

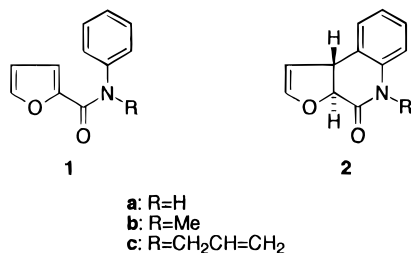
# 1:1 and 2:1 Inclusion Complexes of (*R,R*)-(-)-*trans*-2,3-Bis(hydroxydiphenylmethyl)-1,4-dioxaspiro[4.4]nonane with *N*-Allylfuran-2-carboxanilide Which upon Irradiation in the Solid State Give (-)- and (+)-Photocyclization Products, Respectively

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It has been reported that irradiation of furan-2-carboxanilide (**1a**) and *N*-methylfuran-2-carboxanilide (**1b**) in MeOH gave the *rac-trans*-dihydrofuran derivatives, **2a** and **2b**, respectively, in addition to some photoreaction products.<sup>1</sup> In order to control this reaction, we have now carried out photolysis of **1** in an inclusion complex with the title chiral host compound **3**, using our previously reported technique,<sup>2</sup> and we have succeeded in preparing optically active **2** as the sole isolable product. Furthermore, either optically pure (-)-**2** or (+)-**2** are obtained readily by using the title (*R,R*)-(-)-chiral host compound **3b**. This is the first report of such product chirality control employing just one enantiomer of a host compound.

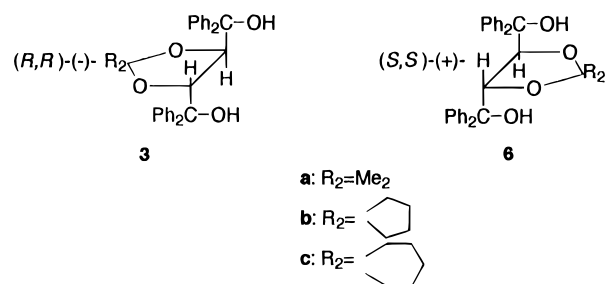


In preparation experiment of inclusion complex crystals of host **3b**<sup>3</sup> and the *N*-allyl derivative **1c** involving their cocrystallization from ether, two kinds of complex crystals of **3b** and **1c** in 1:1 (**4**) and 2:1 (**5**) host:guest ratios were obtained. Colorless prisms of **4** and colorless needles of **5** can easily be separated mechanically. The two complex crystals **4** (3180 (OH) and 1620 cm<sup>-1</sup> (C=O)) and **5** (3630, 3420, and 3280 (OH) and 1600 cm<sup>-1</sup> (C=O)) can also be identified by the IR spectral absorptions indicated. Photoirradiation<sup>4</sup> of a suspension of powdered 1:1 complex (**4**) (1.4 g) in water (80 mL) containing hexadecyltrimethylammonium bromide (0.2 g) as a surfactant was carried out at room temperature for 77 h under stirring. The reaction product was filtered, air-dried, and chromatographed on silica gel using toluene–AcOEt (10:1) as an eluent gave (-)-*trans*-photocyclization product **2c** of 96% ee (0.22 g, 50% yield, mp 102–104 °C, [α]<sub>D</sub> -289° (c 0.5, MeOH)); IR 1710 cm<sup>-1</sup> (C=O); <sup>1</sup>H NMR

δ 4.21 and 4.34 (1H each, d, *J* = 18.4 Hz, CH), 4.37 and 4.81 (1H each, q, CH<sub>2</sub>), 5.18 (2H, m, =CH<sub>2</sub>), 5.69 (1H, q, =CH of furan ring), 5.88 (1H, m, =CH of allyl group), 6.68 (1H, t, =CH of furan ring), and 7.06–7.29 (4H, m, ArH).

On the other hand, similar irradiation of the 2:1 complex **5** gave the other enantiomer (+)-**2c**. Photoirradiation of powdered **5** (2 g) in water (80 mL) containing hexadecyltrimethylammonium bromide (0.2 g) was carried out at room temperature for 48 h under stirring. Workup of the reaction mixture as above gave (+)-**2c** of 98% ee (0.33 g, 86% yield, mp 102–104 °C, [α]<sub>D</sub> +293° (c 0.4, MeOH)). IR and <sup>1</sup>H NMR spectra were identical to those of (-)-**2c**. The optical purity of (-)-**2c** and (+)-**2c** was determined by HPLC on the chiral stationary phase Chiralcel OD<sup>5</sup> using hexane–iPrOH (9:1) as eluent. The *trans*-structure of (-)-**2c** and (+)-**2c** was elucidated by comparison of their <sup>1</sup>H NMR spectra with those reported for *rac-2b* which shows two methine protons of the dihydrofuran ring at δ 4.09 and 4.18 (1H each, d, *J* = 18.5 Hz). The coupling constant of **2c** is comparable to that of **2b**.

This procedure is very convenient for the preparation of both (-)-**2c** and (+)-**2c**, since both these enantiomers can be prepared using just the one enantiomeric host **3b**. When a 2:1 mixture of **3b** and **1c** is crystallized from ether, only the 2:1 complex crystal (**5**) is formed, although crystallization of their 1:1 mixture gives a mixture of **4** and **5**. These results show that the 2:1 complex is more stable and easily formed. The IR carbonyl absorption band of **1c** in **5** (1600 cm<sup>-1</sup>) appears at lower wavenumber than that of **1c** in **4** (1620 cm<sup>-1</sup>). This suggests that a stronger hydrogen bond between **1c** and **3b** is present in **5**. In **5**, the **1c** molecules would be more tightly bound and more regularly arranged by the two surrounding **3b** molecules rather than just the single one. That the optical and chemical yields of **2c** obtained from **5** are higher than those from **4** support these ideas.



In the **4** and **5** crystals, achiral molecules of **1c** would be arranged in chiral conformations so as to produce (-)- and (+)-**2c**, respectively, upon photocyclization. Unfortunately, these chiral arrangements of **1c** molecules in **4** and **5** have not been observed directly by X-ray crystal analysis, because adequate crystalline samples are not available. However, the chiral arrangements of **1c** in **4** and **5** were observed by measurement of CD spectra of Nujol mulls (Figures 1 and 2).<sup>6</sup> For comparison of the CD spectra of **4** and **5**, 1:1 (**7**) and 2:1 (**8**) inclusion complexes of **1c** with the (*S,S*)-(+)-enantiomer of **3b** (**6b**) were prepared and their CD spectra were also measured. The shapes of the CD spectra were unchanged after

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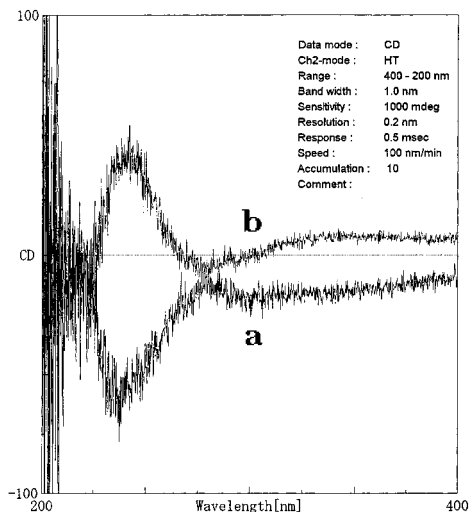
(2) Toda, F. *Synlett* **1993**, 303. Toda, F. *Acc. Chem. Res.* **1995**, *28*, 480.

(3) Seebach, D.; Beck, A. K.; Imwinkelried, R.; Roggo, S.; Wonnacott, A. *Helv. Chim. Acta* **1987**, *70*, 954. Toda, F.; Tanaka, K. *Tetrahedron Lett.* **1988**, *29*, 551.

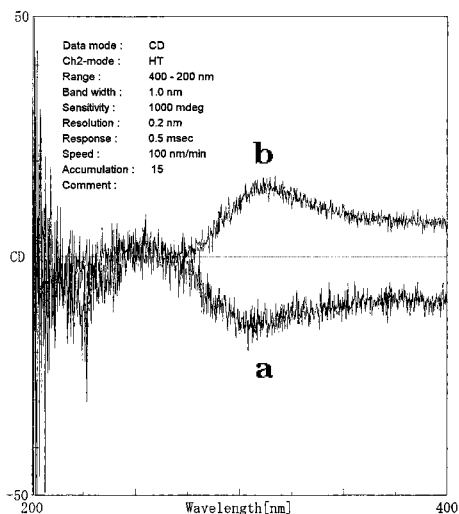
(4) Photoirradiations were carried out in a water suspension by using a 100 W high pressure Hg-lamp under air.

(5) Chiralcel OD is available from Daicel Chemical Ind. Ltd., Himeji, Japan.

(6) CD Spectra were measured on Nujol mulls using a JASCO J-720 spectropolarimeter.



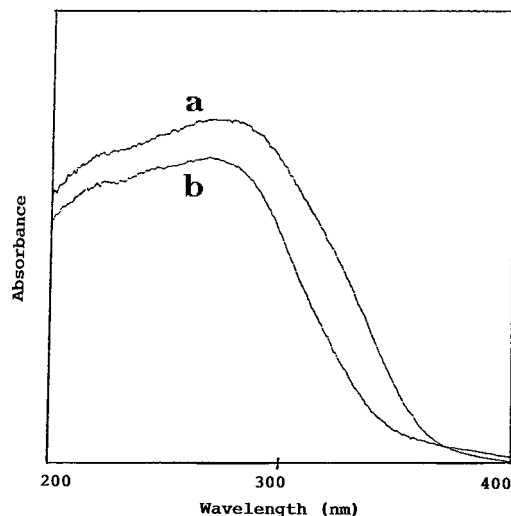
**Figure 1.** CD spectra of **4** (a) and **7** (b) as Nujol mulls at a concentration of 5 mg sample in 10 mg of liquid paraffin and employing 10 accumulations and 100 nm/min scanning speed.



**Figure 2.** CD spectra of **5** (a) and **8** (b) as Nujol mulls at a concentration of 5 mg sample in 10 mg of liquid paraffin and employing 15 accumulations and 100 nm/min scanning speed.

rotation of the samples by 90°. The CD spectra show that **1c** molecules in **4** and **7** are arranged with opposite chirality (Figure 1). In fact, similar photoirradiation gave (+)-**2c** of 96% ee in 52% yield. This is also the case for **5** and **8** (Figure 2), and photoirradiation of **8** gave (-)-**2c** of 98% ee in 85% yield. The CD spectra of **4** and **7** are quite different from those of **5** and **8**. The large CD absorption at 240 nm corresponds to the UV absorption of **1c** in MeOH at 256 nm. On the other hand, the CD absorptions of **5** and **8** around 300 nm correspond to those of their UV absorptions in the solid state at 280 nm (Figure 3).<sup>7</sup> The UV absorption bands of **5** and **8** appeared at longer wavelength than that of **1c** in MeOH. The UV absorption of **5** and **8** in the solid state also appeared at slightly shorter wavelength than that of **4** and **7** (Figure 3). These results indicate that **1c** molecules in **5** and **8** have slightly more planar structure than do **1c** molecules in MeOH and in **4** and **7**.

Previously we have reported that inclusion complexation occurs just by mixing powdered host and guest



**Figure 3.** UV spectra of **4** (a) and **7** (b) in the solid state.

compounds in the solid state.<sup>8</sup> The mixing method was also applicable to the complexation of **1c** and **3b**; however, in this case, only the 1:1 complex **4** was formed. Mixing of powdered **3b** and **1c** in 1:1 and 2:1 ratios in the solid state using a small amount of liquid paraffin followed by irradiation in a water suspension gave (-)-**2c** of 98% ee (10%) and (-)-**2c** of 97% ee (16%), respectively, in the yields indicated. It is interesting that the relatively unstable complex **4** is formed predominantly by the solid state complexation method.

The alternative host **3a**<sup>3</sup> formed only a 1:1 inclusion complex with **1c** (mp 130–132 °C) on crystallization from ether, and its photoreaction in a water suspension gave (+)-**2c** of 93% ee in 20% yield. On the other hand, the host **3c**<sup>3</sup> formed only a 2:1 complex with **1c** (mp 112–115 °C) by the crystallization method, and its photoreaction gave (+)-**2c** of 98% ee in 77% yield. Remarkably, however, the mixing of powdered **3c** and **1c** in both 1:1 and 1:2 ratios gave 1:1 complexes whose photoreaction gave (-)-**2c** of 49% ee (16%) and (-)-**2c** of 54% ee (11%), respectively, in the yields indicated.

Photoirradiation of the 1:1 complex of **3a** with **1c** gave (+)-**2c**, although the irradiation of the 1:1 complex of **3b** and **1c** (**4**) gave (-)-**2c**. In these two complexes, the **1c** molecules should be arranged in opposite chiral forms, and we intend to confirm this by X-ray analysis.

Although **1a** did not form an inclusion complex with any of **3a**, **3b**, or **3c**, in contrast **1b** formed a 1:1 complex with both of **3b** and **3c**. Irradiation of the 1:1 complex of **1b** with **3b** (mp 122–123 °C) in a water suspension for 40 h gave (-)-**2b** of 8% ee in 25% yield. However, the 1:1 complex of **1b** with **3c** (mp 149–151 °C) was inert to the photoreaction conditions.

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(7) UV spectra in the solid state were measured using a Shimadzu multipurpose recording spectrophotometer MPS-2000.

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