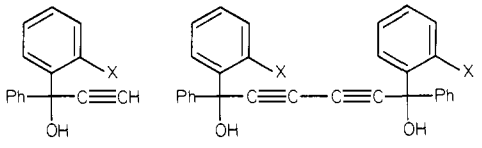
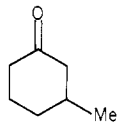


1

2

2a, X = H 2c, X = Cl
2b, X = F 2d, X = Br



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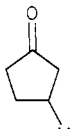

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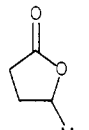

5

study of the 1:2 complex of **2a** and acetone that a hydrogen bond between OH of **2a** and acetone forces the latter in the vicinity of the saturated carbon of the former in the complex.[2b,c] These data suggest the potential for optical resolution of a guest molecule by complexing with optically active **2b–d**. Oxidative coupling of 100% optically pure 1-(*o*-halophenyl)-1-phenylpropyn-1-ol (**1b–d**), which had been obtained by previously reported resolution method,[3] gave in almost 100% ee[4] **2b** (mp 166–168 °C, $[\alpha]_D$ 47.7°[4]), **2c** (mp 127–129 °C, $[\alpha]_D$ 122°), and **2d** (mp 139–141 °C, $[\alpha]_D$ 129°), respectively. By this method, both the *d*- and *l*-enantiomers of **2b–d** were prepared in 100% ee. In all cases of the optical resolution, 100% ee **2b–d** were used.

When a solution of *l*-**2c** (19.2 g, 39.8 mmol) and *dl*-**3** (17.8 g, 159 mmol) in ether–petroleum ether (1:1, 100 mL) was kept at room temperature for 6 h, a 1:2 complex of *l*-**2c** and *d*-**3** (25.5 g, 91%,[5] $[\alpha]_D$ −85.8°) was obtained as colorless prisms. Upon heating the complex, 28% ee *d*-**3** (8.0 g, 90%,[5] $[\alpha]_D$ +4.0° ($CHCl_3$)) was obtained by distillation.[6] The remaining *l*-**2c** was 100% optically pure. Two recrystallization of the 1:2 complex of *l*-**2c** and the 28% ee *d*-**3** (25.5 g) from ether–petroleum ether (1:1, each 80 mL) gave the complex (11.6 g, 41%, $[\alpha]_D$ −84.0°) that, on distillation, gave 66% ee *d*-**3** (3.5 g, 39.3%, $[\alpha]_D$ +9.5° ($CHCl_3$)). When the same recrystallization was repeated twice for the complex prepared from *l*-**2c** and the 66% ee *d*-**3** (3.7 g), the 1:2 complex of *l*-**2c** and 100% ee *d*-**3** (4.1 g, 15%, mp 78–79 °C, $[\alpha]_D$ −71.7°) was obtained. By further recrystallization, the $[\alpha]_D$ value of the complex did not change. Upon heating the complex, 100% ee *d*-**3** (1.16 g, 13%, $[\alpha]_D$ +14.4° ($CHCl_3$), lit.[7] +14.4° ($CHCl_3$, *c* 0.01)) was obtained after distillation.

This resolution method was not effective for 2-methylcyclohexanone and only the 2% ee *d*-enantiomer was obtained in 95% yield by a single complexation with *l*-**2c**. This suggests that the distance between the chiral center and the carbonyl group in the guest molecule is crucial to the efficiency of resolution. In support of this, **4** and **5** were resolved quite efficiently by this method. Complexation of *l*-**2c** (7.7 g, 16 mmol) and *dl*-**4** (6.3 g, 64 mmol) in ether–petroleum ether (1:1, 50 mL) at room temperature for 6 h gave the 1:1 complex of *l*-**2c** and *l*-**4** (9.4 g, 86%, $[\alpha]_D$ −20.2°). Seven recrystallizations of the above complex from ether–petroleum ether (1:1, each 30 mL) gave the 1:2 complex of *l*-**2c** and 100% ee *l*-**3** (0.87 g, 8%, mp 61–63 °C, $[\alpha]_D$ −126°), the $[\alpha]_D$ value of which did not change by further recrystallization. When the complex was heated, 100% ee *l*-**4** (0.19 g, 6%, $[\alpha]_D$ −148°) was obtained by distillation.

Similar complexation of *l*-**2c** (13.4 g, 27.7 mmol) and *dl*-**5** (11.1 g, 111 mmol) gave the 1:2 complex of *l*-**2c** and *l*-**5** (18.5 g, 98%, $[\alpha]_D$ +5.1°). Recrystallization of the complex from ether–petroleum ether (1:1, each 50 mL) was repeated 12 times to give the 1:2 complex of *l*-**2c** and 100% ee *d*-**5** (0.95 g, 5%, mp 94–95 °C, $[\alpha]_D$ −81.3°). Heating of the complex resulted in 100% ee *d*-**5** (0.25 g, 4.5%, $[\alpha]_D$ +30.1°, lit.[8] +33.3° (neat)).

When *d*-**2c** was used instead of *l*-**2c** for the resolution of **3**, **4**, and **5**, the other enantiomers *l*-**3**, *d*-**4**, and *l*-**5** were obtained, respectively, in almost the same yields as those by *l*-**2c**. For example, when a solution of *d*-**2c** (8.1 g, 16.7 mmol) and *dl*-**5** (6.7 g, 67 mmol) in ether–petroleum ether (1:1, 100 mL) was kept at room temperature for 6 h, a 1:2 complex of *d*-**2c** and *l*-**5** (11.2 g, 98%, $[\alpha]_D$ +88.8°) crystallized out, which on distillation gave 17% ee *l*-**5** (3.15 g, 94%, $[\alpha]_D$ −5.2°). Recrystallization of the complex from ether–petroleum ether (1:1, each 30 mL) was repeated 12 times to give the 1:2 complex of *d*-**2c** and 100% ee *l*-**5** (0.69 g, 6%, mp 93–95 °C, $[\alpha]_D$ +81.3°). By heating the complex, 100% ee *l*-**5** (0.17 g, 5%, $[\alpha]_D$ −30.1°) distilled out.

Although **2d** showed almost the same efficiency as did **2c** for the resolution, **2b** was much less effective. One complexation of *dl*-**5** with *l*-**2d** followed by distillation gave 19% ee *d*-**5** (95%), even though the same treatment of *dl*-**5** with *l*-**2b** gave *dl*-**5** (87%). When recrystallization of the 1:2 complex of *l*-**2d** and 19% ee *d*-**5** from ether–petroleum ether (1:1) was repeated 12 times, 89% ee *d*-**5** (11%) was obtained after distillation.

The quite efficient optical resolution by the complexation method is probably due to a favorable packing of host and guest molecules in the crystal. The channel formed by optically active **2** includes one enantiomer of a guest selectively and results in more stable complex rather than to include the other enantiomer. X-ray structural study of the complex of *l*-**2c** and *d*-**3** is in progress.

Acknowledgment. We thank Professor Ryoji Noyori of Nagoya University for helpful comments and discussions.

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(4) The enantiomeric excess (% ee) was determined by NMR analysis in $CDCl_3$ by using the chiral shift reagent, tris[3-(heptafluoropropylhydroxymethylene)-*d*-camphorato]europium(III), Eu(hfc)$_3$ (Aldrich, 99+%). The % ee values are accurate within the limits of error (±5%) of the NMR instrument used, JASCO, FX-100.

(5) All yields of the optical resolution were calculated on the basis of the theoretical amount of the optical isomer contained in the initial *dl*-compound.

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Crystal and Molecular Structures of 2,11-Dithia- and 1,3,10,12-Tetrathia[3.3](2,6)pyridinophanes

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The conformational aspects of 2,11-dithia[3.3]metacyclophanes, prepared as precursors for the corresponding [2.2]metacyclophanes and/or [2.2]metacyclophane-1,9-dienes, have been well studied[1] via the convenient ^1H NMR spectral probes present in the form of the "internal" proton(s) or substituents. Conversely, relatively little is known about the stereochemistry of the structurally related [3.3](2,6)pyridinophanes, which lack these probes. Initial ^1H NMR studies on pyridinophanes **1** and **2** suggested a rapid syn–anti isomerization in bis(sulfide) **1**;[2a] while in tetrasulfide **2**, conjugative factors have been proposed to play a role in raising the energy barrier to ring inversion.[3] Moreover in solution

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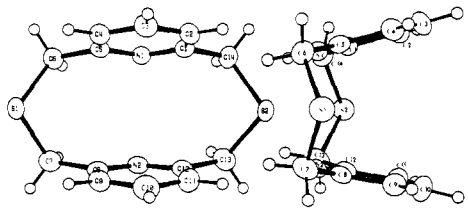
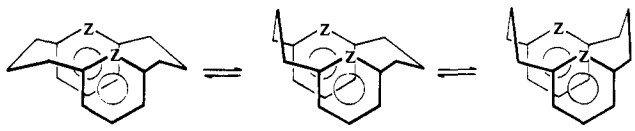


Figure 1. ORTEP drawings (side, front views) of cyclophane 1.

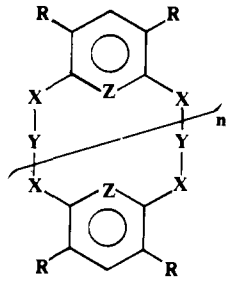
Scheme I



a b c

syn-[3.3]metacyclophanes have been thought to exist in three rapidly interconverting isomeric forms a–c (Scheme I),[4] whereas X-ray data have provided evidence for the crown-like configuration a in the parent *syn*-2,11-dithia[3.3]metacyclophane (**3**)[5] as well as **4**.[6] On the other hand, a 4:1 distribution of conformers a and b has been found in the crystal structure of the dimethyl syn analogue (**5**)[7] of **3**.

We report herein single-crystal X-ray structure determinations of [3.3]pyridinophanes **1** and **2** and present evidence that **1** *and*



1, X = CH_2; Y = S; Z = N; R = H; n = 1
2, X = S; Y = CH_2; Z = N; R = H; n = 1
3, X = CH_2; Y = S; Z = CH; R = H; n = 1
4, X = S; Y = S; Z = CH; R = OCH_3; n = 1
5, X = CH_2; Y = S; Z = CCH_3; R = H; n = 1
6, X = CH_2; Y = S; Z = N; R = H; n = 2
7, X = CH_2; Y = S; Z = N; R = H; n = 3
8, X = CH_2; Y = O; Z = N; R = H; n = 1

2 *exist as the specific syn conformers both in solid state and solution.*

Phane **1**, as shown in Figure 1, is found to exist as the syn conformer a[8] in the solid state, with approximate symmetry C_{2v}, an SS distance of 6.180 (1) Å, and torsion angles (NCCS) of 112–121°. The single-bond character of the CS bonds is supported by the average length of 1.810 (3) Å (1.82 Å for C—S and 1.62 Å for C=S bonds).[9] The average CSC bond angle of 102.6 (3)° is slightly smaller than that found in related carbophanes (104–109°).[5]

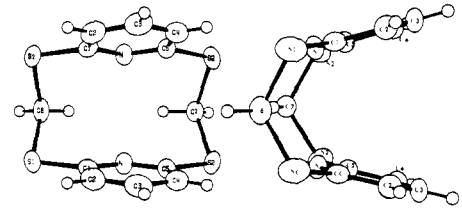


Figure 2. ORTEP drawings (side, front views) of cyclophane 2.

Table I. ^{1}H NMR Spectral Data (δ)

	H-4	H-3,5	CH_2
1	7.25 (t, 7.3)	6.94 (d, 7.3)	3.99 (s)
2[3]	7.21 (7.8)	6.87 (7.8)	5.57 (brs)
6[2b]	7.53 (t)	7.30 (d)	3.77 (s)
7	7.50 (t, 7.3)	7.18 (d, 7.3)	3.75 (s)

Phane **2**, as depicted in Figure 2, is shown to also possess the syn conformation c in the crystal state.[10] This is the first, to the best of our knowledge, *syn*-[3.3]metacyclophane existing in this conformation. The molecule has exact C_s and approximate C_{2v} symmetry in the crystal. The short C6–C7 distance of 4.6 Å and dramatically diminished torsion angles (NCSC) of ca. 48° characterize this geometry. Although the shorter (pyridine) C1–S1 bond length of 1.784 (3) Å is suggestive[11] of slightly increased multiple-bond character (i.e., the thioimidate moiety), the bridging C6–S1 bond length of 1.797 (4) Å is indicative of single-bond character. The juxtaposition of methylene protons to the N atoms (2.5 Å) may infer hydrogen bonding; however, the spatial orientation of these hydrogens is not favored for optimal hydrogen bonding.[12] The W conformation in **1** and the lack of it in **2** are probably the results of heteroatom (N–S) repulsions.

In solution, the conformational preference of **1** was easily ascertained by chemical shift comparison (Table I) of its pyridyl protons with those of 2,11,20-trithia[3.3.3]- (**6**) and 2,11,20,29-tetrathia[3.3.3.3](2,6)pyridinophane (**7**).[13] Therefore, the upfield shift (δ = 0.24–0.36) experienced by the pyridyl protons in **1** is supportive of the syn conformation in solution. No temperature dependence has been reported[2a] for the methylene signal in **1** down to −50 °C, thus indicating that **1** is still undergoing conformational equilibration among the isomeric forms a, b, and c.

Contrary to the reported[3] syn–anti equilibrium for **2** in solution, the $\Delta G^{\ddagger}$ of 12.2 kcal/mol is best explained by a mobile syn conformation [a ⇄ b ⇄ c] in view of the invariant pyridine region in the ^{1}H VTNMR spectrum; while at −50 °C, conformer **2c** is the preferred frozen orientation. Cyclophane **8**[14] is probably also in the syn conformation on the basis of similar chemical shift differences (Δδ = 0.3–0.4) exhibited between **8** and its larger, more flexible homologues.

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Registry No. 1, 25117-68-4; **2**, 80693-51-2.

Supplementary Material Available: Experimental details, tables containing bond lengths, bond angles, torsion angles, and interatomic distances, and atomic coordinates and anisotropic temperature factors for **1** and **2** are given (9 pages). Ordering information is given on any current masthead page.

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