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Enantioselective Photoreaction Occurring in a Chiral Bimolecular Crystal Formed from Acridine and *R*-(–)- or *S*-(+)-2-Phenylpropionic Acid

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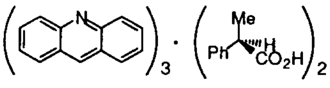
Abstract: Irradiation of a chiral bimolecular crystal formed from acridine and *R*-(–)- or *S*-(+)-2-phenylpropionic acid caused photodecarboxylation followed by stereoselective condensation to give three optically active products. The radical coupling paths in the crystal lattice are discussed. © 1997 Elsevier Science Ltd.

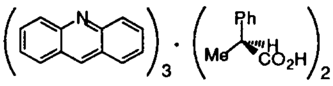
A chiral bimolecular crystal can cause stereoselective bimolecular reaction.[1] Because the initial enantiomeric molecular arrangement in the crystal lattice is retained even during a radical involving reaction due to the small thermal motion of molecules, leading to the formation of chiral products. In an ultimate case utilizing a chiral bimolecular crystal constructed from achiral compounds, absolute asymmetric synthesis can be achieved, although such successful examples are scarecely reported.[2-4] At the present time, however, it is difficult to predict whether or not a chiral bimolecular crystal can be obtained from achiral molecules. A methodology for overcoming the difficulty is to prepare a chiral bimolecular crystal by combining a chiral compound with a second achiral component. We already reported such an example of the preparation of a chiral CT crystal using 1,2,4,5-tetracyanobenzene and *S*-(+)-2-(6-methoxy-2-naphthyl)propanoic acid and the stereoselective condensation retaining the initial chirality in some extent.[1] Although numbers of chiral inclusion complexes[5] using chiral host compounds such as chiral tartaric acid derivatives and chiral salts[6] combined with unreactive chiral auxiliary such as chiral amines or chiral acids were already reported, the reaction types were limited in unimolecular reactions. Here we prepared enantiomorphous bimolecular crystals **1R** and **1S** combined with acridine (**1**) and *R*-(–)-2-phenylpropionic acid (**R**), and **1** and *S*-(+)-2-phenylpropionic acid (**S**) and examined the photoreactivities.

Chiral **1R**



1 **R**

Chiral **1S**



1 **S**

The chiral bimolecular crystal **1R** was prepared by spontaneous crystallization from a 3:2 solution of **1** and **R** in ethanol.[7] The melting point of **1R** is 73 °C, which is between those of **1** (179 °C) and **R** (29 °C). The crystal **1R** was also formed by only grinding together a 3:2 mixture of **1** and **R** without the solvent in a mortal for a few tens minutes. Under the grinding conditions, the **R** component was liquid at room temperature before **1R** crystallized. The **1R** crystals thus obtained was identified by the coincidence with the melting point, IR spectrum and powder X-ray diffraction pattern of **1R** which was prepared by crystallization from the ethanol solution. The opposite handed crystal **1S** was similarly obtained by the both methods of recrystallization from the solution and grinding of **1** and **S**. Here **R** and **S** seem to play a role as a kind of solvent in the formation of the bimolecular crystals.

The 3:2 crystal **1R** was found to be chiral with the space group $P2_1$ by X-ray structure analysis (Figure 1).[8] It is very natural due to the coexistence of the chiral component **R** in the crystal. The absolute configuration of

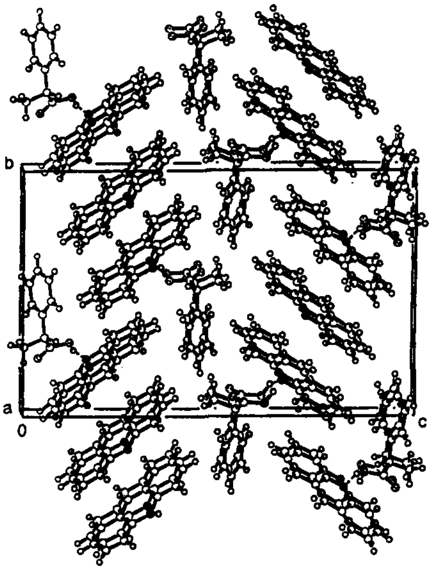
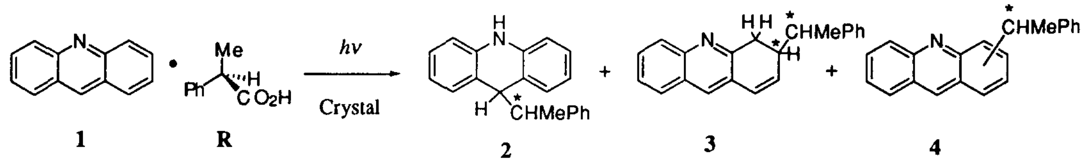
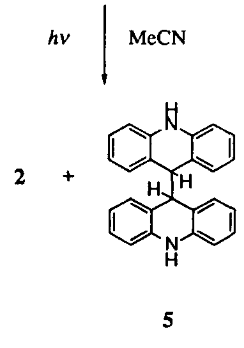


Figure 1. Packing diagram of the crystal **1R** along *a* axis. Black and dotted atoms present N and O atoms, respectively.





	Conv. (%)		Yield (%), $[\alpha]_D^{20}$			
	1	R or S	2	3	4	5
Crystal **1R**	35	64	16 [+2.0]	12 [+3.8]	5 [+47.8]	-
Crystal **1S**	44	87	19 [−1.5]	17 [−2.2]	4 [−45.4]	-
1+**R** (1:1) in MeCN	94	89	56 [0]	-	-	20

Scheme 1

1R was confirmed by the internal reference of **R**. Two kinds of hydrogen bonding pairs of **1** and **R** are formed with the N•••OH distances of 1.57 Å and 1.89 Å and with the dihedral angles of acridine plane and carboxyl plane of 4.81° and 13.79°, and a remaining acridine molecule does not form hydrogen bond. In a unit cell (Z = 2), the four hydrogen bonding pairs and the two acridine molecules are packed and further stacking forms a column structure along *a* axis.

The pulverized crystal of **1R** (2.00 g) was placed between Pyrex glass plates and irradiated with a 400 W high-pressure mercury lamp under argon for 3 h at 15 ℃. The irradiated mixture was submitted to TLC (silica gel, 40:1 benzene-ethyl acetate) followed by preparative HPLC (C_{18} column, methanol-water) to give three products **2**[9], **3**[10] and **4**[11] shown in Scheme 1. The $[\alpha]_D^{20}$ values of **2**, **3** and **4** obtained were +2.0 (c=2.0, ethyl acetate), +3.8 (c=0.32) and +47.8 (c=0.34), respectively, which implies the the chirality of **R** is transferred to **2**, **3** and **4**. The opposite handed crystal **1S** also caused the similar photodecarboxylative condensation to give the three products **2**, **3** and **4** with minus $[\alpha]_D^{20}$ values (Scheme 1). The e.e. determination for the formation of optically actvive **2**, **3** and **4** using a chiral HPLC column was not successfully done.

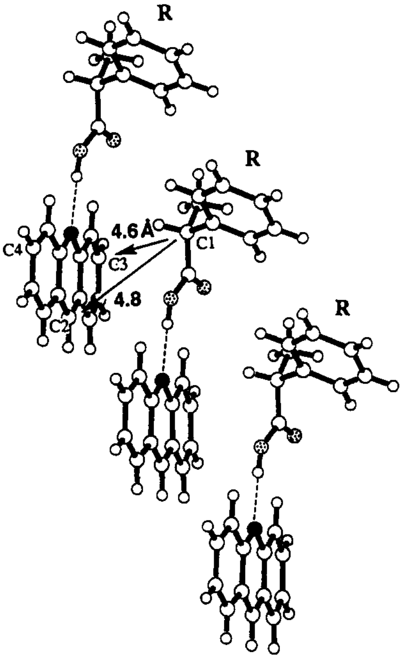


Figure 2. Radical coupling path in the crystal **1R**. Black and dotted atoms present N and O atoms, respectively.

Upon irradiating **1R**, electron transfer, proton transfer and then decarboxylation occur to give •CHMePh radical and hydroacridine radical species. Next C1---C2 radical coupling is caused in highest priority due to the short distance of 4.8 Å and the highest charge density[4] on the hydroacridine radical, while the original configuration of •CHMePh is retained due to the restricted motion in the crystal lattice to lead to the formation of the optically active **2** (Figure 2). The C1---C3 front attack by the active •CHMePh radical with the distance of 4.6 Å should introduce another asymmetric carbon at the coupling position in **3**; the condensation product **3** can be diastereomeric. The C1---C4 coupling with the distance of 6.1 Å gives other diastereomer **3** in less priority. The reason why **1 S** gave the minus $[\alpha]_D^{20}$ values can be similarly explained.

On the other hand, photolysis in the solution phase of **1** and **R** resulted in the formation of the optically inactive **2** and biacridane (**5**) (Scheme 1),[12] which suggests that the original •CHMePh radical species caused racemization due to the higher mobility in the solution before coupling with the hydroacridine radical between C1 and C2.

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7. Chiral crystal **1R**: light yellow rod; mp 73-75 °C (from EtOH); IR (KBr) 2487 (H-bonding, broad), 1879 (H-bonding, broad), 1710 cm^{-1} (C=O). Anal. calcd for $C_{57}H_{47}N_3O_4$ (3:2): C, 81.67; H, 5.90; N, 4.81%. Found: C, 81.70; H, 5.65; N, 5.01%.
8. Crystal data of chiral crystal **1R**: M =838.02; 0.30 x 0.10 x 0.30 mm; monoclinic; space group $P2_1$; a =5.808(4), b =15.617(4), c = 24.671(3) Å, β = 91.47(3)°; V = 2237(1) $Å^3$; Z = 2; D_c = 1.244 g cm^{-3}; GOF 1.45. The structure was solved by direct method (SIR88) and refined by the full-matrix least-squares procedure to R = 0.050 and R_w = 0.075 for 2476 independent observed reflections [$F_o > 3\sigma(F_o)$] of total 4518 reflections with 2θ < 50.0°.
9. Selected data for **2**: mp 140-142 °C (MeCN); IR (KBr) 3374 cm^{-1} (NH); ^{1}H NMR ($CDCl_3$) δ 6.56-7.19 (m, 13H), 5.87 (broad s, 1H), 4.05 (d, J=7.0 Hz, 1H), 2.95 (quintet, J=7.0 Hz, 1H), 1.12 (d, J=7.0 Hz, 3H); UV λ_{max} (MeCN) 356 (log ε 2.39), 282 (3.14), 249 nm (2.80). Anal. calcd for $C_{21}H_{19}N$: C, 88.37; H, 6.72; N, 4.91%. Found: C, 88.46; H, 6.97; N, 4.92%. $[\alpha]_D^{20}$ +2.5 (c=2.0, ethyl acetate).
10. Selected data for **3**: mp 101-106 °C (MeCN); IR (KBr) no NH; ^{1}H NMR ($CDCl_3$) δ 7.19-8.26 (m, 12H), 6.52 (broad t, J=7.0 Hz, 1H), 6.17 (dd, J=7.0, 1.5 Hz, 1H), 5.83 (dd, J=7.0, 1.5 Hz, 1H), 4.11 (quintet, J=7.0 Hz, 1H), 1.29 (d, J=7.0 Hz, 3H). Anal. calcd for $C_{21}H_{19}N$: C, 88.37; H, 6.72; N, 4.91%. Found: C, 88.13; H, 6.90; N, 5.23%. $[\alpha]_D^{20}$ +3.8 (c=0.32, ethyl acetate).
11. Selected data for **4**: not solidified; IR (neat) no NH; ^{1}H NMR ($CDCl_3$) δ 7.20-8.52 (m, 13H), 4.32 (q, J=7.0 Hz, 1H), 1.77 (d, 7.0 Hz, 3H). Anal. calcd for $C_{21}H_{17}N$: C, 89.00; H, 6.06; N, 4.94%. Found: C, 88.82; H, 6.32; N, 4.87%. $[\alpha]_D^{20}$ +47.8 (c=0.34, ethyl acetate).
12. Photolysis in solution phase. A solution of **1** (0.896 g, 5 mmol) and **R** (0.751 g, 5 mmol) in 100 ml of acetonitrile was internally irradiated with a 100 W high-pressure mercury lamp under argon bubbling for 3 h at room temperature. Filtration of the irradiated solution gave 0.177 g of biacridane **5** in 20% yield as a solid. The filtrate was submitted to preparative TLC (silica gel, 40:1 benzene-ethyl acetate) to give 0.801 g of **2** in 56% yield as a white crystal. The melting point and spectral data were consistent with those in ref. 9. $[\alpha]_D^{20}$ 0 (c=2.5, ethyl acetate). The recoveries of **1** and **R** were 6% and 11%, respectively.

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