Molecular and crystalline structure of cycloheptanespiro-3′(4′H)-6′,7′,8′,9′-tetrahydrocyclohexa[b][1,4]thiazole-2′(5′H)-thione from powder synchrotron X-ray diffraction data

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Molecular and crystalline structure of cycloheptanespiro-3′(4′H)-6′,7′,8′,9′-tetrahydrocyclohexa[b][1,4]thiazole-2′(5′H)-thione from powder synchrotron X-ray diffraction data

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A series of bidentate nitrogen–sulfur pro-ligands has been designed and synthesized with the purpose of introducing a structural modification that favours the tetrahedral site distortions of metalloprotein systems with metallic centers surrounded by ligands containing two N atoms and two S atoms as donor groups. Some of these new pro-ligands were obtained only as powders. Here we present the molecular and crystalline structure of cycloheptanespiro-3′(4′H)-6′,7′,8′,9′-tetrahydrocyclohexa[b][1,4]thiazole-2′(5′H)-thione (I) solved and refined from powder synchrotron X-ray diffraction data. Two independent molecules comprising a total of 36 non-H atoms were obtained from the direct-methods solution and refined against the powder X-ray diffraction data using the Rietveld method. The molecular conformations of the heterocyclic benzothiazine ring, the fused heptenyl ring and the heptanyl spiro ring are thoroughly discussed and compared with VASP theoretical calculations and other related structures. The packing of molecules in (I) is based on hydrogen bonds of the type N—H⋯S and hydrophobic C—H interactions.

1. Introduction

Biomimetic inorganic chemistry is concerned with the synthesis and detailed electronic and structural characterization of model molecules that approach one or more properties of a protein-active metal site (Holm & Solomon, 2004). Composition, ligand type, site topology and oxidation state are among the properties that can be duplicated. In particular, efforts have been made (Solomon et al., 2004; Halcrow & Christou, 1994; Malachowski et al., 1999; Karlin et al., 1997) to reproduce the pseudo-tetrahedral coordination spheres of metal ions linked with pro-ligands containing two N atoms and two S atoms as donor groups, since biological systems use this type of environment in the coordination of metal ions such as CuII in plastocyanin or azurin (Roat-Malone, 2002), NiII in nickel-hydrogenase (Kain & Schwederski, 1994) and ZnII in the so-called zinc finger proteins involved in the activation and regulation of the DNA transcription (Auld, 2001). Recently, Contreras et al. (2001, 2005, 2006) modified the reaction conditions proposed by Bordás et al. (1972) in their seminal synthetic studies and synthesized a series of nitrogen–sulfur pro-ligands. The aim of the study was to investigate the geometry and steric effects of the chelate formation of the new pro-ligands with the various biometals responsible for biological activity in metalloproteins. Some of the [NS] pro-ligands have only been obtained as powders. Here we discuss the molecular and crystal structure of cycloheptanespiro-3′(4′H)-6′,7′,8′,9′-tetrahydrocyclohexa[b][1,4]thiazole-2′(5′H)-thione,
Table 1
Experimental details.

<table>
<thead>
<tr>
<th>Crystal data</th>
<th>Chemical formula</th>
<th>Mr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cell setting, space group</td>
<td>C_{15}H_{23}NS_{2}</td>
<td>281.46</td>
</tr>
<tr>
<td>Temperature (K)</td>
<td>298</td>
<td></td>
</tr>
<tr>
<td>a, b, c (Å)</td>
<td>13.11563 (4), 21.32201 (6), 11.75591 (3)</td>
<td></td>
</tr>
<tr>
<td>β (°)</td>
<td>113.9899 (1)</td>
<td></td>
</tr>
<tr>
<td>V (Å³)</td>
<td>3003.57 (2)</td>
<td></td>
</tr>
<tr>
<td>Z</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>D_{x} (Mg m⁻³)</td>
<td>1.245</td>
<td></td>
</tr>
<tr>
<td>Radiation type</td>
<td>Synchrotron</td>
<td></td>
</tr>
<tr>
<td>μ (mm⁻¹)</td>
<td>1.99</td>
<td></td>
</tr>
<tr>
<td>Specimen form, colour</td>
<td>Cylinder (particle morphology: thin powder), yellow</td>
<td></td>
</tr>
<tr>
<td>Specimen size (mm)</td>
<td>40.0 × 1.5 × 1.5</td>
<td></td>
</tr>
<tr>
<td>Specimen preparation temperature (K)</td>
<td>298 (1)</td>
<td></td>
</tr>
</tbody>
</table>

Data collection

| Diffractometer        | Inet ID31, ESRF Grenoble, France |
| Data collection method | Specimen mounting: borosilicate glass capillary; mode: transmission; scan method: step |
| 2θ (°)                | 2θ_min = 3.00, 2θ_max = 65.96, increment = 0.003 |

Refinement

| R factors and goodness-of-fit | R(F) = 0.050, R_exp = 0.061, R_exp = 0.025, S = 2.51 |
| Wavelength of incident radiation (Å) | 1.25248 (3) |
| Excluded region(s)           | None |
| Profile function             | Pseudo-voigt |
| No. of parameters            | 293 |
| H-atom treatment            | Constrained |
| (Δ/σ)_{max}                 | 0.07 |

Computer programs used: GSAS (Larson & Von Dreele, 2007), EXPO2004 (Altomare et al., 2004), PLATON (Spek, 1990), DIAMOND 2.1 (Brandenburg, 2001).

which was determined using synchrotron powder diffraction data.

2. Experimental

2.1. Synthesis of cycloheptanespiro-3'(4'H)-6',7',8',9'-tetrahydrocyclohexa[1,4]thiazole-2'(5'H)-thione (I)

Compound (I) was synthesized from cycloheptanone (25 ml, 200 mmol; Aldrich, 99%) dissolved in a solution of NH₄OH 29% v/v (Sigma-Aldrich, ≥ 97%) at a temperature of 273 K. After 10 min Cs₂ (29 ml, 300 mmol), previously purified as described elsewhere (Gordon & Ford, 1972), was added with continuous agitation for 24 h at a temperature of 268 K. The solvent was evaporated under vacuum until a yellow crystalline powder was obtained. Yield of the overall reaction: 12.13 g (23%). The diagram shows the synthetic route of (I). Rectangular microcrystals were obtained by evaporation of the recrystallization solvent (3:1 acetone, Fluka, ≥ 99.5%): water; m.p. 472–473 K. Mass spectroscopy (MS) data using electronic ionization showed P⁺, m/z (I %): C_{15}H_{23}NS_{2}, 281.25 (15%). FT-IR spectra on a KBr pellet (3% p/p) gave the following bands: ν (cm⁻¹) (ν_{as}/ν_{s} asymmetric/symmetric absorption bands, s = strong, m = medium, w = weak, bb = broad) ν(N—H): ν_{as}(C=C) + ν_{s}(C≡N); ν_{as}(C≡C); ν_{as}(C=N) + ν_{s}(C=S); ν_{s}(S—CH₂—); ν_{s}(CSS—): 3428(w), 2924(s), 2850(m), 1544(m), 1516(m), 1390(m), 1251(m).

2.2. Powder data collection

Powder X-ray diffraction data were collected with the high-resolution powder X-ray diffractometer on beamline ID31 at ESRF (Fitch, 2004), selecting X-rays from the white undulator source with wavelength 1.25248 (Å). Small quantities of (I) were lightly ground with a pestle in an agate mortar and introduced into a 1.5 mm diameter borosilicate glass capillary, mounted on the axis of the diffractometer and spun during measurements. Data were collected at room temperature for several hours, normalized against monitor counts and detector efficiencies, and rebinned into steps of 2θ = 0.003°.

3. Results

3.1. Structural solution and refinement

The auto-indexing program DICVOL91 (Boultit & Louër, 1991) indexed the diffraction pattern in a monoclinic cell, with cell parameters a = 13.11563 (4), b = 21.32201 (6), c = 11.75591 (3) Å, and β = 113.9899 (1)° (refined) and figures-of-merit M_{21} = 102.7 (de Wolff, 1968) and F_{21} = 441.2 (0.0016, 29) (Smith & Snyder, 1979). Systematic absences unequivocally assigned the space group as P2₁/c (No. 14). The cell volume suggested that there were two independent molecules of (I) within the asymmetric unit. The extraction of 2021 unique reflections in the 2θ range 3.00–65.96° from the powder diffraction data by the Le Bail method (Le Bail et al., 1988) and the crystalline structure solution by direct methods were carried out using the routines implemented in the program EXPO2004 (Altomare et al., 2004). All 36 non-H atoms from the two independent molecules were found in the best E-map. The model was refined by the Rietveld method (Rietveld, 1969) using the program GSAS (Larson & Von Dreele, 2007). The H atoms were placed in calculated positions with restricted geometries using the HIDIX command of the program SHELXL (Sheldrick, 2008). The peak shapes were modeled using the pseudo-voigt peak-shape function (Thompson et al., 1987), which included the axial divergence correction at low angle (Finger et al., 1994) and the anisotropic...
line-shape broadening model (Stephens, 1999). Background was initially determined manually and then modeled using the Chebyschev polynomial function. In the final stages of the refinement, the diffuse scattering function 1 was used to model the background of the capillary. Weighted soft constraints on bond distances ($^{A_0}$) and angles ($^{^\circ}$) were applied using the average values obtained from related structures found in the Cambridge Structural Database (CSD, Version 5.28, January 2007; Allen, 2002): one hit with the benzothiazine ring, eight hits with the cycloheptenyl ring and two hits with the cycloheptanyl ring. The isotropic displacement coefficients were refined in blocks: one $U_{iso}$ for the non-H atoms of the benzothiazine ring, one $U_{iso}$ for the remaining non-H atoms in the fused heptenyl ring and one $U_{iso}$ for the non-H atoms in the heptanyl spiro ring. Finally, the isotropic displacement coefficients of each of the H atoms were refined as 1.2 times the value of the temperature factor of their riding non-H atom. With this refinement routine, the use of the Marquardt damping factor was not necessary since the refinement was stable and convergence was readily achieved. Finally, to determine if the diffraction data contain systematic errors or if modeling of the peak shape and background was correct, a refinement without a model (Le Bail et al., 1988) was conducted. The refinement produced excellent agreement factors: $R_p = 0.037$, $R_w = 0.042$ and $\chi^2 = 3.014$; therefore, the above problems were ruled out. Table 1 shows experimental details for the data collection, structural solution and the Rietveld refinement.

3.2. Solid-state ab initio calculations

Periodic, solid-state calculations were performed using the Vienna ab initio simulation package VASP (Kresse & Hafner, 1993; Kresse & Furthmuller, 1996). The following execution parameters were used: GGA-PBE PAW potentials (Kresse & Joubert, 1999), electronic convergence at $10^{-5}$ eV, an optional cut-off controlling the accuracy of the calculations set to 400 eV, Davidson-blocked iterative optimization of the wavefunctions in combination with reciprocal space projectors (Davidson, 1983), a $2 \times 1 \times 2$ k-mesh for the reciprocal space integration with a Monkhorst–Pack scheme (Monkhorst & Pack, 1976), and a Methfessel–Paxton smearing with a width of 0.2 eV for energy corrections (Methfessel & Paxton, 1989). Atomic-coordinate-only optimizations of (I) were performed.

Figure 1
Final observed (points), calculated (lines) and difference profiles for the Rietveld refinement for (I): (a) low-angle data; (b) high-angle data.
using the experimental cell parameters and atomic positions obtained from the X-ray powder diffraction Rietveld refinement. The structure was evaluated and compared with the structure obtained from X-ray powder diffraction.

4. Discussion

4.1. Molecular conformation

Fig. 2 shows the atom labeling and molecular conformation of the two independent molecules of (I) in the asymmetric unit. Selected average bond angles and distances of the benzothiazine ring (A in the diagram), the fused cycloalkene and spiro rings (B and C in the diagram) are shown in Table 2, which are compared with those obtained from VASP calculations and with the related compound 5,6,7,8-tetrahydro-4H-3,1-benzothiazine-2(1H)-spirocyclohexane-4-thione [Casti-
rings are more flexible than smaller cyclic rings and, therefore, by the rings in each of the molecules. Heptenyl and heptanyl which arises from the slightly different conformations adopted (only present in one of the molecules in the asymmetric unit), weak intramolecular non-classical C—H bonds, which play the role of keeping the extended chains together. Finally, there is a weak intramolecular non-classical C—H · · · N hydrogen bond (only present in one of the molecules in the asymmetric unit), which arises from the slightly different conformations adopted by the rings in each of the molecules. Heptenyl and heptanyl rings are more flexible than smaller cyclic rings and, therefore, chair, while C11/C26, C10/C25, C15/C30 and C14/C29 are coplanar (with a maximum deviation of 0.17 Å), representing the seat of the chair.

4.2. Hydrogen bonds

Hydrogen bonds are summarized in Table 3. Fig. 3 shows the two independent molecules (black and white) linked by N—H · · · S hydrogen bonds with a donor–acceptor average distance of 3.44 Å, forming extended chains along the [50,10] direction. These chains can be represented by two graph symbols according to the acceptor atom: \([C_2(12)]_{51}\) and \([C_2(12)]_{53}\). Moreover, the combination of the 2,1 screw axis and the \(c\)-glide plane build up the entire crystal, as shown in Fig. 4. In addition to the classical hydrogen bonds, there are several weak non-classical C—H · · · S hydrogen bonds, which play the role of keeping the extended chains together. Finally, there is a weak intramolecular non-classical C—H · · · N hydrogen bond (only present in one of the molecules in the asymmetric unit), which arises from the slightly different conformations adopted by the rings in each of the molecules. Heptenyl and heptanyl rings are more flexible than smaller cyclic rings and, therefore, positional disorder phenomena and structures with \(Z' > 1\) have been reported in the literature [de Costa et al., 1994 (SUMMUI); Ohlbach et al., 1996 (NADWUK); Schulze et al., 2002 (AFUPAS); Albov et al., 2004 (ATUYAP); Amitina et al., 2004 (DANGOP); Ianelli et al., 1995 (ZAYJUE); Zhang et al., 1993 (HABROR)].

4.3. Summary

Using synchrotron powder diffraction data the structure of the compound cycloheptanespiro-3(4'H)-6,7,8,9-tetrahydrocyclohexa[b][1,4]thiazole-2(5'H)-thione (I) was determined. The structural solution was attained using direct methods [EXPO2004 (Altomare et al., 2004)], and located the two independent molecules in the asymmetric unit. The quality of the crystalline sample and the excellent diffraction data attainable at beamline ID31, ESRF, allowed a detailed structural characterization of the compound. VASP theoretical calculations confirmed the correct characterization of the structure.

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References

research papers


