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Generation of Chirality in a Two-Component Molecular Crystal of Acridine and Diphenylacetic Acid and Its Absolute Asymmetric Photodecarboxylating Condensation

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Abstract: Despite the fact that acridine (**1**) and diphenylacetic acid (**a**) are achiral compounds, a chiral two-component molecular crystal (**1·a**) in which two molecules are self-assembled in a 1:1 molar ratio by hydrogen bonding crystallizes spontaneously from an acetonitrile solution. The space group is $P2_12_12_1$, which is typical chiral space group. Both handed crystals (−)-**1·a** and (+)-**1·a** can be prepared as desired on a large scale by seeding. The two phenyl planes and the carboxyl plane of the diphenylacetic acid molecule in the crystal (−)-**1·a** have torsions in the same direction as the blades of a propeller. The oppositely handed crystal (+)-**1·a** has minus torsion angles. Irradiation of (−)-**1·a** or (+)-**1·a** caused stereospecific decarboxylating condensation to give an excess of the chiral compound {(−)-**3**} or {(+)-**3**} in about 35% ee, respectively, as the main product. The absolute configurations of the reactant (−)-**1·a** and the product (−)-**3** could be determined to be (*M*)-(−)-**1·a** and (*S*)-(−)-**3** by the Bijvoet method based on anomalous dispersion of an oxygen atom of (−)-**1·a** and a sulfur atom of the trifluoromethanesulfonate salt of methylated (−)-**3** during X-ray crystallographic analysis. Upon irradiating (*M*)-(−)-**1·a**, the diphenylmethyl radical and the hydroacridine radical are produced via electron transfer from **a** to **1** and subsequent proton transfer followed by decarboxylation. The next radical coupling occurs with the shortest distance of 5.1 Å between the two preradical carbon atoms in the crystal lattice to afford (*S*)-(−)-**3** as the major enantiomer. On the other hand (*R*)-(+)-**3** can be produced as the minor enantiomer by coupling over a longer distance of 6.8 Å, resulting in a ca. 2:1 of S:R ratio, i.e., about 35% ee. The radical coupling is necessarily accompanied by a slight movement of the radical species in the crystal lattice, in contrast to the well-known topochemical [2+2] photocycloaddition.

Introduction

Optically active molecules necessarily form chiral crystals.[1] However, even if a molecule is not chiral, a chiral conformation such as may be caused by molecular torsion, can induce crystallization into a chiral crystal structure. For instance, a crystal of benzophenone is chiral (space group $P2_12_12_1$) by virtue of the propeller-like arrangement of the phenyl rings.[2] Such crystals can be distinguished by knowing whether the space group is chiral or not. A large number of chiral one-component crystals that are composed of achiral organic compounds are already known and compiled in the JCPDS crystal data series and the Cambridge Crystallographic Data Centre. Statistically, the most frequent chiral space groups are $P2_12_12_1$ and $P2_1$ of 65 chiral space groups, which are included in 230 possible space groups. However, chiral “two-component molecular crystals”[3] composed of two achiral compounds are scarcely known until now except for certain types of charge-transfer complexes.[4] In the course of our study of the photochemistry of two-component molecular crystals,[5−9] we found that a chiral two-component molecular crystal (**1·a**) spontaneously crystallizes from a solution of acridine (**1**) and diphenylacetic acid (**a**) in acetonitrile. Further we succeeded in carrying out an absolute asymmetric synthesis by the solid-state photoreaction of chiral **1·a**.

Thus, chiral crystals composed of optically inactive molecules can be useful as the reactants for absolute asymmetric syntheses, because the chiral environment in the crystal lattice can cause a stereospecific reaction due to the low mobility of molecules in the crystalline state. In fact, since the first successful absolute asymmetric [2+2] photocycloaddition in the solid state by Elgavi et al.,[10] more than 10 absolute asymmetric photochemical syntheses have been achieved.[11] However, most of these were unimolecular (intramolecular) reactions caused in one-component crystals such as the di-π-methane photorearrangement of dibenzobarrelenes and the Norrish type II photorearrangement by Scheffer et al.,[12−15] the Norrish type II photocyclization of

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(3) The term “two-component molecular crystal” used in this paper defines a crystal in which two different organic compounds form a molecular compound through intermolecular forces.

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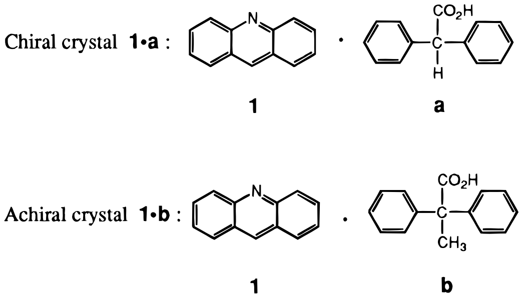
oxoamides to β-lactams by Toda et al.,[16−18] and the [2+2] photocyclization of imides and thioamides by Sakamoto et al.[19,20] Bimolecular (intermolecular) examples are limited to [2+2] photocycloadditions in one-component crystals[21,22] and two-component molecular crystals.[10] Recent excellent work by Suzuki et al. also involves the [2+2] photocycloaddition of a chiral crystalline charge-transfer complex of bis[1,2,5]thiadiazolotetracyanoquinodimethane and *o*-divinylbenzene via a single crystal-to-single crystal transformation.[23]

Unimolecular reactions for solid-state asymmetric synthesis have the advantage of not requiring specific crystal packing arrangements. However, as our study showed,[5] bimolecular reactions of two-component molecular crystals can in principle lead to a greater variety of reaction types such as addition[6] and decarboxylation[7−9] than in the case of unimolecular reactions.[11,24,25] For example, even if a simple compound is not photosensitive, the formation of a two-component molecular crystal in which a second component is combined as a sensitizer can induce photoreactivity by electron-transfer sensitization.[7] We report in this paper that crystal chirality is generated in a two-component molecular crystal **1·a** and that an absolute asymmetric synthesis can be achieved by a solid-state photodecarboxylating condensation. In addition, the reaction stereochemistry could be mapped out by determining the absolute configurations of the reactant and product and correlating them with a given crystal reaction.

Results and Discussion

Generation of Chirality. A 1:1 chiral two-component molecular crystal **1·a** of acridine **1** and diphenylacetic acid **a** could be prepared by slow evaporation of an equimolar solution of **1** and **a** in acetonitrile at room temperature (Scheme 1). The crystal exists as light-yellow rods, and the melting point is 101 °C, which is lower than the melting points of the components **1** (107 °C) and **a** (148 °C). There exist both enantiomorphous crystals (−)-**1·a** and (+)-**1·a**. The single crystals that gave enantiomeric excesses of (−)-**3** and (+)-**3** were named (−)-**1·a** and (+)-**1·a**, respectively. By seeding we could easily obtain crystals with the same chirality as the seed crystal.

Scheme 1



A single crystal of (−)-**1·a** (ca 3 mg), prepared by seeding, was cut into two pieces. One piece was pulverized and irradiated with a xenon lamp through a UV transparent filter under argon for 1 h at −30 °C. The photoproduct consisted of an excess of (−)-**3** in 33% ee by HPLC analysis with a chiral column. The second piece was submitted to X-ray crystallographic analysis. The crystal is orthorhombic and belongs to the chiral space group $P2_12_12_1$ (Table 1). The absolute configuration could be determined with a fairly high degree of certainty by the Bijvoet method based on anomalous dispersion of the oxygen atom with Cu Kα radiation.[26] The details are described in the Experimental Section. Figure 1 shows the molecular packing in (−)-**1·a** for the correct absolute configuration. The molecular pair of **1** and **a** is connected through O−H···N hydrogen bonding with an H···N distance of 1.92 Å and an O−H···N angle of 148° (Figure 2A). The angle between the acridine plane and the carboxyl plane of the molecular pair is 35.5°. The two phenyl planes and the carboxyl plane of the diphenylacetic acid molecule in the crystal (−)-**1·a** have torsions in the same direction as the blades of a propeller. The three torsion angles of (−)-**1·a** are positive as listed in Table 2. All four molecular pairs present in the unit cell have the same absolute configuration (Figure 1). If the diphenylacetic acid molecule is compared to three blades of a propeller, a helix generates around the H1−C1 bond in a counterclockwise direction. That is, the helicity around H1−C1 bond is minus (Figure 2A).[27] Therefore the crystal (−)-**1·a** should be designated as (*M*)-(−)-**1·a**. The oppositely handed crystal (+)-**1·a** has minus torsion angles (Table 2) and the helicity is plus (Figure 2B). The molecular pairs (*M*)-(−)-**1·a** and (*P*)-(+)-**1·a** have a mirror image relationship (Figure 2A,B).

On the other hand, the crystal (**a**) of diphenylacetic acid alone is achiral (Table 1, space group $P2_1/n$). Because the antipodal molecules of diphenylacetic acid form a dimer through the hydrogen bonding O−H···O with the distance H···O of 1.73 Å (Figure 2C), the positive and negative torsion angles exist together in the dimer (Table 2). Therefore, the chiralities of the two molecules in the crystal **a** is compensated and does not appear. Preparation of the chiral crystal **1·a** from an equimolar solution of **1** and **a** by seeding followed by evaporating the solvent completely resulted in the crystals with the same absolute configuration as the seed crystal in a nearly quantitative yield. This was deduced from the ee values (35−39%) of the photoproduct (**3**) obtained from the whole pulverized crystals in the vessel, which were consistent with those from the single crystals in Table 3. This indicates that the phenyl and carboxyl groups of molecule **a** are sufficiently mobile in solution to allow M to P inversion, despite the fact that such motions are difficult to accomplish with space filling molecular models.

We tried to find additional chiral two-component molecular crystals based on similar propeller-shaped molecules. 2,2-

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Table 1. X-ray Crystallographic Data for Molecular Crystals and Products

	a	(−)-**1·a**	{(−)-**3**}$_2$·MeOH	(−)-**7**	**1·b**
formula	$C_{14}H_{12}O_2$	$C_{27}H_{21}NO_2$	$C_{53}H_{46}N_2O$	$C_{28}H_{24}NO_3SF_3$	$C_{28}H_{23}NO_2$
f_w	212.25	391.47	726.96	511.56	405.50
space group	$P2_1/n$	$P2_12_12_1$	$P1$	$P2_1$	$P2_1/n$
Z	4	4	1	4	4
cell constants					
a, Å	12.254(4)	14.908(4)	9.871(1)	13.363(5)	12.717(6)
b, Å	7.226(3)	25.367(6)	17.6408(9)	10.277(4)	13.061(9)
c, Å	12.737(2)	5.457(3)	6.1787(9)	18.792(4)	13.542(5)
α, deg	90.00	90.00	90.280(7)	90.00	90.00
β, deg	90.99(2)	90.00	107.31(1)	107.42(2)	105.57(3)
γ, deg	90.00	90.00	101.002(6)	90.00	90.00
V, Å^3	1127.6(6)	2063(1)	1006.1(2)	2462(1)	2166(2)
D_{calcd}, g cm^{-3}	1.250	1.260	1.200	1.380	1.243
μ, cm^{-1}	0.83	6.25	0.70	16.38	0.78
radiation	Mo Kα	Cu Kα	Mo Kα	Cu Kα	Mo Kα
$2\theta_{max}$, deg	50.0	110.0	50.0	120.0	50.0
scan mode	$\omega-2\theta$	$\omega-2\theta$	$\omega-2\theta$	$\omega-2\theta$	$\omega-2\theta$
no. of reflns measd	2273	10378	3771	10456	4187
no. of unique reflns	2168	1570	3548	3901	4000
no. of $I > 3.00\sigma(I)$	1418	1501	3161	3445	1852
no. of variables	149	275	687	673	290
R, %	3.6	4.3	3.3	6.5	5.2
R$_w$, %	5.7	5.8	5.0	10.2	6.7

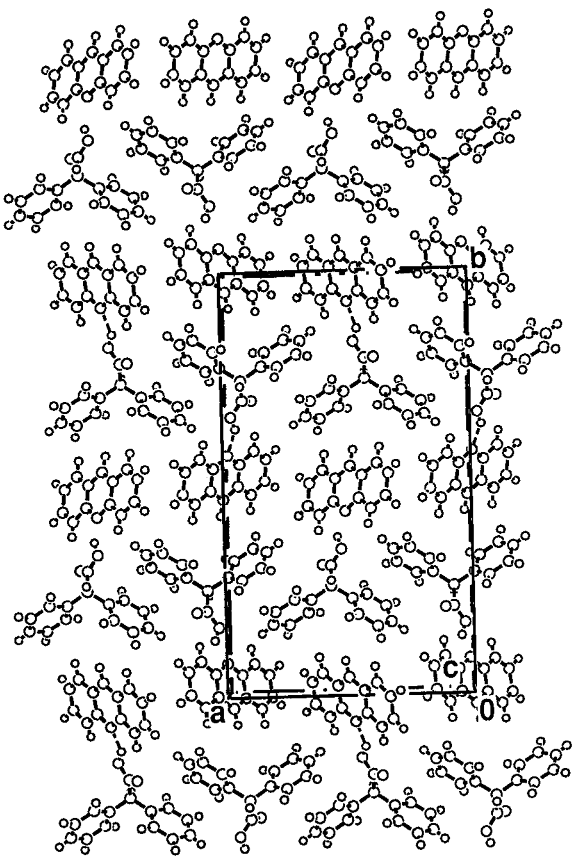

Figure 1. Molecular packing in the unit cell of the chiral crystal (−)-**1·a** of acridine (**1**) and diphenylacetic acid (**a**).

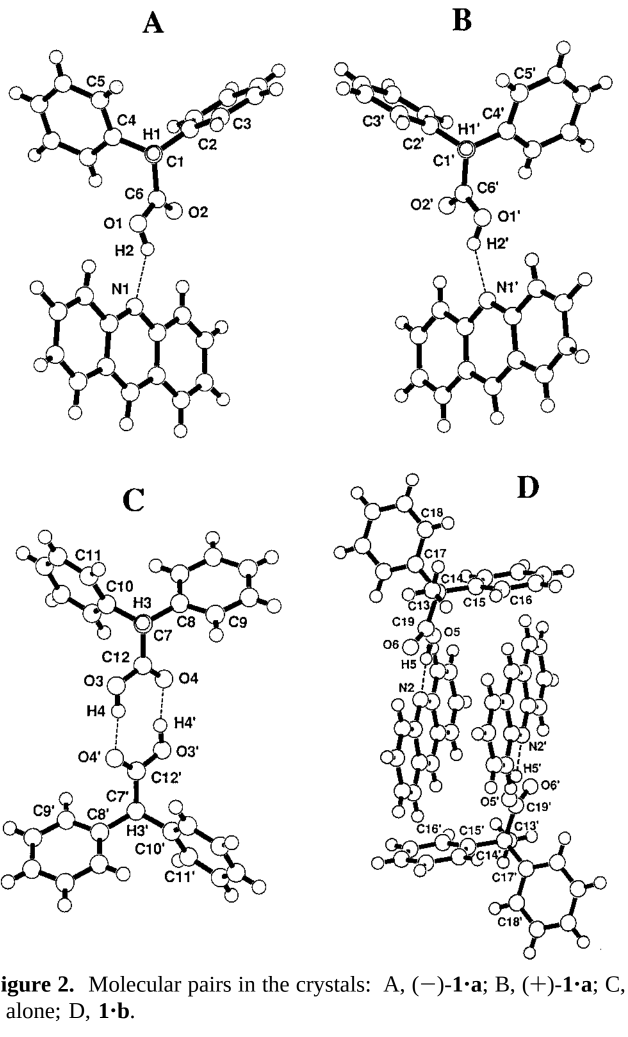

Figure 2. Molecular pairs in the crystals: A, (−)-**1·a**; B, (+)-**1·a**; C, **a** alone; D, **1·b**.

Diphenylpropionic acid (**b**), which is a methyl-substituted derivative of **a**, was selected (Scheme 1). A two-component molecular crystal (**1·b**) could be prepared by slow evaporation of an equimolar solution of **1** and **b** in ethanol. The 1:1 crystal is yellow and the melting point is 139 °C, which is between that of **1** (107 °C) and **b** (178 °C). However, the crystal was not chiral (achiral space group $P2_1/n$) as shown in Table 1. The molecular arrangement in the unit cell has a center of symmetry as illustrated in Figure 3. The molecular pair of **1** and **b** is connected through O−H···N hydrogen bonding with an H···N distance of 1.83 Å and an O−H···N angle of 157° (Figure 2D). Enantiomeric molecular pairs with plus and minus torsion angles in **b** compensate the chirality in the crystal **1·b** (Table 2).

Why does **1·b** not share the same chiral crystallization of **1·a**? Figure 4 shows the stacking arrangements of two molecular pairs in the crystals (−)-**1·a** and **1·b**. The molecular pairs of **1** and **a** in the crystal (−)-**1·a** (A) stack in a head-to-

Table 2. Torsion Angles in the Crystals

	torsion angle (deg)
	(−)-**1·a**
H1−C1−C2−C3	13.0
H1−C1−C4−C5	50.3
H1−C1−C6−O1	33.9
	(+)-**1·a**
H1′−C1′−C2′−C3′	−13.0
H1′−C1′−C4′−C5′	−50.3
H1′−C1′−C6′−O1′	−33.9
	a
H3−C7−C8−C9	52.8
H3−C7−C10−C11	27.3
H3−C7−C12−O3	48.2
H3′−C7′−C8′−C9′	−52.8
H3′−C7′−C12′−C11′	−27.3
H3′−C7′−C12′−O3′	−48.2
	1·b
C13−C14−C15−C16	17.0
C13−C14−C17−C18	74.9
C13−C14−C19−O6	11.8
C13′−C14′−C15′−C16′	−17.0
C13′−C14′−C17′−C18′	−74.9
C13′−C14′−C19′−O6′	−11.8

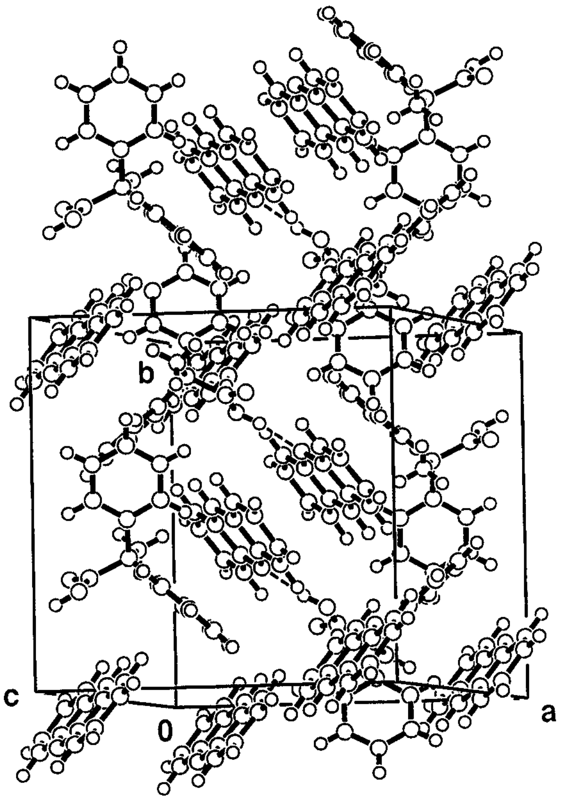

Figure 3. Molecular packing in the achiral crystal **1·b** of acridine (**1**) and 2,2-diphenylpropionic acid (**b**).

head fashion with a distance of 5.46 Å along the *c* axis, while two molecular pairs of **1** and **b** stack in a head-to-tail arrangement with a center of symmetry. The reason that **1·b** (B) cannot be arranged in a head-to-head stacking along an axis as in (−)-**1·a** is most probably due to the steric hindrance of the bulky methyl group (van der Waals radius 1.8 Å) of the molecule **b**.

Absolute Asymmetric Decarboxylating Condensation. Crystals of (−)-**1·a** prepared by seeding were pulverized and irradiated with a 400 W high-pressure mercury lamp through Pyrex glass (>290 nm transparent) under argon for 3 h at 15 °C on a preparative scale. Solid-state photodecarboxylation occurred to give three products (Scheme 2). The main product was a chiral condensation compound (**3**) with $[\alpha]^{20}_{D}$ −30 (from MeCN, *c* 0.2, ethyl acetate) and a melting point of 155 °C (from MeCN) in 35% ee and in 37% chemical yield. Minor products were the achiral condensation product (**4**) and diphenylmethane (**5**). Irradiation of the enantiomorphous crystals (+)-**1·a** resulted in the formation of **3** with $[\alpha]^{20}_{D}$ +30 (*c* 0.2, ethyl acetate) and a melting point of 150 °C (from MeCN) in 33% ee and in 38% yield. In contrast to the solid-state photoreaction, irradiation of a solution of **1** and **a** in acetonitrile did not produce **3** but gave instead the achiral condensation product **4** and 1,1,2,2-tetraphenylethane (**6**) in 74% and 24% yield, respectively, at complete conversion of **a** (Scheme 2).

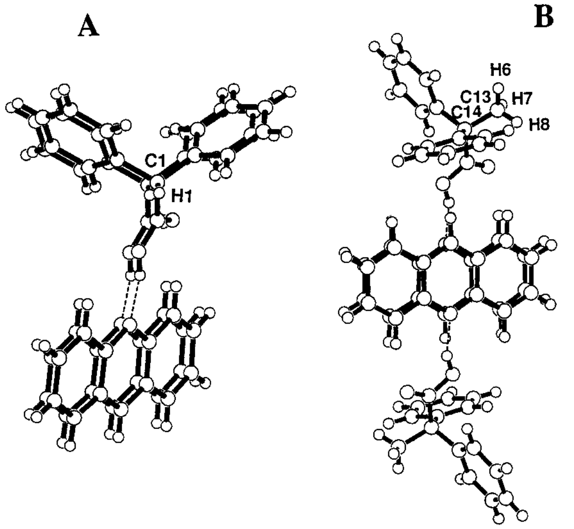

Figure 4. Molecular pair stackings in the crystals: A, (−)-**1·a**; B, **1·b**.

Table 3 summarizes the influence of irradiation time, temperature, and wavelength on the solid-state photoreaction, examined by using single crystals (2−3 mg) of (−)-**1·a** and (+)-**1·a** followed by HPLC analysis. The irradiation of (−)-**1·a** at 10 °C for 1 h gave (−)-**3** in 36% ee and in 50% yield at the conversions of 28% and 45% of **1** and **a**, respectively. The photoreactivity was retained even at −70 °C with an accompanying slight decrease of the reaction rate and the yield of **3**. However, the ee value was not changed; almost constant values of 33−39% ee were obtained for photolyses in the temperature range 10 to −70 °C. This result is different from those of the several reports,[19,20,23] in which absolute asymmetric [2+2] photocycloaddition at lower temperature led to higher ee values due to a decrease of the thermal motion in the crystals. Prolonged irradiation for 5 h led to high conversion of **1** and **a** (52% and 71%, respectively) and to a low yield of **3** due to partial decomposition. However, even in this case the ee value was unchanged. In addition, the reaction could be brought about by irradiation using not only UV light (290−390 nm) but also visible light (>390 nm). The crystal **1·a** has an absorption band at wavelength 200−450 nm, which is almost the sum of those of the components **1** (200−450 nm) and **a** (200−300 nm). Therefore this reaction can be induced by the excitation of the acridine molecule **1** at >390 nm, and **1** acts as the excited species in the crystal **1·a** (Scheme 3).

Thus, the absolute asymmetric photodecarboxylating condensation of single crystals of (−)-**1·a** and (+)-**1·a** under various conditions gave **3** in the constant ee value of about 35%. As described above, this value coincides with the ee values of 33% and 35% obtained by the photoreaction on a preparative scale of crystals (−)-**1·a** and (+)-**1·a**, respectively, prepared by seeding. However, chiral crystals of **1·a** prepared without

Scheme 2

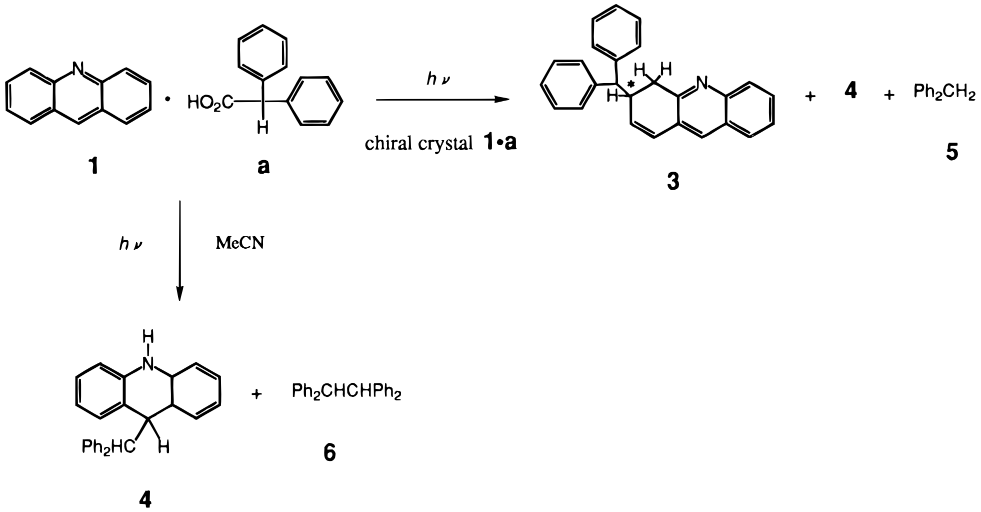

Table 3. Photoreaction of the Chiral Single Crystal **1·a**

	irradiation			conversion (%)		yield[a] (%)			ee (%)
crystal	°C	h	nm	**1**	**a**	**3**	**4**	**5**	**3**
(−)-**1·a**	10	1	290−390	28	45	50	2	11	(−) 36
(−)-**1·a**	−30	0.5	290−390	6	13	58	2	8	(−) 35
(−)-**1·a**	−30	1	290−390	22	31	48	4	9	(−) 33
(−)-**1·a**	−30	5	290−390	52	71	28	2	6	(−) 33
(−)-**1·a**	−30	1	>390	39	63	39	2	9	(−) 36
(−)-**1·a**	−70	1	290−390	12	23	34	2	4	(−) 39
(+)-**1·a**	−30	1	290−390	23	35	51	4	9	(+) 37
(+)-**1·a**	−30	1	>390	31	51	32	2	7	(+) 35

[a] Yield based on consumed **a**.

seeding afforded different ee values of 36%, 27%, 22% with minus optical rotations and 20%, 24%, 30% and 33% with plus rotations by irradiation in separate vessels. These results indicate that crystals of both absolute configuration (−)-**1·a** and (+)-**1·a** are deposited simultaneously from solution without seeding. Therefore, the seeding method is necessary to prepare crystals of a desired chirality.

Determination of the absolute configurations of the reactant and the product is most important to discuss the reaction path in the crystal lattice. The absolute configuration of (−)-**1·a** is already determined (Figures 1 and 2). The molecular structure of (−)-**3** could be determined by X-ray structure analysis of {(−)-**3**}$_2$·MeOH (Table 1). However, because oxygen is not sufficiently heavy for the determination of absolute configuration by anomalous dispersion, a sulfur atom was introduced by preparing the trifluoromethanesulfate salt {(−)-**7**} of methylated (−)-**3**, which did not affect the configuration of the asymmetric carbon.[28] The absolute configuration of (−)-**7** could be determined as (*S*) with a high degree of certainty by the Bijvoet method based on the anomalous dispersion ($\Delta f'' = 0.557$ for Cu Kα radiation) of sulfur (Figure 5). The details are described in the Experimental Section.

How does the stereospecific condensation reaction occur? Scheme 3 and Figure 5 show the possible reaction mechanism and the radical coupling path, respectively. Irradiation of the crystal excites **1** followed by electron transfer from **a** to **1** to give a cation radical (**8**) and an anion radical (**9**). Proton transfer can then afford diphenylacetate radical (**10**) and hydroacridine radical species (**11**−**14**). The charge densities on **9** by semiempirical PM3[29] in vacuum are localized in the order of N1 (−0.94), C20 and C27 (−0.44), C22, C25, C23 and C24 (−0.28) (for numbering, see Figure 5). On the other hand, the shorter distances between H2 and other atoms, estimated from the crystallographic data, are 1.94, 3.13, 2.94, and 3.31 Å of H2−N1, H2−C20, H2−C27, and H2−C28, respectively; other distances are longer than 4 Å. Both higher charge density and shorter distance are needed to the proton transfer in the crystal lattice, different from that in solution. Hydroacridine radical species **11** and **12**, which satisfy the both conditions, should be preferably produced with their higher stability. Next decarboxylation of **10** gives the diphenylmethyl radical (**15**). In the crystal lattice of (−)-**1a**, the molecular pairs of **1** and **a** stack along the *c* axis with a plane-to-plane distance of 5.46 Å to form a column structure as shown in Figure 5. Radical coupling between ·C1 of **15** and ·C29 of **12** over the shortest distance of 5.11 Å can occur with the highest priority to give (*S*)-(−)-**3** as the major enantiomer. Radical coupling of ·C1 and ·C26 over a distance of 6.52 Å also produces (*S*)-(−)-**3**. On the other hand, (*R*)-(+)-**3** is formed as a minor enantiomer by the radical coupling between ·C1 of **15** and ·C21 and ·C30 of **12** over the longer distances of 6.79 and 8.97 Å, respectively. The *S*:*R* ratio is calculated as ca. 2:1 based on the experimental ee value of ca. 35% ee. The radical coupling is necessarily accompanied by a slightly larger movement of the radical species in the crystal lattice, in contrast to the well-known topochemical [2+2] photocycloaddition, for which a distance of less than 4 Å distance is indispensable.[30]

The reason why **4** and other condensation products are scarcely produced in the solid-state photoreaction (Table 3) is most probably due to the steric hindrance of the bulky radical **15**, different from the solution reaction giving **4** in high yield. In addition, the formation of **5** and the regeneration of **1** are caused by hydrogen abstraction by the diphenylmethyl radical **15** from **11** because the ·C1−H2 distance (3.11 Å) between the radicals **15** and **11** is short enough to abstract the hydrogen H2.[7] The regeneration of **1** is the reason for the lower conversion of **1** than that of **a** (Table 3).

Conclusion

A chiral two-component molecular crystal composed of acridine and diphenylacetic acid, which are achiral molecules, could be prepared by a spontaneous crystallization from an acetonitrile solution. The two-component molecular crystal is

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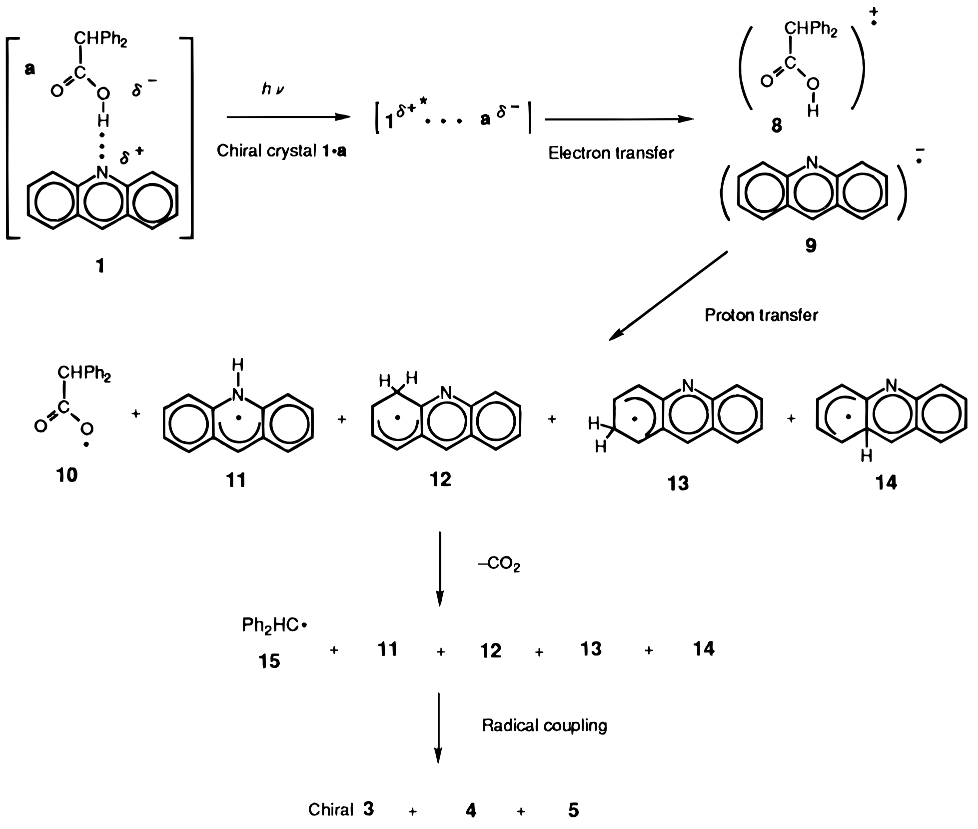
Scheme 3



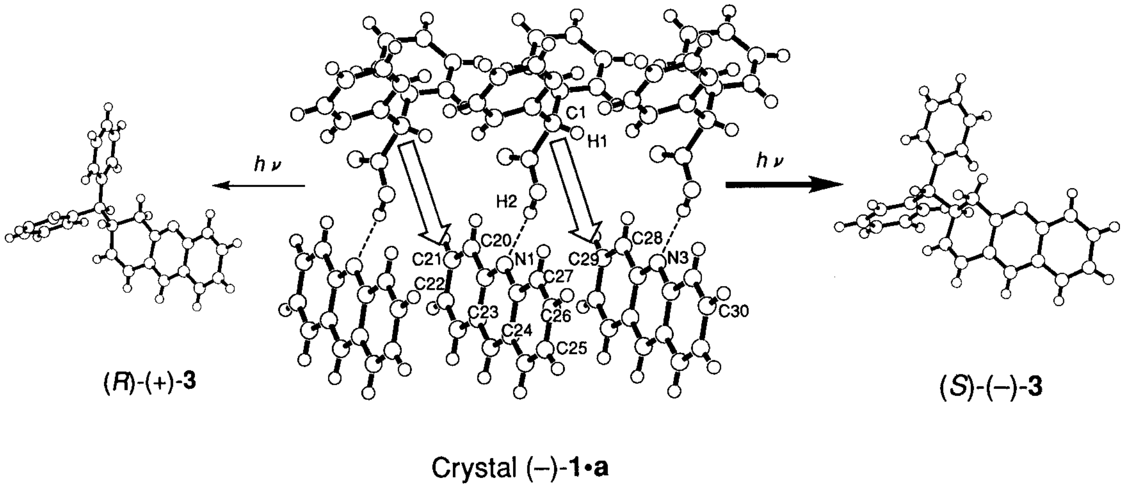


Figure 5. Radical coupling path in the crystal (−)-**1·a**.

photoreactive, and an absolute asymmetric synthesis was successfully achieved by a photodecarboxylating condensation. This work represents a new step in the chiral crystallization of achiral molecules in a two-component system and in solid-state absolute asymmetric synthesis by utilizing a bimolecular process.

Experimental Section

General Methods. ^{1}H NMR spectra were measured on a 60 MHz JEOL PMX-60 spectrometer with tetramethylsilane as an internal standard. IR spectra were recorded on a JASCO FT/IR-8300 spectrophotometer. UV spectra were measured on a Shimadzu UV-3100 and spectrophotometer. UV spectra in solid state were also taken on a Shimadzu MPS 2000 spectrophotometer by a reflection method. Differential scanning calorimetry (DSC) was done on a Rigaku Thermoflex TAS-200 DSC8230D, and melting points (mp) were not corrected. Elemental analysis was carried out with a Yanaco CHN Corder MT-5. HPLC with a photodiode-array detector was used for determining the products on a Waters HPLC system. All the reagents were commercially available.

Preparation of Two-Component Molecular Crystals (1·a and 1·b) of Acridine (1) and Acids (a and b). The chiral two-component molecular crystal **1·a** was prepared by slow evaporation of 1:1 solution of **1** and **a** in MeCN at room temperature. (−)- and (+)-**1·a** could be prepared by the seeding. The crystal **1·b** was prepared by evaporating the 1:1 solution of **1** and **b** in EtOH at room temperature.

(−)- or (+)-**1·a**: light yellow crystal; mp 100−102 °C; IR (KBr) 2490−3085, 1705 cm^{-1}; UV 190−450 nm. Anal. Calcd for $C_{27}H_{21}NO_2$ (1:1): C, 82.84; H, 5.42; N, 3.58. Found: C, 83.26; H, 5.64; N, 3.57.

1·b: dark yellow crystal; mp 138−140 °C; IR 2465−3100, 1700 cm^{-1}; UV 190−450 nm. Anal. Calcd for $C_{28}H_{23}NO_2$ (1:1): C, 82.93; H, 5.73; N, 3.45. Found: C, 83.00; H, 5.86; N, 3.36

Solid-State Photoreaction of Chiral Crystal 1·a. (−)-**1·a** (800 mg) in preparative scale prepared by seeding was pulverized, placed between two Pyrex plates, and irradiated with a 400 W high-pressure mercury lamp for 3 h under argon at room temperature. The irradiated mixture was submitted to preparative TLC (7:1 benzene−ethyl acetate) to give 260 mg of a chiral condensation product **3** in 37% yield and 15 mg of **4** in 2% yield. Pure enantiomers of **3** were separated by HPLC with a Daicel Chiralpak AD preparative column eluting with 2% 2-propanol in hexane. Next recrystallization of (−)-**3** and (+)-**3** from MeCN−MeOH gave the high quality crystals of {(−)-**3**}$_2$·MeOH and {(+)-**3**}$_2$·MeOH, respectively.

3: white crystal, mp 154−155 °C (from MeCN); $[\alpha]^{20}_{D}$ −30 (*c* 0.2, THF); 35% ee (HPLC equipped with a Daicel Chiralpak AD column, 2% 2-propanol in hexane as an eluant); IR (KBr) no NH band; ^{1}H NMR (THF-d_8) δ 6.90−7.90 (m, 15H), 6.50 (dd, *J* 9.0, 1.5 Hz, 1H), 5.83 (dd, *J* 9.0, 3.0 Hz, 1H), 2.80−4.00 (m, 2H); UV (MeCN) λ_{max} 224 (log ϵ 4.61), 254 (4.67), 283 (4.18), 327 (3.76), 343 (3.79) nm. Anal. Calcd for $C_{26}H_{21}N$: C, 89.88; H, 6.09; N, 4.03. Found: C, 90.22; H, 6.26; N, 3.92.

{(−)-**3**}$_2$·MeOH: white crystal, mp 135−137 °C (from MeOH−MeCN); $[\alpha]^{20}_{D}$ −121 (*c* 0.4, THF); optical purity 100%. Anal. Calcd for $C_{53}H_{46}N_2O$: C, 87.55; H, 6.39; N, 3.85. Found: C, 87.65; H, 6.15; N, 3.90.

{(+)-**3**}$_2$·MeOH: white crystal, mp 132−135 °C (from MeOH−MeCN); $[\alpha]^{20}_{D}$ +123 (*c* 0.2, THF); optical purity 100%.

HPLC Study of Solid-State Photoreaction. One single crystal (2−3 mg) was pulverized, placed between two Pyrex plates and irradiated with a 500 W xenon short arc lamp through a UV transparent filter (290−390 nm irradiation) or a UV cut filter (>390 nm irradiation) under argon at appropriate temperatures and times. In the cases of the crystals prepared by seeding or evaporation, 20 mg of powdered crystals was irradiated. The irradiated sample was methylated with CH_2N_2 followed by HPLC analysis (C_{18} column, methanol−water). The results are shown in Table 3.

Preparative Photoreaction of 1 with a in MeCN. A solution of **1** (895 mg, 5 mmol) and **a** (1060 mg, 5 mmol) in MeCN (100 mL) was internally irradiated with a 100 W high-pressure mercury lamp for 2 h under argon at room temperature. After the irradiation, a precipitated product **4** (1270 mg) was separated by filtration of the reaction mixture in 74% yield. The filtrate was submitted to preparative TLC (7:1 benzene−ethyl acetate) to give **6** (200 mg) in 24% yield. The mp (215−216 °C), IR, and ^{1}H NMR signals were in accordance to those of the authentic sample.

4: white needle, mp 254−255 °C (from THF−MeCN); IR 3375 cm^{-1}. ^{1}H NMR could not be measured due to the low solubility in any solvent. Anal. Calcd for $C_{26}H_{21}N$: C, 89.88; H, 6.09;, N, 4.03. Found: C, 90.12; H, 6.30; N, 3.87.

X-ray Structure Analyses. Data collections were performed on a Rigaku AFC7R automatic four-circle X-ray diffractometer equipped with a graphite monochromated Mo Kα (λ = 0.710 69 Å) or Cu Kα (λ = 1.541 78 Å) radiation and a rotating anode. Absorption correction was applied. No degradation of the crystal by X-ray was ascertained in all cases by repeated monitoring of the three representative reflections every 150 reflections. These structures were solved by direct methods and expanded using Fourier techniques. The non-hydrogen atoms were refined anisotropically. Atomic parameters were refined by the full-matrix least-squares method at the final stage. All the calculations were carried out on teXsan crystallographic software package, Molecular Structure Corp. Detail crystal data are summarized in Table 1.

The absolute configuration of (−)-**1·a** was determined very carefully by the Bijvoet method using anomalous despersion during X-ray crystallographic analysis. Although oxygen is a light atom ($\Delta f''$ = 0.032 for Cu Kα radiation), its use as an anomalous scatterer was preferred, because even slight modification of (−)-**1·a** by induction of heavier elements such as sulfur and chlorine may cause changes in the initial crystal structure. One of the single crystal cut into two pieces: half was subjected to reaction, yielding the photoproduct (−)-**3** in 33% ee (measured by HPLC using a chiral column). It was thus classified to be (−)-**1·a**. The second half was fitted to the top of the glass rod and made into a spherical crystal (0.5 mm diameter) by rubbing the surface with a wet cloth in MeCN. Since the space group is $P2_12_12_1$, equivalent Miller indices are (hkl), ($h\,\bar{k}\,\bar{l}$), ($\bar{h}\,k\,\bar{l}$), ($\bar{h}\,\bar{k}\,l$) at the plus side and ($\bar{h}\,\bar{k}\,\bar{l}$), ($\bar{h}\,k\,l$), ($h\,\bar{k}\,l$), ($h\,k\,\bar{l}$) at the minus side. However, structure factors F_o containing $\bar{l}$ of Miller indices were omitted in this evaluation in order to avoid errors due to the absorption of X-ray by the glass rod at minus position of χ-circle. Twenty-five reflections of the Bijvoet pairs were selected in order of larger absolute value $\{0.75 > |\Delta F_c|/\sigma(F_o) > 0.28\}$. The diffraction intensities were measured manually in a low speed due to the weakness of diffraction intensities. By comparisons of $\Delta F_o/\sigma(F_o)$ vs $\Delta F_c/\sigma(F_o)$ for Bijvoet pairs, 22 reflections (88%) of 25 gave opposite plus and minus signs. This result indicates that the absolute configuration is not correct with a high degree of certainty.[26] Therefore, *x*, *y*, and *z* axes were converted; Figures 1, 2, and 5 show correct absolute configuration of (−)-**1·a**.

Single crystals of {(−)-**3**}$_2$·MeOH were obtained by recrystallization from the solution of (−)-**3** in MeCN−MeOH and the crystal structure could be determined by X-ray crystallography (Table 1). However, because oxygen is an insufficiently heavy atom to determine the absolute configuration by Bijvoet method, a sufficiently heavy sulfur atom ($\Delta f''$ = 0.557 for Cu Kα radiation) was introduced in the form of the salt (−)-**7** (mp 135 °C, $[\alpha]^{20}_{D}$ −91, *c* 0.2, MeCN) of methylated (−)-**3** with trifluoromethanesulfonate,[28] which reaction did not change the configuration of the asymmetric carbon of (−)-**3**. The salt (−)-**7** was prepared by reacting (−)-**3** with methyl trifluorosulfate in CH_2Cl_2 followed by recrystallization from CH_2Cl_2. The crystal had a chiral space group $P2_1$ (Table 1). The fluorine atoms of trifluoromethanesulfate were slightly disordered in the crystal. The comparison of ΔF_o vs ΔF_c for Bijvoet pairs resulted in correct trend to be (*S*)-(−)-**7** with 41 reflections (80%) of 51 for $2.0 > |\Delta F_c|/\sigma(F_o)$. Therefore the absolute configuration of (−)-**3** could be successfully determined to be (*S*)-(−)-**3** (Figure 5).

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Supporting Information Available: Tables giving full data collection parameters and further details of refinement, atomic coordinates, anisotropic displacement parameters, bond lengths and angles, torsion angles of four structures reported in this paper (107 pages). See any current masthead page for ordering and Internet access instructions.

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