Pergamon

Tetrahedron: Asymmetry, Vol. 8, No. 20, pp. 3431–3436, 1997

Printed in Great Britain
PII: S0957-4166(97)00460-6
0957-4166/97 $17.00 + 0.00

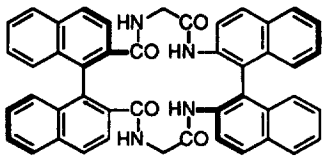
Cyclic polyamides consisting of 1,1′-binaphthyls. 'Chiral twist' of glycine residues

Kyoko Nozaki,* Takakiyo Terakawa, Hidemasa Takaya † and Tamejiro Hiyama
Department of Material Chemistry, Graduate School of Engineering, Kyoto University, Sakyo-ku, Kyoto 606-01, Japan

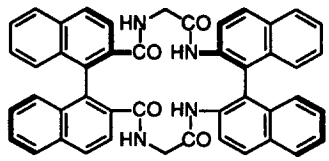
Abstract: Two cyclic polyamides were prepared from glycine and 1,1′-binaphthyls, and their structures have been determined by single-crystal X-ray analysis. Local conformations of glycines are twisted when they are sandwiched between two (*R*)-1,1′-binaphthyls. Glycines are stretched into planer conformations when they are placed between an (*R*)-1,1′-binaphthyl and an (*S*)-1,1′-binaphthyl. Conformations of these two cyclic polyamides in organic solvents and their interaction with other organic molecules are also discussed.

Introduction

Intensive efforts have been devoted to restricting peptide conformation. Two of the most common methods for this purpose are incorporation of amino acids into cyclic peptides[1] and attachment of amino acids to template molecules.[2] As a spacer, we came interested in the use of 1,1′-binaphthyl group which is widely used as a chiral building block.[3] Here we report preparation and characterization of cyclic polyamides **1a** and **1b** both of which consist of two glycine molecules and two chiral 1,1′-binaphthyls.[4] A 'chiral twist' induced by chiral 1,1′-binaphthyls restricts the glycine conformation.



1a



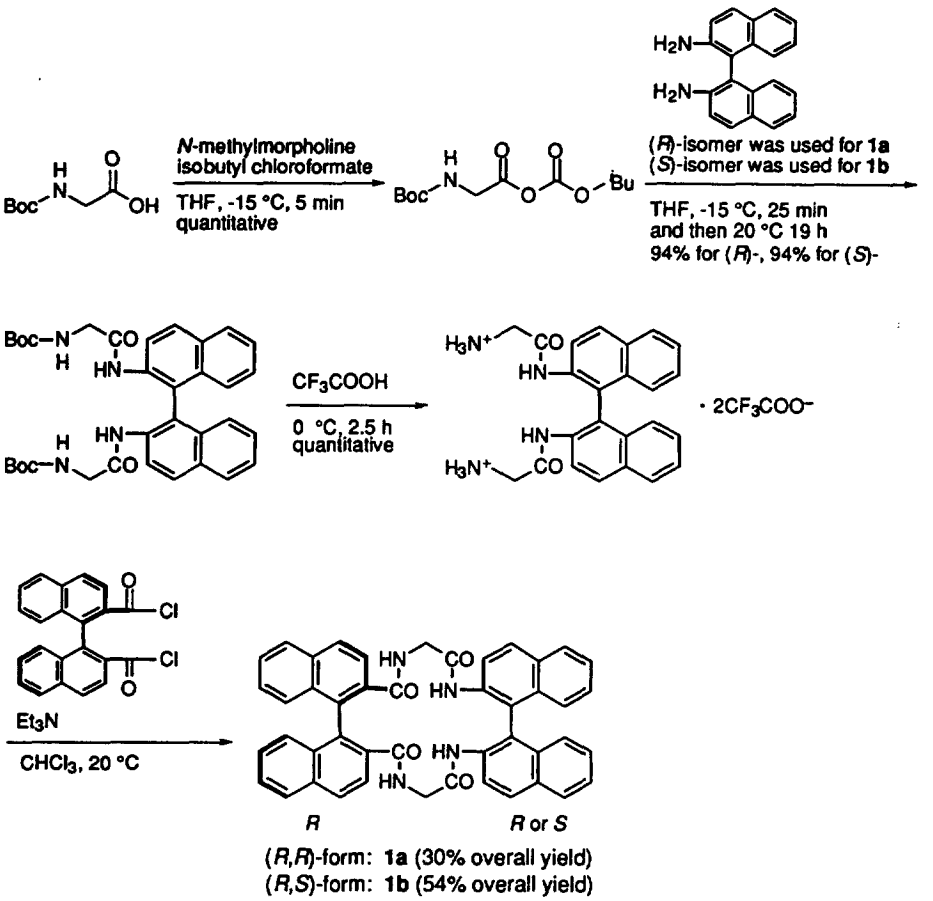
1b

Results and discussions

Cyclic polyamide **1a** has been synthesized from glycine, (*R*)-2,2′-diamino-1,1′-binaphthalene, and (*R*)-1,1′-binaphthalene-2,2′-dicarboxylic acid (Scheme 1). Boc–Gly was attached to (*R*)-2,2′-diamino-1,1′-binaphthalene and then cyclized with (*R*)-1,1′-binaphthalene-2,2′-dicarboxylic chloride. Similarly, **1b**, a diastereomer of **1a**, was prepared from (*S*)-enantiomer of the diamine.

In the solid state, the local conformations of the glycine residues are governed by the chirality of the biaryl spacers. Shown in Figure 1 are ORTEP drawings for the crystal structures of **1a**·(DMSO) and **1b**·$(DMF)_3$ when they were recrystallized from DMSO–THF–hexane and DMF, respectively. The representative bond lengths and dihedral angles are shown as captions. The structure of **1a** is C_1 symmetric and the two glycine units are twisted (Φ=67°; Ψ=26° and Φ=76°; Ψ=6°).[5] An amide proton of (*R*)-2,2′-diamino-1,1′-binaphthyl forms a hydrogen bond with one of the amide oxygen atoms of the (*R*)-1,1′-binaphthalene-2,2′-dicarboxylic acid. The solvent DMSO is incorporated in the crystal by a hydrogen bonding between one of the amide protons of the glycines and the oxygen atom of DMSO.

* Corresponding author. Email: nozaki@NPC05.Kuic.Kyoto-u.ac.jp
† Deceased on 4 October 1995.



Scheme 1.

In contrast, in **1b** the two glycine residues are stretched into planar structure (Φ=153°; Ψ=176° and Φ=171°; Ψ=175°). The conformation of polyamide **1b** is almost C_2 symmetric. Two DMF molecules are bound by intermolecular hydrogen bondings between amide protons of the (*S*)-2,2′-diamino-1,1′-binaphthalene moiety and the oxygen atoms of the DMFs.

Next, the conformations of **1a** and **1b** in organic solvents were investigated on the basis of ^{1}H and ^{13}C NMR spectra. The two glycine residues of **1a** are equivalent at 20°C in DMSO-d_6 and $CDCl_3$ (Figure 2(a) and (b)). Similarly, the two naphthyls in each binaphthyl are equivalent. Thus, it is suggested that cyclic polyamide **1a** is in C_2 symmetric structure in these solvents.

In DMSO-d_6, **1b** also maintains its C_2 symmetry which was proven by NMR (Figure 3(a)). In $CDCl_3$, the crystals of **1b**·$(DMF)_3$ are soluble (Figure 3(b)). After a few minutes, however, aggregation of **1b** occurred and precipitates appeared gradually. Shown in Figure 3(b) is a ^{1}H NMR spectra of **1b**·$(DMF)_3$ in $CDCl_3$ which was taken before the precipitates appeared. Lower concentration of 0.01 M is employed to retard the aggregation. Interestingly, broadening was observed in the peak due to one of the two methylene protons of each glycine unit.

From a 0.040 M solution of **1b**·$(DMF)_3$ in $CHCl_3$, 42% of the originally dissolved **1b** was recovered as precipitates by filtration through a glass filter G4 after 15 min at 20°C. Addition of a hydrogen bond acceptor inhibited the self aggregation. For example, the recovery of **1b** from the same solution was reduced to 6.0% in 1 h in the presence of two mol amounts of Boc–Gly. From DMSO solution of

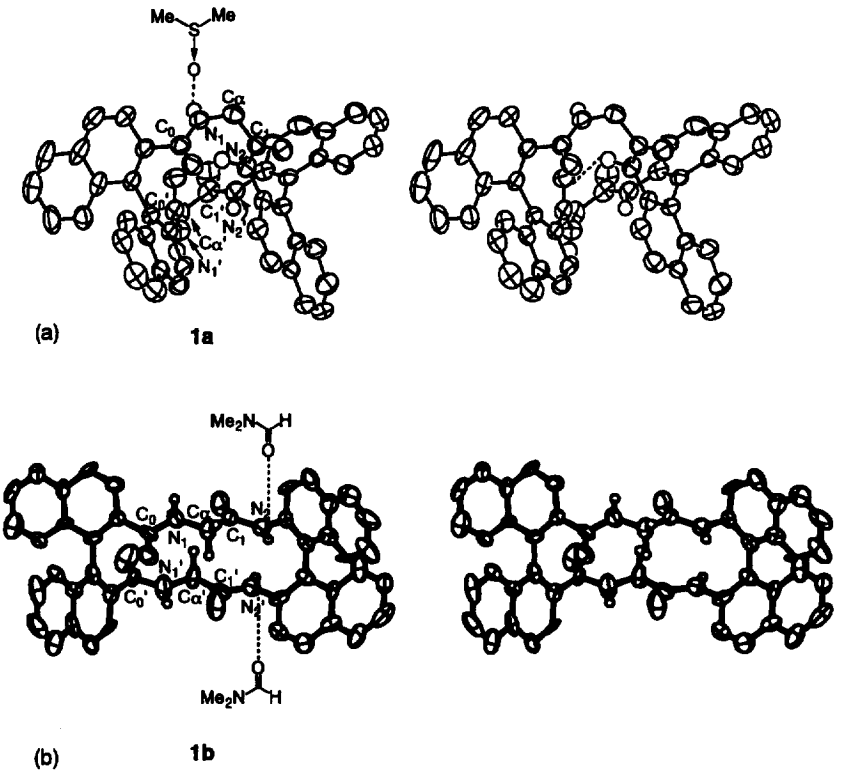


Figure 1. Stereoviews of ORTEP drawings for (a) **1a**·(DMSO) and (b) **1b**·$(DMF)_3$. Solvent molecules and the hydrogen atoms not involved in the discussion are omitted. Hydrogen bondings are shown as dotted lines. (a) C_0–N_1–$C\alpha_1$–C_1 66.6(9), N_1–$C\alpha_1$–C_1–N_2 26.4(7), C_0'–N_1'–$C\alpha_1'$–C_1' 75.7(9), N_1'–$C\alpha_1'$–C_1'–N_2' 6.1(8), H (attached to N_2)-O (attached to C_0') 2.26. $P2_12_12_1$, Z=4, a=18.0341(42) Å, b=28.3709(97) Å, c=9.1861(23) Å, V=4700(2) $Å^3$. (b) C_0-N_1-$C\alpha_1$-C_1 153(1), N_1-$C\alpha_1$-C_1-N_2 176(1), C_0'–N_1'–$C\alpha_1'$–C_1' 171(1), N_1'–$C\alpha_1'$–C_1'–N_2' 175(1). $P2_12_12_1$, Z=6, a=14.780(8) Å, b=29.279(7) Å, c=11.327(7) Å, V=4901(4) $Å^3$.

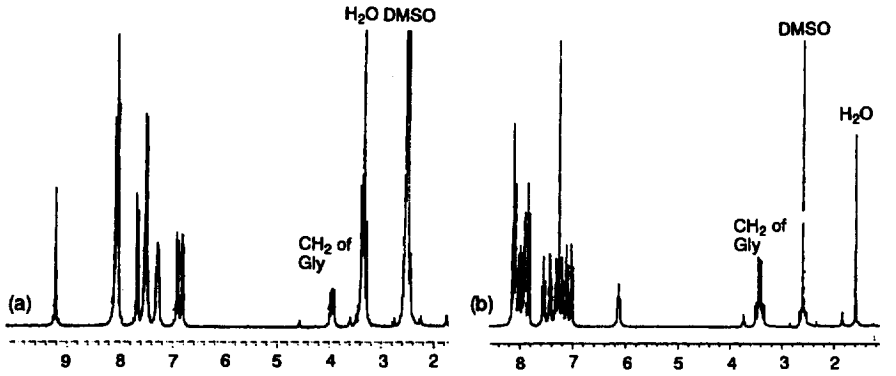


Figure 2. ^1H NMR spectrum of **1a**·(DMSO) in (a) DMSO-d_6 (0.01 M) and (b) $CDCl_3$ (0.01 M). In both charts, the methylene of each glycine residue and the two naphthyls in each binaphthyl group are equivalent.

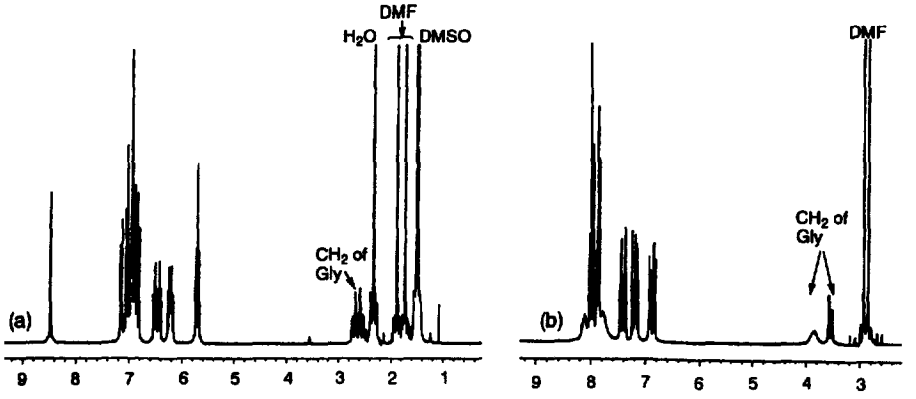


Figure 3. ^{1}H NMR spectrum of **1b**·(DMF)$_3$ in (a) DMSO-d_6 (0.01 M) and (b) $CDCl_3$ (0.01 M). In both charts, the methylene of each glycine residue and the two naphthyls in each binaphthyl group are equivalent. Peak broadening is observed for one of the two methylene protons of each glycine residue in (b).

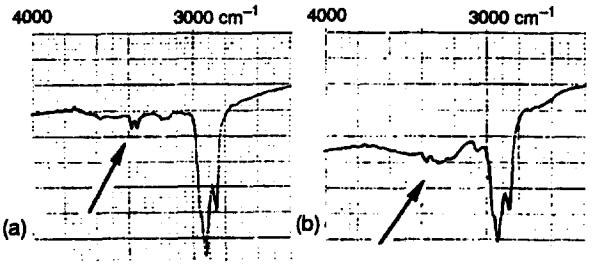


Figure 4. IR spectra of (a) **1b**·(DMF)$_3$ complex and (b) precipitate of **1b** from $CHCl_3$. In the region of 3400–3300 cm^{-1}, two sharp amido N–H stretching bands are observed in (a) due to the two different types of amides (ArCON*H*Cα– and –CαCON*H*Ar) while those are broadened in (b).

1b, no precipitate was observed. In contrast to these results with **1b**, no precipitate appeared from the **1a** solution in $CHCl_3$ even after 24 h. Because the glycine residues of **1b** are in planar conformations in the solid state, such β-sheet-type intermolecular hydrogen bonding[6] may be responsible for the aggregation. In fact, infrared spectrum of this aggregate suggests that the amide protons are involved in random hydrogen bondings. That is, the sharp amide–proton peaks observed in the crystal form of **1b**·(DMF)$_3$ (Figure 4(a)) broadened in the aggregate (Figure 4(b)).

Interactions of cyclic polyamides **1a** and **1b** with some organic molecules were investigated in $CDCl_3$ by ^{1}H NMR. When a racemic mixture of methyl phenyl sulfoxide was mixed with **1a**·(DMSO) in $CDCl_3$, a split was observed for the singlet due to the methyl group of methyl phenyl sulfoxide (Figure 5(a)). Accordingly, **1a** worked as a shift reagent to separate the peaks of enantiomers. Similar phenomenon was observed with **1b**·(DMF)$_3$ (Figure 5(b)). Addition of **1a**·(DMSO) to a $CDCl_3$ solution of Ac–Gly–Gly–OEt changed the chemical shift of either AcNHC*H*$_2$CONHCH$_2$COOEt or AcNHCH$_2$CONHC*H*$_2$COOEt (Figure 6). Both of these interactions suggest the possible utilization of cyclic polyamides **1a** and **1b** for molecular recognitions.

In this study, two cyclic polyamides **1a** and **1b** have been synthesized and their conformations in solid have been revealed. Their behaviors in solution were also investigated.

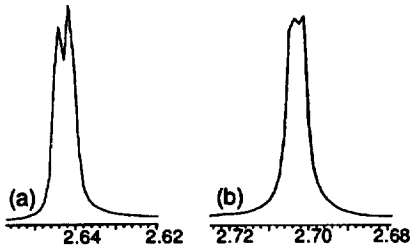


Figure 5. ^{1}H NMR spectra of the methyl group of methyl phenyl sulfoxide (0.01 M in $CDCl_3$) in the presence of (a) **1a**·(DMSO) (0.01 M) and (b) **1b**·$(DMF)_3$ (0.01 M).

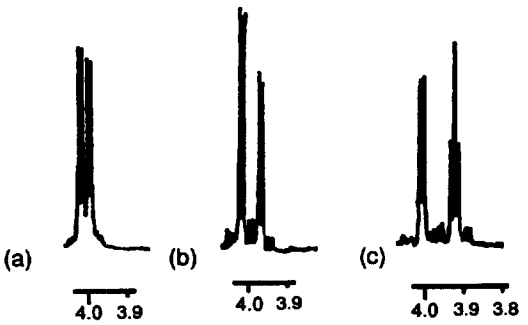


Figure 6. ^{1}H NMR spectra of the underlined methylene groups of AcNHCH_2CONHCH_2COOEt (0.01 M in $CDCl_3$) in the presence of **1a**·(DMSO). (a) without **1a**·(DMSO), (b) 0.006 M of **1a**·(DMSO) and (c) 0.020 M of **1a**·(DMSO).

Experimental section

Preparation of 1a and 1b

Boc–Gly (4.46 mmol) was coupled with isobutyl chloroformate (4.05 mmol) in the presence of *N*-methylmorpholine (4.05 mmol) in dry THF (20 mL) at −15°C. To the solution was added (*S*)-2,2′-diamino-1,1′-binaphthalene (2.03 mmol) and the mixture was stirred at −15°C for 25 min and at 20°C for 19 h. After aqueous workup, the resulting Boc–Gly-(*S*)-1,1′-binaphthyl-2,2′-diamine was recrystallized from CH_2Cl_2/hexane (1/1) (94% yield). (*R*)-1,1′-Binaphthalene-2,2′-dicarboxylic acid[7] (2.03 mmol) was dissolved in thionyl chloride (10 mL) and stirred at reflux temperature for 10 h. After removal of the volatile components, the residue was mixed with Gly-(*S*)-1,1′-binaphthyl-2,2′-diamine·CF_3COOH (2.03 mmol) and triethylamine (16.0 mmol) in chloroform (100 mL) and the mixture was stirred at 20°C for 45 h. After workup, the product was purified by column chromatography on silica gel (EtOAc/hexane=3/1). Reprecipitation from DMSO–ether gave **1b** in 30% overall yield. mp (DMSO–ether) 319.5–319.8°C (decomp.). $[\alpha]_D^{23}$ −13.1 (*c* 1.0 DMSO). ^{1}H NMR (DMSO-d_6) δ 9.33 (s, 2H), 7.92–7.69 (m, 12H), 7.51 (s, 2H), 7.37–7.26 (m, 4H), 7.10–7.01 (m, 4H), 6.81 (d, 2H, J=8.25 Hz), 6.73 (d, 2H, J=8.25 Hz), 3.74–3.57 (m, 4H); ^{13}C NMR (DMSO-d_6) δ 168.45, 134.32, 133.87, 133.30, 133.19, 132.74, 132.54, 131.02, 127.94, 127.78, 127.39, 127.21, 126.74, 126.31, 126.24, 125.93, 125.75, 125.37, 124.98, 124.50, 123.90, 42.45. Anal. Found: C, 74.01; H, 4.82; N, 7.47. Calcd. for **1b**·(DMSO): C, 73.64; H, 4.89; N, 7.16. **1a** was prepared analogously in 54% overall yield. **1a**: mp (DMSO–ether) 257.0–257.9°C (decomp.). $[\alpha]_D^{23}$+3.6 (*c* 1.0 $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ 8.17–7.83 (m, 14H), 7.59–7.00 (m, 12H), 6.06 (dd, 2H, J=7.26, 4.95 Hz), 3.50 (dd, 2H, J=15.18, 4.95 Hz), 3.36 (dd, 2H, J=15.18, 7.26 Hz); ^{13}C NMR ($CDCl_3$) δ 169.31, 168.05, 134.61, 134.09, 133.46, 132.94, 132.76, 132.38, 131.61, 129.42, 129.25, 128.59, 128.10, 127.66, 127.01, 126.69, 126.09, 125.84, 125.61, 123.76, 123.68, 123.27, 45.09. Anal. Found: C, 75.50; H, 4.57; N, 7.48. Calcd. for **1a**·$(DMSO)_{0.5}$: C, 75.89; H, 4.74; N, 7.53.

Self aggregation of ***1b*** *in* $CHCl_3$

When the **1b**-DMF complex was dissolved in $CHCl_3$ (1 mL) at 20°C, precipitates gradually appeared. The precipitates were collected in 15 min by filtration using a glass filter (G4) and dried *in vacuo* to give solvent free **1b** in 42% (11.9 mg, 0.0169 mmol).

Acknowledgements

We are grateful to Professor Shunsaku Kimura (Kyoto University) for helpful discussions.

References

1. For example, (a) S. J. Miller, R. H. Grubbs, *Chemtracts; Org. Chem.* **1995**, *8*, 363. (b) C. Gilon, D. Halle, M. Chorev, Z. Selinger, G. Byk, *Biopolymers* **1991**, *31*, 745. (c) R. M. J. Liskamp, *Recl. Trav. Chim. Pays-Bas* **1994**, *113*, 1. (d) M. Kahn, *Synlett* **1993**, 821.
2. For example, (a) J. P. Schneider, J. W. Kelley, *Chem. Rev.* **1995**, *95*, 2169. (b) I. Ernest, J. Kalvoda, C. Sigel, G. Rihs, H. Fritz, M. J. J. Blommers, F. Raschdorf, E. Francotte, M. Mutter, *Helv. Chim. Acta.* **1993**, *76*, 1539. (c) D. W. Choo, J. P. Schneider, N. R. Graciani, J. W. Kelly, *Macromolecules* **1996**, *29*, 355. (d) J. S. Nowick, D. L. Holmes, G. Mackin, G. Noronha, A. Shaka, E. M. Smith, *J. Am. Chem. Soc.* **1996**, *118*, 2764.
3. E. Weber, F. Vögtle, in *Host Guest Complex Chemistry I*; F. Vögtle Ed.; Springer-Verlag: New York, 1981.
4. (a) V. Brandmeier, M. Feigel, *Tetrahedron* **1989**, *45*, 1365. (b) Btandmeier, V.; Feigel, M.; Bremer, M. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 486.
5. For the nomenclature, see, *Biochemistry* **1970**, *9*, 3471.
6. (a) H. Maeda, Y. Gatto, S. Ikeda, *Macromolecules* **1984**, *17*, 2031. (b) A. Brack, L. E. Orgel, *Nature* **1975**, *256*, 383. (c) H. Maeda, K. Ooi, *Biopolymers* **1981**, *20*, 1549. (d) W. F. DeGrad, J. D. Lear, *J. Am. Chem. Soc.* **1985**, *107*, 7684.
7. T. Ohta, M. Ito, K. Inagaki, H. Takaya, *Tetrahedron Lett.* **1993**, *34*, 1615.

(Received in Japan 12 August 1997)