The First *in Situ* Observation of Intramolecular Rotation and Cyclization of Anilide by an X-ray Study: Partial Single-Crystal to Single-Crystal Photocyclization of *N*-Methyl-*N*-{(*E*)-methylmethacryloyl}anilide in Inclusion Crystals

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Solid-state reactions can be observed *in situ* by X-ray diffraction provided that the process under observation is single-crystal to single-crystal in nature.[1] Photochemical reactions in single crystals can be controlled to some extent by irradiation far into the long wavelength absorption tail.[2] This technique was applied to the inclusion crystals **I** which consist of chiral host (−)-**1** and guest **2** (Scheme 1, host/guest = 1:1).[3]

Photoirradiation of powdered crystals of **I** with a 400-W high-pressure mercury lamp for 150 h at room temperature gave (−)-**3** in 98% ee (yield 46%).[4] The absolute configuration of the photoproduct can be predicted from the beginning conformation of the anilide. The C−N−C(=O)−C torsion angle of the backbone is important to describe the chirality in molecular conformation shown in Figure 1a. The C7−N6−C14−C15 angle is −19.5(7)°. The sign of this torsion angle will not be inverted even if some intramolecular rotation of the unsaturated group will take place (Scheme 2). It is expected that the photocyclization starts from the conformation where the central C=C−N−C(=O)−C=C moiety is in a shape like a portion of the helix. However, the beginning orientation of the methylmethacryl moiety of anilide **2** in crystal **I** is not suitable for cyclization as shown in Figure 1a. The intramolecular rotation of the guest molecules is expected before cyclization. To see what really happens in crystals, an experiment of photoirradiation to the single crystals has been carried out.

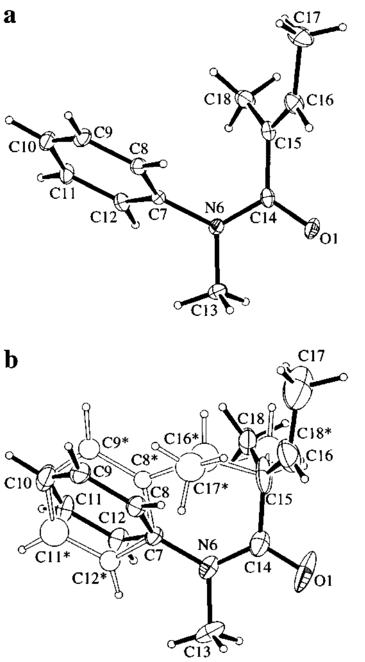
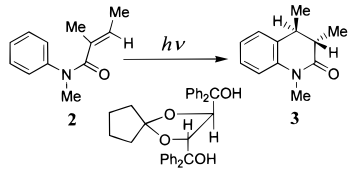


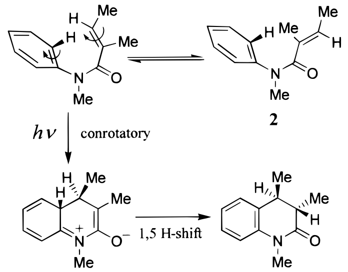
Figure 1. Molecular structure of guest **2** in (a) **I** and (b) **I′** (after photoirradiation). Thermal ellipsoids are plotted at the 10% probability level. Atoms with asterisks in (b) have a site occupancy factor of 26(1) %.

Scheme 1



2 **3** (−)-**1**

Scheme 2



2 (−)-**3**

Crystals were photoirradiated with a 250-W ultrahigh-pressure Hg lamp through band-pass filter BP365 (transmission factor 50% at 365 nm, half-height width 10 nm).[5] The reaction was very slow, and the changes in the lattice constants were monitored by X-ray four-circle diffractometer Rigaku AFC-7R with Mo Kα radiation. As the reaction proceeded, the X-ray diffraction ability of the crystal decreased. X-ray intensities were measured after photoirradiation for 143 h (the crystal after photoirradiation is denoted as **I′**).[6]

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(3) The host (−)-**1** was derived from (+)-tartaric acid. (a) Seebach, D.; Beck, A. K.; Imwinkelried, R.; Roggo, S.; Wannacott, A. *Helv. Chim. Acta* **1987**, *70*, 954−974. (b) Toda, F.; Tanaka, K. *Tetrahedron Lett.* **1988**, *29*, 551−554.

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(5) The UV−vis spectra of the acetonitrile solution of **I**, which is deposited, show a strong $\pi-\pi^*$ absorption maximum at 199 nm with a weak n−π^* absorption at around 250 nm. The absorption is negligible for wavelengths longer than 340 nm. The light from a ultrahigh-pressure Hg lamp has a main component at 365 nm in the region of wavelength longer than 340 nm. Therefore, a band-pass filter BP365 (T = 50% at 365 nm) was used for the incident light to penetrate a single crystal and to proceed with photoreaction homogeneously. If the band-pass filter was not used, the crystals degraded quickly.

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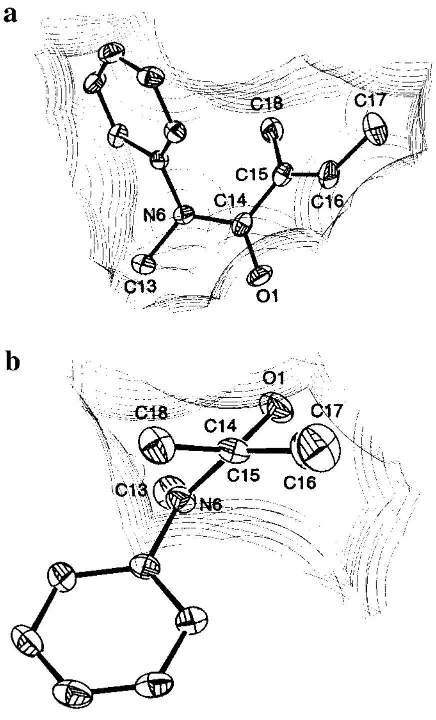

Figure 2. (a) Sections of the reaction cavity of guest **2** in **I** parallel to the plane defined by O1, C14, and C15, with a shift from −1 to +1 Å (the C16 and C17 atoms are located upward *ca.* 1 Å, and the C18 is located downward *ca.* 1 Å). (b) Sections of the reaction cavity perpendicular to the C14−C15 bond axis and through the C16 or the C17 atom (the C17 atom is located upward by 1.5 Å to the C16 and C18 atoms). Positions of C16 and C18 will be exchanged by the intramolecular rotation of the methylmethacryl group.

The disordered structure of guest in **I′** is shown in Figure 1b. The solid lines indicate the original structure of the guest. The open lines correspond to the cyclized product, (−)-**3**, with occupancy 26(1)%.[7] The dihedral angle between the *N*-phenyl group of the reactant, C7, C8, C9, C10, C11, C12, and that of the product, C7, C8*,C9*, C10, C11*, C12*, is 36(1)°. It became clear that the photoreaction of the guest molecules really occurred inside the crystal.

The proposed reaction mechanism is illustrated in Scheme 2. Intramolecular rotation of the methylmethacryl group seems to be caused thermally by the photoirradiation. It is expected that the photocyclization starts from the conformation where the central C=C−N−C(=O)−C=C moiety is in a shape like a portion of the helix. By photoirradiation, the helical bond sequence becomes flat as two C=C bonds approach each other. When the conjugated trienes are converted to a six-membered ring, the hydrogens at positions 1 and 6 will conrotate in a way such that they do not collide. Afterward, a 1,5 hydrogen shift will occur in a suprafacial manner, and the *trans*-isomer will be obtained. In the upper left structure of Scheme 2, the helix of the C=C−N−C(=O)−C=C moiety is left-handed according to the negative sign of the C−N−C(=O)−C torsion angle, and the photoproduct is (−)-**3**. If the molecular conformation of the guest **2** is a mirror image, the C−N−C(=O)−C torsion angle is positive, and the photoproduct will be (+)-**3**.

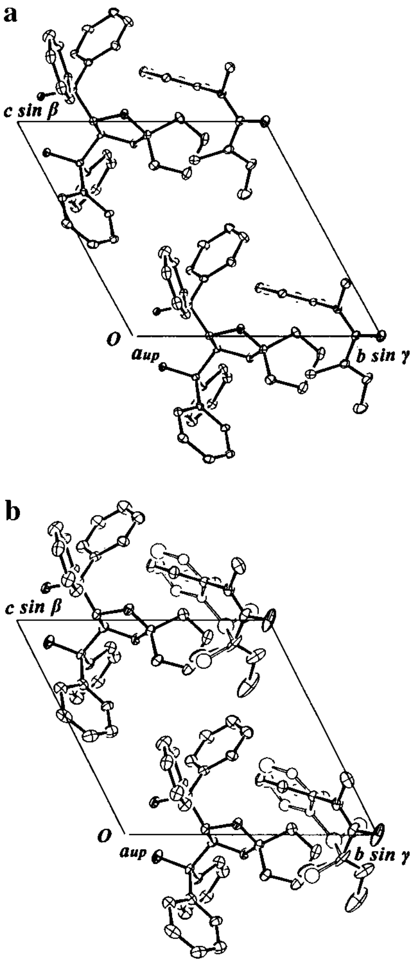

Figure 3. Projection of the crystal structure along *c* of (a) **I** and (b) **I′** (after photoirradiation). Thermal ellipsoids are plotted at the 10% probability level.

The reaction cavity of guest **2** in **I** was analyzed using the program CAVITY[8] to see if the methylmethacryl group might rotate around the C14−C15 bond axis by 180°. In Figure 2a, positions of the C16 and C18 atoms will be exchanged by intramolecular rotation, and the C17 atom will be accommodated in the cavity. Figure 2b is a projection of the cavity around the C16, C17, and C18 atoms perpendicular to the C14−C15 rotation axis. Of course, the rotation around the C14−C15 bond is not allowed at the beginning by the intermolecular steric repulsion. In contrast to the crystal, the intramolecular rotation seems very active in solution because of the rather low energy barrier. By photoirradiation, the temperature of the crystal will be increased, and the space becomes sufficient for 180° rotation by chance. Photocyclization of a guest molecule will alter the reaction cavity of the neighboring unit-cell, and the photoreaction may proceed like the domino effect.

Host molecules play an important role in keeping the crystal lattice during the reaction. As shown in Figure 3, their positional parameters in the crystal were almost unchanged with an increase in their displacement parameters U_{eq} of *ca.* 1.5 times after the photoirradiation, whereas U_{eq} of atoms of the guest increased 1.9 times on average with photoirradiation.

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Supporting Information Available: UV−vis absorption spectra of **I** in CH_3CN, and X-ray structural information on **I** and **I′** (PDF). X-ray crystallographic file (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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[6] Chemical formula: $C_{33}H_{32}O_4 \cdot C_{12}H_{15}NO$, M_r 681.87. Crystal data before photoirradiation (**I**): triclinic, $P1$, $Z = 1$, $a = 10.283(1)$ Å, $b = 10.295(1)$ Å, $c = 10.141(1)$ Å, $\alpha = 118.29(1)°$, $\beta = 92.79(1)°$, $\gamma = 84.00(1)°$, $V = 940.2(2)$ Å^3, $D_x = 1.204$ Mg m^{-3}, $R = 0.056$. After photoirradiation for 143 h (**I′**): $a = 10.224(2)$ Å, $b = 10.476(3)$ Å, $c = 10.024(3)$ Å, $\alpha = 116.84(2)°$, $\beta = 93.15(2)°$, $\gamma = 83.69(2)°$, $V = 952.2(5)$ Å^3, $D_x = 1.189$ Mg m^{-3}, $R = 0.068$.

[7] Positions of the C8*, C9*, C11*, C12*, C16*, and C17* atoms were located on difference syntheses and refined isotropically. The positions of hydrogen atoms and C18* were calculated geometrically and fixed.

[8] Ohashi, Y.; Yanagi, K.; Kurihara, T.; Sasada, Y.; Ohgo, Y. *J. Am. Chem. Soc.* **1981**, *103*, 5805−5812.