Pergamon

Tetrahedron: Asymmetry Vol. 6, No. 1, pp. 101-104, 1995
Elsevier Science Ltd
Printed in Great Britain
0957-4166/95 $9.50+0.00

0957-4166(94)00362-9

Chirality Memory Controlled by the Crystal Lattice of a Molecular Compound

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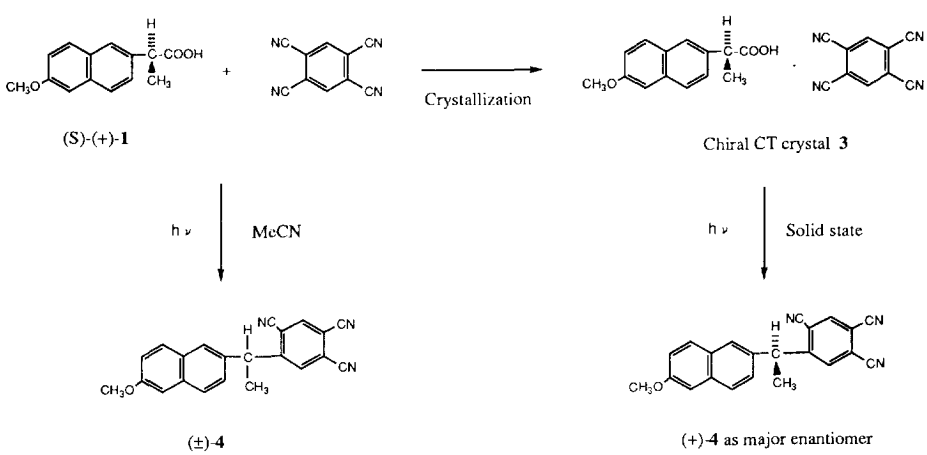
Abstract: Irradiation of crystalline charge transfer complex **3** formed between (S)-(+)-2-(6-methoxy-2-naphthyl)propanoic acid **1** and 1,2,4,5-tetracyanobenzene **2** is shown to lead to the optically active decarboxylated-coupled product (+)-**4** in high yield and substantial enantiomeric excess. In this process the configuration of the stereogenic carbon in **1** is retained to some extent by the control of the crystal lattice. The factors which affect the reaction of the molecular crystals were also examined. The relationship between the reactivity and the crystal structure is discussed.

There are several strategies for solid-state asymmetric syntheses.[1] One of them is the so-called absolute asymmetric synthesis involving the reactions of chiral crystals composed of achiral molecules containing a prochiral group.[1-8] However, the asymmetric crystallization of achiral molecules is very serendipitous. The methodology to overcome this problem is to use a removable remote chiral auxiliary approach, in which a chemically reactive but achiral molecule is derivatized with an unreactive remote chiral auxiliary (e.g. chiral amines or amino acids etc.) which ensures the crystallization in a homochiral space group.[1,2,9] Alternatively, crystallization of achiral but reactive molecules in some chiral hosts (e.g. cyclodextrins or tartaric acid derivatives etc.) by host-guest complexation also guarantees the formation of homochiral crystals.[10,11] In the course of our studies on solid-state photoreactions between two different organic molecules, we have developed several reactions which occur in the crystal lattice of molecular compounds.[12-14] As part of an effort for this purpose, in the present communication we report the use of a chiral crystal of a molecular compound formed between an optically active substrate (S)-(+)-2-(6-methoxy-2-naphthyl)propanoic acid (**1**) and 1,2,4,5-tetracyanobenzene (**2**) to afford chirality memory of the stereogenic carbon at which a bond-breaking and making process occurred. The factors which influence the reactivity of the molecular crystals and enantioselectivity of the reaction were also examined.

The charge transfer (CT) crystal **3** was prepared by cooling of a warm solution of an equimolar mixture of **1** and **2** in 3:1 MeCN-MeOH followed by filtration. The melting point of **3** is 168 °C appearing between those of **1** (156 °C) and **2** (266 °C). The CT absorption of **3** in the crystalline state was observed at 433 nm as a broad band. The fluorescence spectrum of **3** measured with a front faced arrangement shows only one broad peak around 510 nm, which is not found in those of **1** and **2** and can be attributed to the emission from the CT excited state. The crystal structure of **3** was determined by single crystal X-ray crystallography.[15]

The pulverized crystal of **3** obtained under ice-water cooling (100mg) was placed between two Pyrex glass plates and irradiated with a 400 W high-pressure mercury lamp under argon for 15 h at 15 °C. A product 1-(2,4,5-tricyanophenyl)-1-(6-methoxy-2-naphthyl)ethane **4**[16] (Scheme 1) was separated by preparative TLC on silica gel (benzene as an eluent) and then purified by preparative HPLC (C_{18} column,10:1 MeOH-H_2O as an eluent). The optical rotation and enantiomeric excess determinations of **4** show the $[\alpha]_D^{20}$ value and e.e. to be +22 (c=0.30, MeOH) and 21.2%, respectively, which implies that the chirality of **1** is transferred to product **4** in the decarboxylating-coupling process of the reaction (Scheme 1). So, the radical species ($ArC\dot{H}Me$) formed in the solid-state reaction may retain its original hybridization state and configuration to some extent because of the restriction of the crystal lattice when it reacts with the anion radical of **2** to form a new C–C bond. Figure 1 illustrates the molecular packing in the crystal **3**. The layer stacking of **1** and **2** shows the CT character with the plane distance of 3.4 Å. The shorter C•–•C distances between the radical $ArC\dot{H}Me$ and the anion radical of **2** are estimated as 4.68 (C1–C2), 4.81 (C1–C3), 4.83 (C1-C4) and 5.24 Å (C1–C5) based on the crystal data (Fig. 1). These values seem slightly large to cause the radical coupling. The production of **4** suggests that the radical species can move in the crystal lattice.

Scheme 1



In order to compare with the solid-state reaction of **3**, the solution photoreaction between **1** and **2** was carried out in acetonitrile.[17] Both of the optical rotation and enantiomeric excess of the product **4** were found to be zero (Scheme 1), which suggests that the radical species[18] (ArĊHMe) formed in this case undergoes the change of hybridization from sp^3 to sp^2 and loses its original configuration in a relatively free environment before it reacts with the anion radical of **2** to form a new C–C bond.

Some factors which influence the reaction of **3** were also examined.[19] The results are shown in Table 1. It was found the rate of the reaction increases with the increasing of the reaction temperature (Entry III–VI). When the photolysis was run at –30 °C, no reaction occurred at all (Entry III). The e.e. value is scarcely affected by increasing the reaction temperature and the conversion. The crystals obtained at a lower temperature undergo faster photolysis with lower enantioselectivity than those obtained at a relatively high temperature (Entry I, IV and VII). The reason is that the reaction proceeded not only in the crystal lattice but also on the surface of the crystallites and the larger contribution of the surface reaction appeared in the crystals obtained at the lower temperature, which gave the smaller size of the crystallites.[20]

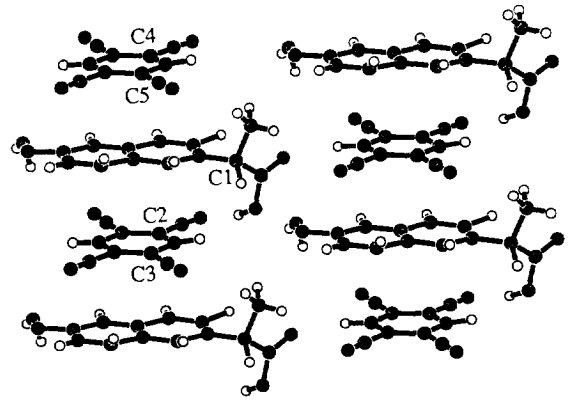


Fig. 1. Molecular packing in **3**

Table 1. Solid-state Photolysis Results of **3**

Entry	T_1[a] (°C)	T_2[b] (°C)	Conv. of **1** (%)	Yield[c] of **4** (%)	Optical yield of **4** (% ee)
I	0	0	2	95	22
II[d]	0	0	2	100	22
III	–30	–20	0	0	–
IV	0	–20	10	89	16
V	15	–20	17	87	14
VI	30	–20	24	83	14
VII	0	–40	17	94	8

[a] T_1, at which the irradiation was carried out.

[b] T_2, at which CT crystal **3** was crystallized.

[c] Yield based on consumed **1**.

[d] The crystal was pulverized for a onger time than in the case of Entry I.

Acknowledgment This work was partly supported by a Grant in Aid for scientific research from the

Ministry of Education, Science and Culture, Japan (No. 06242218).

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15. Yellow color crystal; P1; a = 8.538(5) Å, b = 10.596(6)Å, c = 6.815(6) Å, α = 106.84(6)°, β = 108.60(7)°, γ = 99.84(5)°; Z = 2; R = 5.6%.
16. Spectral data for **4**: m.p. 80–85 °C (MeOH); $[\alpha]_D^{20}$ = +22 (c=0.30, MeOH); e.e. = 21.2% (determined by HPLC using a Chiralpak AD column); UV λ_{max} = (MeCN) 218 nm (log ϵ 4.88), 231 (4.96); IR (KBr) 3040, 2225, 1628, 1482, 1263, 1028, 920, 814 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.90–7.90 (m, 8H), 4.71 (q, J=7.0 Hz, 1H), 3.80 (s, 3H), 1.71 (d, J=7.0 Hz, 3H). Analysis calculated for $C_{22}H_{15}N_3O$: C, 78.32; H, 4.48; N, 12.46%. Found: C, 78.41; H, 4.68; N, 12.31%.
17. Work-up of the photolysis between **1** and **2** in CH_3CN solution. A solution of **1** (1150 mg, 5 mmol) and **2** (890 mg, 5 mmol) in 100 ml of acetonitrile was internally irradiated with a 100 W high-pressure mercury lamp at room temperature for 24 h under the bubbling of argon. After evaporation of the solvent from the irradiated solution, the residue was submitted to prepartive TLC on silica gel (benzene as an eluent) to give 1206 mg (71.6% yield) **4** as pale yellow crystals. The melting point and spectral data are consistent with those mentioned above. $[\alpha]_D^{20}$ = 0, e.e. = 0%. The recoveries of **1** and **2** are 4% and 5%, respectively.
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19. The irradiation was carried out in a 20-mg scale by using a 500 W short arc lamp through a UV cut filter (light transmission, >390 nm) for 24 h at various temperatures. The irradiated mixture was treated with excess diazomethane and then submitted to HPLC analysis by using a Chiralpak AD column.
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21. One of the author (K. D.) is a guest researcher from Zhengzhou University, China.

(*Received in Japan* 21 *October* 1994)