N-(2-Nitrobenzenesulfonyl)-L-alanine methyl ester

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Published
2005

Journal Title
Acta crystallographica. Section E, Structure reports online

DOI
https://doi.org/10.1107/S1600536805014315

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N-(2-Nitrobenzenesulfonyl)-l-alanine methyl ester

The structure of the title compound, C_{10}H_{12}N_{2}O_{6}S, has been determined as part of an ongoing investigation into the preparation of substituted amino acids suitable for the generation of combinatorial libraries. The molecular conformation is stabilized by intra- and intermolecular N—H···O and C—H···O hydrogen-bonding interactions.

Comment

In a previous paper, we reported the structure of N-(2-nitrobenzenesulfonyl)glycine methyl ester (Bornaghi et al., 2005). This work is part of our ongoing investigation into the development of N-substituted amino acids as building blocks for dynamic combinatorial chemistry (Lehn & Eliseev, 2001) and subsequent biological screening. Our synthetic approach utilizes concomitant protection and activation of the amino acid nitrogen with the 2-nitrobenzene sulfonyl (oNBS) group. The oNBS group is introduced with the premise that the electron-withdrawing nature of this group will increase the acidity of the NH proton, ensuring the amide becomes susceptible for further high-yielding N-substituted products.

In this paper, we report the structure of the l-alanine methyl ester compound, oNBS–Ala–OMe, (I), which crystallizes in space group P2_1 with one discrete molecule in the asymmetric unit (Fig. 1). The bond lengths and angles for (I) (Table 1) are in accord with data for structures of related oNBS protected amino acid compounds (Bornaghi et al., 2005; Iacapino et al., 1999; Hammarström et al., 2000; Giraldés et al., 2001). In the structure, the S—N bond lies approximately perpendicular to the plane of the benzene ring, with a torsion angle N1—S1—C1—C2 of 80.3 (3)°. The methyl ester group is planar and folds back over the plane of the benzene ring such that atom O5 is situated directly above atom C1, with C1···O5 = 3.212 (5) Å. The NO2 group is rotated out of the plane of the benzene ring, with a torsion angle O1—N2—C2—C1 of −43.3 (6)°. The nitro atom O2 forms weak intramolecular N—H···O hydrogen bonds with the H atom on N1 (Table 2). N1 is also involved in intermolecular N—H···O hydrogen bonding to the sulfonyl atom O4 to form a polymeric chain along the c
axis (Table 2 and Fig. 2). The crystal structure is stabilized also by a number of intra- and intermolecular C—H···O hydrogen-bond interactions (Table 2).

**Experimental**

Triethylamine (5.06 g, 0.05 mol) was added dropwise to a solution of l-alanine methyl ester hydrochloride (2 g, 0.014 mol) and 2-nitrobenzene sulfonyl chloride (3.5 g, 0.016 mol) in anhydrous dichloromethane (DCM, 50 ml). The reaction mixture was stirred at room temperature for 18 h, diluted with DCM (50 ml) and then washed with 2 M HCl (2 × 100 ml), 1 M NaHCO₃ (1 × 100 ml), saturated brine (1 × 100 ml) and dried over MgSO₄. The volatiles were removed under reduced pressure to give a yellow residue. The title compound was obtained in 70.8% yield following recrystallization from a mixture of ethyl acetate and hexane (m.p. 359 K). ¹H NMR (CDCl₃, 200 MHz): δ 1.48 (d, 3H, J = 6.6 Hz, CH₃), 3.52 (s, 3H, OCH₃), 4.25 (m, 1H, αCH), 5.92 (br. s, 1H, NH), 7.76 (m, 1H, ArH), 7.92 (m, 1H, ArH), 8.07 (m, 1H, ArH). MS (LRMSES): m/z 289 [M + H]⁺, 311 [M + Na]⁺.

**Crystal data**

C₇H₁₂N₂O₆S

\( M_r = 288.29 \)

Monoclinic, \( P_2_1 \)

\( a = 8.845 (3) \) Å

\( b = 13.335 (5) \) Å

\( c = 5.5203 (10) \) Å

\( \beta = 95.10 (2) ^\circ \)

\( V = 648.5 (3) \) Å³

\( Z = 2 \)

**Data collection**

Rigaku AFC-7R diffractometer

\( \omega-2\theta \) scans

1708 measured reflections

1608 independent reflections

1252 reflections with \( I > 2\sigma(I) \)

\( R_{int} = 0.033 \)

\( \theta_{max} = 27.5^\circ \)

\( D_x = 1.476 \) Mg m⁻³

Mo Kα radiation

Cell parameters from 25 reflections

\( \beta = 12.8-17.0^\circ \)

\( \mu = 0.27 \) mm⁻¹

\( T = 298 \) K

Prism, colorless

0.40 × 0.20 × 0.15 mm

**Refinement**

Refinement on \( F^2 \)

\( R[F^2 > 2\sigma(F^2)] = 0.036 \)

\( wR(F^2) = 0.106 \)

\( S = 1.02 \)

1668 reflections

173 parameters

H-atom parameters constrained

\( w = 1/[\sigma(F^2) + (0.0631P)^2] \)

where \( P = (F^2 + 2F_O^2)/3 \)

\( \Delta/\sigma(\Delta)_{max} = 0.018 \)

\( \Delta p_{max} = 0.20 e \) Å⁻³

\( \Delta p_{min} = -0.21 e \) Å⁻³

Extinction correction: SHELXL07

Extinction coefficient: 0.041 (7)

Absolute structure: Flack (1983)

Flack parameter = 0.24 (12)

**Table 1**

Selected geometric parameters (Å, °).

<table>
<thead>
<tr>
<th></th>
<th>D—H—A</th>
<th>D—H</th>
<th>H···A</th>
<th>D—A</th>
<th>D—H—A</th>
</tr>
</thead>
<tbody>
<tr>
<td>S1—O3</td>
<td>1.246 (3)</td>
<td>0.85</td>
<td>0.94</td>
<td>1.121 (5)</td>
<td>0.95</td>
</tr>
<tr>
<td>S1—O4</td>
<td>1.433 (3)</td>
<td>0.65</td>
<td>0.74</td>
<td>1.322 (5)</td>
<td>0.95</td>
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<tr>
<td>S1—N1</td>
<td>1.613 (3)</td>
<td>0.85</td>
<td>0.94</td>
<td>1.455 (6)</td>
<td>0.95</td>
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<tr>
<td>S1—Cl</td>
<td>1.776 (3)</td>
<td>0.94</td>
<td>1.03</td>
<td>1.468 (5)</td>
<td>0.95</td>
</tr>
<tr>
<td>O1—N2</td>
<td>1.212 (5)</td>
<td>0.95</td>
<td>1.04</td>
<td>1.485 (5)</td>
<td>0.95</td>
</tr>
<tr>
<td>O2—N2</td>
<td>1.200 (5)</td>
<td>0.95</td>
<td>1.04</td>
<td>1.485 (5)</td>
<td>0.95</td>
</tr>
<tr>
<td>O3—S1—O4</td>
<td>1.109 (18)</td>
<td>0.56</td>
<td>0.65</td>
<td>1.212 (4)</td>
<td>0.95</td>
</tr>
<tr>
<td>O3—S1—N1</td>
<td>1.085 (17)</td>
<td>0.56</td>
<td>0.65</td>
<td>1.212 (3)</td>
<td>0.95</td>
</tr>
<tr>
<td>O3—S1—C1</td>
<td>1.059 (15)</td>
<td>0.56</td>
<td>0.65</td>
<td>1.212 (3)</td>
<td>0.95</td>
</tr>
<tr>
<td>N1—S1—C1</td>
<td>1.086 (15)</td>
<td>0.56</td>
<td>0.65</td>
<td>1.212 (3)</td>
<td>0.95</td>
</tr>
<tr>
<td>C8—O6—C9</td>
<td>1.162 (2)</td>
<td>0.56</td>
<td>0.65</td>
<td>1.212 (3)</td>
<td>0.95</td>
</tr>
<tr>
<td>S1—N1—C7</td>
<td>1.202 (19)</td>
<td>0.56</td>
<td>0.65</td>
<td>1.212 (3)</td>
<td>0.95</td>
</tr>
<tr>
<td>O1—N2—O2</td>
<td>1.249 (4)</td>
<td>0.56</td>
<td>0.65</td>
<td>1.212 (3)</td>
<td>0.95</td>
</tr>
<tr>
<td>O1—N2—C2</td>
<td>1.163 (3)</td>
<td>0.56</td>
<td>0.65</td>
<td>1.212 (3)</td>
<td>0.95</td>
</tr>
</tbody>
</table>

**Table 2**

Hydrogen-bonding geometry (Å, °).

<table>
<thead>
<tr>
<th></th>
<th>D—H—A</th>
<th>D—H</th>
<th>H···A</th>
<th>D—A</th>
<th>D—H—A</th>
</tr>
</thead>
<tbody>
<tr>
<td>N1—H1···O1</td>
<td>0.86</td>
<td>2.39</td>
<td>2.999 (5)</td>
<td>128</td>
<td></td>
</tr>
<tr>
<td>N1—H1···O4</td>
<td>0.86</td>
<td>2.39</td>
<td>2.999 (5)</td>
<td>128</td>
<td></td>
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<tr>
<td>C3—H3···O3</td>
<td>0.95</td>
<td>2.44</td>
<td>3.376 (6)</td>
<td>146</td>
<td></td>
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<tr>
<td>C6—H6···O4</td>
<td>0.95</td>
<td>2.40</td>
<td>3.280 (5)</td>
<td>107</td>
<td></td>
</tr>
<tr>
<td>C6—H6···O5</td>
<td>0.95</td>
<td>2.53</td>
<td>3.339 (5)</td>
<td>144</td>
<td></td>
</tr>
<tr>
<td>C7—H7···O4</td>
<td>0.95</td>
<td>2.49</td>
<td>3.263 (4)</td>
<td>103</td>
<td></td>
</tr>
<tr>
<td>C9—H9···O5</td>
<td>0.95</td>
<td>2.29</td>
<td>2.668 (7)</td>
<td>103</td>
<td></td>
</tr>
</tbody>
</table>

Symmetry codes: (i) x, y, z; (ii) −x, ½+y, −z; (iii) x, y, 1−z.
C—H H atoms were constrained as riding atoms, with C—H = 0.93–0.96 Å and $U_{iso}(H) = 1.2U_{eq}(C)$. The N—H H atom was located in a difference map and constrained as a riding atom with N—H = 0.86 Å and $U_{iso}(H) = 1.2U_{eq}(N)$. The absolute configuration, determined with low precision from anomalous scattering effects, is in accord with the known configuration of the starting material.

Data collection and cell refinement: MSC/AFC-7 Diffractometer Control Software for Windows (Molecular Structure Corporation, 1999); data reduction: TEXSAN for Windows (Molecular Structure Corporation, 2001); program(s) used to solve structure: TEXSAN for Windows; program(s) used to refine structure: TEXSAN for Windows and SHELXL97 (Sheldrick, 1997); molecular graphics: ORTEP-3 (Farrugia, 1997); software used to prepare material for publication: TEXSAN for Windows and PLATON (Spek, 2003).

We acknowledge financial support of this work by Griffith University and the Eskitis Institute of Cell and Molecular Therapies.

References