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Optical activity of benzophenone and thiobenzophenone generated by spontaneous crystallization and inclusion complexation with cholic acid

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Abstract—The solid state CD spectra were measured for enantiomorphous crystals of benzophenone **1** and 4,4'-dimethylbenzophenone **2**. The helicity of the constituent molecules was determined from the sign of the Cotton effect corresponding to the ketone $n-\pi^*$ transition. In addition the crystalline 1:2 inclusion complexes of the ketone **1** and thiobenzophenone **4** with cholic acid were prepared and their CD spectra were measured. The observed negative Cotton effect sign of **1**-CA and positive one for **4**-CA corresponding to the lowest energy $n-\pi^*$ transitions were correlated with the *M* and *P* helicity of the enclathrated guest molecules, respectively. The helicity of the guest molecules was confirmed by X-ray crystal structure analyses.
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1. Introduction

Generation of chirality in achiral compounds is considered one of the most intriguing topics in organic solid state chemistry.¹ Molecules devoid of stereogenic centers can adopt chiral conformations caused by internal torsion. Usually such compounds are conformationally labile in solution due to a rapid interconversion between the enantiomers. However, they may occasionally form optically active crystals with the component molecules frozen in a chiral conformation. Spontaneous generation of chirality is a relatively rare phenomenon that occurs when the racemic mixture crystallizes as a conglomerate, that is, an equimolar mixture of enantiomorphous crystals from which a suitable single crystal can be selected.² It can be illustrated by the asymmetric crystallization of glycine,³ benzil,^{4,5} 1,1-binaphthyl⁶ or more recently 1,2-bis(*N*-benzoyl-*N*-methylamino)benzene and *N*-(4-chlorophenyl)-*N'*-cyanoguanidine.⁷

Sometimes seeding the sample of the equilibrating enantiomers with the desired form may lead to a conversion of the whole quantity of the racemate into a single enantiomer (complete asymmetric transformation).^{2b,6}

Chiral crystals formed of achiral compounds have attracted growing attention as starting materials or catalysts in asymmetric synthesis.^{1,8} They may also be responsible for the origin of homochirality in biomolecules.⁹ Unfortunately, the asymmetric crystallization of achiral compounds without external chiral influence is a rare and highly unpredictable phenomenon. A different approach to generate optical activity in symmetric molecules offers inclusion complexation with chiral hosts.^{5,10,11} Recently we have shown that naturally occurring cholic acid (CA) is particularly well suited for this purpose.^{5,10} The guest molecules embedded in the crystal lattice of CA are forced to assume a chiral conformation that can be detected by solid state circular dichroism (CD) measurements. Since the configuration of CA is well established, the X-ray crystallographic analysis of single crystals of the inclusion compounds makes possible unequivocal assignment of the absolute configuration of the guest molecules.

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