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Spectral characterization and crystal structure of 5-spiro-(3-methyl-2,6-diphenyl-tetrahydropyran-4-yl)-4,5-dihydro-[1,3,4]thiadiazole

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ABSTRACT

The synthesis of new 1,3,4-thiadiazoline derived from 3-methyl-2,6-diphenyltetrahydropyran-4-one, via the corresponding thiosemicarbazone, is described. The synthesis, spectral characterization and crystal structure of 5-spiro-1,3,4-thiadiazoline of 2,6-diphenyl-3-methylpyran is reported. Spectral techniques employed include ^{1}H NMR, ^{13}C NMR, HOMOCOSY, HSQC, HMBC, NOESY correlation techniques, mass and IR. The conformation of the compound is established on the basis of ^{1}H NMR spectral data, MOPAC calculation and the single crystal X-ray analysis.

1. Introduction

Several natural products including antibiotics possess the oxane (pyran) ring skeleton. The pyran nucleus can frequently be recognized in the structure of numerous naturally occurring carbohydrates and synthetic compounds with interesting biological and pharmacological properties [1–4]. Thiosemicarbazones exhibit various biological activities and are extensively applied in medicine particularly in the treatment of tuberculosis [5,6]. The Δ^2-1,3,4-thiadiazolines also exhibit biological behavior [7–11].

There are few general routes to obtain 1,3,4-thiadiazolines. Holmberg and Sandström proposed the reaction between an aldehyde or a ketone with substituted thiohydrazides [12]. Evans and Taylor [13] found that 1,3-dipolar cycloaddition between chlorodiazabutadiene and thiourea rendered 4-amidine-1,3,4-thiadiazolines. However, the preparation of this heterocyclic ring is mostly achieved by heterocyclization of thiosemicarbazones [14], as reported by Andreae et al. [15], Somogyi [16] and Kubota et al. [17]. In view of these findings and in a further stage of our work on the synthesis of heterocycles [18], here we describe the synthesis, structural and spectral studies of 5-spiro-(3-methyl-2,6-diphenyltetrahydropyran-4-yl)-4,5-dihydro-[1,3,4]thiadiazole.

2. Experimental

The IR spectrum was recorded in AVATAR-330 FT-IR spectrophotometer (Thermo Nicolet) and only noteworthy absorption levels (reciprocal centimeters) are listed. ^{1}H NMR spectrum was recorded at 400 MHz on BRUKER AMX 400 MHz spectrophotometer using $CDCl_3$ as solvent and TMS as internal standard. ^{13}C NMR spectrum was recorded at 100 MHz on BRUKER AMX 400 MHz spectrophotometer in $CDCl_3$. ^{1}H–^{1}H COSY, phase-sensitive NOESY and one-bond ^{1}H–^{13}C correlations spectra were recorded on BRUKER AMX 500 NMR spectrometer using standard parameters. 0.05 M solutions of the sample prepared in $CDCl_3$ were used for recording 2D NMR spectra. The tubes used for recording NMR spectra are of 5 mm diameter. The FAB mass spectrum was recorded on a JEOLSX 102/DA-6000 mass spectrometer using Argon/Xenon (6 kV, 10 mA) as the FAB gas. The accelerating voltage was 10 kV and the spectra recorded at room temperature. The theoretical conformation calculation were performed on a personal computer using PM3 (MNDO Hamiltonian) available in MOPAC version 7.2 [19]. Unless otherwise stated, all the reagents and solvents used were of high grade and purchased from Fluka and Merck. All the solvents were distilled prior to use.

2.1. X-ray data collection, structure solution and refinement

Single crystals suitable for diffraction were obtained by the slow evaporation of a solution of the compound in ethanol. The colorless

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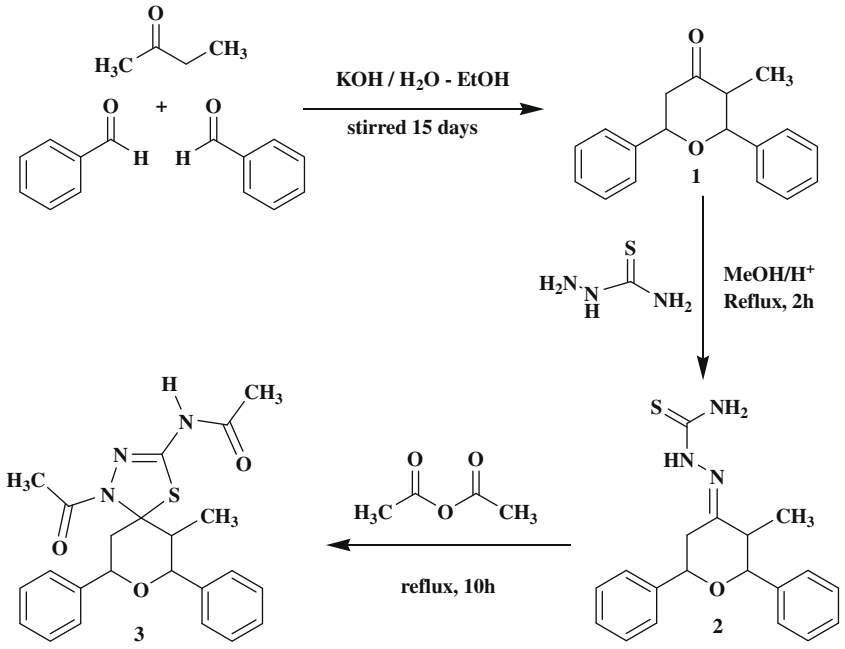

Scheme 1. Schematic diagram showing the synthesis of compound **3.**

crystal of the compound having appropriate dimensions of 0.30 × 0.20 × 0.20 mm was mounted on a glass fiber with epoxy cement for the X-ray crystallographic study. Bruker axs kappa apex2 CCD diffractometer equipped with graphite monochromated Mo Kα (λ = 0.71073 Å) radiation was used for the measurement of data. The collected data were reduced using the SAINT program and structural refinement was carried out by Full-matrix least-squares on F^2 (SHELXL-97) [20]. Molecular graphics employed include ORTEP and PLATON [21]. Data center allogated the deposition number CCDC 697342.

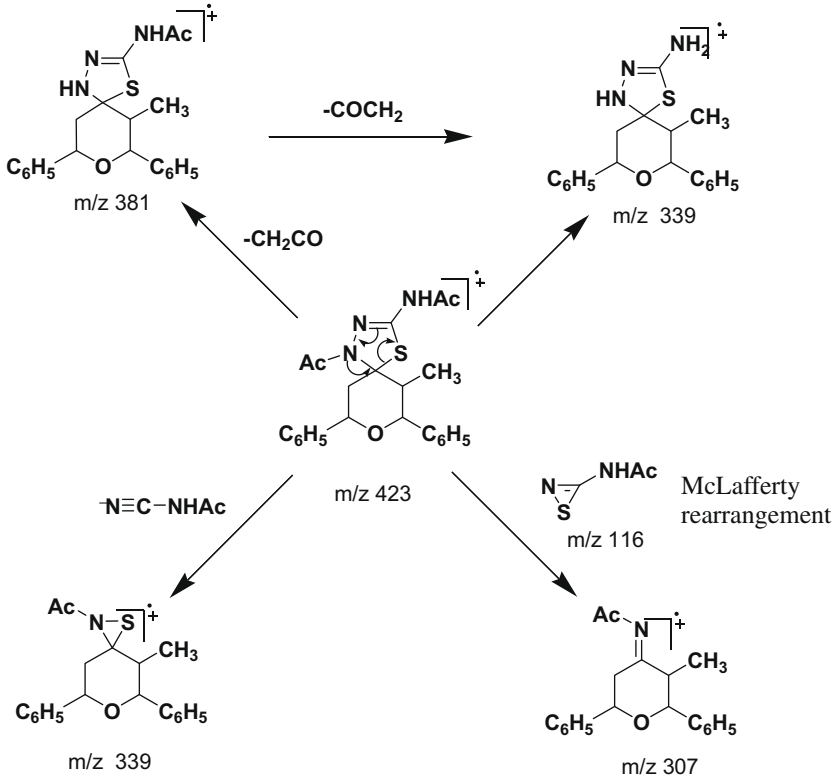

Fig. 1. Mass spectral fragmentations of the compound **3.**

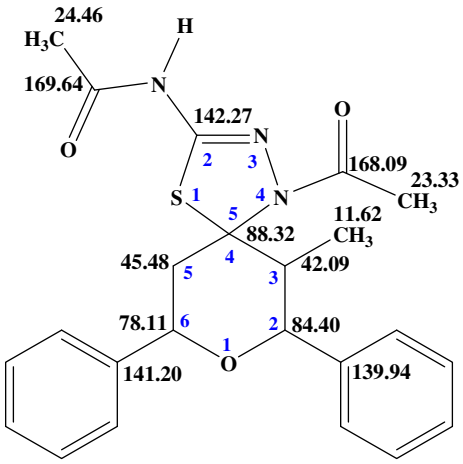

Fig. 2. ^{13}C chemical shift values in (δ) ppm and carbon numbering of the compound **3.**

2.2. Synthesis of compound **3**

Compound **3** was synthesized as shown in Scheme 1. The parent 3-methyl-2,6-diphenyltetrahydropyran-4-one **1** was prepared by the literature precedent of Japp and Maitland [22]. The pyran-4-one further converted into their thiosemicarbazone **2** by condensation with thiosemicarbazide in the presence of concentrated hydrochloric acid in methanol medium [23]. Compound **2** (0.025 mol) was treated with freshly distilled acetic anhydride and the mixture was refluxed for 10 h on a water bath (90–100 °C). The removal of solvent from the cooled reaction mixture in vacuo afford 5-spiro-(3-methyl-2,6-diphenyltetrahydropyran-4-yl)-4,5-dihydro-[1,3,4]-thiadiazoles **3** which is recrystallized from 96% ethanol. M.p. 126 °C, yield: 91%.

3. Results and discussion

3.1. IR spectral studies

IR spectral data confirms the presence of characteristic groups present in the compound. The bands at 1700 cm^{-1} and 1663 cm^{-1} are for the amide carbonyl groups present in tertiary and secondary amides, respectively. The C=N stretching frequency appears at 1625 cm^{-1}. The band at 3251 cm^{-1} is assigned for the NH stretching frequency. Aromatic C—H stretching bands occur in the region 3088 cm^{-1}. Carbon to carbon stretching vibrations within the ring occurs at 1498 cm^{-1}.

3.2. Mass spectral analysis of the compound **3**

Mass spectra of this heterocyclic compound resemble the observed rupture pattern, although the relative abundance and the *m/z* relationship are characteristic for the synthesized compound **3**, in agreement with that observed for similar heterocycles derived from aldehydes [16]. The proposed fragmentation model is presented in Fig. 1.

3.3. NMR spectral studies of compound **3**

Ring closure may be observed by the disappearance in the ^{13}C NMR spectrum of the signal at 179.70 ppm corresponding to the thiocarbonyl, the appearance of the signal at 88.32 ppm assigned to C-4 and the signals of the carbonyl and methyl moieties of the

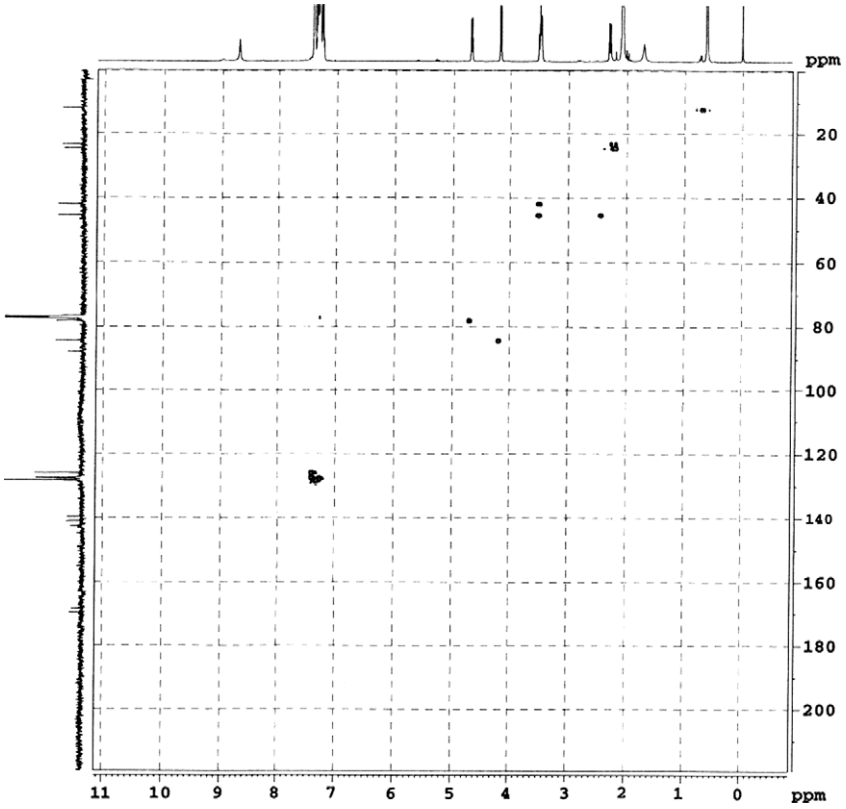

Fig. 3. The HSQC correlation spectrum of the compound **3.**

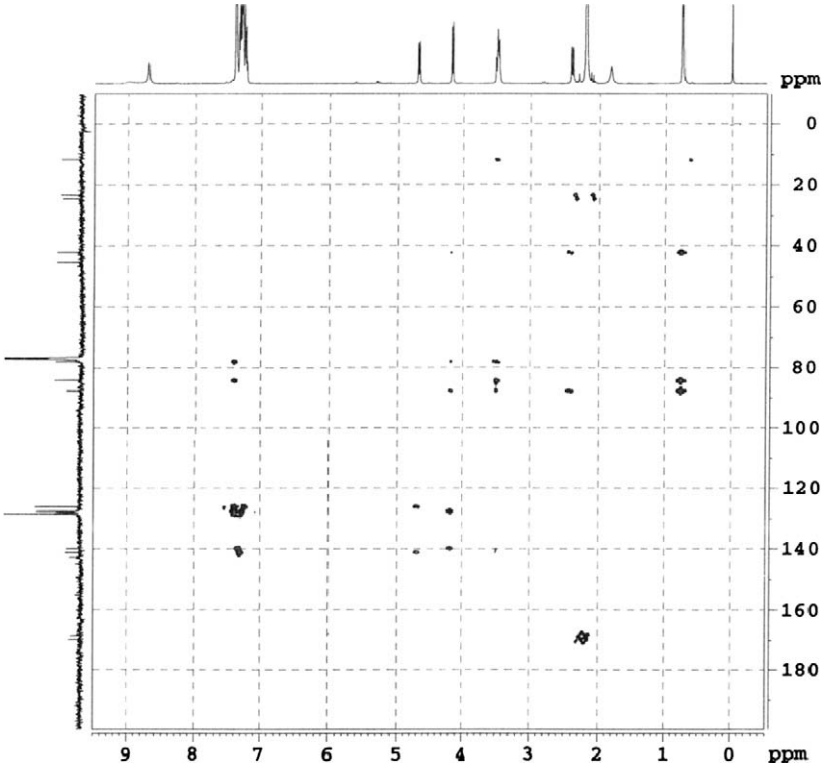

Fig. 4. The HMBC correlation spectrum of the compound **3.**

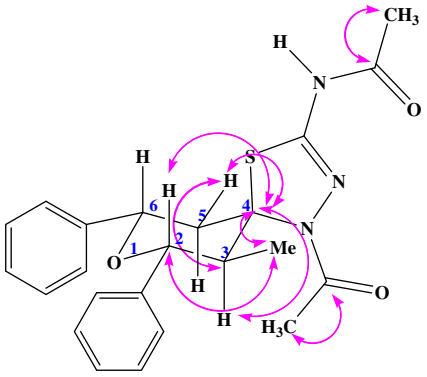

Fig. 5. The HMBC correlations of the compound **3.**

acetyl groups incorporated to the molecule. The C=N signal is around 142.27 ppm. The ^{13}C chemical shift value of compound **3** is depicted in Fig. 2 with carbon numbering. The ^{13}C chemical shift values are unambiguously assigned by HSQC and HMBC spectra (Figs. 3 and 4). The HMBC correlations are shown in Fig. 5, respectively.

In the HSQC spectrum of compound **3**, the carbon signal at 88.32 does not have HSQC correlation whereas there are notable HMBC correlations with H-2a, H-3a, H-5a, H-5e and 3-CH_3 protons which confirm that the signal at 88.32 is for spiro carbon (C-4).

Moreover, the carbon signal at 45.48 ppm having HSQC correlation with two proton signals at 3.46 and 2.42 ppm, respectively, which confirms that the carbon signal at 45.48 ppm is a methylene carbon (C-5).

The ^{1}H NMR spectral data used to determine the conformation of the compound **3**. The ^{1}H NMR spectral assignments have been made based on the characteristic signal, positions of functional groups, spin multiplicity and 2D NMR (^{1}H–^{1}H HOMOCOSY, HSQC, HMBC and NOESY) spectral data. The ^{1}H chemical shift values and the HOMOCOSY correlation of compound **3** are shown in Fig. 6. The NOESY correlations are shown in Fig. 7. HOMOCOSY

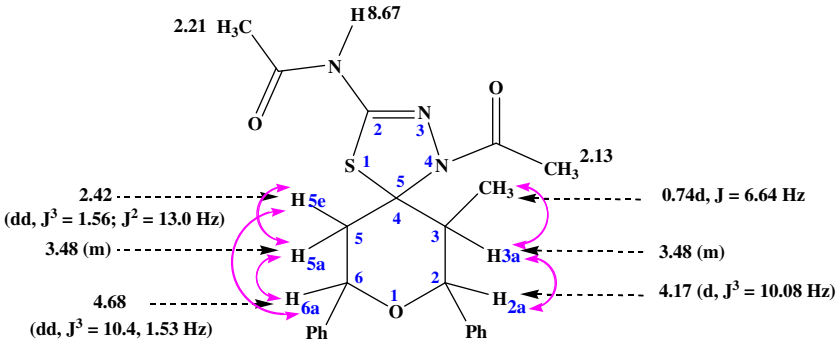

Fig. 6. ^{1}H chemical shift values in (δ) ppm with ^{1}H–^{1}H HOMOCOSY correlation of the compound **3.**

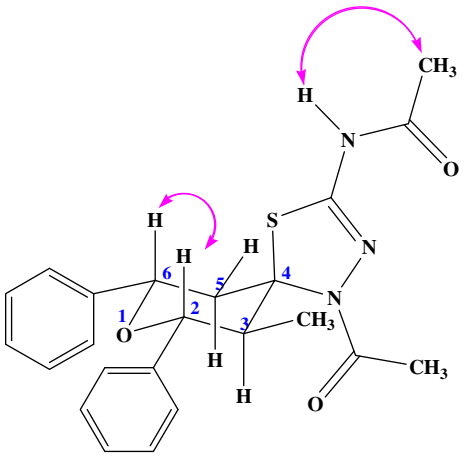

Fig. 7. The NOESY correlation of the compound **3.**

and NOESY correlations spectra are shown in Figs. 8 and 9, respectively. The signals appeared as double doublet and multiplet in the region of 7.21–7.40 ppm with 10 protons integral are due to the phenyl protons present at C-2 and C-6. Among the two signals the double doublet at 7.41–7.38 has strong NOE with the double doublet at 4.68 and doublet at 4.17 ppm (Fig. 8), which suggest that the double doublet at 7.41–7.38 ppm is due to the *ortho* protons of the phenyl groups at C-2 and C-6. Deshielding of the *ortho* protons has been attributed to the lone pair of electrons on the oxygen in the pyran heterocycle. The rest of the phenyl protons are merged together to give multiplet at about 7.21–7.34 ppm. In the higher frequency region there are two signals as double doublet at 4.68 ($^3J_{6a,5a}$ = 10.40 Hz; $^3J_{6a,5e}$ = 1.56 Hz) and doublet at 4.17 ($^3J_{2a,3a}$ = 10.08 Hz) with one proton integral each. From the multiplicity of those signals the higher frequency signal (4.68 ppm) is assigned as H-6a proton and relatively lower frequency signal is assigned (4.17 ppm) as H-2a proton. Both the signals are confirmed from its HOMOCOSY (Fig. 6), NOESY (Fig. 7) and HSQC (Fig. 3) correlation spectra. In the lower frequency region there is a double doublet at 2.42 (J^2 = 13.0 Hz; J^3 = 1.56 Hz) with one proton integral is assigned as H-5e on the basis of their multiplicity and vicinal coupling constant. Consequently, the multiplet at 3.48 ppm with two protons integral is for H-3a and H-5a, which is unambiguously assigned from the HSQC correlation spectra. The two protons linked to C-5 of the pyran nucleus were thus found to be 1.06 ppm separation. The marked difference between the protons linked to C-5 would not only result from the inductive effect exerted by the heteroatoms, but rather due to a spatial effect probably exerted by the acetyl groups.

In the NOESY spectrum (Fig. 7), NOE was observed between the proton linked to the nitrogen atoms and the least shielded methyl moiety, that is to say, the methyl moiety of the acetamide group linked to C of the heterocycle; therefore, the methyl moiety that appears at a higher field is the one belonging to the N-acetyl group. Considering both acetyl groups, the one located on N-4 of the heterocycle is nearer the pyran ring and could present some type of interaction with the hydrogen atoms in position C-3 and C-5; however, no NOE effect was observed between the methyl moiety of this acetyl group and the hydrogen atoms belonging to the pyran system.

3.4. Conformation of the compound **3**

The observed chemical shifts, vicinal coupling constants and splitting pattern strongly support that the synthesized compound is in normal chair confirmation with equatorial disposition of the

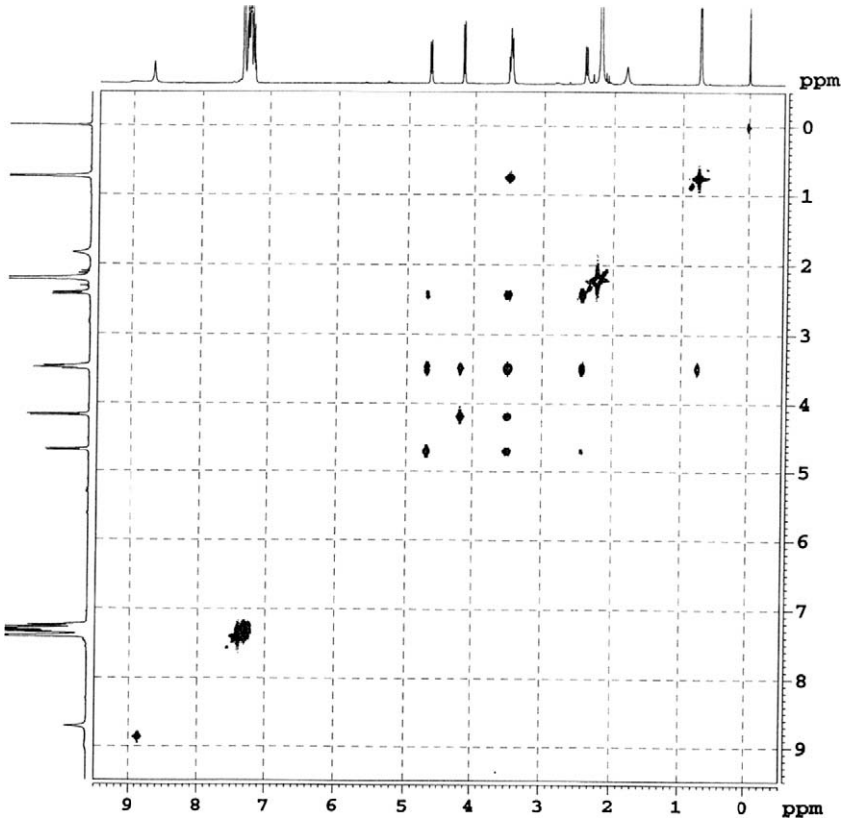

Fig. 8. The COSY correlation spectrum of the compound **3.**

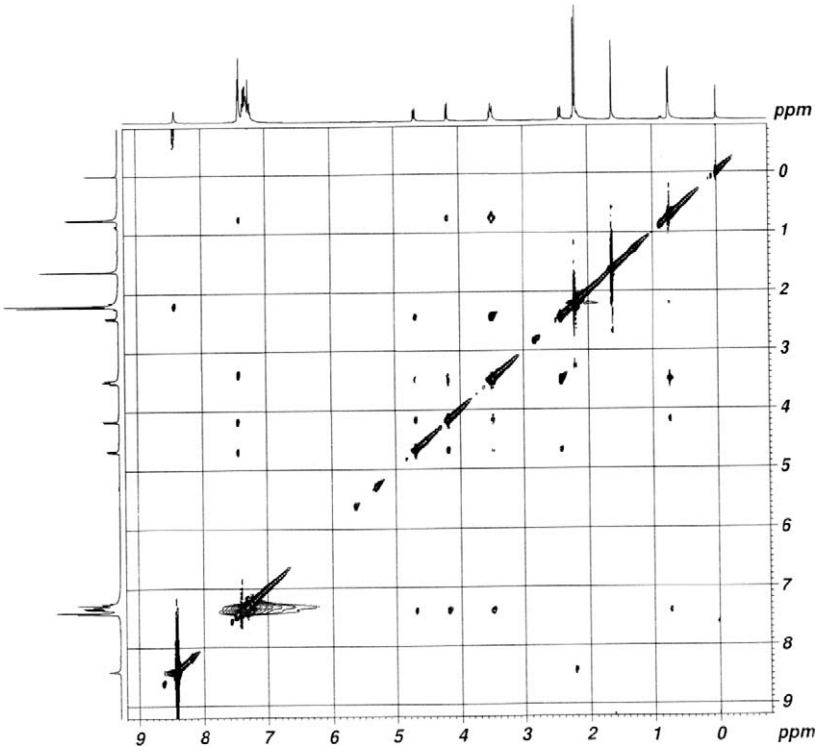

Fig. 9. The NOESY correlation spectrum of the compound **3.**

phenyl rings present at C-2 and C-6 and methyl group at C-3 position of the pyran moiety.

There are two possible orientations of the N-acetyl group of thiadiazoline moiety whether the 4-N-acetyl group at equatorial or axial. In order to avoid the 1,3-diaxial interaction the N-acetyl group prefer the equatorial than axial orientation confirmed from NMR spectral data of the compound **3**.

The carbon chemical shift values of the compound **1** and their parent thiopyran-4-one **3** and difference between them also reproduced in Table 1. As a result, the benzylic carbons at C-2 and C-6 are not much affected. An interesting point has been observed for the compound **3** as C-3 carbon is resonances at shielded region than the C-5 carbon unlike in parent ketone [24]. This is may be due to the anisotropic effect exerted by carbonyl group of the thiadiazoline moiety at N-4 which deshielded the methyl carbon at C-3.

^{1}H NMR spectral data of the compound **3** gives the information about the orientation of the spiro-C-S bond and C-N-acetyl bond. The proton chemical shift values of pyran ring protons of compound **3**, parent ketone **1** and the difference between them are given in Table 2.

Table 1
^{13}C chemical shift values of **1**, **3** and difference between them (δ) in ppm.

Compound	C-2	C-3	C-4	C-5	C-6	3-CH_3
1	85.97	51.65	207.09	50.16	79.39	9.48
3	84.40	42.09	88.32	45.48	78.11	11.62
1–3	1.57	9.65	118.48	4.68	1.28	−2.14

Table 2
^{1}H chemical shift values of **1**, **3** and difference between them (δ) in ppm.

Compound	H-2a	H-3a	H-5a	H-5e	H-6a	3-CH_3
1	4.33		2.71		4.81	0.86
3	4.17	3.48	3.48	2.42	4.68	0.74
1–3	0.16	−0.77	−0.77	0.29	0.13	0.12

Perusal of Table 2, the benzylic (H-2a and H-6a) protons are not much affected by the thiadiazoline moiety whereas the axial protons at C-3 and C-5 are deshielded 0.77 ppm and the equatorial proton at C-5 is shielded about 0.3 ppm which are due to the anisotropic effect of the carbonyl group present at N-4 of the thiadiazoline moiety as shown in Fig. 10.

From these inferences, the carbonyl group of acetyl group at N-4 of thiadiazoline moiety is oriented in the plane of equatorial proton of C-5 and equatorial methyl group at C-3 and above the plane of axial protons at C-3 and C-5. As a result the C—N-acetyl bond oriented at equatorial.

This hypothesis is supported by the optimized energy results obtained from PM3 calculation. The PM3 calculation was carried out for both the possible chair conformations Fig. 11 (N-acetyl group at axial orientation) and Fig. 12 (N-acetyl group at equatorial

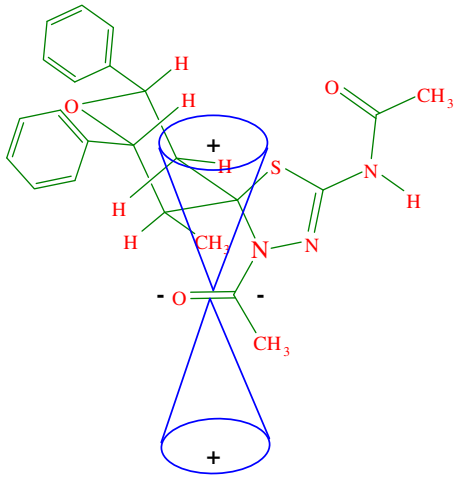

Fig. 10. Anisotropic effect on H-5e and 3-CH_3 protons (+shielding region and −shielding region).

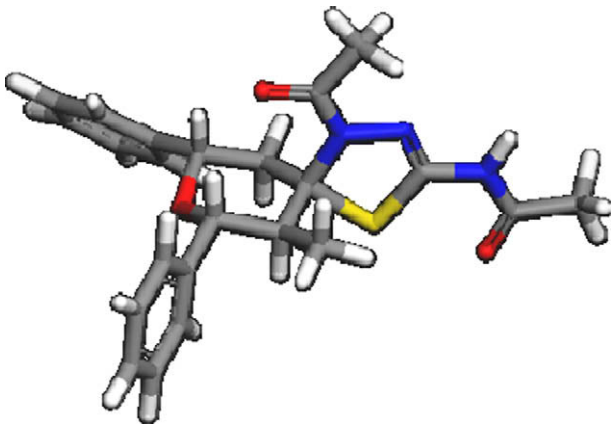

Fig. 11. The optimized structure of the compound **3** with optimized energy 12.89 (kJ/mol).

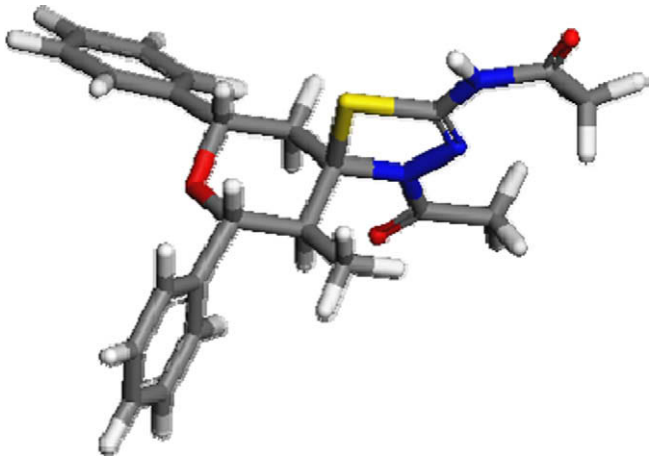

Fig. 12. The optimized structure of the compound **3** with optimized energy 1.78 (kJ/mol).

orientation), in which the later optimized at lower energy (1.78 kJ/mol) than the former (12.89 kJ/mol). The equatorial orientation of N-acetyl group of thiadiazoline moiety further confirmed from their selected bond angles and torsion angles derived from PM3 calculation method and X-ray diffraction studies.

3.5. Crystal structure

The compound **3** crystallizes into an orthorhombic lattice with $P2_12_12_1$ symmetry. Crystal data and structure refinement of compound **3** is shown in Table 3. The ORTEP diagram of compound **3** is shown in Fig. 13, displacement ellipsoids is drawn at 50% probability level. The saturated pyran ring adopts a distorted chair conformation, as shown by the torsion angles around the bonds involving the ring atoms. These torsion angles deviate from the ideal value of 56° reported for the chair conformation of cyclohexane [25]. The C—C bond lengths of the aryl rings are in the range 1.366 (3)–1.375 (4) Å, while the bond angles are in the range 117.8 (2)–122.2 (2)°. The equatorial dispositions of the phenyl groups are revealed by the torsion angles involving the exo atom and the other three ring atoms; these vary from −179.0 (4)° to 177.9 (3)°, as observed also in a pentasubstituted cyclohexan-1-one derivative [26]. Torsion angle of −67.93° and 170.94° perceived by H(5)—C(5)—C(4)—C(23) and H(4)—C(4)—C(5)—H(5), respectively, confirms the methyl group

Table 3
Crystal data and structure refinement of compound **3.**

Empirical formula	$C_{23}H_{25}N_3O_3S$
Formula weight	423.52
Temperature	293(2) K
Wavelength	0.71073 Å
Crystal system, space group	Orthorhombic, $P2_12_12_1$
Unit cell dimensions	a = 11.069(5) Å α = 90°
	b = 14.681(5) Å β = 90°
	c = 13.910(5) Å γ = 90°
Volume	2260.4(15) Å^3
Z, calculated density	4, 1.244 mg/m^3
Absorption coefficient	0.171 mm^{-1}
F(0 0 0)	896
Crystal size	0.30 × 0.20 × 0.20 mm
Theta range for data collection	2.30–27.93°
Limiting indices	$-14 \leqslant h \leqslant 14$, $-19 \leqslant k \leqslant 19$, $-18 \leqslant l \leqslant 18$
Reflections collected/unique	24,921/5423 [R(int) = 0.0348]
Completeness to theta = 25.00	99.9%
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9665 and 0.9504
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	5423/0/290
Goodness-of-fit on F^2	1.025
Final R indices [$I > 2\sigma(I)$]	R1 = 0.0467, wR2 = 0.1199
R indices (all data)	R1 = 0.0652, wR2 = 0.1341
Absolute structure parameter	0.03(9)
Largest diff. peak and hole	0.442 and −0.200 eA^{-3}

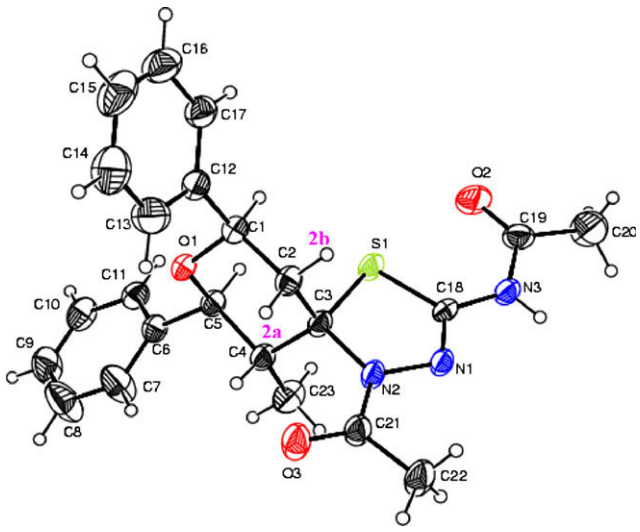

Fig. 13. The ORTEP diagram of the compound **3**, showing 50% probability displacement ellipsoids.

present at C-5 is in axial and methyl group at C-5 is in equatorial orientation. The sum of the bond angles around N2 atom [347.8 (18)°] indicates the sp^2 hybridization. The torsion angles C(22)—C(21)—N(2)—N(1) [−3.31°] and C(22)—C(21)—N(2)—C(3) [−177.01(3)°] indicate that atoms C(21) and C(22) lie in the plane of the five-membered ring (N2—N1—C18—S1—C3). Also the torsion angles C20—C19—N3—C18 [177.89°], O(2)—C(19)—N(3)—C(18) [−1.25 (3)°], C(19)—N(3)—C(18)—S(1) [6.39°] and C(19)—N(3)—C(18)—N(1) [174.47(2)°] indicate that the substituted moiety at C(18) lie in the plane of the ring to which it is attached. The dihedral angles (2a)—C(2)—C(3)—S(1) [−173.33°], H(2b)—C(2)—C(3)—S(1) [−52.80°], H(2a)—C(2)—C(3)—N(2) [−58.93°] and H(4)—C(4)—C(5)—H(5) [170.94°] which clearly indicates the equatorial orientation of N-acetyl group. The selected bond length, bond angles and torsion angles obtained from PM3 calculation data of the compound **3** are in good agreement with XRD-data which are shown in Table 4.

Table 4
Geometric parameters of compound **3**.

Geometric parameters	XRD	PM3 calculation
Bond length (Å)		
C(6)—C(7)	1.375(4)	1.342
C(6)—C(11)	1.366(3)	1.334
C(21)—O(3)	1.213(3)	1.268
C(3)—S(1)	1.852(2)	2.000
C(3)—N(2)	1.480(3)	1.537
C(18)—N(1)	1.263(3)	1.303
Bond angle (°)		
C(21)—N(2)—N(1)	111.26(17)	112.88
C(11)—C(6)—C(7)	117.8(2)	117.21
C(7)—C(6)—C(5)	122.2(2)	121.12
C(21)—N(2)—N(1)	119.15(18)	120.70
C(18)—N(1)—N(2)	111.26(17)	120.02
N(1)—N(2)—C(3)	117.39(17)	122.67
C(21)—N(2)—N(1)	119.15(18)	120.09
C(18)—N(1)—N(2)	111.26(17)	112.88
N(1)—C(18)—N(3)	119.48(19)	118.89
C(19)—N(3)—C(18)	126.0(2)	124.17
O(2)—C(19)—N(3)	121.1(3)	120.69
Torsion angle (°)		
C(1)—C12)—C(17)—C(16)	177.9(3)	178.07
C(5)—O(1)—C(1)—C(12)	−179.0(3)	−178.94
C(22)—C(21)—N(2)—N(1)	−3.3(4)	−2.26
C(22)—C(21)—N(2)—C(3)	−177.1(3)	−174.90
O(2)—C(19)—N(3)—C(18)	−1.25(3)	176.01
C(19)—N(3)—C(18)—S(1)	6.39(3)	−3.2
C(19)—N(3)—C(18)—N(1)	174.47(2)	172.10
H(2a)—C(2)—C(3)—S	−173.33	−175.23
H(2b)—C(2)—C(3)—S	−52.80	−57.43
H(2a)—C(2)—C(3)—N(2)	−58.93	−62.56
C(1)—O(1)—C(5)—C(6)	−172.26	−174.99

4. Conclusion

Conformation of title compound was carried out using NMR spectral data, X-ray diffraction. The semiempirical molecular orbital calculation (PM3) also carried out to investigate the conformational preference of N-acetyl group of 1,3,4-thiadiazoline moiety. The results show that the title compound exist in chair conformation with equatorial orientations of two phenyl groups at C-2, C-6, methyl group at C-3 carbons and N-acetyl group of thiadiazoline moiety. The results obtained from NMR spectra are in good agreement with those from X-ray crystallography and MOPAC (PM3) calculation.

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References

[1] C.L. Stevens, P. Blumbergs, D.H. Otterbach, J.L. Stronming, M. Matsuhashi, D.N. Dietzler, J. Am. Chem. Soc. 86 (1964) 2937;
C.L. Stevens, P. Blumbergs, F.A. Daniher, J. Am. Chem. Soc. 85 (1963) 1552.
[2] N.D. Heindal, J.R. Reid, J. Heterocycl. Chem. 17 (1980) 1087.
[3] R.H. Bradbury, J.E. Revett, J. Med. Chem. 34 (1991) 151;
R.H. Bradbury, Heterocycles 32 (1991) 449.
[4] M. Dohaz, S. Rekas, J. Acta Pol. Pharm. 52 (1995) 35;
S.G. Komurcu, S. Rollas, Z. Yilmaz, A. Ceuikbas, Drug Metab. Drug Interact. 12 (1995) 161.
[5] H.K. Shukla, N.C. Desai, R.R. Astik, K.A. Thaker, J. Indian Chem. Soc. (1984) 168.
[6] N.C. Desai, H.K. Shukla, B.P. Parekh, K.A. Thaker, J. Indian Chem. Soc. (1984) 455.
[7] K. Pan, M.K. Scott, D.H.S. Lee, L.J. Fitzpatric, J.J. Crooke, R.A. Rivero, D.I. Rosenthal, A.H. Vaidya, B. Zhao, A.B. Reiz, Bioorg. Med. Chem. 11 (2003) 185.
[8] K.Y. Jung, S.K. Kim, Z.G. Gao, A.S. Gross, N. Melman, K.A. Jacobson, Y.C. Kim, Bioorg. Med. Chem. 12 (2004) 613.
[9] A. Foroumadi, A. Asadipour, M. Mirzaei, J. Karimi, S. Emami, IL Farmaco 57 (2002) 765.
[10] A.R. Jalilian, S. Sattari, M. Bineshmarvasti, M. Daneshtalab, A. Shafiee, IL Farmaco 58 (2002) 63.
[11] R. Leung-Toung, J. Wodzinska, W. Li, J. Lowrie, R. Kukreja, D. Desilets, K. Karimian, T.F. Tam, Bioorg. Med. Chem. 11 (2003) 5529.
[12] (a) B. Holmberg, Arkiv. Kemi 7 (1954) 517;
(b) J. Sandstron, Adv. Heterocycl. 9 (1968) 165.
[13] D. Evans, D.R. Taylor, J. Chem. Soc. Chem. Commun. (1982) 188.
[14] M.A. Martins Alho, N.B. D'Accorso, J. Heterocycl. Chem. 34 (1997) 1415.
[15] S. Andreae, E. Schmitz, H. Seeboth, J. f. prakt. Chem. 328 (1986) 205.
[16] L. Somogyi, Tetrahedron 47 (1991) 9305.
[17] S. Kubota, Y. Ueda, K. Fujikane, K. Toyooka, M. Shibuya, J. Org. Chem. 45 (1980) 1473.
[18] C. Ramalingan, S. Balasubramanian, S. Kabilan, Synth. Commun. 34 (6) (2004) 1105;
C. Ramalingan, S. Balasubramanian, S. Kabilan, Heterocycl. Commun. 10 (2/3) (2004) 187;
C. Ramalingan, S. Balasubramanian, S. Kabilan, Synth. Commun. 33 (9) (2003) 443;
S. Balasubramanian, C. Ramalingan, S. Kabilan, Indian. J. Chem. 41B (2002) 2402;
S. Balasubramanian, C. Ramalingan, S. Kabilan, Synth. Commun. 33 (17) (2003) 2979;
C. Ramalingan, S. Balasubramanian, S. Kabilan, M. Vasudevan, Med. Chem. Res. 12 (1) (2003) 26;
C. Ramalingan, S. Balasubramanian, S. Kabilan, M. Vasudevan, Eur. J. Med. Chem. 39 (2004) 527;
C. Ramalingan, S. Balasubramanian, S. Kabilan, M. Vasudevan, Med. Chem. Res. 12 (1) (2003) 41;
S. Balasubramanian, C. Ramalingan, G. Aridoss, P. Parthiban, S. Kabilan, Med. Chem. Res. 13 (5) (2004) 297;
S. Balasubramanian, C. Ramalingan, G. Aridoss, S. Kabilan, Eur. J. Med. Chem. 40 (2005) 694;
S. Balasubramanian, G. Aridoss, P. Parthiiban, S. Kabilan, Biol. Pharm. Bull. 29 (1) (2006) 125;
G. Aridoss, S. Balasubramanian, P. Parthiban, S. Kabilan, Eur. J. Med. Chem. 42 (2007) 860.
[19] J.J.P. Stewatt, MOPAC 2000 V 1.3 User's Manual, Fujitsu Limited, 2000.
[20] G.M. Sheldrick, SHELXS-97 Program for the Solution of Crystal Structures, University of Gottingen, Gottingen, Germany, 1997.
[21] A.L. Spek, PLATON, in: A Multipurpose Crystallographic Tool, Utrecht University, Utrecht, The Netherlands, 1999.
[22] F.R. Japp, W. Maitland, J. Chem. Soc. 85 (1904) 1473.
[23] S. Umamatheswari, J. Jayapratha, S. Kabilan, Eur. J. Med. Chem., submitted for publication.
[24] K. Ramalingam, K.D. Berlin, J. Org. Chem. 44 (1979) 471;
V. Baliah, G. Mangalam, Indian J. Chem. 16B (1978) 213.
[25] P.S. Kalsi, Stereochemistry: Conformation and Mechanism, New Age International, New Delhi, 1997. p. 236.
[26] T.R. Sarangarajan, K. Panchanatheswaran, K. Thanikachalam, R. Jeyaraman, Acta Crystallogr. E 58 (2002) o1053–o1054.