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Growth and characterization of 2-(meta-methoxyphenyl) thiazolidine

K. S. RAJU, S. ESWARAMOORTHY
Department of Crystallography and Biophysics, University of Madras, Guindy Campus, Madras – 600 025, India

R. UMARANI, P. RAJALINGAM
Polymer Division, Central Leather Research Institute, Adyar, Madras – 600 020, India

2-(meta-methoxyphenyl) thiazolidine (hereafter called 2mmpT) has medicinal importance, as the five-membered thiazolidine ring happens to be the active part of penicillin. This material has been synthesized and crystallized. The crystals are needle-shaped and of dimensions $0.3 \times 0.5 \times 1.5\,mm^3$ using X-ray diffraction technique, oscillation and Weissenberg patterns of the sample are taken. It is shown that the crystal is monoclinic and the unit cell parameters are found to be $a = 1.007(5)$ nm, $b = 0.545(3)$ nm, $c = 1.720(8)$ nm and $\beta = 71.3(3)°$. The space group is $P2_1/c$.

From IR absorption spectrum of the sample, the characteristic peak pertaining to NH at $3250\,cm^{-1}$ has been identified. The proton magnetic resonance (PMR) spectrum of the sample unambiguously supports the proposed structure of the compound. It has been confirmed that thiazolidine complex in the present case is a cyclic and not a linear one. The implications are discussed.

1. Introduction

The medicinal importance of synthetic materials has initiated a collaboration between organic chemists, pharmacologists and solid state physicists. This has lead to synthesis and the investigation of characterizational aspects to find the crystallinity, conformity of the functional groups and thereby the chemical aspects. Thiazolidine is one such material belonging to the important group of heterocyclic compounds. It is a saturated molecule with sulphur and nitrogen atoms in positions 1 and 3 respectively (Fig. 1). Thiazolidines only appeared in literature in 1937. The importance of thiazolidine lies in its moiety being present in the penicillin molecular structure (Fig. 2). The discovery of penicillin from the fungi *penicillum notatum* and its remarkable and valuable biological activity and the urge to accomplish its synthesis initiated intensive research in the field of thiazolidines.

Thiazolidine derivatives have diverse biological activities such as bactericidal, pesticidal, fungicidal, insecticidal, tuberculostatic, anti-inflammatory and anti-oxidant. Thiazolidine derivatives are also potential anti-radiative agents [1, 2]. The conformations of cystamine and thiazolidine are reported in aqueous solution using NMR spectroscopy [3]. Thiazolidines act as anti-oxidants for bone fats and sunflower seed oil [4]. Thiazolidines behave as the active functional groups incorporated in flavour enhancing activities [5]. Thiazolidine complexes are used as aroma additives for food or tobacco; 5 p p m producing aroma taste evaluation of meat nut coffee. The presence of N–C–S linkages has been postulated to account for the antifungal activity [6]. Thiazolidine derivatives are, having hypoglycemic action [7], effective hypertensive agents [8], as well as for applications for the treatment of anginopectories, arrhythmia and thrombosis [9].

It is thought worthwhile to crystallize and thereafter to characterize a 2mmpT sample employing (a) X-ray diffraction studies, (b) density measurements, (c) infrared absorption studies and (d) proton magnetic resonance studies.

2. Experimental and observations

2.1. Preparation of the sample

A mixture of β-mercaptoethylamine hydrochloride (10 g, 0.09 mol), and m-methoxybenzoldehyde (20 g, 0.15 mol) in absolute ethanol (100 ml) is heated in a steam-bath for 10 min. It is cooled, concentrated and the solution is made alkaline using potassium carbonate solution. The free base has been filtered and the pale yellow shiny powder recrystallized using petroleum ether. The melting point is found to be 62° C (with 73% yield). The 2mmpT compound is dissolved in ethanol and on slow evaporation tiny needle-shaped crystals are formed of the order of $0.3 \times 0.5 \times 1.5\,mm^3$ in size.

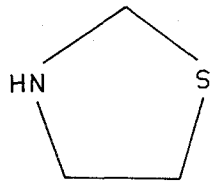

Figure 1 Thiazolidine ring.

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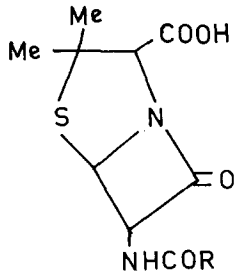

Figure 2 Penicillin molecular structure.

2.2. X-ray diffraction studies

A good single crystal is chosen to carry out X-ray studies. The crystal is put into a Lindaman's tube, to avoid the crystal being affected by adhesives, and mounted on a goniometer head. With the needle axis as spindle axis, oscillation and Weissenberg patterns are recorded (Figs 3 and 4). The cell parameters *a*, *b* and *c* are measured and the symmetry conditions studied. The oscillation pattern reveals $m\times$ symmetry. This suggests that the crystal belongs to monoclinic or higher symmetry system. As the Weissenberg pattern reveals no symmetry conditions and the angle between the two axes is measured as 71° it is confirmed that the crystal is monoclinic.

In order to assign the space group another mounting is made along the *a* axis. The systematic absences are studied and recorded in Table I. From the systematic absences and symmetry conditions the space group is fixed as $P2_1/c$. Different 2θ values for different $h01$ and $0k1$ values are measured and the cell parameters are refined using the programme CELN [10].

2.3. Density measurements

The density of a specimen, such as 2mmpT in the present case, is usually determined by the flotation method using two solvents, one of high density and the other of low density. This method is not reliable owing to the solubility of the sample in most solvents. The experimental density of the sample in the present work is measured by liquid displacement with petroleum spirit as the medium. Weights of ten samples in air and their loss of weight on complete immersion in the liquid have been computed

$$\varrho_{exp} = \frac{\text{Weight of the sample in air}}{\text{Loss of weight of the sample under liquid}} \times \text{Density of the Liquid}$$

The average value of the experimental density is determined as $1.43\,g\,cm^{-3}$, which agrees reasonably well with the density calculated from X-ray diffraction data ($\varrho_{cal} = 1.45\,g\,cm^{-3}$).

TABLE I Crystal data of 2mmpT

Molecular formula	$C_{10}H_{13}NSO$
System	Monoclinic
Cell constants	
a	1.007(5) nm
b	0.545(3) nm
c	1.720(8) nm
β	71.3 (3)°
Systematic Absences	
$0k0$: k odd absent	21: screw along *b*
$h0l$: l odd absent }	*c* glide
$00l$: l odd absent }	perpendicular to *b*
Space Group	$P2_1/c$
Z	4
V	$0.89413\,nm^{-3}$
ϱ_{exp}	$1.43\,g\,cm^{-3}$
ϱ_{cal}	$1.45\,g\,cm^{-3}$

2.4. Infrared absorption studies

The infrared absorption spectrum of the sample (Fig. 5) is taken in KBr matrix, recorded using SHIMEDZU-IR, 408, Japan. The characteristic peaks pertaining to the chemical groups associated with the sample have been identified [11, 12] and recorded in Table II.

The absorption peaks relating to NCS, NH and CH_2 fully satisfy the chemical groups representing five-membered thiazolidine moiety. The strong peaks relating to the CH and C=C groups correspond quite

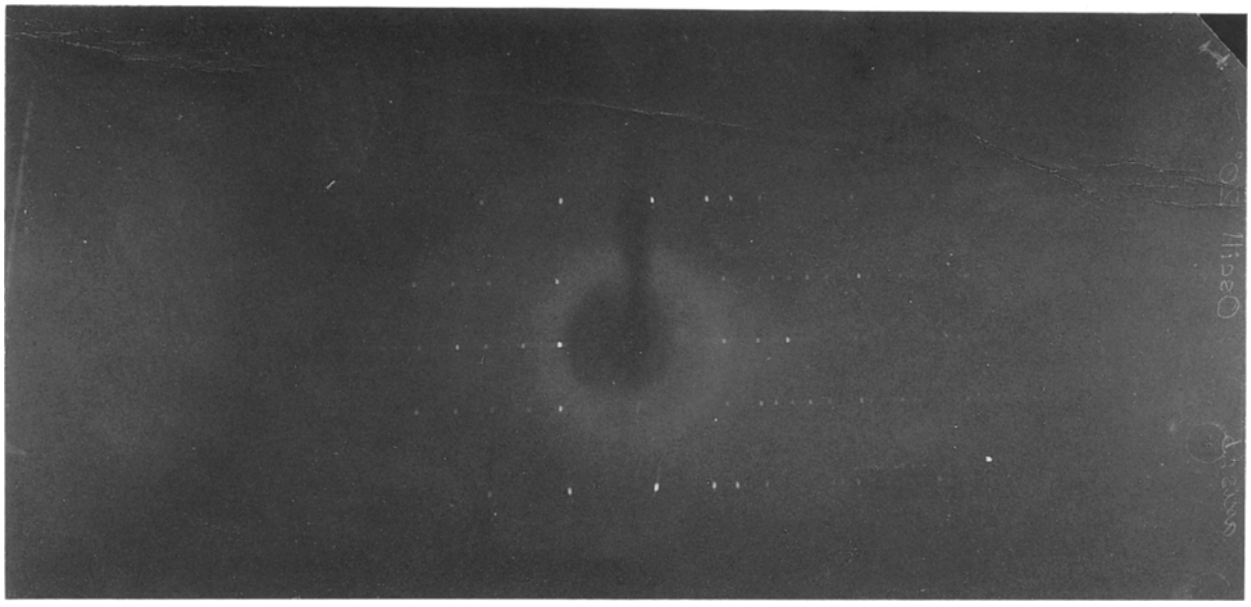

Figure 3 Oscillation pattern of 2mmpT sample.

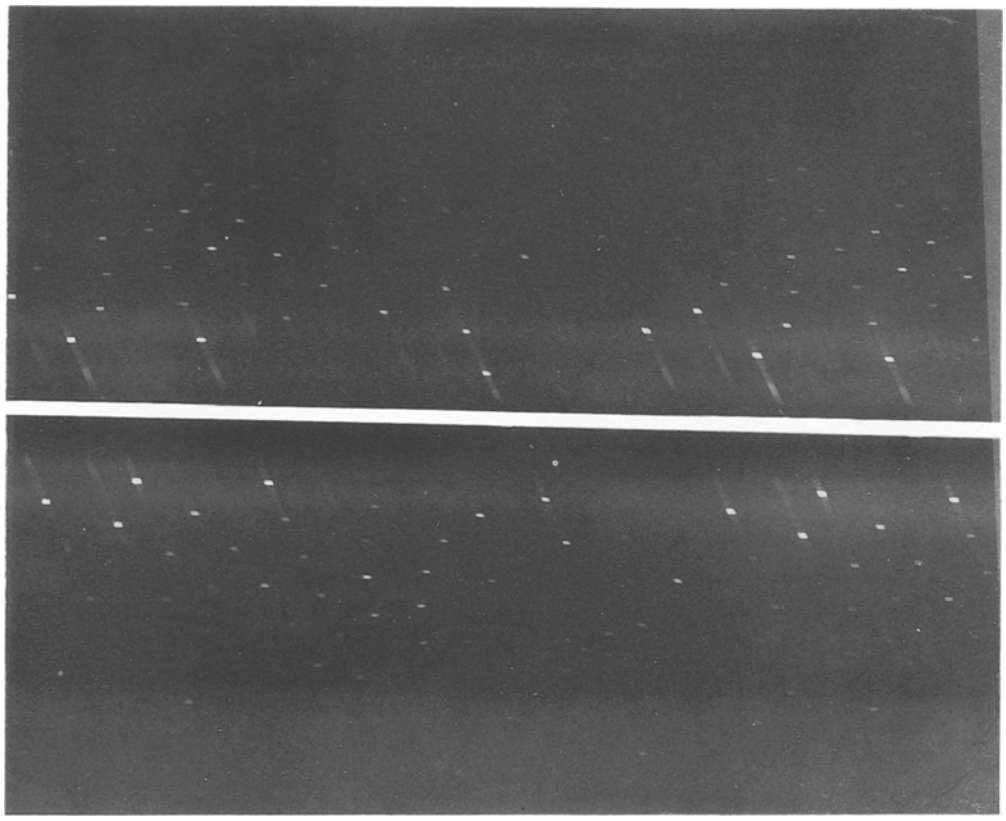

Figure 4 Weissenberg pattern of 2mmpT sample.

well to the presence of phenyl ring. There is no individual peak relating to the $-OCH_3$ group. This may be due to the fact that the absorption peak at $1450\,cm^{-1}$ relating to the CH_2 group may be the contribution of not only the two CH_2 groups of thiazolidine but also of a CH_2 group forming a part of the methoxyl group $-OCH_3$ attached to the phenyl ring.

It is worth mentioning that NH is the only functional group in the IR spectrum and the other groups come under the "fingerprint region" less than $1600\,cm^{-1}$. In order to further establish the chemical groups of 2mmpT, proton magnetic resonance study was undertaken.

2.5. Proton magnetic resonance (PMR) studies

The PMR spectrum of 2mmpT is recorded using VARIAN EM-390 Instrument and is taken in CCl_4 matrix (Fig. 6).

The PMR spectrum exhibits a broad singlet at $\sigma 1.8$ nm due to NH, a complex multiplet around $\delta 2.83$ to 3.40 due to the hydrogen atoms of the methylene groups, a sharp 3H singlet at $\delta 3.66$ due to methoxyl hydrogens, another sharp 1H singlet at $\delta 5.2$ due to benzylic hydrogen and a complex 4H multiplet at $\delta 6.4$ to 7.2 due to aromatic hydrogens. A $\delta 6.4$ to 7.2 multiplet corresponding to the aromatic hydrogens is possible due to their asymmetry positions in the phenyl ring, when $-OCH_3$ is in the meta position, on the other hand $-OCH_3$ in the para position would reveal the presence of two 2H doublets with A_2B_2 patterns. In the present case a multiplet formation strongly suggests that $-OCH_3$ is in the meta position.

TABLE II Characteristic absorption peaks in IR spectrum of 2mmpT

Groups	Wave number (cm^{-1})	Reference
N–C–S	500	[11]
NH	3250	[12]
CH_2	1450	[12]
CH, C=C	2950, 1600	[12]

3. Discussion

The characterization by X-ray diffraction studies reveals the crystallinity sample, as monoclinic with and space group $P2_1/c$. The density of the sample is of the order of $1.43\,g\,cm^{-3}$, in agreement with the calculated density ($1.45\,g\,cm^{-3}$) from X-ray diffraction studies. The prominent peak at $3250\,cm^{-1}$ in the IR

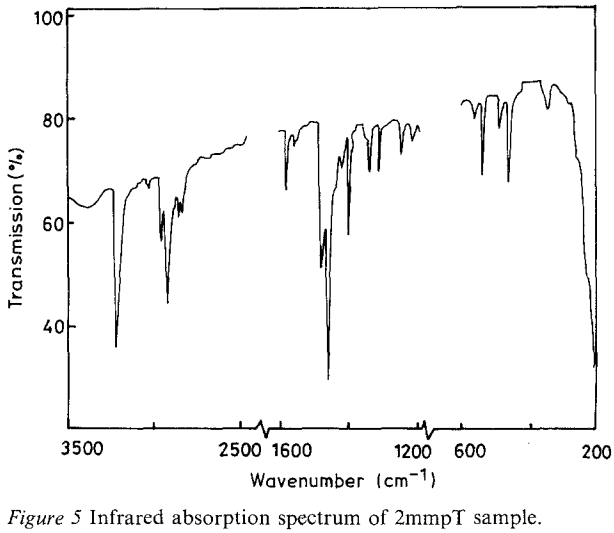

Figure 5 Infrared absorption spectrum of 2mmpT sample.

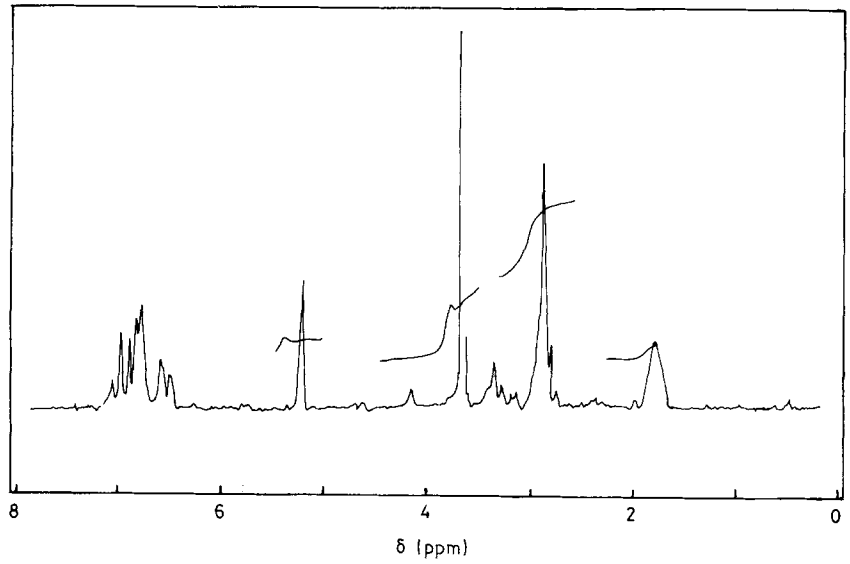

Figure 6 Proton magnetic resonance spectrum of 2mmpT sample.

spectrum of the sample observed suggests the presence of an NH group in the thiazolidine part of the 2mmpT sample; this is further supported by the PMR spectrum of the sample showing a broad peak at $\delta 1.8$ relating to the NH present in the thiazolidine group. The prominent peaks relating to the hydrogen atoms of the methylene groups, the 3H singlet due to methoxyl hydrogens, hydrogen linkages with benzylic and a complex 4H multiplet due to an aromatic group are easily identified in the PMR spectrum establishing the presence of a thiazolidine ring, phenyl ring and OCH_3 attached in the meta position. It is concluded that the PMR spectrum of 2mmpT unambiguously supports the proposed structure of the compound (Fig. 7). The final conformational of the structure and molecular formula will be carried out by X-ray analysis and reported later.

4. Conclusion

The following conclusions are drawn from the above methods of characterization.

(1) The sample 2mmpT is crystalline belonging to the monoclinic system and having space group $P2_1/c$.

(2) The experimental density of the sample agrees with the calculated density ($\varrho_{exp} = 1.43$, $\varrho_{cal} = 1.45\,g\,cm^{-3}$).

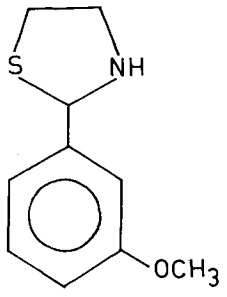

Figure 7 Proposed structure of 2mmpT sample.

(3) The infrared spectrum establishes the presence of a NH group in the sample.

(4) The PMR spectrum supports unambiguously the proposed structural formula for 2 mmpT as shown in Fig. 7.

Acknowledgment

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