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Solid-state structural properties of 2,4,6-trimethoxybenzene derivatives, determined directly from powder X-ray diffraction data in conjunction with other techniques

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Abstract

Structural properties of 2,4,6-trimethoxybenzaldehyde, 2,4,6-trimethoxybenzyl alcohol and 2,4,6-trimethoxyacetophenone have been determined directly from powder X-ray diffraction data, using the direct-space Genetic Algorithm (GA) technique for structure solution followed by Rietveld refinement. Structural similarities and contrasts within this family of materials are elucidated. The work illustrates the value of utilizing information from other sources, including spectroscopic data and computational techniques, as a means of augmenting the structural knowledge established from the powder X-ray diffraction data.

Keywords: Powder X-ray diffraction; Structure determination; Molecular conformation; Solid state NMR; DFT calculations

1. Introduction

Within the last decade or so, new opportunities have been created for carrying out complete structure determination of organic molecular solids directly from powder diffraction data [1], particularly through the development of the direct-space strategy for structure solution [2]. Such techniques are essential for structure determination of the wide range of materials that cannot be prepared as single crystals of suitable size and/or quality for investigation by single crystal X-ray diffraction techniques. Recent advances in methodology within the field of structure determination from powder X-ray diffraction data are such that organic molecular crystal structures of moderate complexity can now be determined fairly routinely by this approach. Nevertheless, structure determination from powder X-ray diffraction data is not a "black-box" technique, and careful attention is required to ensure the correctness of the structure obtained. In this regard, an important aspect, illustrated in the present paper, is to recognize the advantages of using information derived from other sources, including spectroscopic data and/or computational techniques, in conjunction with the powder X-ray diffraction data as a means of augmenting the structural information determined from the diffraction data.

This paper reports the structure determination of three related organic molecular materials (Fig. 1): 2,4,6-trimethoxybenzaldehyde (denoted **1**), 2,4,6-trimethoxybenzyl alcohol (denoted **2**) and 2,4,6-trimethoxyacetophenone (denoted **3**). In each case, structure determination has been carried out directly from powder X-ray diffraction data using our direct-space Genetic Algorithm (GA) technique [3] for structure solution, followed by Rietveld refinement [4]. Materials **1**–**3** are of interest as part of a wider research effort on dendrimeric materials, as they are precursors for some of the targeted families of dendrimers in this research.

2. Experimental details and methodology

Compound **1** was obtained from Aldrich and re-crystallized from dichloromethane/methanol (1:10). Compound **2**

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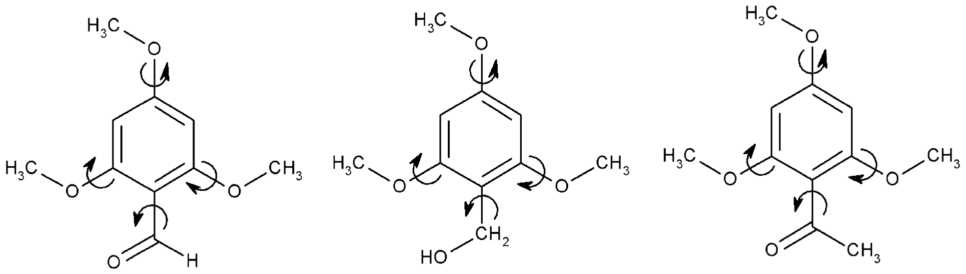

1 **2** **3**

Fig. 1. Molecular structures of **1**, **2** and **3**. The arrows indicate the variable torsion angles in the direct-space structure solution calculations from powder X-ray diffraction data.

was synthesized by reduction of **1** using $LiAlH_4$ in dry THF, purified by column chromatography on silica gel (dichloromethane/methanol, 1:30) and re-crystallized from acetone/hexane (1:4). Characterization of **2** was carried out using standard techniques (solution-state ^{1}H and ^{13}C NMR and mass spectrometry). To allow solid state ^{2}H NMR studies to be carried out on **2**, a sample of **2** deuterated in the hydroxyl group (denoted **2**-d) was prepared by refluxing **2** for 24 h in CH_3OD/D_2O (1:5). The suspension was then extracted with dry dichloromethane, dried over sodium sulphate, and evaporated under reduced pressure to afford the crude product, which was re-crystallized from acetone/hexane (1:4). Infrared and NMR spectroscopic experiments on **2**-d indicated that the level of deuteration was ca. 65%. Compound **3** was obtained directly from Aldrich, and used without further purification. For each material, the question of whether the crystal structure contains water or solvent of crystallization was assessed by dissolving an amount of the material in dry $CDCl_3$ and then recording the liquid state ^{1}H NMR spectrum of the resultant solution. In all cases, there was no evidence for the presence of any water or solvent molecules within the materials **1**–**3** (we note that the same test has been used previously [3d] to assess the presence of water in a crystalline hydrate phase). Furthermore, the solid state ^{13}C NMR spectrum recorded for **1** (see below) is consistent with the conclusion that no solvent (dichloromethane or methanol) molecules are present in the crystal structure.

For measurement of the powder X-ray diffraction patterns of **1**–**3**, the samples were ground using a mortar and pestle and loaded into a borosilicate glass capillary (0.7 mm diameter). Powder X-ray diffraction data were recorded at ambient temperature in transmission mode on a Bruker D8 diffractometer ($CuK\alpha_1$ radiation, Ge-monochromated; VANTEC detector covering 12° in 2θ; total 2θ range 4–70°; step size 0.017°; data collection time 10 h).

Specific details of the structure determination of **1**–**3** from powder X-ray diffraction data are discussed in Section 3. In each case, following indexing (carried out using one or more of the programs ITO [5], TREOR [6] and DICVOL [7]) and pattern decomposition/profile fitting (carried out using the Le Bail technique [8]), structure solution was carried out using a single-population version of the direct-space GA structure solution program EAGER [1g,3,9]. As discussed in Section 3, each of the structures **1**–**3** has one molecule in the asymmetric unit (but different space groups), and in the GA structure solution calculation, each trial structure was defined by a total of 10 variables: $\{x, y, z, \theta, \varphi, \Psi, \tau_1, \tau_2, \tau_3, \tau_4\}$. The four variable torsion angles in each of the molecules **1**–**3** are defined in Fig. 1. In the GA calculation in each case, the population comprised 100 trial structures (with the initial population generated at random). In the evolution of the population from one generation to the next generation, 50 mating operations and 25 mutation operations were carried out. In each case, the correct structure solution was obtained within 20 generations or less. The best trial structure (i.e. the trial structure with lowest R_{wp}) obtained after 20 generations was used as the initial structural model for Rietveld refinement, which was carried out using the GSAS program package [10]. In the Rietveld refinement, standard restraints were applied to bond lengths and bond angles, and planar restraints were applied to the phenyl rings. The restraints on bond lengths and bond angles were relaxed gradually as the refinements progressed. Isotropic displacement parameters were refined for the non-hydrogen atoms. Hydrogen atoms were placed at calculated positions with a fixed value ($0.05\,\text{Å}^2$) for the isotropic displacement parameter. As discussed elsewhere [3d,4c,4d], careful consideration of the quality of fit achieved in the Rietveld refinement is a crucial component of the validation of the final structural information reported.

Solid state NMR spectra were recorded for powder samples of **1** (^{13}C NMR) and **2**-d (^{2}H NMR) on a Chemagnetics CMX-Infinity 300 spectrometer (75.48 MHz for ^{13}C; 46.08 MHz for ^{2}H). The high-resolution solid state ^{13}C NMR spectrum of **1** was recorded under conditions of $^{13}C \leftarrow {}^{1}H$ cross-polarization (CP), magic angle sample spinning (MAS), high power ^{1}H decoupling using the TPPM decoupling technique, and total suppression of spinning sidebands (TOSS) (CP contact time, 10 ms; recycle delay, 30 s; MAS frequency, 4 kHz). The broad-line ^{2}H NMR spectrum of **2**-d (for a non-spinning sample) was recorded using the standard quadrupole echo pulse sequence at several temperatures between 223 and 293 K (^{2}H 90° pulse length, 2 μs; recycle delay, 6–30 s depending on temperature).