Achiral Molecules Move and Order Themselves in a Chiral Form in Host-Guest Inclusion Crystals

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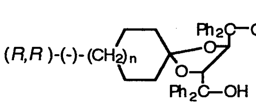
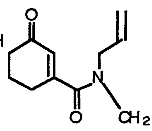
When optically active host compound was mixed with achiral guest compound in the solid state, host-guest inclusion crystals were formed by molecular movement and the achiral molecules became arranged in a chiral form in the inclusion crystals. Mixing of powdered (+)-host crystals with powdered (-)-guest crystals which are formed by a chiral arrangement of achiral guest molecules gave inclusion crystals of the (+)-host and the (+)-guest molecules newly produced through an inversion of the (-)-guest molecules during the complexation in the solid state.

We have reported that irradiation of powdered 2:1 inclusion crystals of *(R,R)*-(-)-trans-2,3-bis(hydroxydiphenylmethyl)-1,4-dioxaspiro[4.4]nonane (**1a**)[1,2] and *N*-allyl-*N*-benzyl-3-oxo-1-cyclohexenecarboxamide (**2**) which had been prepared by recrystallization of these from ether, in a water suspension which contains alkylsulfate as a surfactant at room temperature for 10 h gave (-)-**3** of 100% ee in 90% yield.[3] Similar treatment of 2:1 inclusion crystals of *(R,R)*-(-)-trans-2,3-bis(hydroxydiphenylmethyl)-1,4-dioxaspiro[5.4]decane (**1b**)[1,2] and **2** prepared by recrystallization from benzene gave (-)-**3** of 100% ee in 87% yield.[3] Since the photoreaction of **2** itself in MeCN gives a mixture of *rac*-**3** and an isomeric photocycloaddition product,[4] it is clear that the steric course of the photoreaction is controlled efficiently by the chiral host compound **1**. It is probable that molecules of **2** are arranged in a chiral form in the inclusion complex with **1**. The chirality of **2** in the inclusion complex would result, for example, by locating the allyl group above the cyclohexenone ring (**2A**). When the *(S,S)*-(+)-enantiomer of the host **1** is used, the allyl group would be located below (**2B**) and (+)-**3** is produced by the irradiation.


1
a : n = 0
b : n = 1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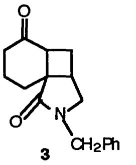
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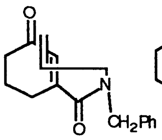
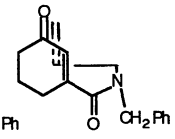
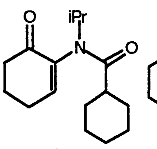

2A


2B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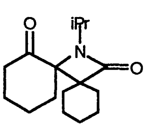
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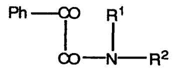
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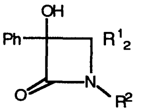
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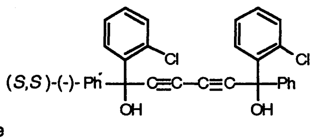
8

a : $R^1 = R^2 = Me$
b : $R^1 = Me$; $R^2 = iPr$
c : $R^1 = Et$; $R^2 = iPr$
d : $R^1 = nPr$; $R^2 = iPr$
e : $R^1 = R^2 = iPr$

a : $R^1 = H$; $R^2 = Me$
b : $R^1 = H$; $R^2 = iPr$
c : $R^1 = Me$; $R^2 = Et$
d : $R^1 = Me$; $R^2 = nPr$
e : $R^1 = Me$; $R^2 = iPr$

Interestingly, however, we found that the same inclusion complex of **1** and **2** as that prepared by recrystallization can be obtained just by mixing **1** and **2** in the solid state and that photoirradiation of the inclusion crystals obtained by mixing gives optically active photoreaction product. For example, an occasional mixing of powdered **1a** of about 50-100 µm diameter and a half molar amount of oily **2** using an agate mortar and pestle for 1 h in order to avoid solidification gave the IR spectroscopically identical 2:1 inclusion complex crystal of **1a** and **2** with that obtained by the recrystallization method. Photoirradiation of the complex in a water suspension for 10 h gave (-)-**3** of 99% ee[5] in 48% yield. Similar mixing of **1b** and **2** in the absence of solvent for 1 h followed by irradiation for 10 h gave (-)-**3** of 87% ee in 40% yield. These data clearly show that inclusion crystals of **1** and **2** in which achiral molecules of **2** are arranged in a chiral form produced just by mixing both components. Such molecular movement in the solid state and arrangement in a chiral form are not special for **2** but are rather common. For example, mixing of powdered **1a** and an equimolar amount of powdered *N*-isopropyl-*N*-2-(1-oxocyclohex-2-enyl)cyclohexanecarboxamide (**4**) followed by irradiation gave the photocyclization product (-)-**5** of 81% ee in 37% yield. Photoirradiation of **4** in acetone gives *rac*-**5** together with an isomeric photocycloaddition product.[6]

N,N-Dialkylphenylglyoxylamide **6** also forms an inclusion complex on mixing with **1** and the achiral molecules of **6** are arranged in a chiral form in the inclusion crystal. Occasional mixing of oily **6a** with an equimolar amount of powdered *(R,R)*-(-)-**1a** or the *(S,S)*-(+)-enantiomer of **1a** of about 50-100 µm diameter for 1 h followed by irradiation in a water suspension for 10 h gave (-)-**7a** of 78% ee (54%) or (+)-**7a** of 65% ee (50%), respectively in the yields indicated. Similar treatments of oily **6b** with **1a** or of oily **6d** with **1b** followed by photoirradiation gave (-)-**7b** of 87% ee (45%) or (-)-**7d** of 93% ee (39%), respectively in the yields indicated.

Very interestingly, irradiation of the 1:1 inclusion complex of **1b** and **6a** which had been prepared by mixing both components in the absence of solvent gave (+)-**7a** of 45% ee in 42% yield, although the same irradiation of the complex prepared by recrystallisation of **1b** and **6a** from toluene gave the other enantiomer (-)-**7a** of 100% ee in 40% yield. The type of chiral

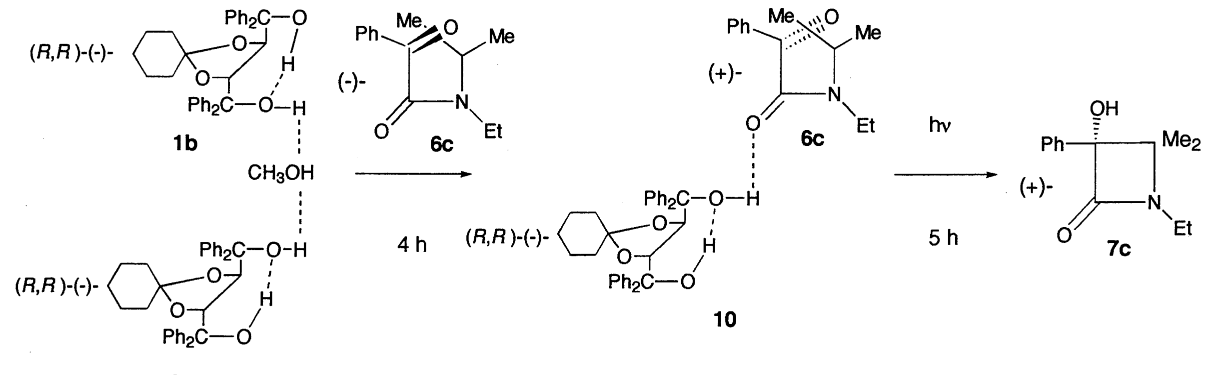

Figure 1. Conversion of the chirality of **6c** through inclusion complexation.

arrangement of **6a** molecules varies depending on the conditions of the inclusion complexation experiment.

Chiral arrangement of **6a** molecules in an inclusion crystal with *(S,S)*-(-)-1,6-di(*o*-chlorophenyl)-1,6-diphenylhexa-2,4-diyne-1,6-diol (**8**)[7] also depends on the conditions of the inclusion complexation experiment. Recrystallisation of **8** and **6a** from ether gives a 1:1 inclusion complex, which upon irradiation affords (-)-**7a** of 100% ee in quantitative yield.[8] X-ray structure study of the inclusion complex showed that **6a** is arranged in a chiral form.[8] However, irradiation of the inclusion crystal prepared by mixing **8** and **6a** gave *rac*-**7a**. In the latter crystal, **6a** molecules would not be arranged in a chiral form. Interestingly, however, both inclusion crystals are thermally interconvertible. After melting (mp 126-127 °C), the former is solidified by cooling to give the latter, but the latter is converted to the former by heating gradually and melts again at 126-127 °C.

It has been reported that **6e** forms chiral crystals in which **6e** molecules are arranged in a chiral form produced by a 90° twisting around the single bond between two CO groups,[9] and that irradiation of the chiral crystals gives optically active **7e** of 93% ee in 74% yield.[10] This time, we found that **6c** also forms chiral crystals which upon irradiation gives optically active **7c**. Although **6e** forms inclusion crystals neither with **1** nor **8**, **6c** forms an inclusion complex with **1** both by recrystallisation and solid state complexation procedures. Especially, 1:1 inclusion crystals of **1b** with **6c** are easily obtained by mixing a 2:1 MeOH complex (**9**) of **1b** and **6c**. The complexation in the solid state can be followed by its IR spectrum. As the complexation proceeds, hydrogen bonded υOH absorption between **1b** and MeOH (3550 cm^{-1}) decreases and finally disappears, and a new hydrogen bonded υOH absorption between **1b** and **6c** (3250 cm^{-1}) appears and increases (Figure 1). The complexation was completed within 4 h. Irradiation of the resulting inclusion complex (**10**) of **1b** with **6c** gave (+)-**7c** of 76% ee.

Very interestingly, by mixing powdered **9** and powdered (-)-crystals of **6c**, 1:1 inclusion crystals of **1b** and (+)-**6c** were formed. Firstly, (-)-crystals of **6c** were prepared in large quantity by adding one piece of a (-)-crystal of **6c** as a seed crystal during recrystallization of **6c** from ether. Photoirradiation of powdered (-)-crystals of **6c** in the solid state gave (-)-**7c** of 80% ee in 54% yield. Secondly, a 1:1 inclusion complex of **9** and (+)-**6c** (**10**) was obtained by mixing powdered **9** and (-)-crystals of **6c**. The (+)-arrangement of **6c** molecules in **10** can be proven by its photoirradiation in a water suspension for 5 h which gives (+)-**7c** of 76% ee in 72% yield. Interconversion between the molecular arrangement of **6c** in the (-)- and (+)-forms easily occurs by the complexation with chiral host **1** in the solid state. In other words, molecules move easily in the solid state and change their chiral arrangement according to the chiral circumstances in the crystal.

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