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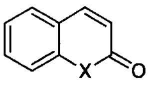
Enantioselective Single-Crystal-to-Single-Crystal Photodimerization of Coumarin and Thiocoumarin in Inclusion Complexes with Chiral Host Compounds

Koichi Tanaka, Fumio Toda,* Eiko Mochizuki, Nobuyoshi Yasui, Yasushi Kai, Ikuko Miyahara, and Ken Hirotsu

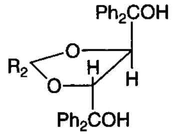
Dedicated to Professor Masazumi Nakagawa on the occasion of his 83rd birthday

Some examples of single-crystal-to-single-crystal photoreactions have been reported,[1–5] but only a few of these involve enantioselective reactions and they are all intramolecular photocyclization reactions.[3–5] For example, the enantioselective photocyclization of *N*,*N*-dibenzyl-1-cyclohexenecarbothioamide to an optically active β-thiolactam has been reported to proceed in a single-crystal-to-single-crystal manner.[4] We have now found that the single-crystal-to-single-crystal enantioselective photodimerization of coumarin (**1a**) or thiocoumarin (**1b**) proceeds efficiently in inclusion complexes with (*R*,*R*)-(−)-*trans*-bis(hydroxydiphenylmethyl)-2,2-dimethyl-1,3-dioxacyclopentane (**2a**) or (*R*,*R*)-(−)-*trans*-2,3-bis(hydroxydiphenylmethyl)-1,4-dioxaspiro[4.4]nonane (**2b**), respectively.



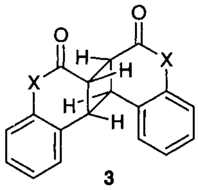
1

a: X = O
b: X = S



2

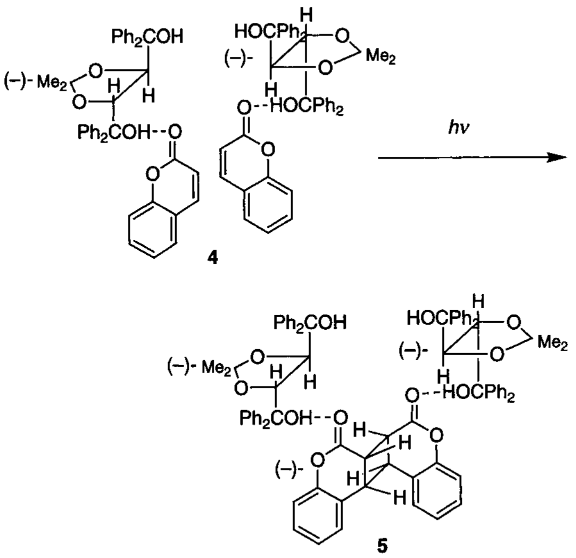
a: $R_2 = Me_2$
b: R_2 =



3

a: X = O
b: X = S

When a solution of a 1:1 mixture of **1a** and (−)-**2a** in a mixture of EtOAc and hexane was kept at room temperature for 3 h, a 1:1 inclusion complex (**4**) was obtained as colorless needles.[6] Irradiation of **4** in the solid state with a 400 W high-pressure Hg lamp (Pyrex filter, room temperature, 4 h) gave a 2:1 complex (**5**)[6] of (−)-**2a** with (−)-**3a** [Eq. (1)]. The crystals were still clear after photoirradiation and the reaction proceeded in a single-crystal-to-single-crystal manner throughout the reaction. The (−)-*anti*-head-to-head dimer **3a** was isolated by exchange with DMF. A 1:1 complex of (−)-**2a** with DMF was obtained as colorless needles in 99% yield after recrystallization of the 2:1 complex **5** from DMF/H_2O (5/1). Concentration of the filtrate left the optically pure (−)-*anti*-head-to-head dimer **3a**, which was isolated as colorless prisms in 89% yield. The optical purity of (−)-**3a** was determined by comparison of its $[\alpha]_D$ value to that of enantiomerically pure **3a**.[7] Optically pure (+)-**3a** was obtained when the host compound (+)-**2a** was used instead of (−)-**2a**.



(1)

This result shows that two molecules of **1a** are arranged in chirally related positions, which gives the optically active *anti*-head-to-head dimer **3a** by [2+2] photodimerization. This

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[*] Prof. F. Toda, Dr. K. Tanaka
Department of Applied Chemistry, Faculty of Engineering
Ehime University, Matsuyama, Ehime 790–8577 (Japan)
Fax: (+81)899-927-9923.

Dr. E. Mochizuki, Dr. N. Yasui, Prof. Y. Kai
Department of Materials Chemistry, Osaka University
Yamadaoka 2–1, Suita, Osaka 565–0871 (Japan)

Dr. I. Miyahara, Prof. K. Hirotsu
Department of Chemistry, Faculty of Science, Osaka City University
Sugimoto-cho, Sumiyoshi-ku, Osaka 558–8585 (Japan)

1433-7851/99/3823-3523 $ 17.50+.50/0

chiral arrangement of the achiral molecule **1a** in the inclusion complex **4** can easily be detected by measurement of the CD spectra of its Nujol mull. The 1:1 complex of **1a** with (+)- and (−)-**2a** showed CD spectra with a near mirror symmetry (Figure 1). The CD absorptions at 225, 275, 300, and 330 nm disappeared after photoirradiation of **4**, and the new CD absorption of **5** at 240 nm appeared. The photodimerization of **4** was also monitored by measurement of the IR spectra from Nujol mulls. The ν_{CO} absorption of **1a** in **4** at 1700 cm^{-1} decreased gradually and finally disappeared after 4 h of photoirradiation and a new ν_{CO} absorption from the presence of **3a** in **5** appeared at 1740 cm^{-1}.

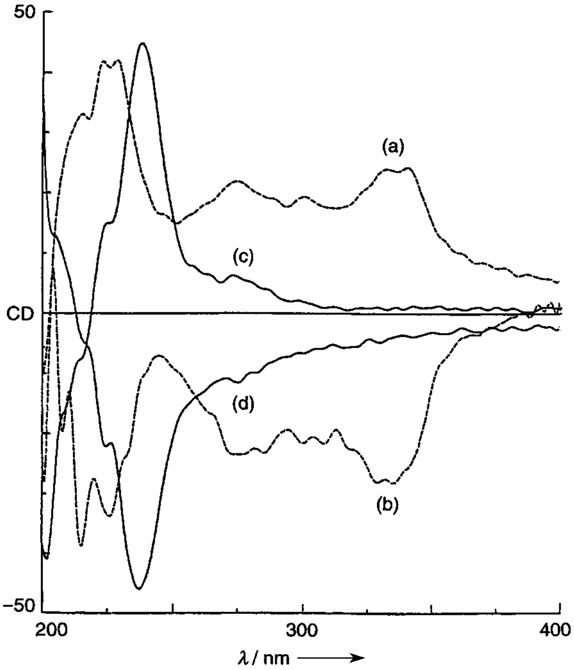


Figure 1. CD spectra in Nujol mulls: a) 1:1 complex of **1a** with (+)-**2a**; b) 1:1 complex of **1a** with (−)-**2a**; c) 2:1 complex of (+)-**2a** with (+)-**3a**; d) 2:1 complex of (−)-**2a** with (−)-**3a**.

The single-crystal-to-single-crystal nature and the steric course of the photodimerization of coumarin (**1a**) to (−)-*anti*-head-to-head dimer **3a** in the inclusion complex **4** were investigated by X-ray crystallographic analysis and X-ray powder diffraction studies. X-ray crystallographic analysis showed that two molecules of **1a** each form a hydrogen bond between the C40=O6 atom and the H(O4) atom of a separate molecule of **2a** and are arranged in the direction that gives the *anti*-head-to-head dimer **3a** on photodimerization; the distance between the two ethylenic double bonds being short enough (3.59 and 3.42 Å) to react easily and topochemically (Figure 2).[8] The bond distances of the cyclobutane ring connecting C38-C38* and C39-C39* atoms are 1.6 and 1.57 Å, respectively, after photoirradiation (Figure 3).[9] According to the X-ray structure analysis of the inclusion complexes **4** and **5** the *a* axis contracts as photodimerization proceeds while the *b* and *c* axes remain virtually unchanged. The changes in lattice constants from **4** to **5** resulting from photoreaction were −2.45, −0.02, and +0.35 Å for *a*, *b*, and *c*, respectively. As seen in Figure 3 the cyclobutane ring forms approximately along the *a* axis. This corresponds well to the anisotropic changes in the lattice constants.

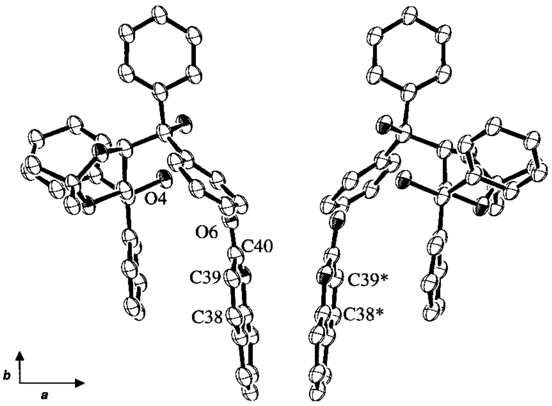


Figure 2. ORTEP drawing of the molecular structure of the 1:1 complex (**4**) of **1a** with (−)-**2a** (viewed along the *c* axis). All hydrogen atoms are omitted for clarity. The distances between C39 and C39*, and C38 and C38* are 3.59 and 3.42 Å, respectively.

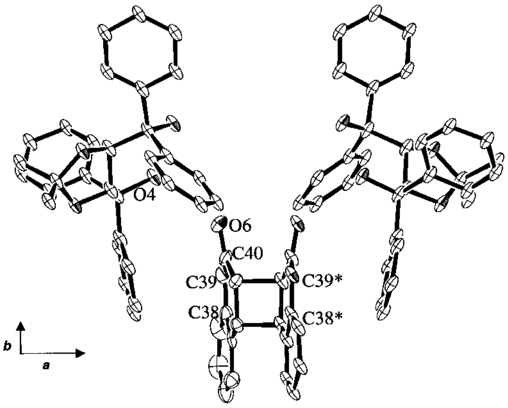
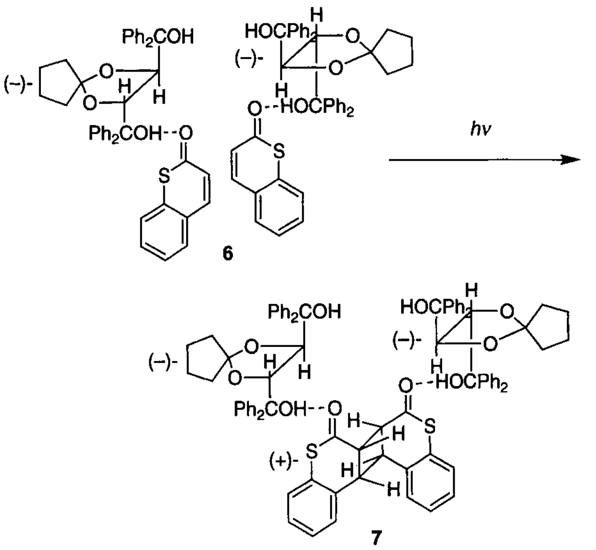


Figure 3. ORTEP drawing of the molecular structure of the 2:1 complex (**5**) of (−)-**2a** with (−)-**3a** (viewed along the *c* axis). All hydrogen atoms are omitted for clarity. The bond lengths C39−C39*, and C38−C38* are 1.57 and 1.60 Å, respectively.

X-ray powder diffraction patterns were measured on a Rigaku RINT 2000 X-ray diffractometer using Cu$_{K\alpha}$ radiation. The peaks at $2\theta = 8.90$ and 9.92 disappeared during UV irradiation and new peaks at $2\theta = 5.36$, 8.46, and 10.78 appeared. The original crystal structure had converted almost completely into the new structure after irradiation for 4 h. Remarkably, the peak of $2\theta = 9.92$ (interplanar spacing of (400)), which corresponds to one quarter of the length of the *a* axis, had shifted to $2\theta = 10.78$. The latter peak corresponds to the interplanar spacing of (400) for the 2:1 complex **5**. From these data we conclude that the photodimerization of the 1:1 complex **4** proceeded in a single-crystal-to-single-crystal manner.

The enantioselective photodimerization of thiocoumarin (**1b**) to optically pure (+)-*anti*-head-to-head dimer (**3b**)[10] in the 1:1 inclusion complex (**6**) of **1b** with (−)-**2b** was also found to proceed in a single-crystal-to-single-crystal manner [Eq. (2)]. Photoirradiation of **6** in the solid state (400 W high-pressure Hg lamp, Pyrex filter, room temperature, 2 h) gave a 2:1 complex (**7**) of (−)-**2b** with (+)-**3b** in quantitative



(2)

yield. Compound (+)-**3b** with 100 % ee[11] was isolated in 73 % yield by column chromatography. The crystal-to-crystal nature of this reaction was also confirmed by X-ray powder diffraction spectroscopy.

In conclusion, the photodimerization of inclusion complexes of coumarin or thiocoumarin to the *anti*-head-to-head dimer within chiral host compounds (**2a**, **2b**) proceeded efficiently and enantioselectively. This is the first example of an enantioselective intermolecular photoreaction by a single-crystal-to-single-crystal transformation and it also provides a good example for the study of the mechanism of topochemical reactions in the crystal.

Experimental Section

4: When a solution of **1a** (3.2 g, 21.9 mmol) and (−)-**2a** (10.0 g, 21.5 mmol) in AcOEt/hexane (120 mL, 1/5) was kept at room temperature for 3 h a 1:1 inclusion complex (**4**) was obtained as colorless needles (5.7 g, 43 %, m.p. 95–98 °C).[6] IR (Nujol): $\tilde{\nu}$: 1700 (C=O), 1607 (C=C), 3358 (OH), 3230 cm^{-1} (OH). Elemental analysis calcd for $C_{40}H_{36}O_6$: C 71.37, H 3.99; found: C 71.64 H 3.82.

5: Photoirradiation of **4** (1.0 g, 1.6 mmol) in the solid state with a 400 W high-pressure Hg lamp with a Pyrex filter at room temperature for 4 h gave a 2:1 complex (**5**) of (−)-**1a** with (−)-**3a** in quantitative yield. Colorless needles (m.p. 228–232 °C). IR (Nujol): $\tilde{\nu}$: 1740 (C=O), 3433 (OH), 3262 cm^{-1}(OH). Elemental analysis calcd for $C_{40}H_{36}O_6$: C 71.37, H 3.99; found: C 71.64 H 3.82.

(−)-**3a**: When the 2:1 complex **5** (1.0 g) was recrystallized from DMF/H_2O (5 mL, 5/1) a 1:1 complex of (−)-**1a** with DMF was obtained as colorless prisms (0.86 g, 99 %). Concentration of the filtrate and separation of the 1:1 DMF complex of (−)-**2a** gave optically pure (−)-*anti*-head-to-head dimer **3a** (0.17 g, m.p. 168–169 °C, $[\alpha]_D = -9.1°$($c = 0.19$, benzene), 100 % *ee*) as colorless prisms in 89 % yield after recrystallization from ethyl acetate/hexane.

6: When a solution of **1b** (0.66 g, 4.1 mmol) and (−)-**2b** (2.0 g, 4.1 mmol) in *n*-butyl ether/hexane (30 mL, 5/1) was kept at room temperature for 12 h a 1:1 inclusion complex (**6**) was obtained as colorless needles (2.1 g, 76 %, m.p. 106–108 °C). IR (Nujol): $\tilde{\nu}$: 1618 (C=O), 1582 (C=C), 3358 (OH), 3250 cm^{-1} (OH). Elemental analysis calcd for $C_{42}H_{38}O_5S$: C 77.04, H 5.85; found: C 77.15, H 5.79.

7: Photoirradiation of **6** (1.0 g, 1.5 mmol) in the solid state by using a 400 W high-pressure Hg lamp with a Pyrex filter at room temperature for 2 h gave a 2:1 complex (**7**) of (−)-**2b** with (+)-**3b** in quantitative yield. Colorless needles (m.p. 190–194 °C). IR (Nujol): $\tilde{\nu}$: 1740 (C=O), 3433 (OH), 3262 cm^{-1} (OH). Elemental analysis calcd for $C_{42}H_{38}O_5S$: C 77.04, H 5.85; found: C 77.12, H 5.90.

(+)-**3b**: Complex **7** (1.0 g) was dissolved in toluene (5 mL) and chromatographed on silica gel using toluene/AcOEt (4/1) to give optically pure (+)-**3b** (0.18 g, 73 % yield) as colorless prisms after recrystallization from toluene (m.p. 254–255 °C). $[\alpha]_D = +182°$($c = 0.02$, $CHCl_3$). IR (Nujol): $\tilde{\nu}$: 1681 (C=O), 1655 cm^{-1} (C=O). Elemental analysis calcd for $C_{18}H_{12}O_2S_2$: C 66.64, H 3.73; found: C 66.38, H 3.60.

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[8] Crystal structure analysis of **4**:[12] $C_{40}H_{36}O_6$, $M_r = 612.72$, space group monoclinic $C2$, $a = 35.59(4)$, $b = 9.489(4)$, $c = 10.03(1)$ Å, $\beta = 102.70(4)°$, $V = 3305(4)$ Å^3, $Z = 4$, $\rho_{calcd} = 1.23$ g cm^{-3}, crystal dimensions 0.80 × 0.05 × 0.03 mm, $\mu = 0.82$ cm^{-1}, $T = 293$ K, $R = 0.105$, $Rw = 0.088$, and $S = 2.63$ for 561 parameters and 1291 unique observed reflections with $[I > 3\sigma(I)]$, $\Delta\rho_{max} = 0.37$ e Å^{-3}. Data collection was carried out on a Rigaku RAXIS-CS imaging plate two-dimensional area detector using graphite-monochromated $Mo_{K\alpha}$ radiation ($\lambda = 0.71070$ Å), $2\theta_{max} = 59.5°$. All the crystallographic calculations were performed using the TEXSAN software package of the Molecular Structure Corporation. The crystal structures were solved by direct methods and refined by full-matrix least squares. All non-hydrogen atoms and hydrogen atoms were refined anisotropically and isotropically, respectively.

[9] Crystal structure analysis of **5**:[12] $C_{40}H_{36}O_6$, $M_r = 612.72$, space group monoclinic $C2$, $a = 32.80(3)$, $b = 9.467(3)$, $c = 10.360(4)$ Å, $\beta = 100.27(7)°$, $V = 3164(2)$ Å^3, $Z = 4$, $\rho_{calcd} = 1.29$ g cm^{-3}, crystal dimensions 0.80 × 0.05 × 0.03 mm, $\mu = 0.86$ cm^{-1}, $T = 293$ K, $R = 0.114$, $Rw = 0.097$, and $S = 2.86$ for 560 parameters and 1939 unique observed reflections with $[I > 3\sigma(I)]$, $\Delta\rho_{max} = 0.46$ e Å^{-3}. Data collection and analysis were carried out in a similar way to those for **4**.

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[11] The optical purity was determined by HPLC on a chiral stationary phase (Chiralpak AS column; Daicel Chemical Co. Ltd., Himeji (Japan). The lactone ring of **3a** in complex **5** was opened by acid catalyzed esterification and the optical purity of the total reaction determined as 96 % *ee* by HPLC.

[12] Crystallographic Data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-118773(**4**) and -118774(**5**). Copies of the data can be obtained free of charge on application to CCDC, 12 union Road, Cambridge CB2 1EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk)