

Inclusion Properties of 11b-Substituted 2,3,5,6,11,11b-Hexahydro-3-oxo-1*H*-indolizino[8,7-*b*]indole-5-carboxylic Acid Esters. New Chiral Host Compounds Derived from L-Tryptophan

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New chiral host compounds have been prepared from L-tryptophan and 3-aroylpropionic acids. These hosts show broad inclusion and sorption abilities toward solvent and racemic molecules, and are characterized by X-ray crystallographic analysis, which clarify the one-dimensional channel structures of the hosts, the helical arrangements of the guests, and the occurrence of weak interactions such as C–H···O and C–H···Cl between the hosts and the guests. The TG and DTA data show the high cohesion of the hosts, and the PXRD patterns indicate that the crystal structures of the hosts remain ordered after removal of the guest molecules. These hosts have potential usefulness in the optical resolution of racemic guest molecules such as *s*-butyl chloride and 4-methylcyclohexene.

Inclusion complexes have received much attention because of their potential applications in analytical and synthetic chemistry.[1] A variety of host compounds have been designed and synthesized. Host compounds, such as anthracene–bis(resorcinol), 9-hydroxy-9-fluorenyl derivatives, thiophene-condensed compounds, etc., are well-characterized.[2] Using tartaric acid or lactic acid, chiral host compounds can be synthesized and used for optical resolution.[3] Naturally occurring steroids such as cholic acid, dehydrocholic acid, and their derivatives are good host compounds.[4] Dipeptide-type host compounds are also studied.[5] In these host compounds functional groups such as OH, NH_2, and COOH are used for strong hydrogen bonding. Alkaloidal brucine has no such functional groups, but shows an inclusion ability.[6] In a previous paper, we reported that the cocrystal of $CHCl_3$ and a compound, (5*S*-*trans*)-2,3,5,6,11,11b-hexahydro-3-oxo-1*H*-indolizino[8,7-*b*]indole-5-carboxylic acid methyl ester (**1**) (Chart 1), had a one-dimensional channel-type structure, and the helical network of the host **1** contained a helical arrangement of the guest $CHCl_3$.[7] Modification of the structure **1** was anticipated to produce a new class of chiral host compounds. In this paper, we wish to report on the inclusion and sorption properties of several 11b-substituted 2,3,5,6,11,11b-hexahydro-3-oxo-1*H*-indolizino[8,7-*b*]indole-5-carboxylic acid esters derived from L-tryptophan.

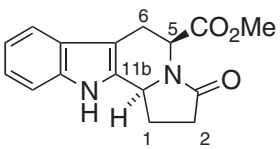

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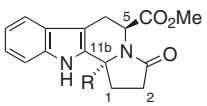
Chart 1.

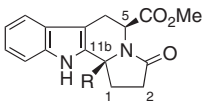
Results and Discussion

Properties of Compounds 2a–7a and 2b–4b. In a previous study, we prepared compounds **2a**–**4a**, **2b**–**4b**, and **5a**–**7a** (Chart 2), and found that the (5*S*-*trans*)-compounds **2a**–**7a** bearing alkyl groups on C-11b in the *trans* relationship with the C-5 methoxycarbonyl group were apt to contain crystalline solvents.[8] Subsequently, the inclusion properties of these (5*S*-*trans*)-compounds were reinvestigated. Upon recrystallizing from benzene, the compounds **4a**–**7a** yielded crystalline inclusion complexes **4a**·C_6H_6 (2:1), **5a**·C_6H_6 (1:1), **6a**·C_6H_6 (2:1), and **7a**·C_6H_6 (2:1), respectively, whereas **2a** and **3a** did not give such crystalline inclusion complexes. Upon recrystallizing from $CHCl_3$, the compounds **6a** and **7a** afforded crystalline inclusion complexes of **6a**·$CHCl_3$ (2:1) and **7a**·$CHCl_3$ (1:1), respectively, whereas **2a**–**5a** did not give crystalline inclusion complexes. The (5*S*-*cis*)-isomers **2b**–**4b** showed no inclusion ability. For the design of host molecules, bulky substituents and rigid basic frameworks are often used to make suitable cavities in crystal structures.[2] Hence, we planned to study the inclusion properties of **6a** and **7a**, and to clarify the crystal structures of their inclusion complexes. The inclusion property of **6a** has been communicated previously.[9]

Preparation of Host Compounds 7b, 7c, 8a, 8b, 8c, and 9. Upon recrystallizing from *s*-BuCl, **6a** gave a stable complex of **6a**·*s*-BuCl (2:1), which was subjected to X-ray crystallographic analysis. Attempts to get a stable inclusion complex of **7a**



2a – 7a



2b – 4b

2a, b R = Me
3a, b R = Et
4a, b R = *n*-Pr
5a R = *i*-Pr
6a R = *t*-Bu
7a R = Ph

Chart 2.

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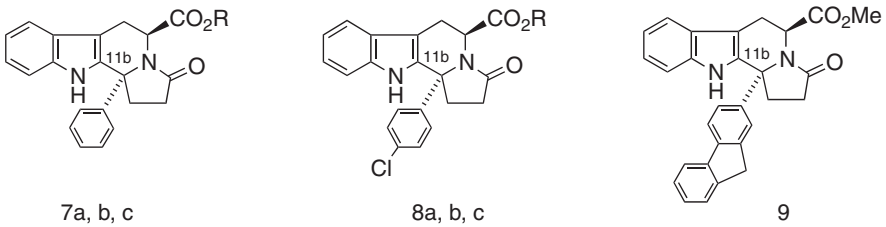

7a, b, c 8a, b, c 9

7a, 8a R = Me 7b, 8b R = Et 7c, 8c R = *n*-Pr

Chart 3.

Table 1. Inclusion Properties of the Hosts **6a**, **7a**, **7b**, **7c**, **8a**, **8b**, **8c**, and **9**

Guest	Host							
	6a	**7a**	**7b**	**7c**	**8a**	**8b**	**8c**	**9**
EtOH	≈0	≈0	≈0	1:1	≈0	3:2	2:3	3:1
i-PrOH	≈0	0	3:1	3:2	≈0	3:2	1:1	1:1
s-BuOH	≈0	≈0	2:1	≈0	≈0	2:1	0	1:1
Acetone	2:1	≈0	2:1	2:1	≈0	2:1	4:3	≈0
EtOAc	2:1	2:1	2:1	3:1	2:1	2:1	3:1	5:1
Benzene	2:1	2:1	3:2	3:1	2:1	1:1	2:1	6:1
$CHCl_3$	2:1	1:1	≈0	5:1	2:1	1:1	1:1[a)]	1:1
s-BuCl	2:1	2:1	≈0	≈0	≈0	2:1	3:1	nc[b)]

a) Recrystallized from $CHCl_3$–hexane. b) nc = Not recrystallized.

were unsuccessful. Subsequently, the methyl ester moiety of **7a** was modified, and the ethyl ester **7b** and the propyl ester **7c** were prepared using 3-benzoylpropanoic acid and the corresponding L-tryptophan esters; however, both **7b** and **7c** did not give stable inclusion complexes. Introduction of a halogen atom in a host molecule is reported to cause different solid-state behavior.[10] Hence, the phenyl group in **7a** was replaced with a *p*-chlorophenyl group, and the methyl ester **8a**, the ethyl ester **8b**, and the propyl ester **8c** were prepared using 3-(4-chlorobenzoyl)propanoic acid and the corresponding L-tryptophan esters. A stable inclusion complex of **8c**·$CHCl_3$ (1:1) was obtained from **8c**. As the modification of the phenyl group in **7a**, the host **9** with a fluorene ring was prepared using 4-(2-fluorenyl)-4-oxobutanoic acid, since acidic hydrogen atoms in the fluorene ring were expected to interact with guest molecules bearing electronegative groups. The *trans* relationships between the C-5 ester moieties and the C-11b substituents in these compounds were confirmed by the ^{1}H NMR double doublet signals of C-5 protons (J = 10–8 and 5–6 Hz) (Chart 3).[8]

Inclusion Properties. The inclusion properties of the host compounds **6a**, **7a**, **7b**, **7c**, **8a**, **8b**, **8c**, and **9** were examined upon recrystallizing from various solvents. The results are summarized in Table 1. The host:guest ratios were determined by ^{1}H NMR after drying the obtained crystals at room temperature for 2 days. The ratio ≈0 is due to immediate or gradual loss of the guest molecules. The individual hosts show slightly different inclusion properties. For example, the guest EtOH in **6a** was apt to escape, whereas **7c** included EtOH in a ratio of 1:1. Upon recrystallizing from *i*-PrOH, **7a** gave guest-free crystals, whereas **7b** included *i*-PrOH in a ratio of 3:1. A transparent complex of **8a**·$CHCl_3$ (1:1) formed by recrystallization changed to opaque guest free crystals by drying at room temperature for several days, whereas **8c**·$CHCl_3$ (1:1) was stable under similar conditions, and suitable for X-ray crystallographic analysis. The compound **9** afforded a stable inclusion complex of **9**·$CHCl_3$ (1:1), and the ratio was also confirmed by elemental analysis. The various ratios shown in Table 1 indicate that interactions between the hosts and the guests are sensitive to the structural modification of the hosts. The host **6a** showed a good inclusion property toward other molecules. Upon recrystallizing from *s*-butyl methyl ether, *s*-butyl acetate, *s*-butyl bromide, *s*-butyl iodide, *s*-butyl amine, and 3-methylcyclohexanone, **6a** yielded the 2:1 complexes with the corresponding solvent molecules, respectively. The host **9** bearing the fluorene ring showed a tendency to include chloroalkanes. Upon recrystallizing from CH_2Cl_2, $ClCH_2CH_2Cl$, and $ClCH_2$-$CHClCH_3$, **9** gave the 1:1 complexes with the corresponding molecules, respectively. The complex **9**·$ClCH_2CH_2Cl$ (1:1) was suitable for X-ray crystallographic analysis.

Table 2. Sorption Properties of the Hosts **6a**, **7a**, **8c**, and **9**

Guests	**6a**	**7a**	**8c**	**9**
s-BuOMe	≈0	≈0	4:1	3:1
2-Me-THF[a)]	≈0	1:1	2:1	1:1
s-BuOAc	5:1	1:1	≈0	4:1
s-BuCl	2:1	0	3:1	1:1
Epichlorohydrin	3:1	1:1	2:1	1:1
3-Chloro-1-butene	3:1	≈0	5:1	2:1
4-Methylcyclohexene	≈0	≈0	≈0	5:1

a) 2-Methyltetrahydrofuran.

Sorption Properties. Upon keeping in contact with the vapor of solvent molecules listed in Table 1, the guest-free **6a**, **7a**, **7b**, **7c**, **8a**, **8b**, **8c**, and **9** were found to incorporate the solvent molecules to some extent. Subsequently, the sorption properties of the guest-free **6a**, **7a**, **8c**, and **9** were examined toward racemic molecules. The guest-free **6a**, **7a**, and **8c** were prepared by recrystallizing from *s*-BuOAc, *i*-PrOH, and *s*-BuOH, respectively. The guest-free **9** was obtained by heating **9**·CH_2Cl_2 (1:1) at 110 °C in vacuo overnight. The individual hosts were exposed to the vapor of racemic molecules in a sealed vessel at room temperature for several days, and the host:guest ratios were determined by ^{1}H NMR after drying the recovered hosts at room temperature for 2 days. The results are summarized in Table 2. The ratio ≈0 is due to immediate or gradual loss of the guest molecules. Broad sorption properties observed in these hosts suggest that they resemble organic analogs of zeolites.[2] On the other hand, guest exchange was

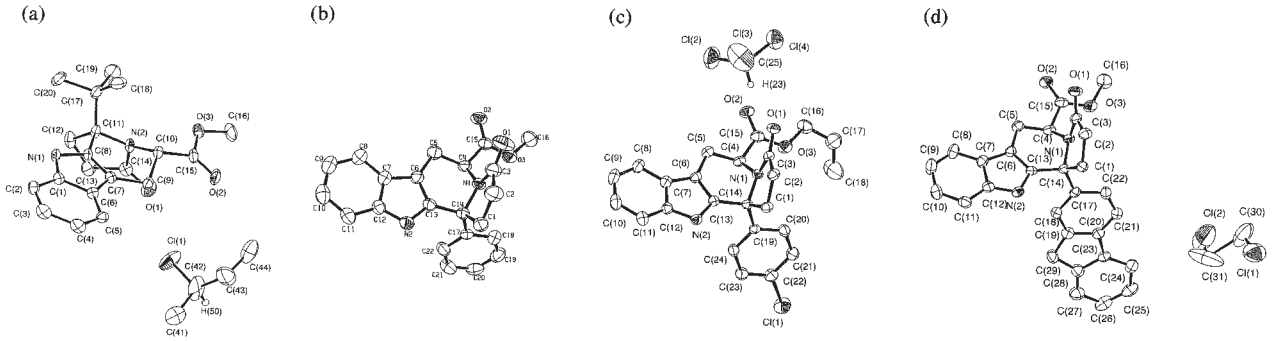

Fig. 1. ORTEP views of (a) **6a**·*s*-BuCl (2:1), (b) **7a**, (c) **8c**·$CHCl_3$ (1:1), and (d) **9**·$ClCH_2CH_2Cl$ (1:1).

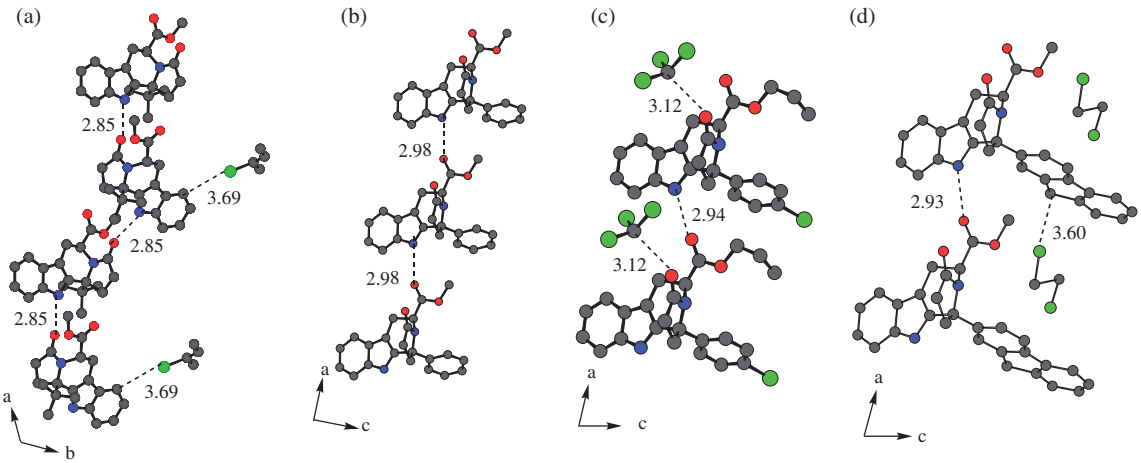

Fig. 2. Hydrogen bonding in (a) **6a**·*s*-BuCl (2:1), (b) **7a**, (c) **8c**·$CHCl_3$ (1:1), and (d) **9**·$ClCH_2CH_2Cl$ (1:1).

examined. For example, upon keeping in contact with the vapor of diethyl ether, **6a**·*s*-BuCl (2:1) gave **6a**·diethyl ether (4:1). The guest exchange in the reverse direction was observed by placing **6a**·diethyl ether (4:1) in the vapor of *s*-BuCl. Accordingly, the host **6a** would incorporate guest molecules mainly by weak van der Waals interactions.

X-ray Crystallographic Analysis. X-ray crystallographic analysis was carried out for the complex of **6a**·*s*-BuCl (2:1), the guest-free **7a**, and the complexes of **8c**·$CHCl_3$ (1:1) and **9**·$ClCH_2CH_2Cl$ (1:1), and the obtained ORTEP views are shown in Figs. 1a, 1b, 1c, and 1d, respectively. The indole and the lactam rings in **6a**·*s*-BuCl (2:1) are twisted with respect to each other, and the torsion angle [N(1)–C(8)–C(11)–C(12)] is −60.0°. The corresponding torsion angles [N(2)–C(13)–C(14)–C(1)] in **7a**, **8c**·$CHCl_3$ (1:1), and **9**·$ClCH_2CH_2Cl$ (1:1) are −52.2, −52.3, and −57.0°, respectively. The torsion observed in these hosts seems to play an important role in their inclusion properties. Figures 2a, 2b, 2c, and 2d show the hydrogen bonding in **6a**·*s*-BuCl (2:1), **7a**, **8c**·$CHCl_3$ (1:1), and **9**·$ClCH_2CH_2Cl$ (1:1), respectively. In **6a**·*s*-BuCl (2:1), a molecule of **6a** is linked to an adjacent molecule of **6a** by the N–H···O interaction between the indole NH and the lactam carbonyl oxygen (N–O distance 2.85 Å), forming a helical chain. There is a weak C–H···Cl interaction between the aromatic ring CH and *s*-butyl chloride (C–Cl distance 3.69 Å).[11] In Fig. 2b, the molecule **7a** is assembled without guest molecules in a one-dimensional fashion, and the interaction between the indole NH and the ester carbonyl oxygen (N–O distance 2.98 Å) is observed. In Fig. 2c of **8c**·$CHCl_3$ (1:1) and Fig. 2d of **9**·$ClCH_2CH_2Cl$ (1:1), molecules **8c** and **9** are similarly assembled in one-dimensional fashions, and there are N–H···O interactions between the indole NH and the ester carbonyl oxygen (N–O distances, 2.94 and 2.93 Å), respectively. In **8c**·$CHCl_3$ (1:1), a weak C–H···O interaction between the chloroform and the lactam carbonyl oxygen (C–O distance 3.12 Å) is observed.[12] The guest dichloroethane in **9**·$ClCH_2CH_2Cl$ (1:1) is surrounded by the fluorene rings, and its orientation might partly be due to a weak C–H···Cl interaction between the acidic methylene hydrogen of the fluorene ring and the dichloroethane (C–Cl distance 3.60 Å). Figure 3a shows a one-dimensional channel structure of the host **6a**, and the cavity includes *s*-butyl chloride with (*R*)-configuration. In **7a**, **8c**·$CHCl_3$ (1:1), and **9**·$ClCH_2CH_2Cl$ (1:1), the channel structures are similarly observed. Previously, we reported the one-dimensional helical arrangement of the guest $CHCl_3$ in the complex of **1**·$CHCl_3$ (1:1).[7] As shown in Figs. 3b, 3c, and 3d, the helical arrangements of the host molecules (**7a**, **8c**, and **9**) and the guest molecules ($CHCl_3$ and $ClCH_2CH_2Cl$) are observed, respectively. Hence, these host molecules derived from L-tryptophan have chiral cavities, which would be useful for the optical resolution of racemic guest molecules.

TGA and DTA. Thermogravimetric analysis (TGA) and differential thermal analysis (DTA) were carried out for **6a**·*s*-BuCl (2:1), **8c**·$CHCl_3$ (1:1), and **9**·$ClCH_2CH_2Cl$ (1:1). The obtained thermograms are shown in Figs. 4a, 4b, and 4c, respectively. The *s*-butyl chloride (bp 68 °C) in **6a**·*s*-BuCl

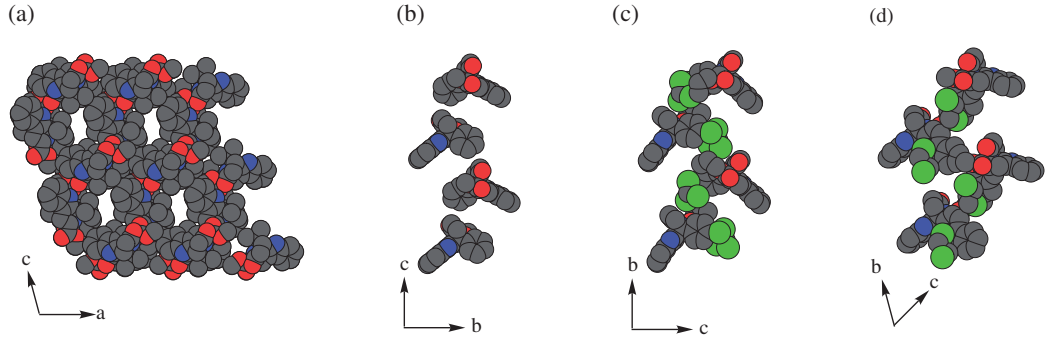

Fig. 3. (a) Space-filling representation of the channel structure of **6a** (guest *s*-BuCl is omitted for clarity). (b) Helical arrangement of **7a**. (c) Helical arrangement of the guest $CHCl_3$ and **8c**. (d) The guest $ClCH_2CH_2Cl$ and **9**. Chlorine atoms of the guests are shown in green.

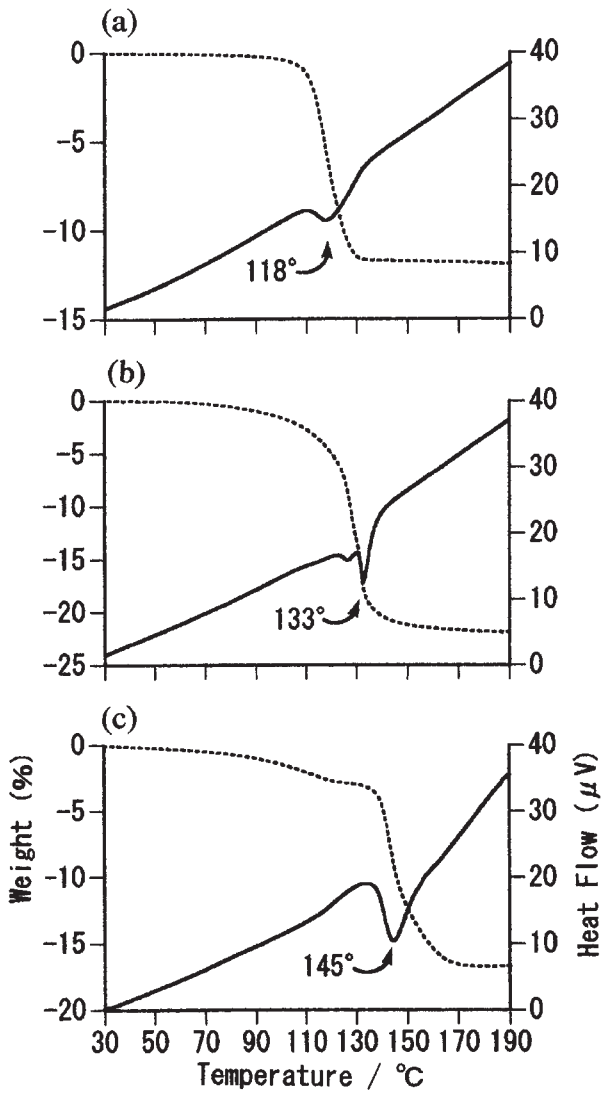

Fig. 4. TGA (·····) and DTA (———) thermograms of (a) **6a**·*s*-BuCl (2:1), (b) **8c**·$CHCl_3$ (1:1), and (c) **9**·$ClCH_2CH_2Cl$ (1:1).

(2:1) prepared by sorption began to leave **6a** at 100 °C and most of the *s*-butyl chloride was released at 130 °C. The weight loss corresponds to the required stoichiometry (9%). The DTA curve showed an endothermic peak at 118 °C due to the guest release process. Similar thermograms were observed for **6a**·*s*-BuCl (2:1) prepared by recrystallization. The chloroform (bp 60 °C) and the dichloroethane (bp 83 °C) in **8c**·$CHCl_3$ (1:1) and **9**·$ClCH_2CH_2Cl$ (1:1) were released above 100 °C, respectively, indicating the high cohesion of the host molecules. The weight losses in **8c**·$CHCl_3$ (1:1) and **9**·$ClCH_2CH_2Cl$ (1:1) are in agreement with the required stoichiometry, 22 and 18%, respectively. These data also suggest the applicability of the host molecules for optical resolution by a complexation and distillation method.[13]

Powder X-ray Diffraction. The properties of the channel structures in **6a**·*s*-BuCl (2:1), **7a**, **8c**·$CHCl_3$ (1:1) and **9**·CH_2Cl_2 (1:1) were examined using powder X-ray diffraction (PXRD). Upon heating at 150 °C in vacuo for 1 h, **6a**·*s*-BuCl (2:1) changed to the guest-free **6a**, which was also obtained from **6a**·*s*-BuOAc (2:1) by drying at room temperature for 3 days. The guest-free **6a** thus obtained again formed **6a**·*s*-BuCl (2:1) by sorption of *s*-butyl chloride. As shown in Figs. 5a and 5b, the PXRD pattern (Fig. 5a) of **6a**·*s*-BuCl (2:1) prepared by recrystallization was identical with that (Fig. 5b) of the complex obtained by sorption. Hence, the channel structure in **6a** is not destructed after removal of the guest molecules. The pattern (Fig. 5c) of the guest-free **6a** prepared from **6a**·*s*-BuCl (2:1) was the same as that (Fig. 5d) of **6a** obtained from **6a**·*s*-BuOAc (2:1). Furthermore, the guest-free **7a** prepared by recrystallization from *i*-PrOH gave the 1:1 complex of **7a**·$CHCl_3$ by sorption, and the PXRD pattern of the thus obtained **7a**·$CHCl_3$ (1:1) was identical with that of **7a**·$CHCl_3$ prepared by recrystallization. Hence, the channel structures of **6a** and **7a** are formed regardless of which recrystallization solvent is used. The PXRD patterns of **8c**·$CHCl_3$ (1:1) and **9**·CH_2Cl_2 (1:1) prepared by recrystallization were very similar to those of the corresponding complexes obtained by sorption, respectively. The guest-free **8c** and **9** were prepared upon heating **8c**·$CHCl_3$ (1:1) and **9**·CH_2Cl_2 (1:1) at 110 °C in vacuo overnight, respectively. Accordingly, the channel structures in **6a**, **8c**, and **9** remain ordered after removal of the guest molecules.

Optical Resolution. The X-ray crystallographic analysis of **6a**·*s*-BuCl (2:1) indicated that the guest *s*-butyl chloride had (*R*)-configuration. Subsequently, we attempted to get (*R*)-*s*-butyl chloride from **6a**·*s*-BuCl (2:1) by distillation. Upon heating at 100–145 °C, **6a**·*s*-BuCl (2:1) prepared by recrystallization afforded (*R*)-*s*-butyl chloride of only 16% enantiomeric excess (ee), which was determined by comparison of the

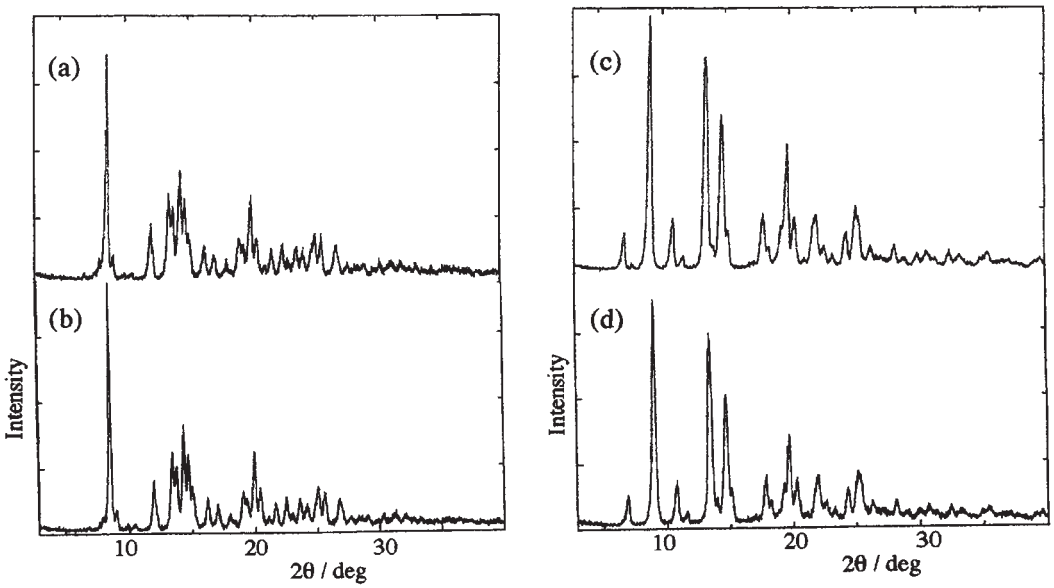

Fig. 5. PXRD patterns of (a) **6a**·*s*-BuCl (2:1) prepared by recrystallization, (b) **6a**·*s*-BuCl (2:1) obtained by sorption, (c) the guest-free **6a** prepared from **6a**·*s*-BuCl (2:1), and (d) the guest-free **6a** obtained from **6a**·*s*-BuOAc (2:1).

Table 3. Optical Resolution of Guest Molecules

Host	Guest	Method[a)]	ee %	Config.[b)]
6a	*s*-BuCl	Re	16	(*R*)-(−)
6a	*s*-BuCl	So	13	(*R*)-(−)
6a	*s*-BuBr	Re	14	(*R*)-(−)
6a	*s*-BuBr	So	8	(*R*)-(−)
6a	3-Methylcyclohexanone	Re	22	(*R*)-(+)
8b	3-Methylhexane	So	10	(*S*)-(+)
8c	4-Methylcyclohexene	So	7	(*R*)-(+)
9	4-Methylcyclohexene	So	21	(*R*)-(+)
9	3-Methylcyclohexene	So	38	(*R*)-(+)

a) Re = Recrystallization method, So = Sorption method. b) Config. = Predominant configuration.

$[\alpha]_D$ value with that reported in the literature (namely, a recrystallization method). On the other hand, **6a**·*s*-BuCl (2:1) obtained by sorption gave (*R*)-*s*-butyl chloride of 13% ee (namely, a sorption method). The resolution of other racemic molecules was examined. The results are summarized in Table 3. The host **9** afforded (*R*)-4-methylhexene and (*R*)-3-methylhexene by the sorption method in 21 and 38% ee, respectively. Of the hosts in this study, **8b** showed a sorption ability toward 3-methylhexane, and afforded (*S*)-3-methylhexane of only 10% ee. 2-Methyltetrahydrofuran, epichlorohydrin, and 3-chloro-1-butene were resolved in poor ee by the sorption method using **6a** or **9**. The low ee % shown by these hosts may be partly due to the racemization at C-5 of the hosts during the preparation. Further modification of the structure **7a** will produce host molecules bearing good recognition ability for chiral alkene and alkane molecules.

Conclusion

(5*S*-*trans*)-11b-Substituted 2,3,5,6,11,11b-hexahydro-3-oxo-1*H*-indolizino[8,7-*b*]indole-5-carboxylic acid esters are a new class of chiral host compounds derived from L-tryptophan, and have broad inclusion and sorption abilities toward various molecules. These hosts with one-dimensional channel structures have potential usefulness for the optical resolution of racemic guest molecules such as *s*-butyl chloride and 4-methylcyclohexene.

Experimental

All melting points are uncorrected. ^{1}H NMR spectra were measured on a Bruker AC300 (300 MHz) in $CDCl_3$ using a $CHCl_3$ signal ($\delta_H = 7.26$) as an internal standard. TGA and DTA thermograms were recorded on a Rigaku TG 8120. PXRD were recorded on a Rigaku RINT 2200. Optical rotations were measured on a Union PM-101.

Preparation of 7b, 7c, 8a, 8b, 8c, and 9. A typical procedure is described for the preparation of **8a**. A mixture of L-tryptophan methyl ester (2.18 g, 10 mmol), 3-(4-chlorobenzoyl)propanoic acid (2.13 g, 10 mmol), DCC (2.06 g, 10 mmol), and CH_2Cl_2 (80 mL) was stirred at room temperature overnight. The resulting solid was removed by filtration. The filtrate was concentrated under reduced pressure to leave an oil, which was dissolved in MeOH (60 mL). To the solution was added acetyl chloride (3 mL). The solution was heated under reflux for 2 h and concentrated under reduced pressure. The residue was partitioned between aqueous $NaHCO_3$ and $CHCl_3$. The organic layer was dried over Na_2SO_4. Evaporation of the solvent under reduced pressure gave an oil, which was crystallized from MeOH to give **8a** (2.62 g, 66%): mp 248–249 °C; $[\alpha]_D$ −45.1° (*c* 1.09, $CHCl_3$); ^{1}H NMR δ 2.26–2.80 (4H, m), 2.93 (1H, dd, J = 16.5, 5.1 Hz), 3.44 (1H, dd, J = 16.5, 11.4 Hz), 3.80 (3H, s), 3.81 (1H, dd, J = 11.4, 5.1 Hz), 7.18 (1H, t, J = 7.5 Hz), 7.25 (1H, t, J = 7.5 Hz), 7.33 (2H, d, J = 8.6 Hz), 7.37 (2H, d, J = 8.6 Hz), 7.43 (1H, d, J = 7.5 Hz), 7.54 (1H, d, J = 7.5 Hz), and 8.37 (1H, brs). Found: C, 66.59; H, 4.89; N, 7.05%. Calcd for $C_{22}H_{19}ClN_2O_3$: C, 66.92; H, 4.85; N, 7.10%.

7b was obtained as the 1:1 adduct of MeOH by crystallization from MeOH (yield 24%). The guest-free crystals of **7b**: mp 231–233 °C; $[\alpha]_D$ −24.2° (*c* 1.00, $CHCl_3$); ^{1}H NMR δ 1.31 (3H, t, J = 7.1 Hz), 2.25–2.77 (4H, m), 2.92 (1H, dd, J = 16.0, 5.2 Hz), 3.45 (1H, dd, J = 16.0, 11.1 Hz), 3.88 (1H, dd, J = 11.1, 5.2 Hz), 4.29 (2H, q, J = 7.1 Hz), 7.15–7.60 (9H, m), and 8.18 (1H, brs).

Table 4. Crystallographic Data for **6a**·0.5C_4H_9Cl, **7a**, **8c**·$CHCl_3$, and **9**·$C_2H_4Cl_2$

	6a·0.5C_4H_9Cl	**7a**	**8c**·$CHCl_3$	**9**·$C_2H_4Cl_2$
Formula	$C_{22}H_{28.5}Cl_{0.5}N_2O_3$	$C_{22}H_{20}N_2O_3$	$C_{25}H_{24}Cl_4N_2O_3$	$C_{31}H_{28}Cl_2N_2O_3$
Crystal system	monoclinic	orthorhombic	orthorhombic	monoclinic
Space group	$P2_1$	$P2_12_12_1$	$P2_12_12_1$	$P2_1$
a/Å	11.458(6)	9.1645(9)	8.600(9)	8.95(2)
b/Å	14.666(7)	12.535(1)	14.73(2)	12.57(3)
c/Å	13.447(7)	16.033(2)	20.47(4)	12.93(3)
β/deg	108.740(6)	90	90	108.75(2)
V/Å^3	2139(1)	1841.8(3)	2592(5)	1376(4)
Z	4	4	4	2
D_{calcd}/g cm^{-3}	1.200	1.300	1.389	1.320
Reflection collected	5074	3033	22414	11640
Unique reflections	3686	2285	4687	5777
No. of variables	496	264	308	341
R; R_w	0.0795; 0.0728	0.0520; 0.0540	0.0551; 0.0656	0.0637; 0.0857
Goodness of fit	1.844	1.757	1.227	1.029

Found: C, 73.93; H, 5.84; N, 7.50%. Calcd for $C_{23}H_{22}N_2O_3$: C, 73.78; H, 5.92; N, 7.48%. **7c** was obtained as guest-free crystals by crystallization from MeOH (yield 77%): mp 212–213 °C; $[\alpha]_D$ −24.8° (*c* 0.50, $CHCl_3$); ^{1}H NMR δ 0.98 (3H, t, J = 7.4 Hz), 1.73 (2H, m), 2.25–2.82 (4H, m), 2.92 (1H, dd, J = 16.0, 5.2 Hz), 3.45 (1H, dd, J = 16.0, 11.1 Hz), 3.90 (1H, dd, J = 11.1, 5.2 Hz), 4.19 (2H, t, J = 6.6 Hz), 7.18 (1H, t, J = 7.6 Hz), 7.23–7.50 (7H, m), 7.55 (1H, d, J = 7.6 Hz), and 8.23 (1H, brs). Found: C, 74.12; H, 6.22; N, 7.23%. Calcd for $C_{24}H_{24}N_2O_3$: C, 74.20; H, 6.23; N, 7.21%.

8b was obtained as the 1:1 adduct of $CHCl_3$ by crystallization from $CHCl_3$ (yield 72%). Recrystallization from MeOH gave the guest-free crystals of **8b**: mp 199–201 °C; $[\alpha]_D$ −33.4° (*c* 1.06, $CHCl_3$); ^{1}H NMR δ 1.32 (3H, t, J = 7.1 Hz), 2.25–2.75 (4H, m), 2.91 (1H, dd, J = 16.1, 5.1 Hz), 3.44 (1H, dd, J = 16.1, 11.2 Hz), 3.82 (1H, dd, J = 11.2, 5.1 Hz), 4.28 (2H, q, J = 7.1 Hz), 7.16 (1H, t, J = 7.7 Hz), 7.25 (1H, t, J = 7.7 Hz), 7.31 (2H, d, J = 9.1 Hz), 7.37 (2H, d, J = 9.1 Hz), 7.42 (1H, d, J = 7.7 Hz), 7.53 (1H, d, J = 7.7 Hz), and 8.28 (1H, brs). Found: C, 54.34; H, 4.22; N, 5.12%. Calcd for $C_{23}H_{21}ClN_2O_3$·$CHCl_3$: C, 54.57; H, 4.20; N, 5.30%. **8c** was obtained as the 1:1 adduct of *i*-PrOH by crystallization from *i*-PrOH (yield 67%). Recrystallization from *s*-BuOH gave the guest-free crystals of **8c**: mp 223–225 °C; $[\alpha]_D$ −27.2° (*c* 2.00, $CHCl_3$); ^{1}H NMR δ 0.98 (3H, t, J = 7.4 Hz), 1.71 (2H, m), 2.25–2.80 (4H, m), 2.91 (1H, dd, J = 15.9, 5.2 Hz), 3.44 (1H, dd, J = 15.9, 10.9 Hz), 3.84 (1H, dd, J = 10.9, 5.2 Hz), 4.16 (2H, t, J = 6.5 Hz), 7.17 (1H, t, J = 7.7 Hz), 7.26 (1H, t, J = 7.7 Hz), 7.31 (2H, d, J = 8.5 Hz), 7.38 (2H, d, J = 8.5 Hz), 7.43 (1H, d, J = 7.7 Hz), 7.54 (1H, d, J = 7.7 Hz), and 8.42 (1H, s). Found: C, 55.11; H, 4.50; N, 5.10%. Calcd for $C_{24}H_{23}ClN_2O_3$·$CHCl_3$: C, 55.37; H, 4.46; N, 5.17%.

9 was prepared using 4-(2-fluorenyl)-4-oxobutanoic acid,[14] and crystallized from MeOH (yield 54%): mp 211–213 °C; $[\alpha]_D$ −63.2° (*c* 0.50, $CHCl_3$); ^{1}H NMR δ 2.28–2.78 (4H, m), 2.95 (1H, dd, J = 16.1, 5.2 Hz), 3.47 (1H, dd, J = 16.1, 11.4 Hz), 3.81 (3H, s), 3.85 (2H, s), 3.91 (1H, dd, J = 11.4, 5.2 Hz), 7.16–7.80 (11H, m), and 8.20 (1H, brs). Found: C, 63.15; H, 4.46; N, 4.88%. Calcd for $C_{29}H_{24}N_2O_3$·$CHCl_3$: C, 63.45; H, 4.44; N, 4.93%.

X-ray Crystallographic Analysis. A single crystal of **6a**·*s*-BuCl (2:1) was formed by recrystallization from *s*-BuCl, and a single crystal of the guest-free **7a** was obtained by recrystallization from *i*-PrOH. A single crystal of **8c**·$CHCl_3$ (1:1) was formed upon slow diffusion of hexane vapor into a $CHCl_3$ solution of **8c**, and that of **9**·$ClCH_2CH_2Cl$ (1:1) was obtained by recrystallization from $ClCH_2CH_2Cl$. For the four compounds, each suitable single crystal was sealed in a glass capillary. Data collections were carried out on a Rigaku CCD mercury system fitted with a monochromatic Mo Kα radiation source (l = 0.71069 Å) at room temperature. Six preliminary data frames were measured at 0.5° increments of w to assess the crystal quality and preliminary unit cell parameters. The intensity images were also measured at 0.5° intervals of w. The intensity images were integrated using the Crystal Clear program package, and the empirical absorption correction was applied for the data. The structures were solved by a direct method (SIR-92).[15] All non-hydrogen atoms were refined anisotropically by full-matrix least-squares technique. The geometrical hydrogen atoms were placed in idealized positions, and were included but not refined. Crystallographic data of **6a**·*s*-BuCl (2:1), **7a**, **8c**·$CHCl_3$ (1:1), and **9**·$ClCH_2CH_2Cl$ (1:1) are shown in Table 4. Crystallographic data have been deposited with Cambridge Crystallographic Data Centre: Deposition numbers CCDC-200214 for **6a**·*s*-BuCl (2:1), CCDC-602987 for **7a**, CCDC-602988 for **8c**·$CHCl_3$, and CCDC-602989 for **9**·$ClCH_2CH_2Cl$. Copies of the data can be obtained free of charge via http://www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge, CB2 1EZ, UK; Fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk).

Optical Resolution. A typical procedure is described for the optical resolution of *s*-BuCl by the host **6a**. Upon heating at 100–145 °C, **6a**·*s*-BuCl (2:1) (7.90 g) prepared by recrystallization gave a distillate of (*R*)-*s*-BuCl (0.17 g, 18%): $[\alpha]_D$ −5.8° (*c* 1.7, MeOH), 16% ee.[16] Resolution by the recrystallization method using **6a**: (*R*)-*s*-BuBr of $[\alpha]_D$ −4.7° (*c* 1.71, MeOH) (14% ee),[16] and (*R*)-3-methylcyclohexanone of $[\alpha]_D$ +3.1° (*c* 4.91, MeOH) (22% ee).[17] By the sorption method using **6a**: (*R*)-*s*-BuCl of $[\alpha]_D$ −4.8° (*c* 1.1, MeOH) (13% ee), and (*R*)-*s*-BuBr of $[\alpha]_D$ −2.6° (*c* 1.54, MeOH) (8% ee); using **8b**, (*S*)-3-methylhexane of $[\alpha]_D$ +1.0° (*c* 2.35, MeOH) (10% ee);[18] using **8c**, (*R*)-4-methylcyclohexene of $[\alpha]_D$ +7.7° (*c* 2.48, MeOH) (7% ee);[19] using **9**, (*R*)-4-methylcyclohexene of $[\alpha]_D$ +22° (*c* 1.49, MeOH) (21% ee) and (*R*)-3-methylcyclohexene of $[\alpha]_D$ +34° (*c* 0.32, MeOH) (38% ee).[20]

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