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In Situ Cryocrystallization of Diphenyl Ether: C−H···π Mediated Polymorphic Forms

Angshuman R. Choudhury,[†] Kabirul Islam,[‡] Michael T. Kirchner,[§] Goverdhan Mehta,[‡] and Tayur N. Guru Row*,[†]

Solid State and Structural Chemistry Unit, Department of Organic Chemistry, Indian Institute of Science, Bangalore, 560012 Karnataka, India, School of Chemistry, University of Hyderabad, Hyderabad, 560046 Andhra Pradesh, India

Received June 30, 2004; E-mail: ssctng@sscu.iisc.ernet.in

Polymorphism is a well-recognized phenomenon controlled by subtle interplay of kinetic and thermodynamic factors and most often mediated through intermolecular forces.[1] In situ crystallization of a liquid, the subsequent determination of crystal structure, and the study of intermolecular interactions therein is an area of contemporary interest.[2−8] In most of these studies, intra- and intermolecular interactions play a significant role in generating molecular assemblies, such as those in fluorobenzenes.[2] Hydrogen bonding in cocrystals of acetylene dissolved in acetone and DMSO under high pressure demonstrates the versatility of the in situ crystallization technique.[3] The involvement of kinetic and thermodynamic factors in in situ crystallization suggests the use of this approach to generate polymorphs. Herein, we report for the first time generation of polymorphs employing in situ cryocrystallization technique on diphenyl ether, a liquid whose crystal structure has not been determined previously. It is further demonstrated that only weak intra- and intermolecular C−H···π interactions[9] direct crystal packing in these dimorphs.

Diphenyl ether (mp = 20 °C), widely used by synthetic organic chemists[10] as a high-boiling solvent, was found to grow single crystals of excellent quality when cooled in a refrigerator, but single-crystal structural analysis was not feasible by conventional diffraction techniques. A Lindemann glass capillary of ∼3 cm length and 0.3 mm diameter was filled with diphenyl ether, sealed, and mounted on the Bruker AXS X-ray diffractometer equipped with SMART APEX CCD area detector. The capillary was aligned and then cooled rapidly at 360 K/h using an OXFORD N_2 cryosystem to 250 K. At first attempt, the liquid solidified in the range of 260−255 K, forming reasonably good-quality (but opaque) single crystals in the capillary (Figure 1a). The temperature was allowed to stabilize at 250 K for 30 min, and then 180 frames of 5-s exposure were collected with the 2θ fixed at −25° and a ω width of −1°. These frames were then processed using SMART,[11] and the spots were analyzed using RLATT[11] to determine the unit cell dimensions. The diffraction spots (∼600 in number) selected using RLATT could be indexed to a monoclinic unit cell. Data were collected on three sets of 606 frames with $2\theta = -25°$ and with ϕ values at 0°, 90,° and 180° and with a ω width of −0.3°. The crystal structure was solved and refined using SIR92[12] and SHELXL97[13] separately in the centric space group $P2_1/n$.[14] Several attempts were made to get a transparent, better-quality single-crystal, keeping in view that the previous data were on an opaque crystal. However, most of the attempts using the same procedure yielded polycrystalline solid in the capillary. It was decided to set the N_2 stream temperature to 240 K (10 K less than previous attempt), and then the solid was annealed by shifting the N_2 stream away from the capillary (which allows partial melting of the solid inside the capillary) and reset the N_2 stream once again to ensure the formation of the solid. This procedure was repeated several times, resulting in a transparent single crystal in the capillary (Figure 1b). At this stage, 180 frames were recorded as before, the reflections were analyzed through RLATT, and the cell dimensions were determined using SMART. It is of interest to note that the newly indexed unit cell is orthorhombic! It is also noteworthy that the space group is noncentric, $P2_12_12_1$! It appears obvious that a polymorphic modification of diphenyl ether has been generated. Single-crystal X-ray diffraction data were collected on this form at 240 K following the same strategy.[15]

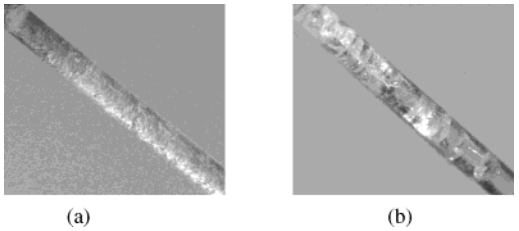

Figure 1. Crystals of the polymorphic forms of diphenyl ether grown in situ in a capillary.

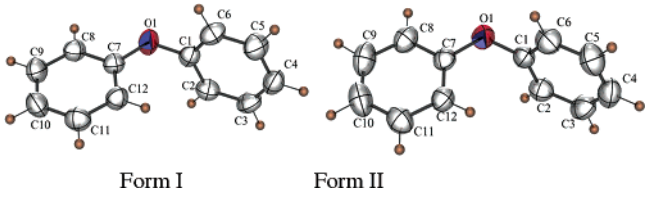

Figure 2. ORTEPs of I and II of diphenyl ether, drawn with 50% ellipsoid probability.

The ORTEPs of the two forms (hereafter I for the centric $P2_1/n$ and II for the noncentric $P2_12_12_1$) are shown in Figure 2 with atom labeling. The molecular conformations in the two forms are similar with the angles between the least-squares planes [PL1 = C1···C6, PL2 = C7···C12] through the phenyl rings being 88.39(7)° and 87.60(4)° and the ∠C1−O1−C7 being 117.9(1)° and 118.3(1)° for I and II, respectively. A significant intramolecular C−H···π interaction[9] is the main reason for locking up the molecular conformation in each case. It is remarkable to note that angles between PL1 and PL2 deviate markedly from a theoretically (RMP2) optimized geometry using a 6-31G basis set in Gaussian 98[16] [∠PL1···PL2 = 67.65°].

Intermolecular C−H···π interactions control the packing of the molecules in the unit cell, thus mediating the generation of two polymorphic forms. In I, the intermolecular C−H···π interactions form a three-dimensional network of molecules (Figure 3a, Table

[†] Solid State and Structural Chemistry Unit, Indian Institute of Science.
[‡] Department of Organic Chemistry, Indian Institute of Science.
[§] School of Chemistry, University of Hyderabad.

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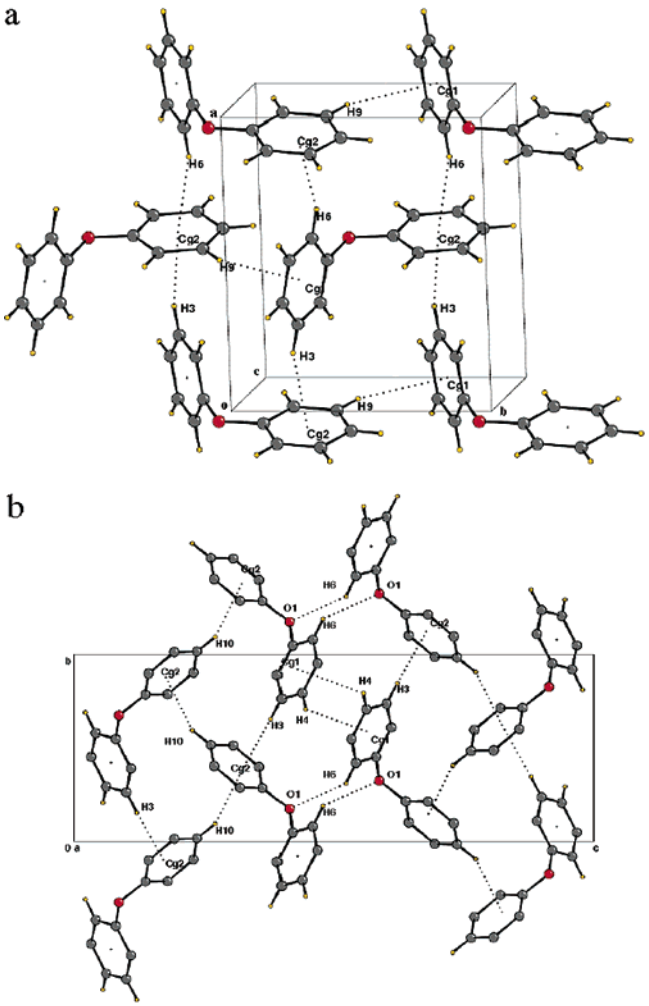

Figure 3. (a) Packing of molecules of diphenyl ether in form I. (b) Packing of molecules of diphenyl ether in form II. Cg1 and Cg2 are the centroids of two phenyl rings C1···C6 and C7···C12.

Table 1. Weak Interactions in the Two Polymorphic Modifications of Diphenyl Ether

D-B···A	D···A/ Å	B···A/ Å	∠D–B···A/ deg	symmetry
		Form I		
C12−H12···Cg1	3.707(1)	3.10(2)	124(2)	x, y, z
C3−H3···Cg2	3.746(3)	2.92(2)	146(1)	$^1/_2 - x, -^1/_2 + y, ^1/_2 - z$
C6−H6···Cg2	3.694(3)	2.88(2)	144(1)	$-^1/_2 - x, -^1/_2 - y, ^1/_2 - z$
C11−H11···Cg1	3.687(2)	2.87(2)	147(2)	$x, 1 + y, z$
		Form II		
C12−H12···Cg1	3.730(2)	3.14(2)	122(2)	x, y, z
C3−H3···Cg2	3.765(2)	2.90(2)	151(1)	$x, y - 1, z$
C4−H4···Cg1	3.788(2)	3.13(2)	128(1)	$^1/_2 + x, ^1/_2 - y, -z$
C10−H10···Cg2	3.792(2)	3.05(2)	135(2)	$1 - x, ^1/_2 + y, ^1/_2 - z$
C6−H6···O1	3.403(2)	2.62(2)	139(1)	$^1/_2 + x, ^1/_2 - y, - z$

1) with C−H···π interactions involving H3 and H6 forming chains along the *a* axis. An additional C−H···π interaction through H11 interlinks these chains. In form II, the C−H···π interactions involving H3 and H10 form a tetramer, while another C−H···π interaction via H4 links neighboring tetramers (Figure 3b, Table 1). Further, a weak intermolecular C−H···O hydrogen bond links neighboring tetramers in form II. This additional C−H···O interaction provides thermodynamic stability to form II and is probably responsible for the monoclinic form being a "*disappearing polymorph*"[17] as several attempts under identical conditions resulted in access to only the orthorhombic form!

To summarize, we have demonstrated polymorphism via in situ crystallization for the first time in a liquid. In the current study, we have shown that, although the molecular conformations are similar, the difference in packing has resulted in the observed ideal "*packing polymorphism*".[1]

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Supporting Information Available: X-ray crystallographic information in CIF format for the two structures and rotation pictures of I and II and figures showing molecular assembly in II. This material is available free of charge via the Internet at http://pubs.acs.org.

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(14) Crystal data: Chemical formula $C_{12}H_{10}O$, Formula weight 170.2, monoclinic, space group $P2_1/n$, $a = 9.961(4)$ Å, $b = 8.022(3)$ Å, $c = 12.274(5)$ Å, $\beta = 106.993(6)°$, $V = 938.0(2)$ Å^3, $Z = 4$, $\rho_{calc} = 1.205$ g cm^{-3}, $T = 250$ K, $\mu = 0.075$ mm^{-1}, reflections measured 6916, unique reflection 1868, observed reflections [$I > 2\sigma(I)$] 1584, R1_obs = 0.054, wR2_obs = 0.116.
(15) Crystal data: Chemical formula $C_{12}H_{10}O$, Formula weight 170.2, monoclinic, space group $P2_12_12_1$, $a = 5.741(2)$ Å, $b = 7.694(2)$ Å, $c = 21.165(7)$ Å, $V = 934.8(1)$ Å^3, $Z = 4$, $\rho_{calc} = 1.209$ g cm^{-3}, $T = 240$ K, $\mu = 0.076$ mm^{-1}, reflections measured 4809, unique reflection 1707, observed reflections [$I > 2\sigma(I)$] 1559, R1_obs = 0.032, wR2_obs = 0.077.
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