Structure of ethyl-[(2-amino-4-phenyl)-5-thiazoyl]acetate

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The crystal structure of ethyl-[(2-amino-4-phenyl)-5-thiazoyl] acetate has been determined by X-ray methods. The compound crystallizes under monoclinic system (space group P2₁/c) with cell parameters: a = 7.586(5) Å, b = 15.475(5) Å, c = 11.543(2) Å and β = 104.56(1)°. The structure has been solved by direct method and refined by full matrix least squares method to final R = 0.052 using 2137 reflections. The molecule on the whole is non-planar and the crystal structure is stabilized significantly by intra-and inter-molecular hydrogen bonds.

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Thiazole-5-acetic acid derivatives have been a useful class of non-steroidal anti-inflammatory agents. The aryl groups at C2 and C5 positions in thiazoles have been of vital importance in minimizing the toxic effects of many anti-arthritis drugs. 2-amino thiazolidine-5-acetic acids have served as model compounds to study the S....O interactions in solid state. In view of the above, the title compound which is known for its anti-microbial and anti-inflammatory activity has been investigated.

Experimental Section

Colourless, needle like single crystals suitable for X-ray diffraction were grown from slow evaporation technique using ethanol. The X-ray intensity data were collected on Enraf-Nonius CAD-4 diffractometer with CuKα radiation. The cell parameters were refined using 25 centered reflections in the range 5 to 70°. Of the 5246 reflections (h, -9 to 9, k, -16 to 18, l, -14 to 14) measured, 2369 were unique and 2137 were observed with Fo>4σ(Fo). The systematic absences h0l for l odd and 0k0 for k odd characterize the space group P2₁/c. The data were corrected for Lorentz and Polarization effects. No absorption correction was applied. The structure was solved by direct methods and refined by full-matrix least-squares method using SHELXL-97 program. Non H-atoms were refined with anisotropic thermal parameters. Hydrogen atoms have been geometrically fixed and refined for isotropic thermal parameters. A sigma weighting scheme was applied and the refinement was continued till final value of R = 0.052. The crystallographic data are summarized in Table I.

Results and Discussion

The fractional co-ordinates and equivalent isotropic temperature factors for non-hydrogen atoms are given in Table II. The bond lengths and bond angles are given in Table III. The selected torsion angles are shown in Table IV. An ORTEP plot of the molecule with 30% probability thermal ellipsoids is shown in Figure 1. The molecule adopts a non-planar arrangement. The phenyl ring at C4 is twisted by an angle of 44.7(1)° with respect to thiazole ring whereas the side chain at C5 is oriented at an angle of 59.8(1)°. These two groups at C4 and C5 are almost eclipsed
with dihedral angle of $15.4(2)^\circ$. The dihedral angles formed between thiazolyl-phenyl ring, thiazolyl-acetate group and phenyl ring-acetate group are shown in Table V. The ring system bonded to the 4-position of thiazole ring are usually twisted by a dihedral angle less than $20^\circ$. But in the present study a twist of $44.7(1)^\circ$ is observed between phenyl and thiazole rings and this large twist is required to prevent the steric interference with $\mathrm{CH}_2\mathrm{COOC}_2\mathrm{H}_5$ group at C5[ C7 ... C12 = 3.342(3)Å, H7 ... H12B = 2.59(5)Å]. This hindrance is also reflected in the
large values of the exocyclic angles C4-C5-C12 = 129.8(2)° and C5-C4-C6 = 126.8(2)° respectively.

The average bond lengths and bond angles of the phenyl ring are normal. The C-H bond lengths are in the range of 0.87-1.01 Å, the observed C-O bond lengths, C13-O2 = 1.495(3) Å and C13-O1 = 1.320(3) Å are comparable with C-O bond lengths of 2-phenyl-[(p-chlorophenyl)-5-thiazoly]acetic acid. as well as relatively high temperature factors of two oxygen atoms may give rise to potential disorder of ester group.10

The bond lengths C2-S1 = 1.733(2) Å and C5-S1 = 1.736(2) Å show appreciable double bond character. The effect of conjugation of the amino group and phenyl group with thiazolyl ring is shown by the bond order C2-N2 = 1.347(3) Å and C4-C6 = 1.484(3) Å. The bond length C4-C6 is almost comparable with 2-phenyl-[(p-chlorophenyl)-5-thiazolyl]acetic acid. The C-N bond distances C2-N2 = 1.347(3) Å, C4-N1 = 1.386(3) Å (single bond) and C2-N1 = 1.306(3) Å (double bond) agree with standard values of C-N single and double bonds.

The confirmation of an CH3COOC2H5 group can be described by the torsion angles S1-C5-C12-C13 = -85.4(2)° and C5-C12-C13-O1 = 80.9(2)°. The torsion angle C13-O1-C14-C15 = 174.7(3)° indicates anti-peri planar relation between the carbonyl carbon and the methyl group. The torsion angle C5-C12-C13-O2 = -99.0(3)° depicts the idea that the two oxygen atoms are lying on the opposite sides. The ester group is in S-cis arrangement across C13-O1 bond which is

Figure 1 - ORTEP plot of the molecule with 30% probability ellipsoids

Figure 2 — Packing diagram of the molecule viewed along a-axis
Table VI — Hydrogen-bonding geometry (Å, °)

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<th>D-H</th>
<th>A</th>
<th>D-H</th>
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<td>C7-H7........O1</td>
<td>1.013(3)</td>
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<td>1.992(3)</td>
<td>2.967(3)</td>
<td>177.58</td>
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<td></td>
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</tbody>
</table>

(i) x,y,z (ii) -x,y-1/2,z+3/2 (iii) -x-1,-y+1,-z+1

indicated by the torsion angle C14-O1-C13-O2=0.0(4)° and C14 is eclipsed with O2.

Molecular Packing

The molecular packing of the molecule along a-axis is shown in Figure 2. The structure appears to be stabilized significantly by the intra- and intermolecular C-H.....O, N-H.....O and N-H.....N hydrogen bonds and intra and intermolecular C-H.....N, C-H.....O and C-H.....N strong and weak interactions. The hydrogen bondings are given in Table VI.

One of the amino hydrogen is inter-molecularly hydrogen bonded with ring nitrogen N1 of the thiazole ring. The carbonyl oxygen of an ester(O2) is in close spatial proximity with the hydrogen of carbon C14 of the methylene carbon 2.49(4)Å. The hydrogen H15C of the methyl group C15 shows the interaction with N2[H15C.....N2 = 2.941(5)Å].

Presence of S.....O interaction in 2-amino-4-thiazolidinone-5-acetic acid has been reported. However, during the present study the distance between O1 and thiazole sulphur S1 atom is 3.492(2)Å and the angle C5-S1.....O1 is 88°. These values suggest that a fairly weak S.....O interaction, may be due to the phenyl ring at C4 which also accounts for the partial conjugation of the heterocyclic ring.

References

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