# A New Chiral Host, (5*S*-*trans*)-11b-(1,1-Dimethylethyl)-2,3,5,6,11,11b-hexahydro-3-oxo-1*H*-indolizino[8,7-*b*]indole-5-carboxylic Acid Methyl Ester: Complexation by a Helical Network

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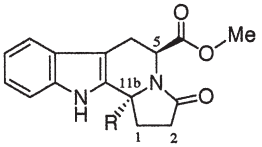
The title L-tryptophan derivative was found to serve as a chiral host and the formation of a helical network with one-dimensional channel was shown by the X-ray analysis of its inclusion complex with (*R*)-*s*-butyl chloride.

Inclusion complexes have received much attention because of their potential applications in analytical and synthetic chemistry.[1] Naturally occurring host compounds such as steroidal cholic acid derivatives, alkaloidal brucine and sparteine are useful for optical resolution of racemic molecules.[2] A variety of inclusion host systems have been designed and synthesized.[3] In a previous paper, we reported the crystal structure of the cocrystal of a L-tryptophan derivative (**1**) with $CHCl_3$: the helical network of the compound **1** contains $CHCl_3$ in a helical arrangement.[4] Attempts to prepare crystalline inclusion complexes of **1** using other recrystallization solvents were unsuccessful. Subsequently, we examined another L-tryptophan derivative, (5*S*-*trans*)-11b-(1,1-dimethylethyl)-2,3,5,6,11,11b-hexahydro-3-oxo-1*H*-indolizino[8,7-*b*]indole-5-carboxylic acid methyl ester (**2**), which had a bulky *t*-butyl group on C-11b in a *trans* relationship to a methoxycarbonyl group on C-5.[5] Here we report inclusion and sorption properties of the compound **2**.




1 R = H
2 R = *t*-Bu
**Scheme 1.**

According to the method reported previously, the compound **2** was prepared from L-tryptophan methyl ester and 5,5-dimethyl-4-oxohexanoic acid.[5] Upon recrystallizing from acetone, EtOAc, and benzene, the compound **2** gave 2 : 1 inclusion complexes of **2** with corresponding solvent molecules, respectively. The 2 : 1 inclusion complexes of **2**·$CHCl_3$ and **2**·$CH_2Cl_2$ were obtained by recrystallization of **2** from $CHCl_3$-hexane and $CH_2Cl_2$-hexane, respectively. Host-guest ratio was determined by $^1$H NMR. Subsequently, we examined an optical resolution ability of **2** toward racemic solvents. Upon recrystallizing from *s*-butyl methyl ether, *s*-butyl acetate, *s*-butyl chloride, *s*-butyl bromide, *s*-butyl iodide, *s*-butyl amine, and 3-methylcyclohexanone, the compound **2** also gave 2 : 1 inclusion complexes of **2** with the corresponding solvent molecules, respectively. The inclusion complex of **2** with *s*-butyl chloride was subjected to X-ray crystallographic analysis.

The ORTEP view of the complex of **2**·*s*-butyl chloride (2 : 1) with atom numbering is shown in Figure 1.[6] The indole and the lactam rings in **2** are twisted each other, and the torsion angle N(1)–C(8)–C(11)–C(12) is 60.0°, which is slightly larger than the corresponding torsion angle (54.9°) in the cocrystal of **1**·$CHCl_3$.

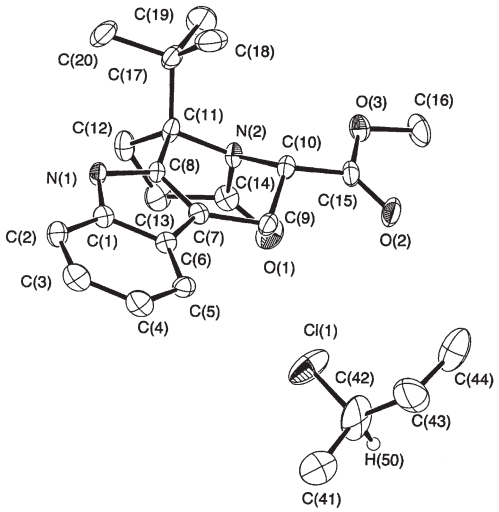



**Figure 1.** ORTEP view of the complex of **2**·*s*-butyl chloride (2 : 1) at the 30% probability level. Although this compound contains two crystallographically independent host molecules with similar structures, only one is shown for clarity.

The torsion observed in **1** and **2** seems to play an important role in their inclusion properties.[4] Molecule **2** is linked to adjacent molecule **2** by the N–H···O interaction between the indole NH and the lactam carbonyl oxygen [N(1)–O(1′) = 2.85 Å], forming helical chain as shown in Figure 2(a). In addition, the host compound **2** forms a helical network with one-dimensional channel as depicted in Figure 2(b). Thus formed chiral cavity includes *s*-butyl chloride with (*R*)-configuration, as shown in Figure 1. There is a weak C–H···Cl interaction between the benzene ring in **2** and *s*-butyl chloride (C(5)–Cl(1) = 3.69 Å).[7]

Upon heating at 150 °C for 1 h, the complex of **2**·*s*-butyl chloride (2 : 1) changed to a guest-free crystal, which again formed the complex of **2**·*s*-butyl chloride (2 : 1) by keeping in contact with the vapor of *s*-butyl chloride. The powder X-ray diffraction patterns of the complexes of **2**·*s*-butyl chloride obtained by recrystallization and by vapor sorption were identical. The transparent inclusion complex of **2**·*s*-butyl acetate changed to an opaque guest-free crystal by keeping at room temperature for 3 days. Thus obtained guest-free crystal of **2** showed the same powder X-ray diffraction pattern as that of the

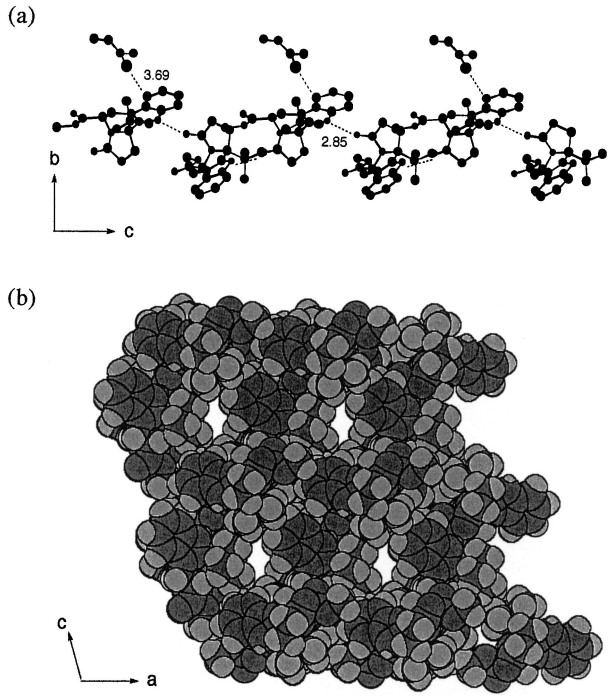



**Figure 2.** (a) Helical chain and hydrogen bonding in the complex of **2**·*s*-butyl chloride viewed along the *a* axis. Hydrogen atoms are omitted for clarity. (b) A space-filling representation of the one-dimensional channel structure of the host **2** viewed along the *b* axis. Guest *s*-butyl chloride is omitted for clarity.

guest free **2** formed from the complex of **2**·*s*-butyl chloride as described above. These facts suggest that the channel of the complex of **2** remains ordered after removal of the guest molecules, and that the guest-free **2** would serve as an apohost.[8] Upon keeping in contact with the vapor of acetone, EtOAc, diethyl ether, and benzene for a few days, the apohost **2** incorporated the guest molecules in the ratio of $2:1 \sim 4:1$. On the other hand, guest exchange was observed. For example, the complex of **2**·*s*-butyl chloride gave the adduct of **2**·diethyl ether (4 : 1) by keeping in the vapor of diethy ether. The guest exchange in the reverse direction was also observed by placing the complex of **2**·diethyl ether in the vapor of *s*-butyl chloride. Accordingly, the compound **2** would incorporate guest molecules mainly by weak van der Waals interactions.

In summary, these preliminary results indicate that the L-tryptophan derivative **2** is a new chiral host and has potential usefulness for optical resolution of non-polar compounds. Modification of the substituents on C-5 and C-11b in **2** will affect crystal structure, inclusion and sorption properties. Further study is now in progress.

**References and Notes**

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6 Crystal data for **2**·*s*-butyl chloride: $C_{22}H_{28.5}Cl_{0.5}N_2O_3$, $M_r$ 386.70, monoclinic, space group $P2_1$, $a = 11.458(6)$ Å, $b = 14.666(7)$ Å, $c = 13.447(7)$ Å, $V = 2139(1)$ Å$^3$, $Z = 4$, $D_{calcd} = 1.200\,Mg\,m^{-3}$, 5074 reflections measured, 3686 [$I > 2\sigma(I)$] used in the refinement, $R = 0.0795$, $wR = 0.0728$. The details of the refinement will be submitted as supporting information.

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