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Enantioselective Intramolecular Aromatic [4 + 4] Photocycloaddition in Crystalline State: Parameters for Reactivity

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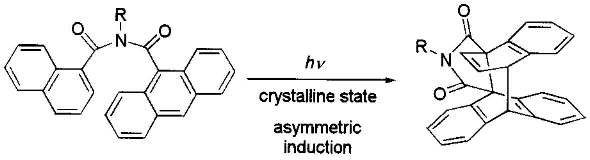
ABSTRACT



Photoreactivity of seven 9-anthryl-*N*-(naphthylcarbonyl)carboxamide derivatives, 1a–g, in their intramolecular [4 + 4] photocycloadditions in solid state is discussed on the basis of their single-crystal X-ray analyses. The distances (d_1 and d_2) between the two carbon atoms to be reacted, the angles (θ_1 and θ_2), and the torsion angle (θ_3) between the anthracene and naphthalene rings were chosen as structural parameters for reactivity. For 1a and 1e, the first example of absolute asymmetric synthesis in [4 + 4] photocycloaddition was attained.

Asymmetric induction using chiral crystals that consist of achiral substrates has been known as absolute asymmetric synthesis.[1] Since the first example of this category of asymmetric induction was achieved by Elgavi et al.,[2] over a dozen examples have been reported.[3] However, the reactions have been limited to rearrangements,[4] Norrish type II photocyclization,[5] and [2 + 2] cycloaddition,[6] and no example of [4 + 4] cycloaddition has been reported, which is a typical photocycloaddition of aromatic compounds.[7] In this paper, we report on the first example of an absolute asymmetric synthesis in [4 + 4] photocycloaddition and demonstrate the usefulness of an iminodicarbonyl group in crystal engineering as a linker to place two moieties in suitable positions to be reacted each other.

Even for achiral or diastereoselective solid-state photocycloadditions, the examples of [4 + 4] cycloadditions[8] were limited compared to the vast examples of [2 + 2] cycloadditions.[9] To have an efficient overlap of two 4π units in a crystalline environment for intramolecular [4 + 4] photocycloadditon, the choice of a functional group as a linker to

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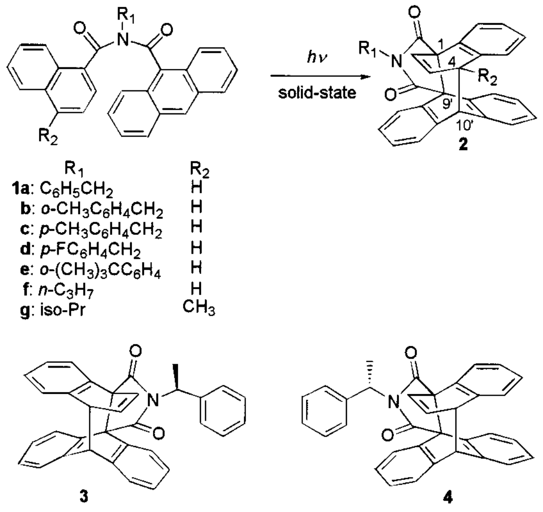
connect these 4π units and its length are very important. According to the rule of five,[10] the linker should have the length of three atoms to construct a five-membered ring, which is the most favorable ring formation in intramolecular photocycloaddition. Amino[11] and propylene[12] linkers were reported to be improper for this purpose because two moieties connected with them did not overlap each other in crystalline state. It is known that *N*-methyl aromatic amides and *N*,*N'*-dimethyl aromatic ureas[13] have the *cis* favorable conformation. By analogy with these, we employed an iminodicarbonyl, which is considered to be a sequence of two amide units, as a linker to connect two 4π units. Two carbonyls are expected to be located nearly on the same plane with the W-shape, which results in an overlapping of two 4π units. To have an asymmetric system, anthracene and naphthalene moieties were introduced as 4π units to be reacted.

Scheme 1



The crystal structures of seven 9-anthryl-*N*-(naphthylcarbonyl)carboxamide derivatives were examined by single-crystal X-ray diffraction analysis, and the relations between their structures and reactivities were investigated. All carboxamides showed structures in which two aromatic rings were laid to overlap each other. Photocycloaddition in solid state was carried out as follows. Powdered single crystals of **1** (ca. 20 mg) were sandwiched between two Pyrex cover glasses and placed in a polyethylene bag, which was irradiated with a 400-W high-pressure mercury lamp for 6 h (3 h for each side of the sample) in an ice−water bath. Out of seven carboxamides examined, **1a**, **1e**, and **1g** showed intramolecular photocycloaddition in solid state to give the [4 + 4] cycloadducts **2a**, **2e**, and **2g** in an almost quantitative yield after complete conversion, and **1f** gave **2f** in 9% yield. However, **1b**, **1c**, and **1d** were unreactive. Melting of the powdered crystals was not observed during and after the irradiation. The crystals of **1a**, **1b**, and **1e** have the chiral space groups $P2_12_12_1$, $P1$, and $P2_1$, respectively, and the others belong to achiral space groups as shown in Table 1.

Table 1. Distances and Angles in Carboxamides **1** Obtained from the X-ray Crystallographic Analysis

compd	space group	d_1 (Å)	d_2 (Å)	θ_1 (deg)	θ_2 (deg)	θ_3 (deg)	$\theta_1 + \theta_2 + \theta_3$ (deg)
1a	$P2_12_12_1$	2.84	4.22	103.8	96.2	38.5	238.5
1b	$P1$	2.85	4.68	108.8	98.3	46.0	253.1
1c	$P\bar{1}$	2.85	4.76	110.8	99.0	47.5	257.3
1d	$P2_1/n$	2.85	4.68	109.4	98.8	48.7	256.9
1e	$P2_1$	2.88	4.31	108.8	94.3	34.8	237.9
1f	$P2_1/c$	2.86	4.47	106.2	100.6	36.0	242.8
1g	$P2_1/n$	2.84	4.35	104.0	98.1	40.4	242.5

Thus, we could expect asymmetric induction in the photocycloaddition of **1a** and **1e** in single crystals if their conformations were preserved during the reaction. This was confirmed by the measurement of $[\alpha]_D$ of the crude **2a** ($[\alpha]^{25}_D = +60°$ ($CHCl_3$, *c* 0.50)) and **2e** ($[\alpha]^{25}_D = -84°$ ($CHCl_3$, *c* 0.50)). The optical purity of **2a** was determined to be 82% ee by HPLC analysis with a chiral column (Daicel Chiralcel OJ; solvent, 10:3 *n*-hexane/*i*-PrOH, containing 0.1% of diethylamine). The optical yield of **2e** was almost quantitative.[14] Single crystal of the cycloadduct **2a** has the chiral space group of $P2_1$.

The absolute configuration of **2a** was determined to be 1*R* and 4*S* from the comparison of their CD spectra with those of the similar diastereomeric [4 + 4] cycloadducts **3**

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(14) Since good separation of enantiomers for **2e** was not obtained by HPLC with a chiral column, enantiomerically pure **2e** was prepared by repeated recrystallization for the optical yield.

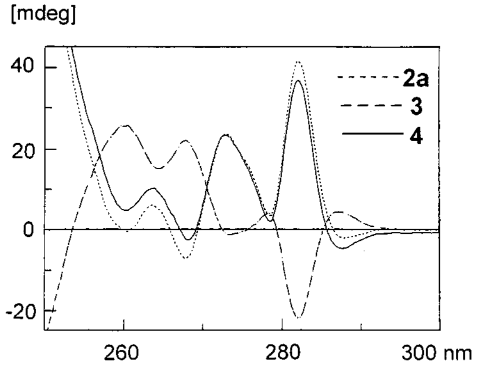


Figure 1. CD spectra of **2a**, **3**, and **4**.

and **4**[15] with known absolute configurations as shown in Figure 1. The signs of Cotton effect for **2a** agreed with that of **4**. Figure 2 shows the ORTEP diagram of **1a** in which the naphthalene and the anthracene rings face each other. In all cases, a similar arrangement of the two aromatic rings was found in the crystalline structures. An iminodicarbonyl linkage worked very well to locate the naphthalene and anthracene moieties in suitable positions to be reacted. To rationalize the reactivity of the carboxamides, distances d_1 and d_2, angles θ_1 and θ_2, and a torsion angle θ_3 (the torsion angle between the naphthalene and the anthracene planes) were selected as the parameters for photocycloaddition from their X-ray structures. These values are summarized in Table 1. The distance d_1 between two carbon atoms, C1 and C9′, is nearly the same, 2.84−2.88 Å, in all compounds. However, the distance d_2 (C4−C10′) varies from 4.22 to 4.76 Å. It has been known that the distance between two π bonds should be within 4.2 Å for their efficient overlapping to be reacted in [2 + 2] photocycloaddition in solid state.[16] In our [4 + 4] photocycloaddition, the distance d_2 of ca. 4.5 Å seems to be the limit for cycloaddition. In the case of **1f**, the cycloaddition was inefficient as a result of the relatively large value of d_2 (4.47 Å). The efficacy of the π-overlapping can also be estimated from the sum of angles θ_1, θ_2, and θ_3. The unreactive imides, **1b**, **1c**, and **1d**, have a value of ($\theta_1 + \theta_2 + \theta_3$) over 250°.

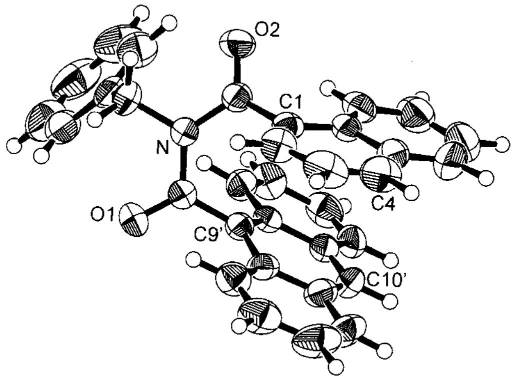
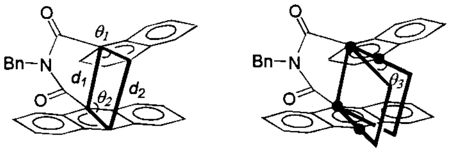


Figure 2. ORTEP diagram for **2a**.

Scheme 2. Structural Parameters for Photocycloaddition: Distances (d_1 and d_2), Angles (θ_1 and θ_2), and a Torsion Angle (θ_3)



As we demonstrated, an iminodicarbonyl group is useful as a linkage to connect two moieties in suitable positions to be reacted in crystalline state. We have established a novel absolute asymmetric synthesis for [4 + 4] photocycloaddition in crystalline state and determined the parameters for cycloaddition.

Acknowledgment. We thank JASCO Co. for the measurements of CD spectra.

Supporting Information Available: Spectral data of **1a**−**g**, **2a**, **2e**, **2f**, and **2g**; X-ray structural information for **1a**−**g**, and **2a** in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.

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