 0.012 mmol) in THF (2 mL) were added NaH (60% oil suspension, 1.5 mg, 0.038 mmol) and benzyl bromide (5.7 μL, 0.048 mmol) successively. The mixture was vigorously stirred for 23 h at room temperature and was added to 2 M hydrochloric acid. The organic materials were extracted with chloroform, and the extracts were washed with water and brine. After the solution was dried over $MgSO_4$, the solvents were removed in vacuo, and the crude product was purified by silica gel chromatography (n-hexane−ethyl acetate) giving the product (9.7 mg, 100%). Mp 201−204 °C (ethyl acetate−n-hexane). $[\alpha]^{27}_D$ −22.9 (*c* 0.610 $CHCl_3$). MS (FAB, NBA) *m/z* 811 (M^+ + 1). UV−vis ($CHCl_3$) λ_{max} (ϵ) 290 nm (3.2×10^4), 303 nm (3.6×10^4). IR (KBr) 2932, 2864, 1642 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$) δ 1.50−1.65 (6 H, m), 1.59 (12 H, br s), 1.66 (6 H, s), 2.17−2.33 (4 H, m), 4.90−5.40 (4 H, br s), 6.27 (2 H, s), 6.75 (2 H, br s), 6.90 (2 H, br s), 7.28 (2 H, d, J = 7.1 Hz), 7.28−7.34 (8 H, m), 7.49 (2 H, dd, J = 7.0, 8.2 Hz), 7.49−7.52 (4 H, m), 8.14 (2 H, d, J = 8.2 Hz). ^{13}C NMR (150 MHz, $CDCl_3$) δ 18.6, 18.8, 22.8, 23.2, 26.3, 29.7, 33.3, 44.8, 52.5, 123.3, 123.5, 125.4, 125.8, 126.2, 126.2, 127.7, 127.7, 128.1, 128.4, 130.1, 130.1, 130.8, 131.0, 135.5, 135.8, 136.5, 137.4, 137.5, 148.9, 168.5.

(*P,P*)-*N,N′,N″,N‴*-Tetrabenzyl[2+2]cycloamide. Mp >300 °C (ethyl acetate−n-hexane). $[\alpha]^{27}_D$ +71.0 (*c* 0.420 $CHCl_3$). MS (FAB, NBA) *m/z* 1622 (M^+ + 2). UV−vis ($CHCl_3$) λ_{max} (ϵ) 309 nm (8.5×10^4). IR (KBr) 2934, 1638 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$, 40 °C) δ −1.86 to −1.70 (2 H, m), −0.47 to −0.36 (2 H, m), 0.02−0.08 (2 H, m), 0.44−0.57 (4 H, m), 0.90−0.99 (2 H, m), 1.00−1.11 (4 H, m), 1.40 (6 H, s), 1.38−1.47 (2 H, m), 1.60−1.75 (2 H, m), 1.66 (6 H, s), 1.72 (6 H, s), 1.81 (6 H, s), 1.92 (6 H, s), 2.54 (6 H, s), 4.28 (2 H, d, J = 13.5 Hz), 4.93 (2 H, d, J = 13.5 Hz), 5.44 (2 H, d, J = 13.5 Hz), 5.52 (2 H, d, J = 13.5 Hz), 6.02 (2 H, s), 6.03 (2 H, s), 6.51 (2 H, s), 6.74 (2 H, s), 7.12 (4 H, d, J = 7.1 Hz), 7.28 (4 H, t, J = 7.3 Hz), 7.32 (2 H, t, J = 7.3 Hz), 7.35 (4 H, d, J = 7.3 Hz), 7.43 (4 H, t, J = 7.7 Hz), 7.44 (2 H, d, J = 6.2 Hz), 7.50 (2 H, s), 7.48−7.55 (5 H, m), 7.63 (2 H, dd, J = 6.2, 8.2 Hz), 7.73 (2 H, s), 7.75 (2 H, t, J = 7.9 Hz), 8.22 (2 H, d, J = 8.2 Hz), 8.29 (2 H, d, J = 8.2 Hz). ^{13}C NMR (150 MHz, $CDCl_3$) δ 18.5, 18.6, 19.0, 19.1, 19.6, 22.1, 22.5, 23.0, 24.7, 35.4, 38.8, 46.0, 51.0, 52.7, 122.7, 122.9, 123.6, 123.7, 125.5, 125.8, 125.9, 126.4, 127.0, 127.5, 127.6, 127.8, 128.0, 128.2, 128.3, 128.4, 128.5, 129.5, 129.8, 129.8, 130.3, 130.9, 131.9, 132.8, 133.6, 135.4, 135.6, 135.8, 136.0, 136.1, 136.3, 136.4, 136.7, 137.8, 142.3, 144.0, 149.8, 169.4, 169.4.

(*P,P*)-[2+2]Cycloamide Catalyzed Addition of Diethylzinc to Aromatic Aldehyde (General Procedures). Under an argon atmosphere, to a mixture of (*P,P*)-**9** (12 mg, 0.01 mmol) and tetrahydrofuran (3 mL) was added 1.6 M *n*-butyllithium (0.048 mmol) in hexane (0.03 mL) at 0 °C. The mixture was stirred for 30 min, and an aldehyde (0.20 mmol) was added. After the mixture was warmed to room temperature, 1 M diethylzinc (0.60 mmol) in hexane (0.6 mL) was added. The mixture was vigorously stirred for 1 day at room temperature, when 2 M hydrochloric acid was added. Organic materials were extracted with chloroform, and the organic layer was successively washed with water and brine. After the solution was dried over $MgSO_4$, the solvents were evaporated in vacuo, and the crude product was purified by silica gel chromatography (n-hexane−ethyl acetate), giving an optically active secondary alcohol. The (*P,P*)-**9** was recovered (>70%). Spectral data of the secondary alcohols were in accordance with the reported data. The optical purity was determined by HPLC analysis using Daicel Chiralcel OB−H (10% 2-propanol in n-hexane). The absolute configuration was determined according to the literature.

(*R*)-1-Phenyl-1-propanol. $[\alpha]^{25}_D$ +16 (*c* 0.97, $CHCl_3$). Literature[19] $[\alpha]_D$ −45.45 (*c* 5.2, $CHCl_3$), (*S*)-configuration.

(*R*)-1-(*p*-Methoxyphenyl)-1-ethanol. $[\alpha]^{22}_D$ +11 (*c* 1.9,

Table 2. Summary of Crystal Data, Data Collection, and Refinement Details

compound	(*P*)-**4**	(*P*,*P*)-**9**	(*P*)-*N*,*N*′-dimethyl[1+1]cycloamide
formula	$C_{42}H_{46}O_6N_2S_2$	$C_{108}H_{144}O_{14}N_4$	$C_{48}H_{48}O_2N_2Cl_6$
M_r	738.96	1722.34	897.64
crystal size, mm	0.2 × 0.3 × 0.4	0.3 × 0.3 × 0.5	0.1 × 0.2 × 0.4
space group	$P2_1$ (No. 4)	$C2/c$ (No. 15)	$P2_12_12_1$ (No. 19)
crystal system	monoclinic	monoclinic	orthorhombic
temp, K	283	150	283
a, Å	10.900(2)	24.038(2)	18.982(2)
b, Å	14.974(2)	12.335(2)	21.336(2)
c, Å	12.060(2)	35.392(2)	11.394(3)
β, deg	112.04(1)	102.29(3)	
V, Å^3	1824.5(5)	10253(1)	4614.4(10)
Z	2	4	4
D_{calcd}, g/cm^3	1.345	1.116	1.292
μ, cm^{-1}	17.00	0.73	18.53
radiation	Cu Kα	Mo Kα	Cu Kα
λ, Å	1.54178	0.71069	1.54178
F(000)	784	3728	1872
no. of unique measd data	3042	9320	4137
no. of unique obsd data	2966 [$I_o > 3\sigma(I_o)$]	4037 [$I_o > 3\sigma(I_o)$]	3170 [$I_o > 4\sigma(I_o)$]
no. of variables	468	574	523
R	0.039	0.085	0.076
Rw	0.052	0.087	0.074
($\Delta\rho$)max, e/Å^3	0.24	0.57	0.48

$CHCl_3$). Literature[20] $[\alpha]^{22}_D$ −17.2 (*c* 5, benzene, 51% ee), (*S*)-configuration.

(*R*)-1-(*p*-Methylphenyl)-1-ethanol. $[\alpha]^{22}_D$ +8.7 (*c* 0.64, $CHCl_3$). Literature[20] $[\alpha]^{22}_D$ −20.4 (benzene, 52% ee), (*S*)-configuation.

(*R*)-1-(*p*-Chlorophenyl)-1-ethanol. $[\alpha]^{22}_D$ +8.7 (*c* 1.2, $CHCl_3$). Literature[20] $[\alpha]^{22}_D$ −10.4 (*c* 5, benzene, 43% ee), (*S*)-configuration.

(*R*)-1-(1-Naphthyl)-1-ethanol. $[\alpha]^{24}_D$ +23 (*c* 1.0, $CHCl_3$). The enantiomeric excess of the adduct was determined by the optical rotation. Literature[21] $[\alpha]_D$ −37.1 (*c* 4.17 $CHCl_3$, 63% ee), (*S*)-configuration.

(*R*)-1-(2-Naphthyl)-1-ethanol. $[\alpha]^{24}_D$ +19 (*c* 1.0, $CHCl_3$). Literature[22] $[\alpha]^{20}_D$ −18.8 (benzene, 44.7% ee), (*S*)-configuration.

X-ray Crystallography. Details of crystal data, data collection, and refinement for the three compounds are concisely summarized in Table 2. The cell and intensity data were collected by using a Rigaku four circle diffractometer (AFC5R). The compound of (*P*,*P*)-**9** is mildly air-sensitive, so that the data were measured at low temperature (150 K) by coating with epoxy-resins. The structures were solved by direct method (SIR92) and refined by using a full-matrix least-squares method. Although most hydrogen atoms were found in D-map, the other atoms were calculated geometrically. The crystal of (*P*)-**4** does not include a solvent molecule. The crystal of (*P*,*P*)-**9** is restricted by a crystallographic 2-fold axis symmetry. A total of 10 ethanol solvents per each (*P*,*P*)-**9** molecule are included, in which the four solvents are included in the cavity of the host molecule and the others are included into the host line channel. The crystal of (*P*)-*N*,*N*-dimethyl[1+1]-cycloamide contained two chloroform molecules per cycloamide and the solvents are included in the crystal lattice. All calculations were carried out by using a teXsan software package (Crystal Structure Analysis Package, Molecular Structure Corporation).

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Supporting Information Available: ^{13}C NMR spectra of **8**−**11**, *N*,*N*″-dimethyl-**8**, *N*,*N*″-dibenzyl-**8**, and *N*,*N*″,*N*‴,*N*⁗-tetrabenzyl-**9** (8 pages). The 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.

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