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EFFECT OF PYRIDINE ON POLYMORPHIC CRYSTALLIZATION OF 1,3-DI(9-ANTHRYL)PROPAN-2-OL. DOES IT AFFECT π/π INTERACTION OR HYDROGEN BONDING?

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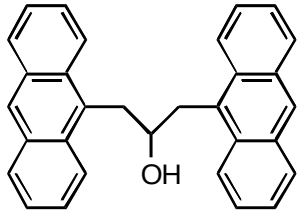
Abstract – Effect of pyridine on polymorphic crystallization of 1,3-di(9-anthryl)propan-2-ol (**1**) is investigated by X-Ray analyses. **1** generally crystallizes in α-form, whereas the 1:1 solvate (γ-form) was obtained from pyridine solution, in which pyridine was shown to serve largely as a hydrogen-bond acceptor preventing hydrogen bonding between molecules of **1** in crystallization process.

INTRODUCTION

Polymorphism[1, 2] is of much importance since physical and chemical behavior in crystalline state is essentially governed by the packing structure. Although polymorphic behavior is not fully understood, it is known that production of polymorphs may often be achieved by adding auxiliaries or replacing solvent. This is explained in such a way that auxiliaries[3, 4] (including solvent molecules)

that can strongly interact with the substrate facilitate to generate other polymorph by their preferential adsorption at some polymorph thus inhibiting its crystal growth. For example, when a thiourea derivative was crystallized from dimethyl sulfoxide (DMSO) solution, the production of a polymorph was observed, that was rationalized in terms of strong hydrogen bond between the substrate and solvent molecules.[5] In these contexts, a variety of intermolecular interactions have been studied, though most auxiliaries are mono-functional. Herein, we have focused our attention on pyridine, which may function as a *bi-functional* auxiliary, e.g. since it is an aromatic compound as well as a basic compound, pyridine might affect crystallization process of aromatic compounds bearing hydrogen-bonding substituent such as hydroxy group. Such aromatic componds, however, have not shown polymorphism; for instance, polymorphism of benzyl alcohol is unknown. We have investigated polymorphic crystallization of 1,3-di(9-anthryl)-2-propanol (**1**).[6] Both the aromatic plane and hydroxy group can interact with pyridine. In additon, according to Desiraju's hypothesis, **1** is a compound possessing a propensity toward polymorphism. In other words, he mentioned in his review[7, 8] that the likelihood of polymorphism may be greater for a molecule having (1) intermediate (C_{11}-C_{20}) molecular weight, (2) flexible conformations, and (3) some different groups



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capable of hydrogen bonding or other interactions. Indeed, **1** possesses one hydroxy group for hydrogen bonding, two anthryl planes for π/π interactions, and a flexible propane backbone.

RESULTS AND DISCUSSION

By slow evaporation of a solution of **1** dissolved in dichloromethane, light yellow prisms, α-form was produced. The X-Ray structure of α-form (Figure 1) shows that two molecules of **1** are associated with the aid of OH/O hydrogen bonding (O•••O distance is 2.81 Å). A plane A (depicted in Figure 1) stacks in parallel with another plane A with an estimated interplanar distance of 3.54 Å. Two plane B's also stack in parallel with slightly shorter interplanar distance (3.52 Å). Thus, the principal packing motives of α-form are OH/O hydrogen bond and π/π interactions. X-ray powder diffraction (XPRD) studies revealed that α-form crystals were obtained from other solvents, such as hexane, chloroform, CCl_4, diethyl ether, ethanol, dioxane, DMSO, and acetone.

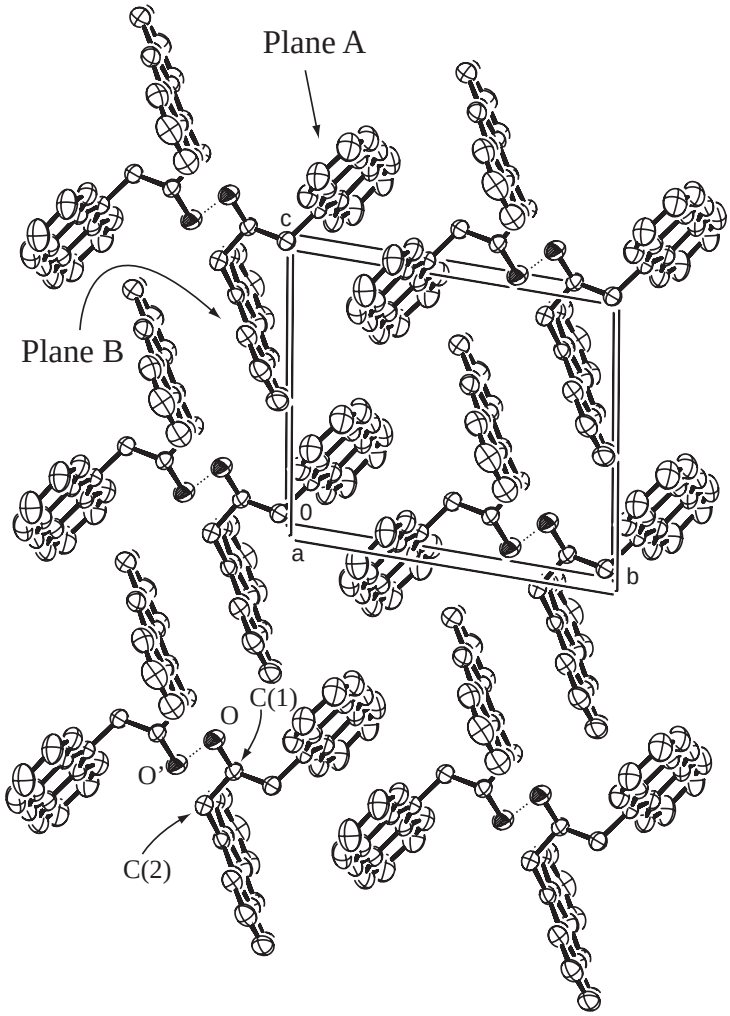

Figure 1. A perspective view of α-form of **1**. For clarity, oxygen atoms are represented by discriminated ellipsoids and hydrogens are omitted. Hydrogen bonds are specified by dotted lines.

Next, we studied influence of benzene, a typical aromatic solvent, on crystallization of **1**. By slow evaporation of benzene solution of **1**, yellow prisms, β-form, were obtained. β-Form is metastable relative to α-form, since DSC (Differential Scanning Calorimetry) analysis showed that β-form was transformed to α-form around 210 ºC. The packing structure of β-form (Figure 2) is considerably different from that of α-form. In β-form, a conformation of **1** is very similar to that in α-form, and hydrogen-bonded association of two molecules of **1** is also found (OH/O distance is 2.91 Å). However, its configuration of the hydrogen-bonded pair is different, so that the packing motif of β-form is distinct. The dihedral angle of C(2)-C(1)-O•••O' is 55° for α-form whereas 154° for β-form. Notably, π/π stacking seems to be less important in β-form. Plane B does not interact with other anthracenes. The π/π interaction between Plane A's is less effective, since the offset between the centroids is larger (2.20 Å) than those in α-form (1.36 and 2.01 Å). The β-form was also obtained from toluene solution, being confirmed by XPRD studies.

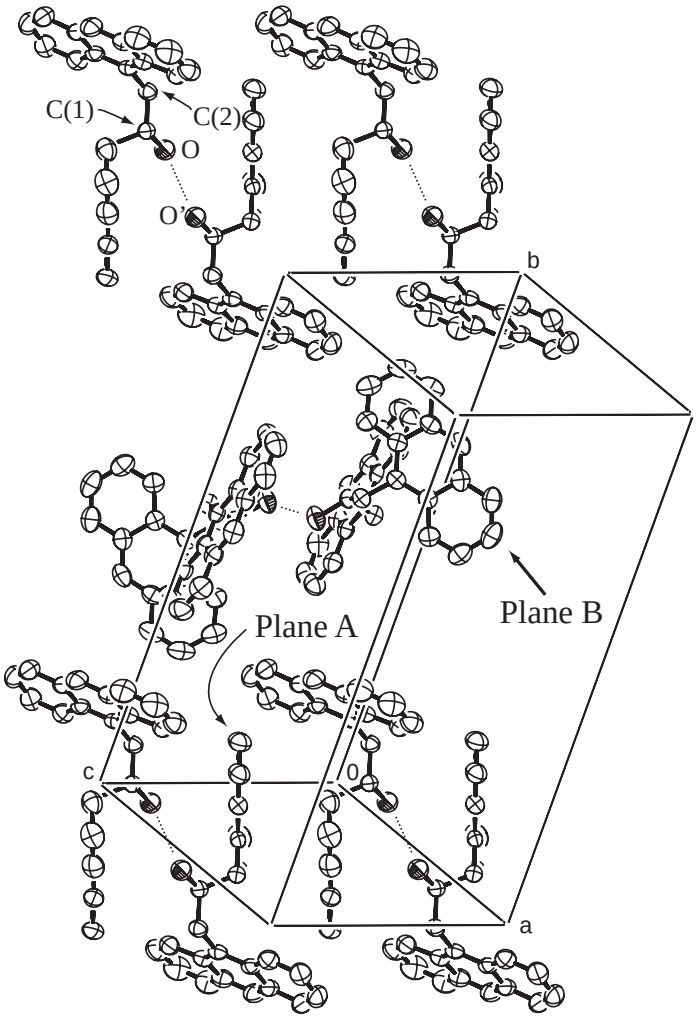

Figure 2. A perspective view of β-form of **1**. For clarity, oxygen atoms are represented by discriminated ellipsoids and hydrogens are omitted. Hydrogen bonds are specified by dotted lines.

Several mechanisms of polymorphic crystallization, such as preferential conformation,[9,10] solubility,[11] or polarity of solvent,[12] have been proposed. These are not in the present cases. Thus, we deduce that the generation of β-form is due to the interactions between **1** and benzene molecules. In benzene solution, the π/π stacking between molecules of **1** would be inhibited by solvent molecules so that β-form is generated. This is supported by the fact that Jorgensen and his coworkers calculated[13] the energy of π/π stacks of anthracene and benzene to be ca. 4 kcal mol^{-1}, which is large enough to provoke polymorphism.

In contrast, the1:1 solvate (γ-form) was obtained from pyridine solution. Since γ-form is thermally so unstable that it gradually loses the guest component at room temperature, X-Ray diffraction studies[13] were performed at –70 ºC. The packing structure of γ-form is depicted in Figure 3. The conformation of **1** is almost identical to those found in α- and β-forms. As indicated in α-form, face-

to-face π/π stacks are observed with interplanar distances of 3.51 Å for both A-A and B-B (the offset values are 1.60 and 1.74 Å, respectively). Intriguingly enough, no hydrogen bond between molecules of **1** exists while **1** and pyridine form hydrogen bond. Namely, the pyridine molecule affected hydrogen bonding between the molecules of 1 rather than the intermolecular π/π stacking on crystallization process of **1**. It should be noted that such potentially hydrogen-bonding solvents such as ether, ethanol, and DMSO, did not afford complex crystals. The complex crystals might be

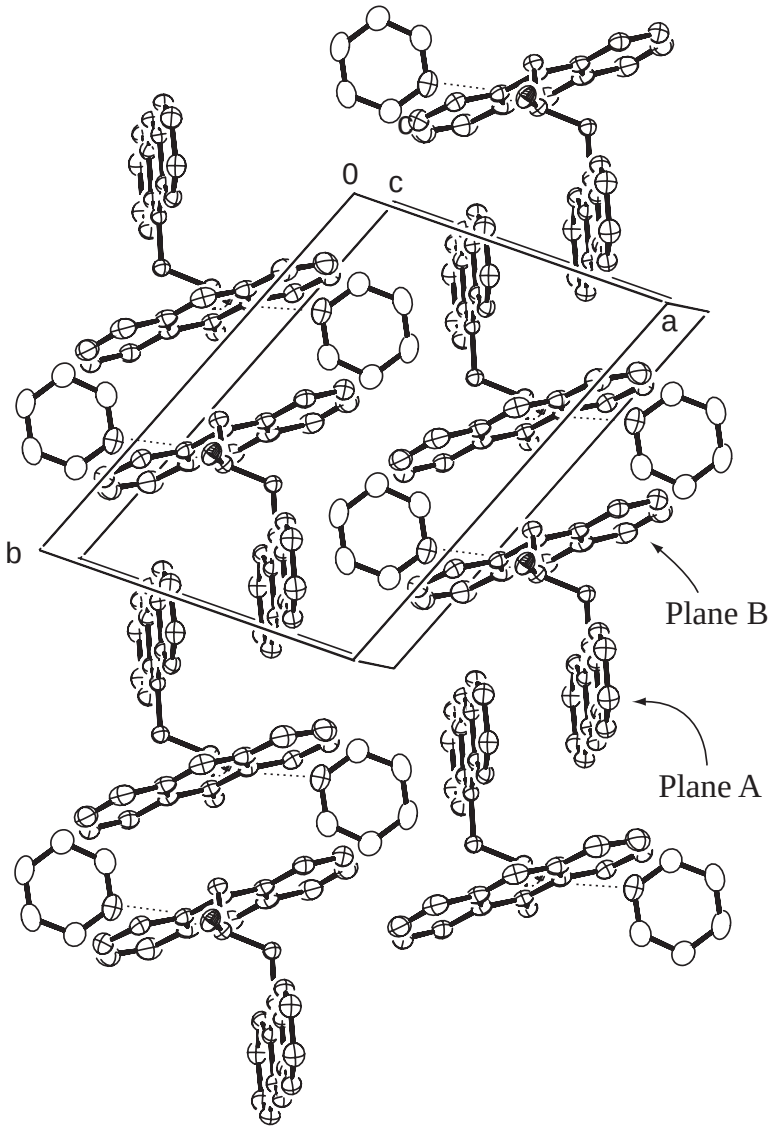

Figure 3. A perspective view of 1:1 solvate of **1** with pyridine (γ-form). For clarity, oxygen atoms are represented by discriminated ellipsoids and hydrogens are omitted. Hydrogen bonds are specified by dotted lines.

generated, however, being too unstable to transform into more stable form and to result in the most stable one, α-form (Ostwald's law of stages).[14] The generation of γ-form is presumably due to larger interaction energy of the hydrogen bond between 1 and pyridine than that of π/π stacking of **1** and

pyridine; otherwise, β-form would be obtained as observed in benzene solution. The bi-functional auxiliary is not only limited to pyridine: when weak intermolecular interactions (such as CH/π, CH/O, and S•••S interactions) are considered, almost all molecules are, more or less, bi-functional (or even multi-functional). Therefore, the result described here will offer a general guideline to understand polymorphism as well as to design crystalline materials and supramolecules in the presence of auxiliaries.

EXPERIMENTAL

Crystal data for α-form of **1**: $C_{31}H_{24}O$, *Fw* = 412.50, triclinic, space group *P*-1, *a* = 10.216(3), *b* = 11.403(4), *c* = 9.685(3) Å, α = 97.47(2)°, β = 99.11(2)°, γ = 102.24(3)°, *T* = 293 K, *Z* = 2, D_{calc} = 1.277 g cm^{-3}, *R1* = 0.048 (*I* > 2σ(*I*)), *wR2* = 0.144 (all data). Crystal data for β-form of **1**: $C_{31}H_{24}O$, *Fw* = 412.50, monoclinic, space group $P2_1/n$, *a* = 24.914(7), *b* = 10.112(2), *c* = 10.216(3) Å, β = 114.20(2)°, *T* = 293 K, *Z* = 4, D_{calc} = 1.261 g cm^{-3}, *R1* = 0.046 (*I* > 2σ(*I*)), *wR2* = 0.127 (all data). Crystal data for **1**-pyridine 1:1 solvate (γ-form): $C_{36}H_{29}NO$, *Fw* = 491.60, triclinic, space group *P*-1, *a* = 11.136(2), *b* = 13.738(2), *c* = 10.204(2) Å, α = 100.08(2)°, β = 114.60(1)°, γ = 104.88(2)°, *T* = 203 K, *Z* = 2, D_{calc} = 1.257 g cm^{-3}, *R1* = 0.049 (*I* > 2σ(*I*)), *wR2* = 0.128 (all data). For all crystals reported in this paper (α-, β-, and γ-forms), all measurement were made on a RIGAKU AFC-5S four-circle diffractometer with Mo-Ka radiation. The crystal structures were solved by direct methods (SHELXS-97)[15] and refined by full-matrix least square methods (SHELXL-97).[15] Crystallographic data have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-165995, 165996, and 165997 for α-, β-, and γ-form, respectively.

Thermal analysis. DSC analysis was performed as follows. Crystals were removed from the mother liquor, blotted dry on filter paper and crushed before analysis. Sample weight was about 3 mg. The temperature range was from ambient temperature to 240 ºC at a heating rate of 10 ºC min^{-1}.

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