

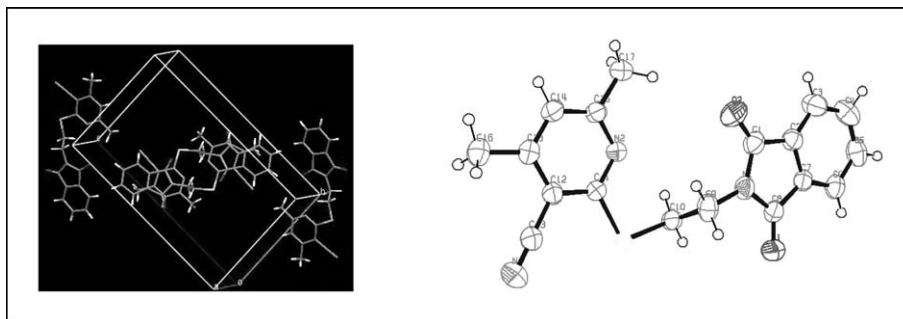
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Weak interactions usually show a versatile property to stabilize the molecular conformation and crystal packing in solid state. Crystal packing and conformational property of the synthesized compound 1(3-cyano-4,6-dimethyl nicotinonitril-1-yl)-3-(phalimido-1-yl)-1-thioxyethane (**2**) is stabilized by CH \cdots O, CH \cdots N, and CH \cdots π interactions.

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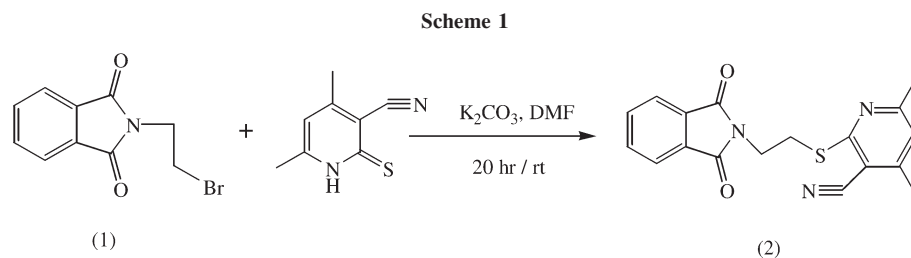
INTRODUCTION

For a long time, chemists tried to understand nature at a level that was purely molecular; they considered only structures and functions involving strong covalent bonds. In contrast, biological structures are usually made from loose aggregates that are held together by weak noncovalent interactions [1]. Weak interactions are hierarchy for formation of supramolecular self assembly in chemical engineering [2]. Stacking interaction keeps aromatic rings swelled up and that plays a vital role in biological structures and function [3]. However, the nature of stacking interaction is still vague [4]. Phthalimide moieties in solid state are engaged due to presence of supramolecular interactions [5]. These interactions depend on the proximal functional groups [6,7]. Various methylene linked N-substituted phthalimide moieties stabilized due to presence of weak nonbonded interactions showing pharmaceutical properties. The crystal structure of 1-methyl-1-phenyl-3-(phthalimidoacetyl)cyclobutane [8] and *N*-(4-methyl-1-piperazinyl)phthalimide [9] molecules are shown to stabilized due to presence of weak CH \cdots O and CH \cdots π interactions. Similarly, the conformation of trimethylene linked 4,6-bis(methareylsulfanyl)-1-phthalimidopropyl-1*H*-pyrazolo[3,4-*d*]pyrimidine stabilized due to presence of intramolecular CH \cdots π interaction. However, fourfold arrangement of crystal packing

was observed in molecule due to the intermolecular stacking interaction in addition to CH \cdots O and CH \cdots N interactions [10]. On the other hand, the crystal structure of 5-[3-(1,3-dioxo-1,3-dihydro-isoindol-2-yl)-propoxy]-3-methyl-1-phenyl-1*H*-pyrazole-4-carboxylic acid ethyl ester was also stabilized due to presence of CH \cdots N, CH \cdots O, and CH \cdots π interactions [11]. Consequently, to study role of weak interactions, we have synthesized the heterodimer, 1(3-cyano-4,6-dimethyl nicotinonitril-1-yl)-3-(phalimido-1-yl)-1-thioxyethane (**2**) linked through dimethylene linker and sulfur as hetero atom.

EXPERIMENTAL

Preparation and characterization. Preparation of 1(3-cyano-4,6-dimethyl nicotinonitril-1-yl)-3-(phalimido-1-yl)-1-thioxyethane (**2**): (Scheme 1). In a 100 mL R.B. flask, 3-cyano,4,6-dimethyl-thiopyridone (0.5 g, 0.003 mole) was dissolved in dry DMF and stirred for 15 min. Anhydrous potassium carbonate (0.41 g, 0.003 mole) was added in it and stirred for 2 h. Stirring was continued for 20 h after adding (**1**) in the reaction mixture. Completion of reaction was monitored through TLC. DMF was removed through rotary evaporator, and residue was extracted by chloroform: water (1:1) (2 \times 20 mL). Organic layer was dried with anhydrous sodium sulfate, and TLC was monitored for purity showing the presence of two compounds. Compounds were purified by column chromatography (EtOAc:



hexane). At 20% EtOAc: Hexane compound was obtained. M.p. 227°C; Yield: 0.03 g (43%); ¹H NMR (CDCl₃, 300 MHz): δ 2.21 (s, 3H, SCH₃), δ 2.37 (s, 6H, CH₃), δ 2.73 (q, 2H, CH₂, *J* = 6), δ 4.06 (t, 2H, CH₂, *J* = 6), δ 4.57 (t, 2H, CH₂, *J* = 6), δ 5.94 (s, 1H, HetArH), δ 8.06 (s, 1H, HetArH), δ 8.71 (s, 1H, HetArH); FAB MS: *m/z* 339 (M+2); Elemental analysis for C₁₈H₁₅N₃O₂S: calcd: C; 64.09%, H; 4.45%, N; 12.46%, Found: C; 64.07%, H; 4.47%, N; 12.46%.

Crystal structure determinations. The cell parameters, space group, and crystal structure were determined from single crystal X-ray diffraction data collected at ambient temperature on Bruker SMART APEX CCD diffractometer. Crystal data, experimental conditions, and structure refinement parameters for (2) are mentioned in Table 1. The structure was solved and refined by using SHELXTL (Sheldrick, 2001) program. Molecular graphics were designed by using ORTEP-3 version 1.08.

RESULT AND DISCUSSION

X-ray quality crystals have been obtained by slow evaporation of compound in acetic acid: MeOH solution at room temperature.

Crystal structure analysis. Title compound is substituted ethane molecule, where one of the carbons has

phthalimide substituent, while other has 3-cyano-4, 6-dimethyl-thiopyridone in place of hydrogen. The phthalimide group was chosen because (a) it is known to exhibit intermolecular stacking (b) it is a bicyclic system, like pyrazolo[3,4-*d*]pyrimidine, (c) it contains a phenyl ring, which is an important acceptor, and (d) it contains an available N atom for linker connection.

In solid state, molecule adopts anticongformation. However, the ring attached through sulfur atom tilted in such a way that nitrogen as well as methyl protons interacted with the Sp²-oxygen atom. The ORTEP diagram with chemical structure is shown in Figure 1.

Table 1

Crystal data, data collection, and structure refinement for 2.

Compound	2
Empirical formula	C ₁₈ H ₁₅ N ₃ O ₂
Formula weight	337.39
Crystal system	Monoclinic
Space group	P 21/n
Unit cell dimensions	
<i>a</i> (Å)	7.5239(9)
<i>b</i> (Å)	11.4933(14)
<i>c</i> (Å)	18.749(2)
β (°)	91.061(2)
Cell volume, <i>V</i> (Å ³)	1621.0(3)
<i>Z</i> , <i>Z'</i>	<i>Z</i> : 4 <i>Z'</i> : 0
<i>R</i> factor (%)	3.77
μ (mm ⁻¹)	0.215
<i>T</i> (K)	294(2)
<i>D</i> (Mg/m ³)	1.382
F(000)	704
hkl range	-8 ≤ <i>h</i> ≤ 8 -13 ≤ <i>k</i> ≤ 13 -22 ≤ <i>l</i> ≤ 22

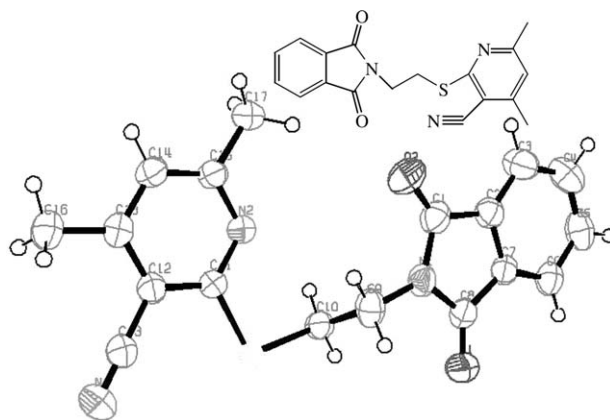


Figure 1. ORTEP diagram with chemical structure of compound 2.

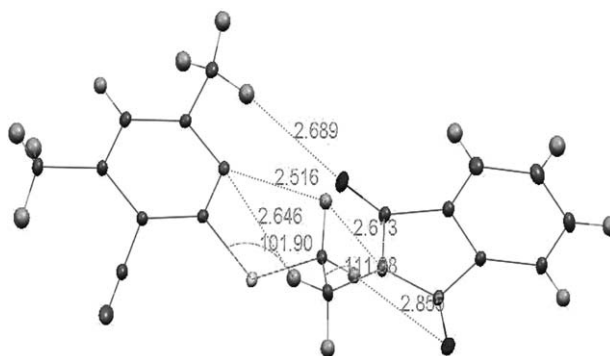


Figure 2. Intramolecular interaction in compound 2.

Table 2
Intramolecular interactions of compound 2.

CH...X	D (C...X)	d (H...X)	< (CHX)
CH9A...N2	3.2	2.64	117.06
CH10B...N2	2.81	2.51	100.10
CH10B...N1	2.64	2.61	70.36
CH10A...O1	3.35	2.85	113.27
CH17A...O2	3.63	2.68	167.09

Intramolecular bifurcated CH...N and CH...O interactions make the molecular stability in anticonformation. The angle formed with methylene carbon to six member and five member rings are 101.90° and 111.98°, respectively (Fig. 2). Data of intramolecular interaction are summarized in Table 2.

Packing of molecule has been stabilized *via* various weak interactions. In the packing diagram, six molecules are arranged in such a way that middle two lie just above the each other due to presence of intermolecular π - π (3.71 Å) interaction. This arene interaction is observed between five member ring of phthalimide and six member ring of thiopyridone moiety, while C=O...S interaction is observed between the sp²-oxygen and divalent sulfur atom having a distance of 3.67 Å (115.09°). Edge to face CH... π interaction (3.42 Å, 98.08°) between centroid of CN group and phenyl hydrogen atom also stabilized the conformational tuning of molecule intermolecularly. The middle pair of two molecules joined with outer molecule of both side *via* CH...O interaction (2.93 Å, 135.69°). As shown in Figure 3, the presence of intermolecular interaction in the molecule has stabilized the conformation.

Ladder-like arrangement of molecular network has been formed by CH...O (2.61 Å, 140.03°) and π - π interaction

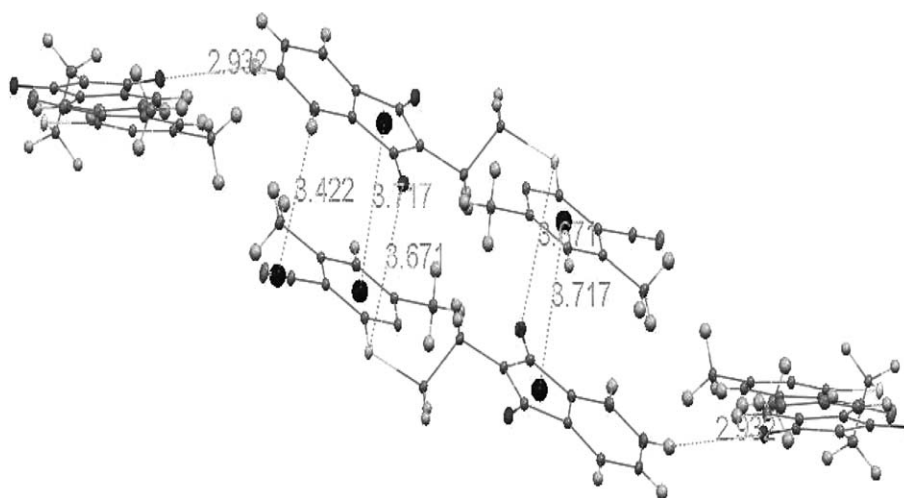


Figure 3. Packing diagram of compound 2 along *b* plane showing intermolecular interaction.

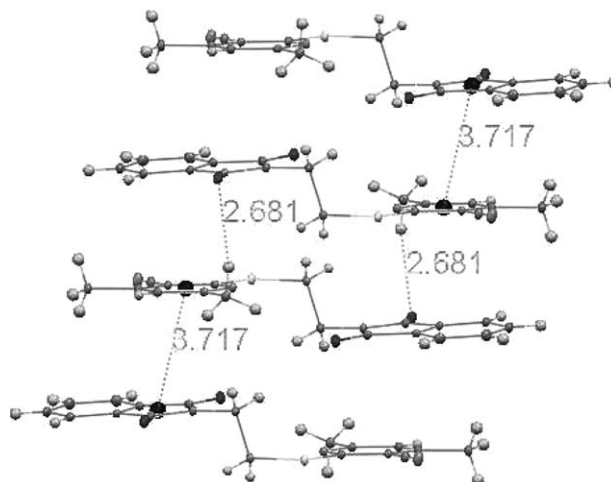


Figure 4. Ladder-like arrangement of molecule stabilized *via* CH...O and π - π interaction.

(3.71 Å) (Fig. 4). However, the bifurcated CH...O [(2.61 Å, 143.03°, 2.64 Å, 152.32°)] interaction stabilized the network of molecule with interesting π - π interaction (3.79 Å) observed between the six member ring of phthalimide and thiopyridone ring of another molecule in Figure 5.

CONCLUSIONS

1(3-cyano-4,6-dimethyl nicotinonitril-1-yl)-3-(phalimido-1-yl)-1-oxypropane was synthesized and characterized by spectroscopic data. Overall, molecular conformation has been stabilized by intra and intermolecular CH...O, CH...N, and CH... π interactions present within it.

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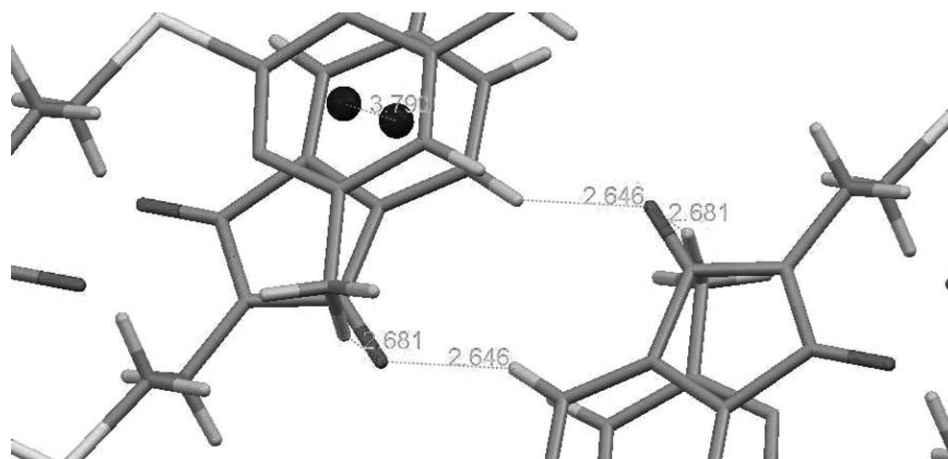


Figure 5. View of bifurcated CH...O interaction and aromatic edge to face π - π interaction.

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