Solvent Switching of Stereoselectivity in [4 + 4] Photocyclodimerization of 2-Anthracenecarboxylic Acid

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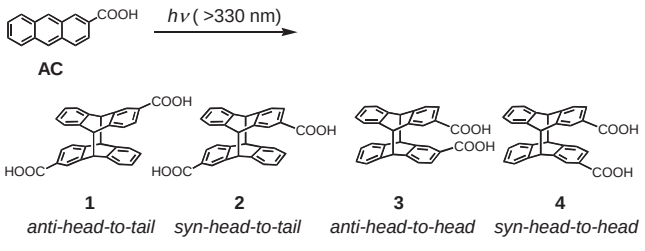
Stereochemistry of the major photocyclodimer is switched from 52% *anti-head-to-head* to 51% *anti-head-to-tail* among the four stereoisomers produced upon irradiation of 2-anthracenecarboxylic acid at low temperatures by changing the solvent from dichloromethane to methanol, through a critical control of the hydrogen bonding and dipole–dipole interactions.

Stereochemical control is one of the most crucial issues in current photochemistry. Hence, a vast variety of strategies have hitherto been employed to manipulate the stereochemical outcome of photochemical reactions by using a variety of ground-state and excited-state interactions, as well as the environmental variants.[1,2] Photocyclodimerization of anthracene derivatives has been studied in considerable details[3–15] and frequently employed as a convenient photochemical glue for connecting two relevant moieties or molecules.[3] However, the stereochemistry of photocyclodimerization of unsymmetrically substituted anthracenes does not appear to have attracted much attention or to have been well studied, although it was reported that *anti*-cyclodimer is favored in a polar solvent upon photocyclodimerization of a couple of 9-substituted anthracenes.[4–9] This would arise from the relatively complex nature of the photoproducts, which contains four stereoisomeric *anti-* and *syn-head-to-tail* (HT) and *anti-* and *syn-head-to-head* (HH) cyclodimers, as exemplified for 2-anthracenecarboxylate (**AC**) in Scheme 1.[13,14] In the present study, we wish to elucidate the factors and mechanisms that control the stereochemical outcome of the photocyclodimerization of **AC** and also to manipulate the product ratio by environmental factors, such as temperature and solvent.

A 4 mL solution of **AC** (0.25 mM) in toluene, dichloromethane, acetonitrile, or methanol was irradiated under an argon atmosphere at various temperatures, by using a 500-W ultrahigh pressure mercury lamp (Ushio Optical Modulex H500) fitted with a UV-35 filter (effective $\lambda > 330$ nm). As the photocyclization is not reversible at the employed wavelengths, a fixed irradiation period of 2 h was employed throughout the work; indeed, a shorter irradiation for 30 min gave practically the same product distribution in dichloromethane at −40 °C. The range of irradiation temperature was set as wide as possible unless **AC** precipitates. After irradiation, the solvent was evaporated and the residue was dissolved in 4 mL of a 1:1 water–acetonitrile mixture, 20 μL of which was subjected to the HPLC analysis on a tandem column of ODS-L (Chemicals Evaluation and Research Institute) and Chiralcel OJ-R (Daicel) eluted with a 6:4 mixture of water and acetonitrile containing 0.1% trifluoroacetic acid. The conversion of **AC** and the product distribution were determined from the integrated area of the relevant peak monitored at 254 nm with an assumption that stereoisomeric cyclodimers **1**–**4** possess the identical extinction coefficients at the detection wavelength. The results thus obtained are shown in Table 1, along with that obtained in an aqueous buffer solution at pH 7.[15]



Scheme 1. Stereoisomeric photocyclodimers **1**–**4** produced upon irradiation of 2-antharacenecarboxylic acid in solution.

Upon irradiation at 20 °C, cyclodimers **1**–**4** were formed in comparable yields in all organic solvents examined. In particular, the four isomers are almost equally produced in less polar toluene and dichloromethane. The result obtained in an aqueous solution exhibits a clearer preference for the HT dimer, probably due to the electrostatic repulsion of **AC**'s carboxylate anions in HH dimers. By lowering the irradiation temperature, the photocyclodimerization became more stereoselective, as might be anticipated. However, the changing profile differs completely in each solvent, critically depending on the solvent properties. In less-polar dichloromethane, *anti*-HH cyclodimer **3** becomes the major product and its relative yield reaches 52% at −50 °C. Although the low solubility of **AC** in toluene did not allow us to examine the photoreaction at lower temperatures,

Table 1. Photocyclodimerization of 2-anthracenecarboxylic acid (**AC**) in various solvents at different temperatures[a]

Solvent	Temp.	Conv.	Product distribution/%				Product ratio		
	/°C	/%	**1**	**2**	**3**	**4**	HT/HH	**1/2**	**3/4**
Toluene[b]	60	98	33	27	22	18	1.5	1.2	1.2
	20	92	24	28	24	24	1.1	0.9	1.0
CH_2Cl_2	20	96	32	22	25	21	1.2	1.5	1.2
	−20	86	33	18	32	17	1.0	1.8	1.9
	−40	70	23	15	47	15	0.6	1.5	3.1
	−50	70	23	12	<u>52</u>	13	0.5	1.9	4.0
CH_3CN	20	89	35	25	21	19	1.5	1.4	1.1
	−40	74	41	19	27	13	1.5	2.2	2.1
CH_3OH	20	90	41	25	21	13	1.9	1.6	1.6
	−50	26	<u>51</u>	15	28	6	1.9	3.4	4.7
	−85	8	48	11	35	6	1.4	4.4	5.8
H_2O[c]	25	75	42	37	12	9	3.8	1.1	1.3

[a][**AC**] = 0.25 mM; irradiated for 2 h at $\lambda > 330$ nm under Ar, unless noted otherwise. [b]Low solubility of **AC** did not allow irradiation at lower temperatures. [c]Ref. 15; [**AC**] = 0.06 mM; irradiated for 40 min in an aqueous buffer solution at pH 7.0; note that the reacting species is not neutral anthracenecarboxylic acid but anionic carboxylate.

the irradiation of **AC** in toluene at 60 °C exhibited the same trend, affording a larger amount of the HH dimers, particularly **1**. In contrast, *anti*-HT cyclodimer **1** is favored in polar protic methanol to afford 51% yield at −50 °C, and polar aprotic acetonitrile exhibits a similar, but less pronounced, tendency. It is thus revealed for the first time that the major photoproduct is switched from **3** to **1** at low temperatures simply by increasing the solvent polarity.

Such contrasting behavior clearly indicates that distinctly different precursor species or transition states are involved in the photocyclodimerization of **AC** in dichloromethane and in methanol at low temperatures. The predominant formation of HT cyclodimers **1** and **2** (in 66% combined yield), particularly **1** (in 51%), upon irradiation in low-temperature methanol is quite reasonable in view of the steric hindrance and the dipole–dipole interactions. However, the selectivity inversion to HH cyclodimers **3** and **4** (65% yield), particularly to **3** (52% yield), observed in dichloromethane at −50 °C needs further rationalization, since the precursors to these cyclodimers should be in a *head-to-head* or similar orientation and are obviously disfavored both sterically and electrostatically.

However, the above discussion is exclusively based on the considerations about the association of monomeric **AC** molecule, which may not be the case in less-polar solvents. We suspected possible intervention of a hydrogen-bonded dimer of **AC** in the ground state, despite the fairly low **AC** concentration employed (0.25 mM). We first examined the fluorescence spectral behavior of **AC** at 0.025–1.0 mM in dichloromethane to observe only slight peak-broadening at higher concentrations and fluorescence intensities proportional to the **AC** concentration (Supporting Information). These results reveal that the fluorescence is not very sensitive to the hydrogen-bonded dimer formation in the present case.

^{1}H NMR spectral examinations (Bruker Avance-400) were conducted at 25 °C with a series of CD_2Cl_2 solutions of **AC** at 0.05–1.0 mM to give the variable chemical shifts shown in Figure 1. Moderate downfield shifts of 0.01–0.02 ppm were induced in particular for H1 and H3 protons of **AC** in the concentration range employed, indicating the intervention of hydrogen-bonded dimer even at room temperature. It is likely that the hydrogen-bonded dimer becomes dominant at lower temperatures.

Crucially, the inherent dipole of **AC** is cancelled in the hydrogen-bonded dimer, and hence the *head-to-head* orientation is favored due to better π–π interactions than the *head-to-tail* one, thus leading to the enhanced formation of **3** and **4** (although the latter is less favored for the steric reasons) at the expense of **1** and **2**, as actually observed upon irradiation in dichloromethane at low temperatures. We now understand why cyclodimers **1**–**4** are less selectively produced in toluene and dichloromethane, and also in acetonitrile and methanol, at 20 °C, where **AC** is almost completely monomeric even in the less-polar solvents and the transition states to all cyclodimers are readily accessible at this temperature. However, as the temperature decreases, the precursors to more-hindered *syn*-cyclodimers **2** and **4** gradually get less accessible relative to those to *anti*-cyclodimers **1** and **3**.

We have shown that the stereochemistry of one of the most representative photocyclodimerizations can be vitally controlled by solvent and temperature. The stereoselectivity of [4 + 4] photocyclodimerization of **AC** was switched from the most stable *anti*-HT to the less-favored *anti*-HH by changing the solvent from methanol to dichloromethane at low temperatures. This was made possible through the critical control of the steric, hydrogen bonding, stacking, and dipole–dipole interactions in the precursor **AC** species by the environmental factors. We believe that this strategy is potentially applicable to a wide variety of photoaddition/cyclization/dimerization reactions, and further studies along this line are currently in progress.

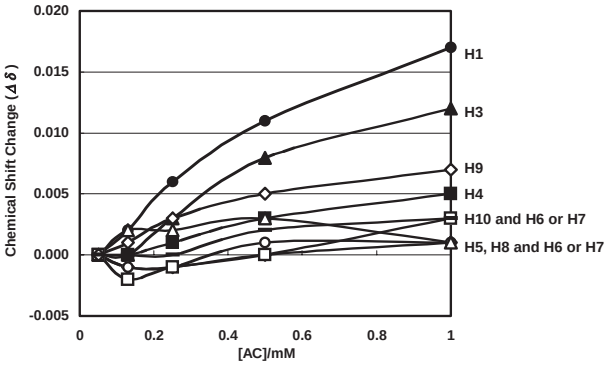


Figure 1. Concentration dependence of the chemical shifts of **AC** protons in CD_2Cl_2 at 25 °C.

References and Notes

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Published on the web (Advance View) June 3, 2006; doi:10.1246/cl.2006.738