

Metastable polymorphic form of isopropylbenzophenone derivative directly obtained by the solid-state photoreaction investigated by *ab initio* powder X-ray diffraction analysis

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Introduction

The crystalline state photoreaction of 2-(2,4,6-triisopropylbenzoyl)((*S*)-1-phenylethyl)benzamide (**1**) undergoes a diastereospecific Norrish type II photocyclization under UV irradiation, producing (*R,S*)-cyclobutenol (**2**). The initial crystalline phase of **1** transforms into the crystalline product phase **2A** upon the UV irradiation with disintegration of the initial single crystalline form. The subsequent recrystallizations always gave a different crystalline product phase **2B** but never the original **2A**. The crystal structure of **2A** is the most important information to understand the solid-state photoreaction of this compound. However, the crystalline phase of **2A** can only be obtained by the photoreaction of **1** as a polycrystalline form and the crystal structure of **2A** cannot be determined by the single crystal diffraction method. Therefore, in this study, the crystal structure of **2A** was directly determined from the high resolution powder X-ray diffraction data in order to elucidate the solid-state photoreaction process of **1**.

Results and Discussions

High resolution synchrotron X-ray powder diffraction data were recorded at ambient condition on beamline 4B2 (Multiple Detector System) at Photon Factory with wavelength 1.20853(2)Å. The sample was loaded on flat sample holder and diffraction measurement was carried out using reflection mode with rotation of the sample holder. Data collection time was ca. 12 hours. From high resolution diffraction data, the crystal structure of **2A** was successfully determined by direct-space method.

Although the powder X-ray diffraction pattern of **1** and **2A** are significantly different, surprisingly, the whole crystal packing was retained during the solid-state photoreaction process. In the photoreaction, the hydrogen atom which was bonded to C13 transferred to O32 and a C-C bond was formed between C13 and C16 giving *R*-cyclobutenol (see Figure 1b). There is a possibility to form a C-C bond between C7 and C16 after an abstraction of the hydrogen atom which is bonded to C7 giving *S*-cyclobutenol. However, this is less preferred because the distance between the abstracted hydrogen atom and O32 is longer. Moreover, the total reaction cavity volume of the *o*-isopropyl group and the phenone group is larger on the reaction side. The difference of reaction cavity volume would also govern the direction of the photoreaction. The crystal structure of **2A** strongly supports this discussion and explains why only the *R*-cyclobutenol is produced in the photoreaction.

As shown in Figure 1b, the molecular conformation in **2B** is almost same as in **2A** except for the terminal isopropyl group. The hydrogen bonds are also similar for **2A** and **2B**. There is one O-H...O intra-molecular hydrogen bond and one N-H...O inter-molecular

hydrogen bond in both **2A** and **2B**. The inter-molecular hydrogen bond of the amide group forms one dimensional chain along the *b* axis in both **2A** and **2B**. However, there is an important difference in the arrangement of these one dimensional chains. Although there are two directions of hydrogen bond chains in **2A**, which are related by the 2_1 screw axis, all hydrogen bond chains point in the same direction in **2B** as shown with the transparent arrows in Figure 1b. Such structural difference seems to cause the difference in the stability of these two polymorphic forms. The lattice energy calculations suggest that **2B** is thermodynamically more stable phase than **2A**. Thus, it was revealed that the crystal structure of **1** transforms into less stable but more similar crystal structure **2A** in the photoreaction process, and the more stable polymorphic form **2B** is obtained by the recrystallization from the solution instead of the metastable form **2A**.

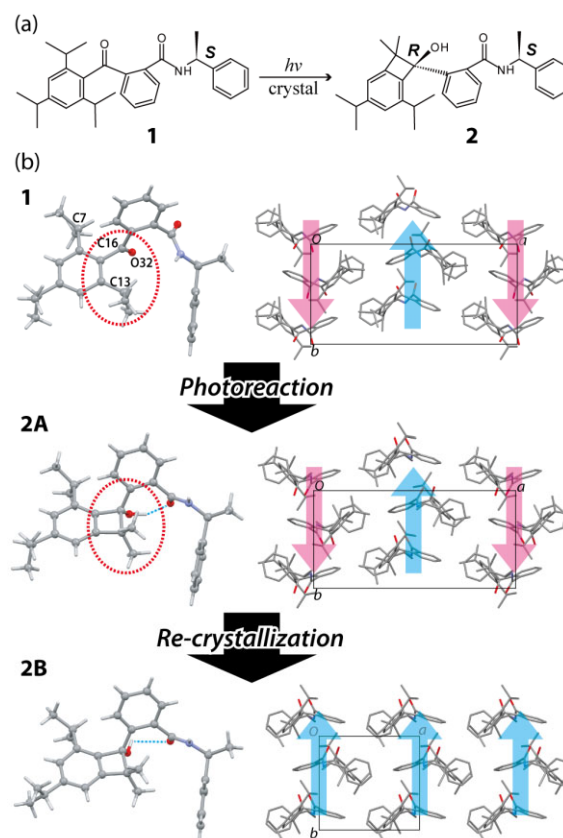


Figure 1: (a) Reaction scheme of **1**. (b) Crystal structures of **1**, **2A** and **2B**. The left side show the molecular structure and the right side show the crystal packing viewed along the *c*-axis.

K. Fujii et al., *CrystEngComm*, 2011, 13, 3197-3201.

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