Available online at www.sciencedirect.com
ScienceDirect
Tetrahedron
Tetrahedron 63 (2007) 9933–9938

Inclusion compounds of L,D-dipeptide with small sulfoxides: flexible sheet structure of (*S*)-phenylglycyl-(*R*)-phenylglycine

Motohiro Akazome,[a,*] Atsushi Hirabayashi,[b] Kyoko Senda[a] and Katsuyuki Ogura[a,b,*]

[a]*Department of Applied Chemistry and Biotechnology, Faculty of Engineering, Chiba University, 1-33 Yayoicho, Inageku, Chiba 263-8522, Japan*
[b]*Graduate School of Science and Technology, Chiba University, 1-33 Yayoicho, Inageku, Chiba 263-8522, Japan*

Received 26 May 2007; revised 18 July 2007; accepted 20 July 2007
Available online 26 July 2007

Abstract—A heterochiral L,D-dipeptide, (*S*)-phenylglycyl-(*R*)-phenylglycine (*SR*-**1**), formed inclusion compounds with some small dialkyl sulfoxides. By their single-crystal X-ray analyses, we observed monolayer structures, where *SR*-**1** molecules are arranged in parallel to construct a wavy sheet. The sulfoxides were accommodated in a channel cavity between the monolayers of *SR*-**1** by hydrogen bonding with $^{+}NH_3$ of *SR*-**1**. Notably, the sheet of *SR*-**1** is so flexible to change its wavy degree in response to the volume of the included sulfoxides. Furthermore, we could analyze the structure of crystalline *SR*-**1** without any sulfoxide, which has a bilayer structure.

1. Introduction

Homochiral L,L-dipeptides have been well studied because they are regarded as a partial structure of proteins. Hitherto, we have reported molecular recognition of organic guest molecules by (*S*)-leucyl-(*S*)-alanine,[1] (*R*)-phenylglycyl-(*R*)-phenylglycine (*RR*-**1**),[2] and (*R*)-(1-naphthyl)glycyl-(*R*)-phenylglycine,[3] which are typical homochiral dipeptides. These dipeptides aggregate to construct a layer and include guest molecules between the layers. In contrast, little attention has been paid to heterochiral L,D-dipeptides, though the chemistry of regularly alternating L,D-oligopeptides has been reported on their intriguing structures[4] such as double stranded helices[5] or peptide nanotubes.[6] Recently, we investigated the inclusion phenomena of (*S*)-phenylglycyl-(*R*)-phenylglycine (*SR*-**1**) crystals that include small amides such as *N*,*N*-dimethylformamide (DMF), acetamide, and *N*,*N*-dimethylacetamide.[7] The crystals have a wavy structure. As a typical example, the crystal structure of *SR*-**1** with DMF is illustrated in Figure 1. These inclusion compounds showed the same interlayer distances along the *b* axis (10.9–11.0 Å). Interestingly, the length of *c* axis expands from 5.2 to 5.9 Å when *N*,*N*-dimethylacetamide is included instead of acetamide.[7] This shows that the *c*-axis of the *SR*-**1** inclusion crystals is variable in response to the volume of the guest amides.

Here, we wish to report that *SR*-**1** also includes sulfoxides like our homochiral dipeptides[1–3] and other artificial host molecules.[8] In the inclusion crystals, guest sulfoxides drastically change the sheet structure of *SR*-**1** from wavy into approximately flat.

2. Results and discussion

2.1. Crystal structures of inclusion compounds of *SR*-1

In the presence of relatively small sulfoxides as a guest molecule, *SR*-**1** was crystallized from a methanol solution to afford a 1:1 inclusion compound (vide infra). Fortunately, we could analyze the inclusion compound of dimethyl sulfoxide (DMSO), ethyl methyl sulfoxide, and diethyl sulfoxide by single-crystal X-ray crystallography. As seen from Figure 2, these inclusion crystals have a wavy sheet structure, which is composed of the curved *SR*-**1** molecules and their wave degree depends on the guest size. The structure of inclusion compound with DMSO is quite similar to that with DMF (Fig. 1) in morphology. In the case of racemic ethyl methyl sulfoxide, both of its enantiomers were included at the same position in the cavity. The sulfoxide in the crystal has a mixed structure of trigonal bipyramidal geometry having the sulfur atom that occupies two coordination sites (S1 and S2). From the ratio of S1/S2=91:9, (*S*)-ethyl methyl sulfoxide is revealed to be the major enantiomer. In order to estimate the enantiomeric ratio of included ethyl methyl sulfoxide by NMR, the recovered sulfoxide was converted to the corresponding diastereomeric *N*-[(*S*)-methoxyphenylacetyl]-sulfoximine[4] and the diastereomeric ratio was 85:15. The

Keywords: Crystal engineering; Inclusion compounds; Dipeptides; Sulfoxides; Molecular recognition.
* Corresponding authors. Tel.: +81 43 290 3388; fax: +81 43 290 2402; e-mail: katsuyuki@faculty.chiba-u.jp

0040–4020/$ - see front matter © 2007 Published by Elsevier Ltd.
doi:10.1016/j.tet.2007.07.061

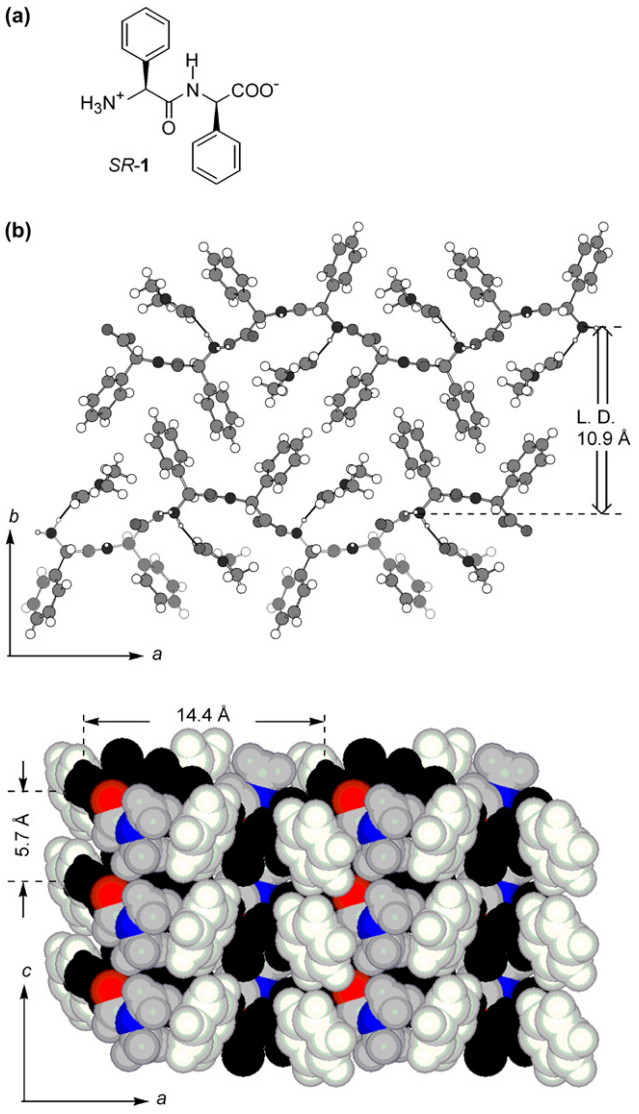


Figure 1. (a) Structure of (*S*)-phenylglycyl-(*R*)-phenylglycine (*SR*-**1**). (b) Crystal structure of the inclusion crystals of *SR*-**1** with dimethylformamide. L.D. is a layer distance measured by PXRD.

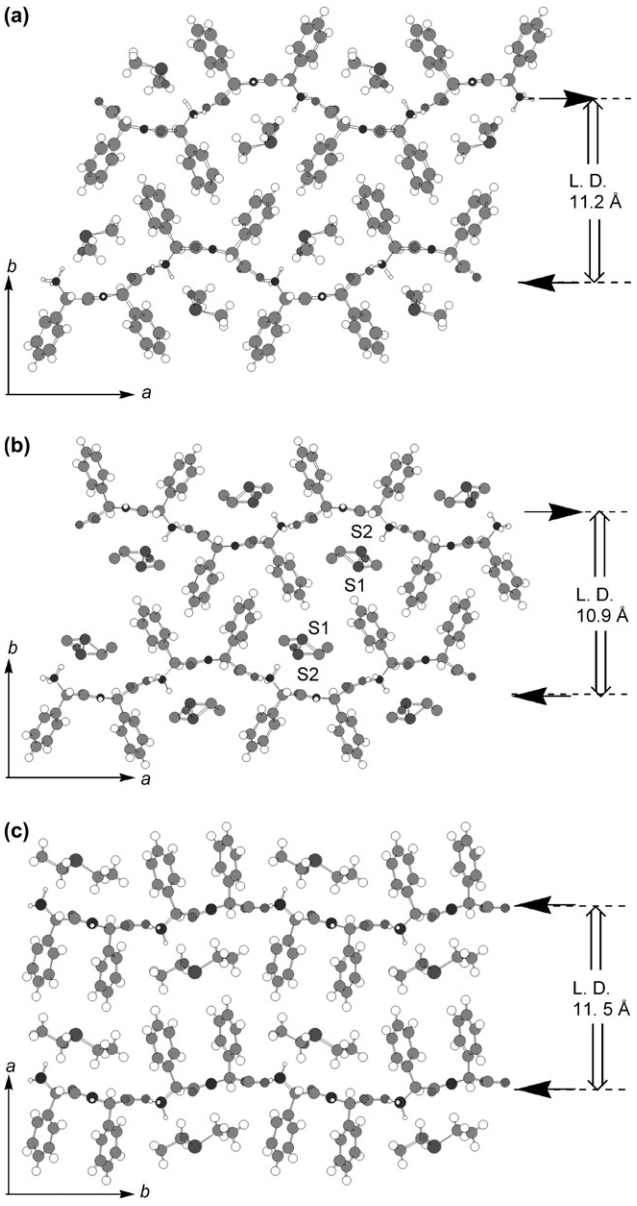


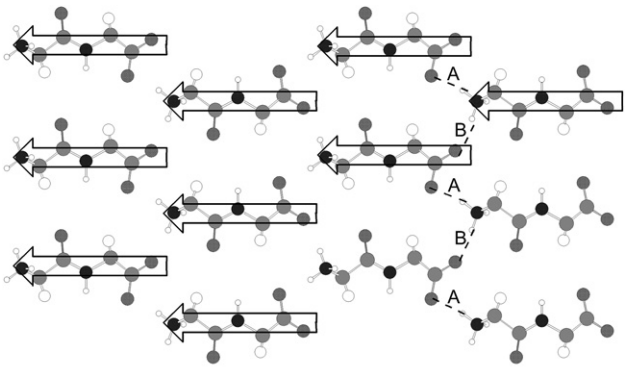
Figure 2. Layer structure of inclusion compounds of *SR*-**1** (*a*-*c* plane). L.D. is a layer distance measured by PXRD: (a) with dimethyl sulfoxide (DMSO); (b) with ethyl methyl sulfoxide; (c) with diethyl sulfoxide.

ratio was close to that of S1/S2 in the crystal structure. In the inclusion crystals with DMSO and ethyl methyl sulfoxide, two phenyl groups of *SR*-**1** are apart from each other, but they interact with the phenyl group of *SR*-**1** in the adjacent sheet. Since the wavy sheets are piled up in antiparallel direction, these crystals have a space group $P2_12_12_1$ (Fig. 2a and b). Interestingly, the sheets of *SR*-**1** in the inclusion compound with diethyl sulfoxide are so approximately flat to stack in parallel (Fig. 2c). Thus, the space group of the crystal becomes $P2_1$. In this case, two phenyl groups of the *SR*-**1** molecule are close to one another and, as a result, do not contact with the phenyl ring of *SR*-**1** in the adjacent sheet. Probably, no benzene–benzene interaction between the layers allows the sheets of *SR*-**1** to stack in the same direction.

All of the inclusion crystals described above have a monolayer structure with a cavity surrounded by the phenyl groups of *SR*-**1**. Two of three ammonio protons of the *SR*-**1** take part in the construction of the sheet structure by hydrogen bonding. The third ammonio proton contributes to the capture of the sulfoxide guests that are accommodated in the cavity between the layers.

The hydrogen bonding distances of the inclusion compounds are summarized in Figure 3. As shown in Figure 3, the glycylglycine backbones of the dipeptides are arranged in parallel by the ionic pairing of carboxyl and amino groups via hydrogen-bonding network: one terminal COO^- bridges two $^+NH_3$ of adjacent dipeptides and the $^+NH_3$ is also bound with two adjacent COO^- groups (O···N). The hydrogen-bonding network of *SR*-**1** resembles to that of a homochiral D,D-dipeptide (*RR*-**1**) with sulfoxides.[2]

In Figure 4, the sheet structures are shown with CPK models. As the alkyl group of the guest sulfoxide increases in volume, the phenyl group of the same *SR*-**1** molecule seems to be pushed out more strongly, so that the *SR*-**1** sheet



Guest	A / Å N---O	B / Å N---O	H-G / Å N---O
MeSOMe	2.72	2.79	2.74
EtSOMe	2.74	2.77	2.80
EtSOEt	2.72	2.76	2.79

R-S-R′ (O, H, H-G, $^{+}NH_2^-$)

Figure 3. Dipeptide backbone and atomic distances of intermolecular hydrogen bonds.

changes from wavy to approximately flat and the unit cell expands from 14.5 to 15.7 Å in *a* axis direction. It should be noted that, if the sheet was flat, the volume of the cavity would become maximum. This is the case when diethyl sulfoxide is the guest. Indeed, larger sulfoxides such as ethyl propyl sulfoxide and ethyl isopropyl sulfoxide were not included at all.

The wall of the cavity consists of two phenyl groups of *SR*-**1**. The C-terminal phenyl groups of *SR*-**1** always adopt the same conformation on the backbone sheet. On the other hand, the conformation of N-terminal phenyl group of *SR*-**1** is drastically changed according to the size of the guest sulfoxide. The similar flipping of the N-terminal phenyl groups was observed in the inclusion crystals of *RR*-**1**.[2b,c]

In the cavity, the alkyl group of the guest sulfoxide is close to the phenyl group of *SR*-**1**: the shortest distances between the alkyl group of the guest and the phenyl group of *SR*-**1** are indicated in red arrows (Fig. 4). The conventional van der Waals limit is ca. 3.7 Å for the C···C (ca. 2.9 Å for the H···C) distance, which is the sum of 2.0 Å for CH_3 (1.2 Å for H) and 1.7 Å for Csp[2].[9] Judging from these values, the distances, 3.72(2.93) Å (dimethyl sulfoxide) and 3.76(2.90) Å (diethyl sulfoxide), meet the criteria of van der Waals contact. It is noteworthy that the C···C distance (3.43 Å) in the inclusion crystal with ethyl methyl sulfoxide is shorter than the sum of van der Waals radii, suggesting the presence of CH–π interaction.[10]

2.2. Crystal structure of *SR*-1 host

We were interested in the crystal structure of *SR*-**1** without any guest, since we could not obtain a single crystal of *RR*-**1**, that is, suitable to X-ray crystallography. Fortunately, we could obtain good-quality single crystals of *SR*-**1** that made us achieve their single-crystal X-ray analysis. In the crystallization of *SR*-**1** in the presence of ethyl isopropyl sulfoxide, *SR*-**1** itself deposited as good-quality crystals that did not include the sulfoxide. The results are

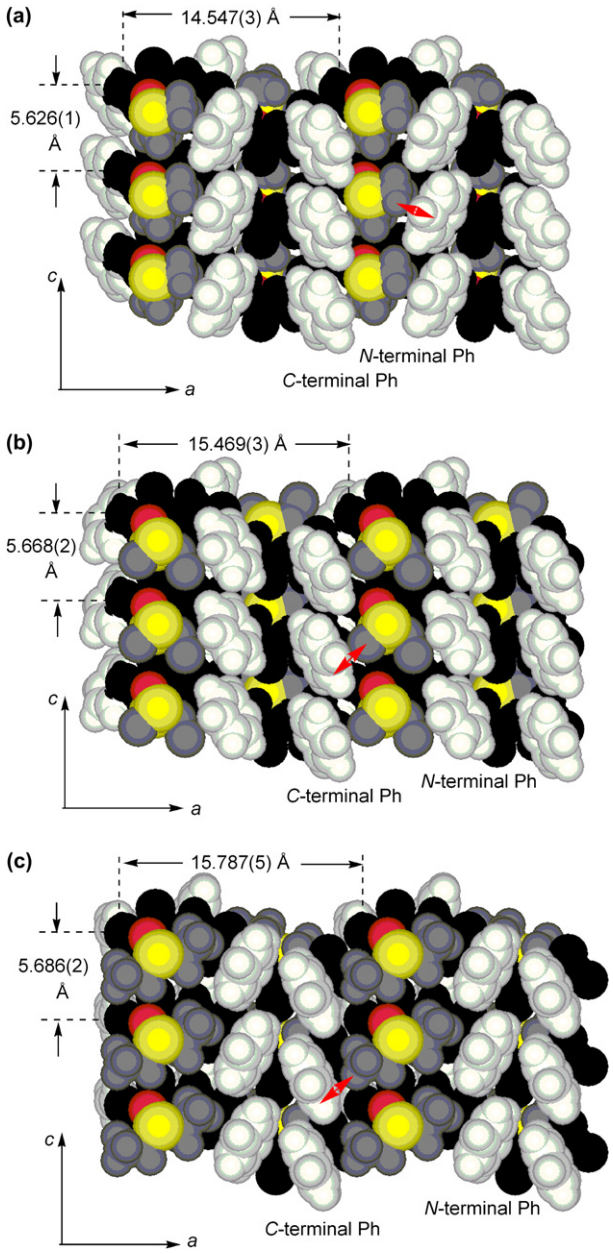


Figure 4. Top views of inclusion crystals (CPK model, *a*-*c* plane): (a) with dimethyl sulfoxide; (b) with ethyl methyl sulfoxide; (c) with diethyl sulfoxide.

summarized in Figure 5. The hydrogen-bonding network of glycylglycine's backbones assembles to form a bilayer structure (Fig. 5a). This is in sharp contrast to the monolayer structure of the above inclusion crystals of *SR*-**1**. As seen from Figure 5b, the hydrogen-bonding network sheet consists of three hydrogen bonds (A–C), which correspond to the hydrogen-bonds (A′–C′) of its opposite sheet. A central amide group, whose trans conformation keeps the glycylglycine backbone linear, does not take part in this hydrogen-bonding network. Two of three ammonio hydrogens are bound with two adjacent COO^- groups to construct the sheet structure (A: 2.67 Å and B: 3.04 Å). The residual one of the ammonio hydrogens binds with COO^- group of *SR*-**1** in the opposite sheet (C: 2.79 Å). Thus, the salt formation between the amino and carboxyl groups constructs the sequence of

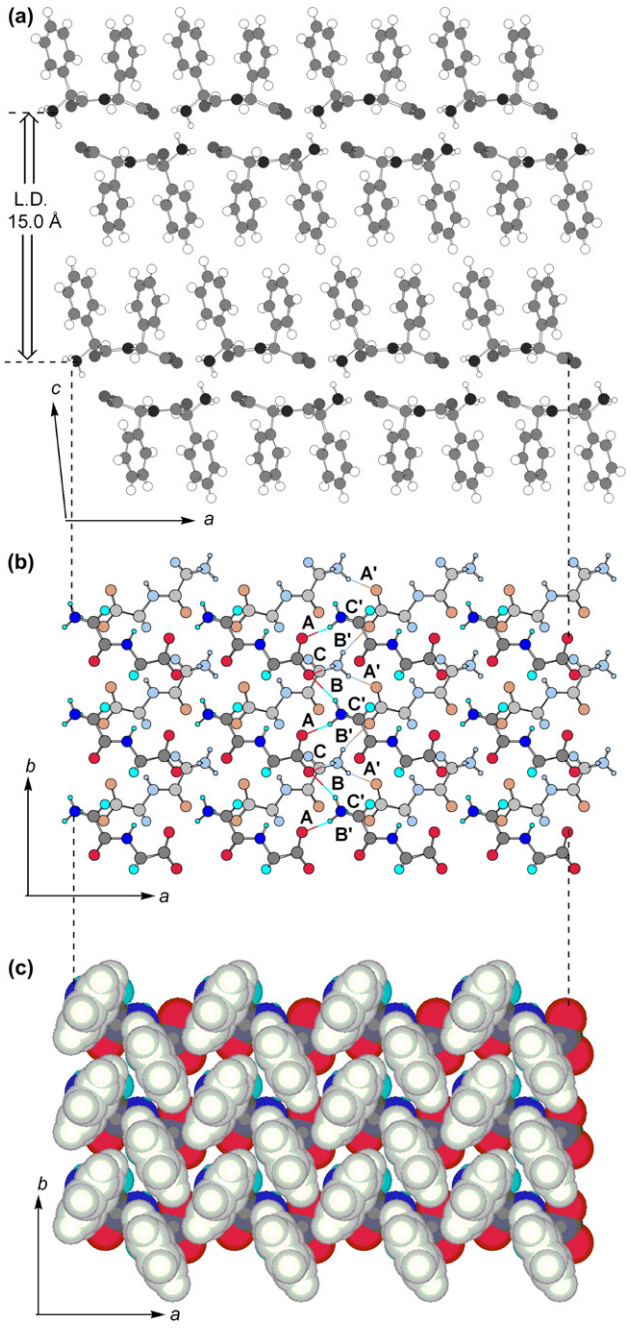


Figure 5. Crystal structure of *SR*-**1**. (a) A bilayer structure (*a*-*c* plane). L.D. is a layer distance measured by PXRD. (b) The offset between two hydrogen bonding layers (*a*-*b* plane). Hydrogen bonds are labelled by A–C and A′–C′. (c) Packing (CPK model) of phenyl groups (*a*-*b* plane).

10-membered rings via four hydrogen bonds (A, C, B′, and C′ in Fig. 5b). These 10-membered rings are often observed in the helical hydrogen-bonding columns (2_1-column) of amine salts of carboxylic acids.[11] As a result, two sheets are close face-to-face via hydrogen bonding to make a bilayer structure. In other words, the bilayer structure in *SR*-**1** crystals changes to a monolayer when they include a sulfoxide guest via hydrogen bonding. Finally, we wish to describe the arrangement of the phenyl groups of *SR*-**1**, which stand perpendicular to the sheet of glycylglycine backbones. Interestingly, all of the phenyl groups stack each other through an edge-to-face benzene–benzene interaction to make the herringbone packing (Fig. 5c). The herringbone motif is a well-known arrangement of phenyl rings in crystal engineering.[12]

3. Conclusion

A heterochiral L,D-dipeptide, (*S*)-phenylglycyl-(*R*)-phenylglycine (*SR*-**1**), has an ability to form inclusion compounds with relatively small sulfoxides such as DMSO, ethyl methyl sulfoxide, and diethyl sulfoxide. In these inclusion compounds, *SR*-**1** molecules arrange in parallel to construct a monolayer sheet. The guest sulfoxides are linked to $^{+}NH_3$ of *SR*-**1** via hydrogen bonding in channel cavity between the layers. In particular, these monolayer sheets of *SR*-**1** are wavy and their wave degree depends on the size of the guest. It is noteworthy that the conformation of the phenyl groups, which construct the sidewall of the cavity, changes in response to the guest volume to make the cavity suitable to the shape of the guest. Furthermore, we could obtain a single crystal of *SR*-**1** without a sulfoxide, which was revealed by its X-ray crystallographic analysis to be a bilayer structure.

4. Experimental

4.1. General methods

NMR spectra were recorded at 300 MHz for ^{1}H NMR. Melting points (decomposition) were measured on a TG-DTA. Elemental analyses were performed at Chemical Analysis Center, Chiba University, Japan. Both of (*S*)- and (*R*)-phenylglycine (99% ee) were purchased from Tokyo Chemical Industry.

4.1.1. X-ray analyses. X-ray powder diffractions were obtained with a MAC Science MXP diffractometer using graphite-monochromated Cu Kα radiation (30 kV, 200 mA). The spectra were measured at room temperature between 2° and 50° in the $2\theta/\theta$-scan mode with steps of 0.01° in 2θ and 4° min^{-1}.

4.1.2. Synthesis of *SR*-1. The preparation of (*S*)-phenylglycyl-(*R*)-phenylglycine [*SR*-**1**] was described in the previous paper.[7] According to the DCC–HOBt method,[13] coupling between (*S*)-*N*-(benzyloxycarbonyl)phenylglycine[14] and (*R*)-phenylglycine benzyl ester *p*-toluenesulfonate[15] provided the protected dipeptide. The deprotection by hydrogenolysis proceeded in the presence of Pd black to afford *SR*-**1**. *SR*-**1**: colorless crystals, mp (dec) 223 °C; $[\alpha]_D^{25}$ −19.6 (*c* 0.94, MeOH); ^{1}H NMR (300 MHz, D_2O+DCl) 7.37 (m, 10H), 5.60 (s, 1H), 5.29 (s, 1H); IR (KBr) 3400, 1693, 1608, 1587, 1496, 1365 (cm^{-1}). Powder X-ray analysis [Å(I/I_0)] 15.4(1.00), 7.58(0.17), 4.59(0.15), 3.76(0.44); Anal. Calcd for $C_{16}H_{16}N_2O_3$: C, 59.65; H, 6.12; N, 7.73. Found: C, 59.41; H, 6.06; N, 7.58.

4.1.2.1. Preparation of inclusion compound of *SR*-1. *SR*-**1** was dissolved in MeOH. After the addition of a sulfoxide (20 equiv) to the solution of *SR*-**1**, the resulting mixture was allowed to stand at an ambient temperature. Then the deposited crystals were collected by filtration and washed

with diethyl ether. The ratios were confirmed by single-crystal X-ray analyses and elemental analyses.

SR-**1**·dimethyl sulfoxide: colorless crystals; dec 164 °C; IR (KBr) 3365, 1680, 1498, 1587, 1377, 1024 (cm^{-1}). Powder X-ray analysis [Å(I/I_0)] 11.2(1.00), 5.19(0.33), 3.80(0.58). Anal. Calcd for $C_{16}H_{16}N_2O_3 \cdot 1.00C_2H_6SO$: C, 59.65; H, 6.12; N, 7.73. Found: C, 59.41; H, 6.06; N, 7.58.

SR-**1**·diethyl sulfoxide: colorless crystals; dec 142 °C; IR (KBr) 3377, 1686, 1592, 1495, 1370, 1010 (cm^{-1}). Powder X-ray analysis [Å(I/I_0)] 11.5(0.59), 11.1(0.10), 5.77(0.13), 3.84(1.00). Anal. Calcd for $C_{16}H_{16}N_2O_3 \cdot 1.00C_4H_{10}SO$: C, 61.52; H, 6.71; N, 7.17. Found: C, 61.14; H, 6.64; N, 7.13.

SR-**1**·ethyl methyl sulfoxide: colorless crystals; dec 136 °C; IR (KBr) 3379, 1676, 1589, 1504, 1375, 1012 (cm^{-1}). Powder X-ray analysis [Å(I/I_0)] 10.9(1.00), 5.02(0.26), 4.66(0.56), 4.21(0.48), 3.80(0.69). Anal. Calcd for $C_{16}H_{16}N_2O_3 \cdot 1.00(C_3H_8SO) \cdot 0.10H_2O$: C, 60.33; H, 6.45; N, 7.41. Found: C, 60.14; H, 6.44; N, 7.17.

According to the Kusumi's methodology,[16] ethyl methyl *N*-[(*S*)-methoxyphenylacetyl]sulfoximine was obtained from the recovered ethyl methyl sulfoxide by a one pot reaction (ethyl methyl sulfoxide/*O*-mesitylsulfonylhydroxylamine/$CHCl_3$ then (*S*)-methoxyphenylacetic acid/PyBOP/HOBt/pyridine).[4] Ethyl methyl *N*-[(*S*)-methoxyphenylacetyl]-sulfoximine (*S*/*R*=85:15 by NMR); colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51–7.24 (m, 5.0H), 4.75 (s, 0.85H, *S* major), 4.74 (s, 0.15H, *R* minor), 3.48–3.20 (m, 2.0H, *S* major and *R* minor), 3.42 (s, 3.0H, *S* major and *R* minor), 3.19 (s, 2.55H, *S* major), 3.12 (s, 0.45H, *R* minor), 1.31 (t, 0.45H, J=7.42 Hz, *R* minor), 1.18 (t, 2.55H, J=7.49 Hz, *S* major).

4.1.3. Crystallograpic data for the inclusion compounds. Data collection was performed on a Mac Science MXC18 four-circle diffractmetor with graphite-monochromated Cu Kα (λ=1.54178) radiation using the 2θ-ω scan technique, and the X-ray intensities were measured up to 2θ=140°. The structures were solved by a direct method *SIR-92*[17] or *SHELXS-97*[18] and refined by a computer program package, *maXus*[19] from MAC Science or *SHELXTL*[20] from Bruker AXS. Hydrogen atoms were calculated in the appropriate position.

4.1.3.1. The inclusion compound of DMSO. $C_{18}H_{22}N_2O_4S$, M=362.45, crystal dimensions 0.80×0.05×0.05 mm, orthorhombic, $P2_12_12_1$, T=298 K, a=14.547(3)Å, b=22.361(5) Å, c=5.626(1) Å, V=1830.0(8) Å^3, Z=4, d_{calcd}=1.316 g cm^{-3}, 2122 reflections measured, 1737 independent, R=0.065, (1331 reflections with $I>1.50\sigma(I)$), Rw=0.056, 259 parameters, with heavy atoms refined anisotropically, residual electron density 0.67/−0.41.

4.1.3.2. The inclusion compound of ethyl methyl sulfoxide. $C_{19}H_{24}N_2O_4S$, M=376.50, crystal dimensions 0.70×0.05×0.05 mm, orthorhombic, $P2_12_12_1$, T=298 K, a=15.469(3) Å, b=21.801(5) Å, c=5.668(2) Å, V=1911.5(7) Å^3, Z=4, d_{calcd}=1.308 g cm^{-3}, 2202 reflections measured, 1808 independent, R=0.072, (1567 reflections with $I>1.00\sigma(I)$), Rw=0.063, 259 parameters, with heavy atoms refined anisotropically, residual electron density 0.29/−0.29.

4.1.3.3. The inclusion compound of diethyl sulfoxide. $C_{20}H_{26}N_2O_4S$, M=390.50, crystal dimensions 0.40×0.30×0.05 mm, monoclinic, $P2_1$, T=298 K, a=11.520(4) Å, b=15.787(5) Å, c=5.686(2) Å, β=93.37(3)°, V=1032.2(6) Å^3, Z=2, d_{calcd}=1.256 g cm^{-3}, 2192 reflections measured, 2019 independent, R=0.042 (1961 reflections with $I>1.00\sigma(I)$), Rw=0.042, 329 parameters, with heavy atoms refined anisotropically, residual electron density 0.28/−0.21.

4.1.4. *SR*-1 host structure. In the course of our trial to make inclusion compounds (vide infra), ethyl isopropyl sulfoxide was not included, but *SR*-**1** crystals suitable for single-crystal X-ray analysis were obtained. $C_{16}H_{16}N_2O_3$, M=284.31, crystal dimensions 0.50×0.10×0.05 mm, monoclinic, $P2_1$, T=298 K, a=15.028(6) Å, b=5.815(2) Å, c=7.952(2) Å, β=95.40(0)°, V=691.8(4) Å^3, Z=2, d_{calcd}=1.365 g cm^{-3}, 1551 reflections measured, 1444 independent, R=0.070, (1444 reflections with $I>1.00\sigma(I)$), $Rw2$=0.175, 191 parameters, with heavy atoms refined anisotropically, residual electron density 0.47/−0.46.

Crystallographic data (excluding structure factors) for the structure in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 648530–648533. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44-(0)1223-336033 or e-mail: deposit@ccdc.cam.ac.uk].

Acknowledgements

This work was supported by a Grant-in-Aid for Scientific Research (C) (no. 18550117) from the Japan Society for the Promotion of Science.

References and notes

1. Akazome, M.; Hirabayashi, A.; Kataoka, K.; Nomura, S.; Ogura, K. *Tetrahedron* **2005**, *61*, 1107–1113.
2. (a) Akazome, M.; Hirabayashi, A.; Ogura, K. *Tetrahedron* **2004**, *60*, 12085–12093; (b) Akazome, M.; Ueno, Y.; Ooiso, H.; Ogura, K. *J. Org. Chem.* **2000**, *65*, 68–76; (c) Akazome, M.; Noguchi, M.; Tanaka, O.; Sumikawa, A.; Uchida, T.; Ogura, K. *Tetrahedron* **1997**, *53*, 8315–8322; (d) Ogura, K.; Uchida, T.; Noguchi, M.; Minoguchi, M.; Murata, A.; Fujita, M.; Ogata, K. *Tetrahedron Lett.* **1990**, *31*, 3331–3334.
3. (a) Akazome, M.; Takahashi, T.; Sonobe, R.; Ogura, K. *Tetrahedron* **2002**, *58*, 8857–8861; (b) Akazome, M.; Takahashi, T.; Sonobe, R.; Ogura, K. *Supramol. Chem.* **2001**, *13*, 109–136; (c) Akazome, M.; Takahashi, T.; Ogura, K. *J. Org. Chem.* **1999**, *64*, 2293–2300; (d) Akazome, M.; Yanagita, Y.; Sonobe, R.; Ogura, K. *Bull. Chem. Soc. Jpn.* **1997**, *70*, 2823–2827; (e) Akazome, M.; Sumikawa, A.; Sonobe, R.; Ogura, K. *Chem. Lett.* **1996**, 995–996.
4. Recent reviews on peptide helices and tubes: (a) Bong, D. T.; Clark, T. D.; Granja, J. R.; Ghadiri, M. R. *Angew. Chem., Int.*

Ed. **2001**, *40*, 988–1011; (b) Karle, I. L. *Acc. Chem. Res.* **1999**, *32*, 693–701.
5. (a) Di Blasio, B.; Benedetti, E.; Pavone, V.; Pedone, C.; Spiniello, O.; Lorenzi, G. P. *Biopolymers* **1989**, *28*, 193–201; (b) Di Blasio, B.; Benedetti, E.; Pavone, V.; Pedone, C.; Gerber, C.; Lorenzi, G. P. *Biopolymers* **1989**, *28*, 203–214; (c) Benedetti, E.; Di Blasio, B.; Pedone, C.; Spiniello, O.; Lorenzi, G. P.; Tomasic, L.; Gramlich, V. A. *Nature* **1979**, *282*, 630.
6. (a) Hartgerink, J. D.; Granja, J. R.; Milligan, R. A.; Ghadiri, M. R. *J. Am Chem. Soc.* **1996**, *118*, 43–50; (b) Ghadiri, M. R.; Granja, J. R.; Milligan, R. A.; McRee, D. E.; Khazanovich, N. *Nature* **1993**, *366*, 324–327; (c) Pavone, V.; Benedetti, E.; Di Blasio, B.; Lombardi, A.; Pedone, C.; Tomasic, L.; Lorenzi, G. P. *Biopolymers* **1989**, *28*, 215–223.
7. Akazome, M.; Senda, K.; Ogura, K. *J. Org. Chem.* **2002**, *67*, 8885–8889.
8. Optical resolution of alkyl sulfoxides using inclusion phenomena has been already reported. (a) Toda, F.; Tanaka, K.; Okada, T. *J. Chem. Soc., Chem. Commun.* **1995**, 639–640; (b) Toda, F.; Tanaka, K.; Mak, T. C. W. *Chem. Lett.* **1984**, 2085–2088; (c) Toda, F.; Tanaka, K.; Nagamatsu, S. *Tetrahedron Lett.* **1984**, *25*, 4929–4932; (d) Arad-Yellin, R.; Green, B. S.; Knossow, M.; Tsoucaris, G. *J. Am. Chem. Soc.* **1983**, *105*, 4561–4571; (e) Allemand, J.; Gredil, R. *Acta Crystallogr.* **1984**, *B38*, 2312–2315.
9. Pauling, L. *The Nature of the Chemical Bond*; Cornell Univ: New York, NY, 1960; p 260.
10. (a) Takahashi, H.; Tsuboyama, S.; Umezawa, Y.; Honda, K.; Nishio, M. *Tetrahedron* **2000**, *56*, 6185–6191; (b) Tsuzuki, S.; Honda, K.; Uchimura, T.; Mikami, M.; Tanabe, K. *J. Am. Chem. Soc.* **2000**, *122*, 3746–3753.
11. (a) Kinbara, K.; Sakai, K.; Hashimoto, Y.; Nohira, H.; Saigo, K. *J. Am. Chem. Soc.* **1996**, *118*, 3441–3449; (b) Kinbara, K.; Sakai, K.; Hashimoto, Y.; Nohira, H.; Saigo, K. *J. Chem. Soc., Perkin Trans. 2* **1996**, 2615–2622.
12. (a) Hunter, C. A.; Lawson, K. R.; Perkins, J.; Urch, C. J. *J. Chem. Soc., Perkin Trans. 2* **2001**, 651–668; (b) Swift, J. A.; Pal, R.; McBride, J. M. *J. Am Chem. Soc.* **1998**, *120*, 96–104; (c) Lewis, F. D.; Yang, J.-S.; Stern, C. L. *J. Am Chem. Soc.* **1996**, *118*, 12029–13037; (d) Hunter, C. A.; Sanders, J. K. M. *J. Am Chem. Soc.* **1990**, *112*, 5525–5534; (e) Desiraju, G. R.; Gavezzotti, A. *J. Chem. Soc., Chem. Commun.* **1989**, 621–623.
13. König, W.; Geiger, R. *Chem. Ber.* **1970**, *103*, 788–798.
14. Doyle, F. P.; Fosker, G. R.; Nayler, J. H.; Smith, H. *J. Chem. Soc.* **1962**, 1440–1445.
15. Zervas, L.; Winitz, M.; Greenstein, J. P. *J. Org. Chem.* **1957**, *22*, 1515–1521.
16. Yabuuchi, T.; Kusumi, T. *J. Am. Chem. Soc.* **1999**, *121*, 10646–10647.
17. Altomare, A.; Cascarno, G.; Giacovazzo, C.; Guagliardi, A.; Burla, M. C.; Polidori, G.; Camalli, M. *J. Appl. Crystallogr.* **1994**, *27*, 435.
18. Sheldrick, G. M. *Acta Crystallogr.* **1990**, *A46*, 467–473.
19. Mackay, S.; Edwards, C.; Henderson, A.; Gilmoer, C.; Stweart, N.; Shankland, K.; Donald, A. *maXus*; University of Glasgow: Scotland, UK, 1999.
20. Sheldrick, G. M. *SHELXTL Version 5.10*; Bruker AXS: Madison, WI, 1997.