Synthesis, and spectroscopic, structural and thermal characterization of p-hydroxybenzenesulfonamide

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Introduction
Sulfonamides are an important class of biologically active compounds formed by at least five different kinds of pharmacological agents. Antibacterial sulfonamides, studied for over 45 years, continue to play an important role in chemotherapy. Those that inhibit the action of carbonic anhydrase have many applications, such as diuretic drugs, antiglaucoma, antiepileptic, or in the treatment of some forms of diabetes (Supuran et al., 2001). Recently, a lot of sulfonamides with important antitumor activity have been found.

Moreover, it should be emphasized further the interest that show sulfonamide complexes with transition metals because of the protective action exerted on cells against oxidative damages caused by oxygen radicals (González-Alvarez et al., 2004).

Some simple aromatic sulfonamides were shown to be inhibitors of carbonic anhydrase II in the nanomolar range, thus demonstrating the importance of these compounds. In the present work the synthesis of p-hydroxybenzenesulfonamide and the study of its spectroscopic and structural properties are shown in view of its subsequent biological assessment and preparation of metal complexes.

Methodology
The synthesis of the substance was carried out by diazotation of sulfanylamide, and the crude product obtained was then recrystallized in ethanol-water until constant melting. The yield of the reaction was 68%. X-ray diffraction measures were carried out at a temperature of 293(2) K using a CAD-4 diffractometer equipped with a rotating Cu anode. For data collection and cell refinement CAD-4 (CAD4 Express Software, 1994) and XCAD-4 (Harm and Wocadlo, 1995) programs were used, respectively. The structure was solved using direct methods with SHELXS-97 program (Sheldrick, 1997a). The model was refined using the least squares method on the F2 basis with SHELXL-97 program (Sheldrick, 1997b). Hydrogen atoms were located from a synthesis of the difference Fourier map, and refined with hydrogen atoms mounted on the bound atom. For structure analysis different programs were used, accounting for software package contained in WinGX (Farrugia, 1997-2003). Differential thermal analysis (DTA), thermogravimetric (TG) and differential thermogravimetric (DTG) analyses were performed in a Shimadzu TGA-50 and DTA-50H equipment at a heating rate of 5°C/min and a flow rate of 50 ml/min under oxygen atmosphere.

FT-IR spectra were recorded in an EQUINOX equipment and Raman spectra were measured with the FRA 106 accessory of the FT-IR Bruker IFS66 equipment, using the excitation line of 1064 nm of Nd:YAG laser.

1H and 13C Nuclear magnetic resonance spectra were obtained from a solution of the compound in CD3CN in a Varian Mercury 200 equipment.

Results
The substance crystallizes in the monoclinic crystal system, P21/a spacial Group. The parameters of the cell are a = 7.5813(19), b = 13.1857(15) and c = 7.994(2) Å, β = 110.22(2)° and Z=4.

Benzene ring has a flat conformation. The C-C distances and C-C-C ring angles do not deviate significantly with respect to the average distances and angles 1.383(5) Å and 120.0(3)°, respectively.
Sulfonamide group shows a distorted tetrahedral conformation with S atom contained in the ring plane. The O-S-O angle = 118.3 (1)° shows the highest deviation from the tetrahedral ideal value equal to 109°. This can be rationalized taking into account that the oxygens of the SO₂ group participate in N-H···O- y O-H···O-type hydrogen bridge interactions, with hydrogens of the NH₂ and OH groups associated to molecules related with an inversion center a = (-x, -y, -z), a net translation b = (-1+x, y, -1+z), and sliding planes parallel to the a axis c = (-1/2+x, 1/2-y, z) and d = (-1/2+x, 1/2-y, -1+z) (see Fig. included in Table 1).

Table 1. Bond distances [Å] and angles [°] of p-hydroxybenzensulfonamide.

<table>
<thead>
<tr>
<th>Bond distances [Å]</th>
<th>Bond angles [°]</th>
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<tbody>
<tr>
<td>N(1)-S(1)</td>
<td>1.610(3)</td>
</tr>
<tr>
<td>S(1)-O(2)</td>
<td>1.435(3)</td>
</tr>
<tr>
<td>S(1)-O(1)</td>
<td>1.438(3)</td>
</tr>
<tr>
<td>S(1)-C(1)</td>
<td>1.754(3)</td>
</tr>
<tr>
<td>O(3)-C(4)</td>
<td>1.345(4)</td>
</tr>
<tr>
<td>C(6)-C(5)</td>
<td>1.378(5)</td>
</tr>
<tr>
<td>C(6)-C(1)</td>
<td>1.394(4)</td>
</tr>
<tr>
<td>C(1)-C(2)</td>
<td>1.380(5)</td>
</tr>
<tr>
<td>C(4)-C(3)</td>
<td>1.381(5)</td>
</tr>
<tr>
<td>C(4)-C(5)</td>
<td>1.390(5)</td>
</tr>
<tr>
<td>C(2)-C(3)</td>
<td>1.375(5)</td>
</tr>
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</table>

Thermal analysis of the substance is shown in Fig. 1. In Fig. 1, an endothermal peak in ATD can be observed at 174.7 °C without mass loss, accounting for the melting point of the substance. The decomposition of the sulfonamide group occurs by an exothermal process at 318 °C, and total decomposition of the substance occurs at around 600 °C.
FT-IR and Raman spectra at room temperature of the substance are shown in Fig. 2, while the observed wave numbers of the most representative groups are displayed in Table 1.

![FT-IR and Raman spectra of p-hydroxybenzensulfonamide.](image)

It is worth mentioning that the tentative assignation of the vibrational modes was performed in comparison with related molecules (Bult and Klase, 1978; Pedregosa et al., 1995; Kanagaraj and Rao, 1992; Macias et al., 2003), and the assistance of semiempiric calculations implemented with MP3 method of the HyperChem package (HyperChem 5, 1996).

**Table 1:** Wave numbers of the representative groups of p-hydroxybenzensulfonamide in cm\(^{-1}\) [a].

<table>
<thead>
<tr>
<th>Raman</th>
<th>FT-IR</th>
<th>Tentative assignations</th>
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<tbody>
<tr>
<td>3479 s</td>
<td>vO-H</td>
<td></td>
</tr>
<tr>
<td>3330 s</td>
<td>v as N-H</td>
<td></td>
</tr>
<tr>
<td>3228 w</td>
<td>3216 s</td>
<td>vs N-H</td>
</tr>
<tr>
<td>1587 m</td>
<td>1588 s</td>
<td>δ NH(_2)</td>
</tr>
<tr>
<td>1321 s</td>
<td>v as SO(_2)</td>
<td></td>
</tr>
<tr>
<td>1143 s</td>
<td>1155 s</td>
<td>vs SO(_2)</td>
</tr>
<tr>
<td>1089 m</td>
<td>1095 s</td>
<td>Rocking NH(_2)</td>
</tr>
<tr>
<td>962 w</td>
<td>v S-N</td>
<td></td>
</tr>
</tbody>
</table>

\(s = \text{strong; } m = \text{medium; } w = \text{weak.}\)

In the \(^1\text{H-NMR}\) spectrum of \(p\)-hydroxybenzensulfonamide the occurrence of a wide singlet assigned to hydrogens of the sulfonamide group can be observed, indicating that they are easily interchangeable.
Conclusions
1. Structural and thermal spectroscopic properties of \( p \)-hydroxybenzensulfonamide were determined for the first time.
2. Geometric parameters obtained from the crystallographic structure are consistent with data from other reported sulfonamides.
3. The crystallographic and spectroscopic information about \( p \)-hydroxybenzensulfonamide will be useful for identifying potential coordination sites to the metal in the series of complexes that are to be studied.

Note: This study was presented at the "XXVI Congreso Argentino de Química", San Luis, Argentina, 2006

References