JOC Note

Formation of Cubane-like Photodimers from 2-Naphthalenecarbonitrile

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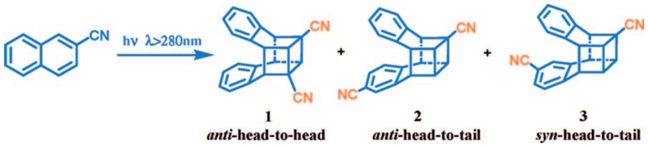

Irradiation of 2-naphthalenecarbonitrile (**2-NpCN**) in solution with a light $\lambda > 280$ nm results in the formation of three rigid cubane-like photodimers, *anti*-head-to-head **1**, *anti*-head-to-tail **2**, and *syn*-head-to-tail **3**, which are not in line with the previously recognized regioselectivity. These cubane-like photodimers have been well characterized by spectroscopic investigation and/or X-ray crystal structural analysis in this work. Moreover, the separation of the optically pure enantiomers of **1**, **2**, and **3** has been achieved by HPLC resolution.

The development of efficient methods for carbon−carbon bond formation is one of the fundamental challenges of organic synthesis. In recent years organic photochemistry has gradually matured to a stage that can offer attractive synthetic routes.[1−12] It is generally accepted that the stable products accessible to a photoexcited molecule are far greater than those accessible to a ground-state molecule since the excited molecule possesses an excess energy content as a result of photon absorption.[1] The fact that light absorption, rather than heat, activates a photochemical reaction allows for selectivity of activation and also allows for the ability to initiate reactions even at very low temperatures. In this context, photocycloaddition is of great interest in view of its significance in σ-bond formation.[2−10]

The photochemical cyclodimerization of anthracenes is one of the oldest known reactions and has been extensively investigated,[11] while the photodimerization of naphthalene derivatives is limited in scope. Unlike anthracene, naphthalene itself does not undergo photodimerization. Only some substituted naphthalene derivatives, such as alkyl 2-naphthoate and 1,8-naphthalenedicarboxylate, have been reported to give cubane-like photodimers.[12−28] Furthermore, the regioselectivity of photodimerization was believed to originate from the fact that (1) the carbon−carbon bonding occurred only between the substituted rings and (2) the substituents were in a head-to-tail orientation.[15,16] Very recently, we found that the highly rigid photodimer of methyl 2-naphthoate,[24] prepared by irradiation of methyl 2-naphthoate in degassed cyclohexane solution with a light $\lambda > 280$ nm, is a new type of C_2-symmetric-chiral cubane-like compound. As we know, the strained cage of cubane molecules, particularly nitrocubanes, has shown promise as high-density energetic materials for use in pharmaceutical and polymer chemistry. Since the first synthesis of cubane, there has been a great deal of effort to functionalize the cubane skeleton.[29−32] In this connection, photocycloaddition of the substituted naphthalene derivatives provides an effective pro-

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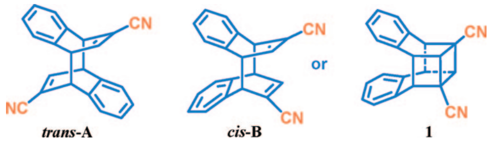
SCHEME 1. The Proposed Structure for the Photodimers of 2-NpCN



tocol for making cubane-like photodimers that cannot be directly obtained by thermal-chemical reaction.

2-Naphthalenecarbonitrile (**2-NpCN**) was reported to form a photodimer in 1971.[33] On the basis of the MS, IR, and ^{1}H NMR spectrum, Zweig[33] assigned the 1,4-bridged structure *trans*-**A** or *cis*-**B** to the photodimers (Scheme 1). Later on, Sasse[34] realized that the spectroscopic data for the photodimer of **2-NpCN** were similar to those of the dimers he had obtained from the naphthalene carboxyl esters, and suggested that the photodimer has a cubane-like structure **1**. In 1984, Albini[35] reinvestigated this reaction and observed that the situation was more complicated. Up to now, there were only three scattered references to this reaction in spite of the easy modification of the carbonitrile functionality. Particular interest in the carbon−carbon formation of cubane-like photodimers with large strain energy and chirality prompted us to study the photodimerization of **2-NpCN**.

In the present work, we report that irradiation of **2-NpCN** in solution results in the formation of three rigid cubane-like photodimers, *anti*-head-to-head **1**, *anti*-head-to-tail **2**, and *syn*-head-to-tail **3**. X-ray crystal structures of **1** and **2** confirm the cubane-like skeleton and a pair of enantiomers interacts with each other via C−H···N hydrogen bonding for **1** and C−H···π and $\pi-\pi$ interactions for **2**. More importantly, the racemic mixtures of **1**, **2**, and **3** have been successfully resolved into their optically pure enantiomers by HPLC. It is worth noting that the arrangement of the carbonitrile functionality is distinctly different in **1**, **2**, and **3**, suggesting that the formation of the photodimers does not lead solely to the unique cubane-like ring system. This finding contrasts to the previously recognized regioselectivity, in which the carbon−carbon bonding occurred only between the substituted rings and the substituents were in a head-to-tail orientation.

The photochemical reaction was carried out at room temperature in a Pyrex tube with a 500-W high-pressure mercury lamp as a light source. Irradiation of **2-NpCN** in degassed acetonitrile solution (0.1 M) with $\lambda > 280$ nm decreased the absorbance at the typical bands for **2-NpCN** (Figure S1, Supporting Information). Monitored by UV absorption spectroscopy, the conversion of the starting material (**2-NpCN**) was close to 23% upon 17 h of photolysis. The reaction mixture was then isolated by chromatographic column over silica, eluted with petroleum ether/ethyl acetate (20/1 in volume). Compounds **1** and **2** were obtained as the products. The parent ion peak ([M + Na$^+$], 329) in the MS (ESI) establishes the dimeric nature of the products. ^{1}H NMR suggests that the framework of the cubane-like structure remains unchanged, similar to that of methyl 2-naphthoate.[24] However, **1** exhibits eight aliphatic and six aromatic protons (Figure S2, Supporting Information), while **2** contains seven aliphatic and seven aromatic protons (Figure S3, Supporting Information). Moreover, the photodimerization was noted to depend on the solvent used. The ratio of **1** to **2** is ca. 8.5:1.5 in acetonitrile but 3:7 in cyclohexane. In spite of the ratios changing with the polarity of solvent, **1** and **2** were obtained exclusively throughout the irradiation. The fact that the higher polarity of solvent favors formation of **1** indicates different polarities for the excimers leading to **1** and **2**.

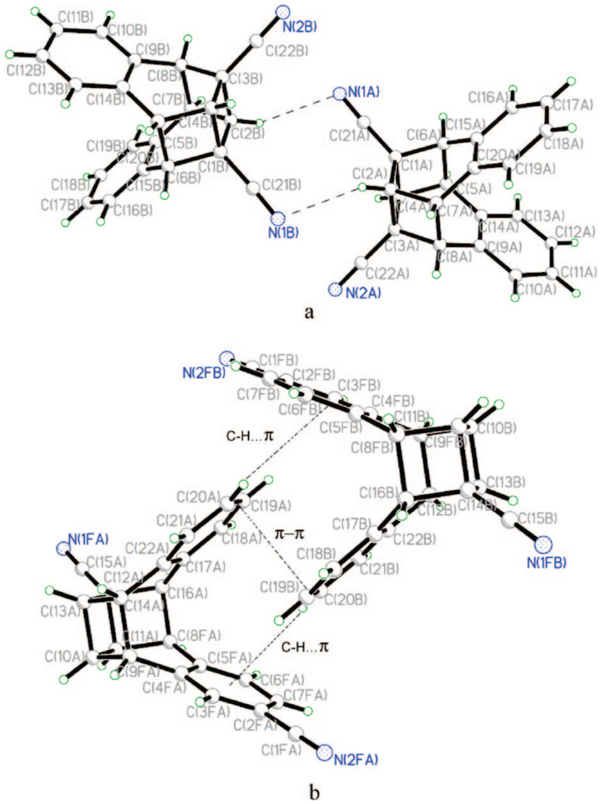


FIGURE 1. (a) Packing diagram of **1**, selected bond lengths (Å): C1−C4, 1.560(2); C2−C3, 1.560(2); C5−C6, 1.582(8); C7−C8, 1.586(2); selected dihedral angles (deg): C6−C5−C14−C9, 73.4(2); C8−C7−C20−C15, 72.1(2); C21−C1−C2−C3, 131.0(3); C22−C3−C4−C1, 128.4(6). (b) Packing diagram of **2**, selected bond lengths (Å): C11−C12, 1.580(3); C10−C13, 1.541(3); C9−C14, 1.559(3); C8−C16, 1.585(3); selected dihedral angles (deg): C4−C5−C8−C16, 72.8(2); C11−C12−C22−C17, 72.6(2); C15−C14−C16−C8, −128.8(2).

Strong support for the structures of **1** and **2** comes from the crystal structural analysis. Single crystals of **1** and **2** were obtained by recrystallization of **1** and **2** from ether/ethyl acetate (3/1 in volume) and ether/dichloromethane (5/1 in volume) solutions, respectively. A colorless single cuboid crystal was used for data collection at 293 K. Both **1** and **2** belong to the monoclinic crystal system (Table S1, Supporting Information). It is evident that the cubane-like structure of **1** is formed by the bonding of C1, C2, C6, and C7 to C4, C3, C5, and C8, while **2** is formed by the bonding of C12, C13, C14, and C16 to C11, C10, C9, and C8, respectively (Figure 1.) The dihedral angles formed by the aromatic rings in both **1** and **2** are around 73°, and torsion angles of C21−C1−C2−C3, C22−C3−C4−C1 in **1** and C15−C14−C16−C8 in **2** are opened out to about 130°. Notably, the arrangement of the carbonitrile functionality is distinctly different in **1** and **2**. **1** has a cubane-like structure with an *anti*-head-to-head conformation, but **2** is *anti*-head-to-tail. These results are not consistent with the previously recognized selectivity, in which bonding only occurred at the substituted rings and the substituents were in head-to-tail orientation.

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Close inspection of Figure 1 further reveals that the mirror images of **1** and **2** cannot overlap with each other. **1** is C_2-symmetric but **2** is not. Both **1** and **2** have a pair of enantiomers combined in one unit cell. Interestingly, two enantiomers of **1** interact with each other in a "head-to-head" manner via C2−H2···N1 hydrogen bonding,[36−38] which may be a result of crystal packing (Figure 1a). The H···N distance of 2.63 Å in C2−H2···N1 with a C−H···N angle of 146.85° is appreciably shorter than the sum of the van der Waals radii for H (1.20 Å) and N (1.55 Å), respectively. On the other hand, a pair of enantiomers of **2** form a symmetrical dimer in a "head-to-head" manner through C−H···π and π−π interactions[38] (Figure 1b). The H···π distance of ca. 3.013 Å suggests that the C20−H20···π intermolecular interaction is crucial in the molecular assembly. When viewed along the *a*-axis in the crystal lattice, the π−π interaction with a distance of 3.327 Å can be observed. These interactions cooperate with each other to afford a synergistic molecular packing of **1** and **2** (Figure S4 and S5, Supporting Information).

It is of significance that the optically pure enantiomers of **1** and **2** can be obtained by HPLC resolution (Figure 2). The resolution was carried out on a chiralcel OT(+) column (Daicel Chemical Industries, Ltd., 4.6 × 250 mm; eluent: *n*-hexane:2-propanol = 7:3; at 5 °C; flow rate 0.5 mL/min; UV detection at 220 nm). The chromatogram displays only one product peak when the reaction mixtures of **1** and **2** are analyzed by HPLC with an achiral Intersil ODS-3 column (Figure 2a,c). Figure 2b shows two product peaks of **1** (first eluting **1a** and second eluting **1b**) with an identical peak area in magnitude within experimental error. The isolated enantiomers of **1a** and **1b** show near mirror image behavior in the circle dichroism (CD) spectra, while their UV−vis absorption spectra are not distinguishable from each other (Figure 3).

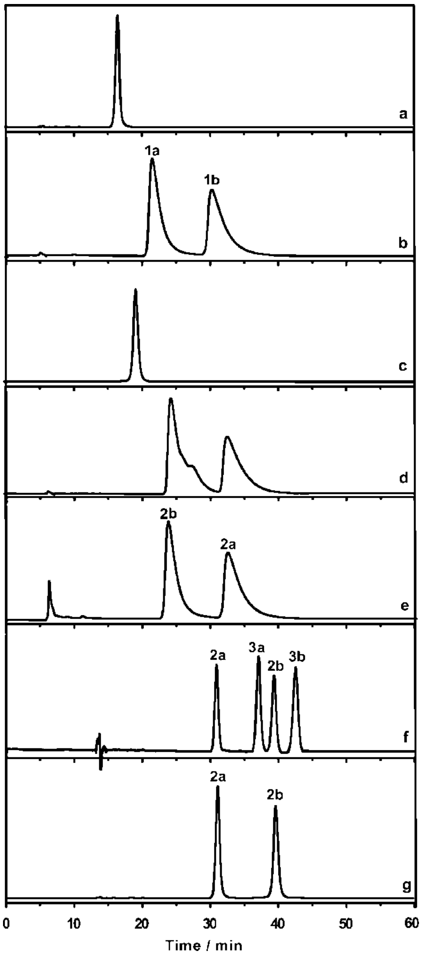

FIGURE 2. Typical HPLC chromatograms of (a) **1** with achiral ODS-3 cholumn; (b) **1** with chiral OT(+) cholumn; (c) the sample of **2** purified by chromatographic column with achiral ODS-3 cholumn; (d) the sample of **2** purified by chromatographic column with chiral OT(+) cholumn; (e) single crystals of **2** with chiral OT(+) cholumn; (f) the sample of **2** purified by chromatographic column with chiral IA cholumn; and (g) single crystals of **2** with chiral OT(+) cholumn.

Unexpectedly, the separation of the racemic mixture of **2** is not straightforward under the same conditions. When the sample of **2** purified by chromatographic column from the reaction mixture was used, peak broadening independent of flow rate (0.5 or 1.0 mL/min) was observed throughout the HPLC resolution (Figure 2d). However, when the single crystals of **2** were used as samples, the peaks were baseline separated (Figure 2e). These results indicate that the sample directly separated from the reaction mixture contains unknown products that cannot be distinguished by achiral Intersil ODS-3 column. In the course of resolving **2**, we finally found that the sample purified by chromatographic column could be separated into four product peaks by chiral IA column (Daicel Chemical Industries, Ltd., 10 × 250 mm; eluent: *n*-hexane:ethanol = 5:5; at room temperature; flow rate 1.0 mL/min; UV detection at 254 nm). As shown in Figure 2f, apart from the chromatograms of **2a** and **2b** from single crystals of **2** (Figure 2g), the other two peaks (**3a** and **3b**) with identical magnitude were detected.

To determine the identity of **3a** and **3b**, we performed the isolation on the chiralcel IA column by HPLC, and achieved **3a** and **3b** subsequently. The MS spectrometry confirms the dimeric nature of **3a** and **3b** with the same parent ion peak ([M + Na^+], 329). Examination of ^1H NMR spectra reveals that **3a** and **3b** contain seven aliphatic and seven aromatic protons. Despite the fact that the ^1H NMR and absorption spectra of **3a** and **3b** are not distinguishable from each other (Figure 3, as well as Figure S6 in the Supporting Information), the two isolated **3a** and **3b** show near mirror image behavior in the CD spectra. Taken all together, **3a** and **3b** are actually a pair of enantiomers deriving from the photodimerization of **2-NpCN**. The similar spectroscopic properties indicate that compounds **2** and **3** are isomeric. In view of the crystal structure of **2**, the only difference is the 2-carbonitrile presented in **3** with a *syn*-head-to-tail structure.

In summary, we have demonstrated that irradiation of **2-NpCN** in solution results in three cubane-like photodimers, *anti*-head-to-head **1**, *anti*-head-to-tail **2**, and *syn*-head-to-tail **3**. The ratio of **1** to **2** and **3** depends on the polarity of solvent used, while that **2** to **3** is almost the same throughout the irradiation. X-ray crystal structural analysis confirms the cubane-like structures of **1** and **2**. The intermolecular C−H···N, C−H···π, and π−π interactions show considerable strength and directionality for the combination of pairs of enantiomers in the crystal packing. It is worth noting that the *anti*-head-to-tail **2** and *syn*-head-to-tail **3** are not consistent with the previously recognized regioselectivity. More importantly, the optically pure enantiomers of **1** [**1a** $[\alpha]^{20}_{D}$ −47.3 (*c* 0.0068, methanol)], **1b** [$[\alpha]^{20}_{D}$ +47.2 (*c* 0.0069, methanol)], **2** [**2a** $[\alpha]^{20}_{D}$ +101.4 (*c*

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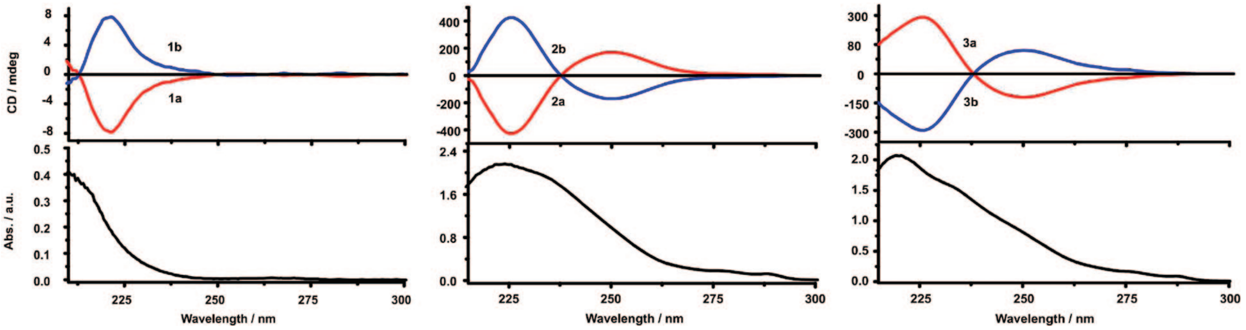

FIGURE 3. The circular dichroism (top) and absorption (bottom) spectra of enantiomers **1a**, **1b** in methanol, **2a**, **2b** and **3a**, **3b** in ethanol, respectively: **1a** (8.8×10^{-5} M), **1b** (8.4×10^{-5} M), **2a** (1.3×10^{-4} M), **2b** (1.3×10^{-4} M), **3a** (9.6×10^{-5} M), and **3b** (9.7×10^{-5} M).

0.0013, ethanol); **2b** $[\alpha]^{20}_{D}$ −101.5 (*c* 0.0013, ethanol)], and **3** [**3a** $[\alpha]^{20}_{D}$ −102.1 (*c* 0.0010, ethanol); **3b** $[\alpha]^{20}_{D}$ +102.2 (*c* 0.0010, ethanol)] can be successfully obtained by HPLC resolution. The easy manipulation and diverse substituted patterns of the photodimers of **2-NpCN** show promise for studying the use of cubane-like photodimers in the area of asymmetric catalysis and chiral assembly.

Experimental Section

Photodimerization of 2-NpCN. The photochemical reaction was carried out at room temperature with a 500-W high-pressure mercury lamp as a light source. **2-NpCN** was dissolved in a degassed acetonitrile (765 mg, 0.1 M) or cyclohexane solution (306 mg, saturated) in a Pyrex tube (diameter: 2.5 cm), which served as a light filter to cut off light below 280 nm and guarantee irradiation with $\lambda > 280$ nm. A quartz jacket with water circulation was used to cool the lamp. The irradiation was monitored by UV−vis absorption spectra. The absorbance at the typical bands for **2-NpCN** was no longer decreased upon 17 h of photolysis, and the conversion of the starting material (**2-NpCN**) was close to 23% in acetonitrile and 13% in cyclohexane. The resulting mixture was concentrated under reduced pressure and purified by a chromatography column on silica with petroleum ether/ethyl acetate (20/1 in volume) to afford **1** and the mixture of **2** and **3** [TLC R_f value for **1** 0.41 and for **2** and **3** 0.32 in petroleum ether/ethyl acetate (5/1 in volume)]. The mixture of **2** and **3** was further separated by HPLC, using a chiral IA column. On the basis of the consumption of the starting material, the yields of **1**, **2**, and **3** are 85% (150 mg), 8% (14 mg), and 5% (9 mg) in acetonitrile and 31% (12 mg), 38% (15 mg), and 31% (12 mg) in cyclohexane.

1: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.09−6.96 (m, 8H), 4.58−4.47 (m, 4H), 3.98−3.96 (d, 2H, *J* = 8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 133.8, 133.0, 128.9, 128.8, 128.4, 128.2, 120.2, 48.9, 43.8, 42.5, 29.8; MS-ESI [M + Na]$^+$ 329. Crystallographic data have been deposited with the Cambridge Crystallographic Data Center as supplementary publication NO. CCDC686516.

2: ^{1}H NMR (400 MHz, CD_3COCD_3) δ 7.37−7.35 (m, 2H), 7.21 (d, 1H, *J* = 7.6 Hz), 7.07−7.02 (m, 4H), 4.71−4.45 (m, 4H), 3.78 (t, 1H, *J* = 7.9 Hz), 3.53−3.45 (m, 2H); MS-ESI [M + Na]$^+$ 329. Crystallographic data have been deposited with the Cambridge Crystallographic Data Center as supplementary publication NO. CCDC686517.

3: ^{1}H NMR (400 MHz, CD_3COCD_3) δ 7.41−7.35 (m, 2H), 7.18 (d, 1H, *J* = 7.8 Hz), 7.09−7.01 (m, 4H), 4.70−4.46 (m, 4H), 3.78 (t, 1H, *J* = 8.0 Hz), 3.53−3.45 (m, 2H); MS-ESI [M + Na]$^+$ 329.

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Supporting Information Available: Absorption spectral changes of **2-NpCN** upon irradiation, ^{1}H NMR and/or ^{13}C NMR spectra of **1**, **2**, and **3**, and crystal structural data (CIF) of **1** and **2**. This material is available free of charge via the Internet at http://pubs.acs.org.

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