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^{1}H and ^{13}C NMR spectral study of some 3,5-bis[(E)-thienylmethylene]piperidin-4-ones

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ABSTRACT

^{1}H and ^{13}C NMR spectra have been recorded for 3,5-bis[(E)-thienylmethylene]piperidin-4-one (**1a**), 3′,3″-dimethyl-3,5-bis[(E)-thienylmethylene]piperidin-4-one (**1b**), 5′,5″-dibromo-3,5-bis[(E)-thienylmethylene]piperidin-4-one (**1c**), their 1-methyl derivatives **2a–c** and 3,5-bis[(E)-thienylmethylene]-2r,6c-diphenylpiperidin-4-one (**3a**). For selected compounds 2D spectra have been recorded. The spectral data are used to study the configuration and conformation of these molecules. The chemical shifts are discussed in light of steric, electronic and magnetic anisotropic effects. The magnetic anisotropic effects of thiophene ring and phenyl group are noteworthy. ^{1}H–^{1}H COSY spectrum of **2b** suggests that long-range ^{1}H–^{1}H coupling, up to seven bonds, is possible in it. HMBC spectrum of **2b** displays the magnetic nonequivalence of C-2 and C-6 and protons at these carbons.

1. Introduction

2,6-Bis(E-arylidene)cyclohexanones and their piperidin-4-one analogues display cytotoxic and anticancer activities [1–5]. Though X-ray crystal data [6–8] have been reported for such compounds, detailed NMR spectral study has not yet been reported on them. Also, chalcones from piperidin-4-ones with substituents at C-2 and C-6 have not been reported. The present article reports the ^{1}H and ^{13}C NMR spectral study of 3,5-bis[(E)-thienylmethylene]piperidin-4-ones (**1a–c**), their 1-methyl derivatives **2a–c** and 3,5-bis[(E)-thienylmethylene]-2r,6c-diphenylpiperidin-4-one (**3a**).

2. Results and discussion

2.1. Synthesis of the compounds and the numbering of atoms

Compounds **1a–c**, **2a–c** and **3a** were synthesized using reactions shown in Scheme 1. The numbering of carbon atoms is shown in Scheme 1. Protons are numbered accordingly. Thus, proton at C-7 is denoted as H-7, proton at C-4′ is denoted as H-4′ and so on. Chemically equivalent nuclei are represented together. Thus, carbons 2 and 6 are represented as C-(2,6). Similarly, protons H-4′ and H-4″ are represented as H-(4′,4″).

2.2. IR and mass-spectra

The IR and mass spectral data are given in Table 1. The carbonyl stretching frequencies of the title compounds are characteristic of carbonyl groups involved in conjugation with a double bond. The N–H stretching frequencies for the compounds **1a–c** and **3a** are in the range of 3331–3291 cm^{-1}. In the mass spectra, for all compounds, molecular ion peak corresponding to the molecular formula is observed.

2.3. Assignments of NMR signals

The signals in the ^{1}H NMR spectra of **1a**, **1b** and **1c** were assigned based on positions, multiplicities and integral values. The ^{13}C signals of **1a** were assigned using the correlations in its HSQC and HMBC spectra. The ^{13}C signals of **1b** were assigned by comparison with **1a** and using correlations in its HMBC spectrum. The ^{13}C signals of **1c** were assigned by comparison with **1a** and **1b**.

All the signals in the ^{1}H NMR spectrum of **2b** were assigned by comparison with **1b**. The ^{13}C signals of **2b** were assigned using the correlations in its HSQC and HMBC spectra. The signals for **2a** and **2c** were assigned by comparison with **2b**.

For **3a**, the proton signals, other than those for the phenyl groups, were assigned by comparison with **1a**. The ^{13}C signals and the ^{1}H signals for the phenyl ring were assigned based on the correlations in its HSQC and HMBC spectra. For **3**, ^{13}C signals were assigned using correlations in its HSQC spectrum.

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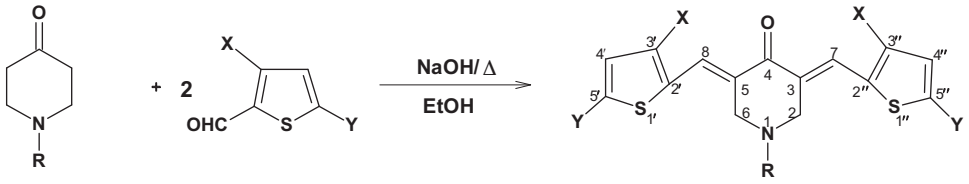


1a, R = X = Y = H

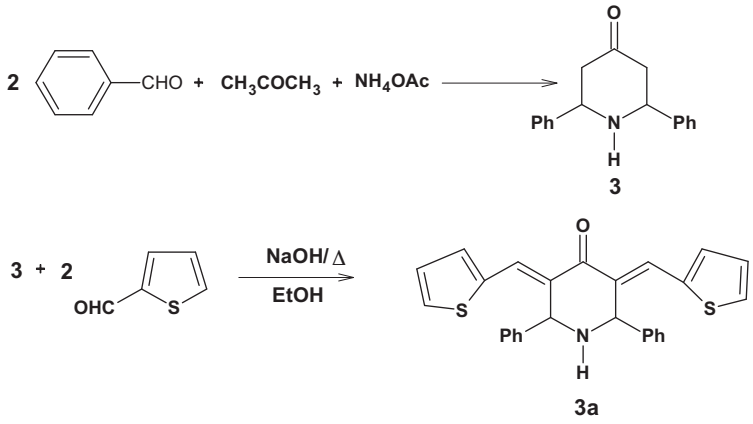
1b, R = Y = H; X = CH_3

1c, R = X = H; Y = Br

2a, R = Me; X = Y = H

2b, R = X = Me; Y = H

2c, R = Me; X = H; Y = Br



Scheme 1.

The ^{1}H chemical shifts are listed in Table 2 and the ^{13}C chemical shifts are listed in Table 3.

2.4. Stereochemistry

2.4.1. Configuration about the C=C bonds

From X-ray crystallographic study it has been found that in **2a**, **2b** and **2c** the configuration about both the C=C bonds is E [6,7]. It has been found [8] that the chemical shift of the vinylic proton in the E-isomers of benzylidenecycloalkanones is about 1 ppm higher than that in the corresponding Z-isomer. The chemical shifts of the vinylic proton in **1a**–**c** and **3a** are close to those observed in **2a**–**c**. Hence, in **1a**–**c** and **3a** the configuration about the C=C bond should be E.

Table 1
IR and mass spectral data.

Compound	IR stretching frequency (cm^{-1})			Mass of parent ion
	C=O	)C=C(	N–H	
1a	1646	1582	3291	287
1b	1646	1583	3300	315
1c	1654	1593	3322	445[a]
2a	1660	1601		301
2b	1660	1591		329
2c	1659	1596		459[a]
3a	1643	1578	3331	439

[a] Corresponds to the mass of molecule with one ^{79}Br and one ^{81}Br.

2.4.2. Conformation of the thiophene ring

Three conformations **A**, **B** and **C** are possible for **1a**–**c** and **2a**–**c** due to rotation of the thiophene ring (Fig. 1). In the NOESY spectrum of **2b** (X = Me; Y = H) the methyl protons of the thiophene ring showed NOE with the vinylic proton. Also there was no NOE between the methyl protons of the thiophene ring and the methylene protons of the piperidine ring. Thus, **2b** should adopt conformation **A** in solution also. By analogy **1a**–**c**, **2a** and **2c** may also be expected to adopt conformation **A** in solution. Compounds **3a** may also be expected to adopt a similar conformation. The preferred conformation of the thiophene group in all these compounds is as that shown in Scheme 1.

2.4.3. Conformation of the piperidine ring

In all these compounds (**1a**–**c**, **2a**–**c**, **3a**) atoms C-3, C-4 and C-5 are sp^2-hybridized. Hence, atoms C(1), C(2), C(3), C(4) and C(5)

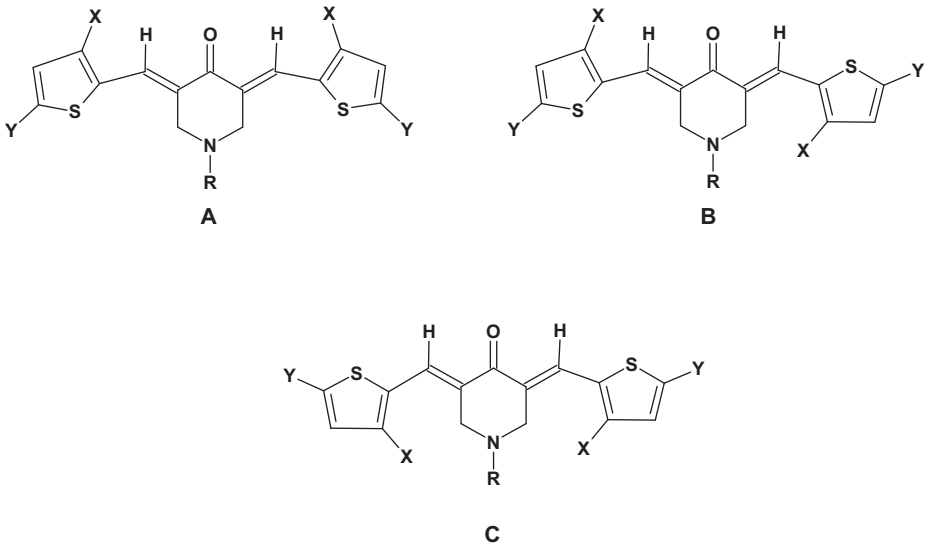


Fig. 1. Possible conformations of compounds **1a–c** and **2a–c**.

might be almost coplanar in these compounds. Indeed by X-ray crystallographic studies [6,7] it has been found that atoms C(1), C(2), C(3), C(4) and C(5) are almost coplanar. The observed torsional angles in **2b** [7] are shown Fig. 2. Two sofa conformations, one with the nitrogen atom above the C(1), C(2), C(3), C(4), C(5) plane and the other with the nitrogen atom below this plane can be written for these compounds. For each sofa conformation two conformations are possible due to inversion at nitrogen. The four possible conformations **SN**, **SN′**, **S′N′** and **S′N** are shown in Fig. 3. For **1a–c** and **2a–c** in any conformation one of the methylene protons will be equatorial like and the other proton will be axial like. The equatorial proton in **SN** and **SN′** is axial in **S′N′** and **S′N** and *vice versa*. The chemical shift of any methylene proton (equatorial or axial) in **S′N** should be the same as that of the corresponding methylene proton in **SN′**. The same is true for conformations **S′N′** and

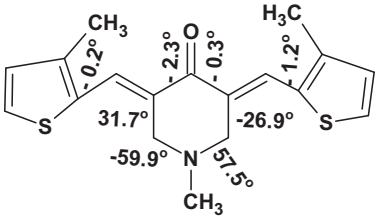
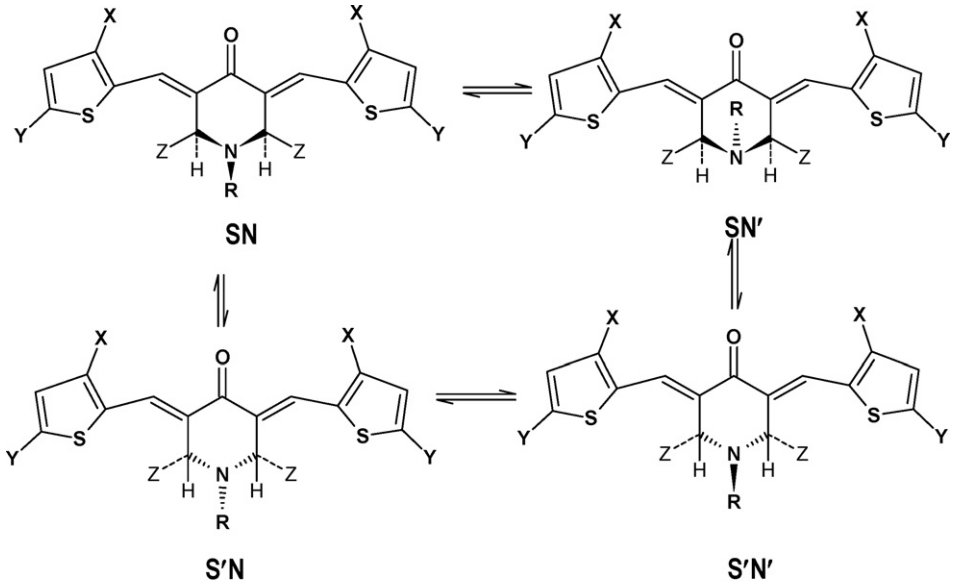


Fig. 2. Observed torsional angles in **2b**.

SN. Conformations **SN** and **S′N′** or conformations **SN′** and **S′N** cannot differ in energy. However, conformations **SN** and **SN′** or **S′N′** and **S′N** should differ in energy. In the ^{1}H NMR spectra of **1a–c** and **2a–c** only one signal is observed for the methylene protons.



For 3a, Z = Ph others Z = H

Fig. 3. Interconvertible sofa conformations of compounds **1a–c**, **2a–c** and **3a**.

Table 2
^{1}H chemical shifts (ppm) of compounds **1a–c**, **2a–c 3a**, **2** and **3**.

Compound	NH/N–CH_3	H-(2,6)	H-(7,8)	H-(3′,3″)	H-(4′,4″)	H-(5′,5″)	(3′,3″)-CH_3
1a	2.21	4.19 (d, *J* = 1.52 Hz)	7.95	7.34 (d, *J* = 3.66 Hz)	7.16 (dd, *J* = 3.66, 5.19 Hz)	7.66 (d, *J* = 5.19 Hz)	–
1b	2.29	4.19	8.04	–	6.98 (d, *J* = 5.19 Hz)	7.47 (d, *J* = 4.88 Hz)	2.43
1c	2.20	4.09 (d, *J* = 2.14 Hz)	7.79	7.11 (d, *J* = 3.97 Hz)	7.08 (d, *J* = 3.97 Hz)	–	
2a	2.59	3.81 (d, *J* = 1.83 Hz)	7.93	7.33 (d, *J* = 3.67 Hz)	7.15 (dd, *J* = 4.17, 5.19 Hz)	7.56 (d, *J* = 5.19 Hz)	
2b	2.58	3.80	8.03	–	6.97 (d, *J* = 5.0 Hz)	7.46 (d, *J* = 5.0 Hz)	2.42
2c	2.59	3.71 (d, *J* = 1.52 Hz)	7.77	7.12 (d, *J* = 3.97 Hz)	7.08 (d, *J* = 3.97 Hz)	–	
3a[a]	2.0	5.59	8.25	7.09	6.96 (dd, *J* = 3.666, 4.88 Hz)	7.37 (d, *J* = 4.88 Hz)	
2	2.07	2.39					
3[b]	2.20	4.09					

[a] *Ortho* 7.06 ppm, *meta* and *para* 6.85 ppm.
[b] *Ortho* 7.48 ppm, *meta* 7.40 ppm and *para* 7.26 ppm.

Hence, it may be concluded that **1a–c** and **2a–c** exist as an equilibrium mixture of conformations **SN**, **SN′**, **S′N′** and **S′N**. The relative population of **SN** should be same as that of **S′N′** and the relative population of **SN′** should be same as that of **S′N**. They are undergoing interconversion at a faster rate so that the methylene protons are seen in an average environment. Indeed the unit cell of **2c** has been found to contain two molecules, one adopting conformation **SN** and the other adopting conformation **S′N′**. In **2a–c** the N-methyl group should prefer equatorial position. Hence, these compounds should largely exist in conformation **SN** and **S′N′**. For **3a** conforma-

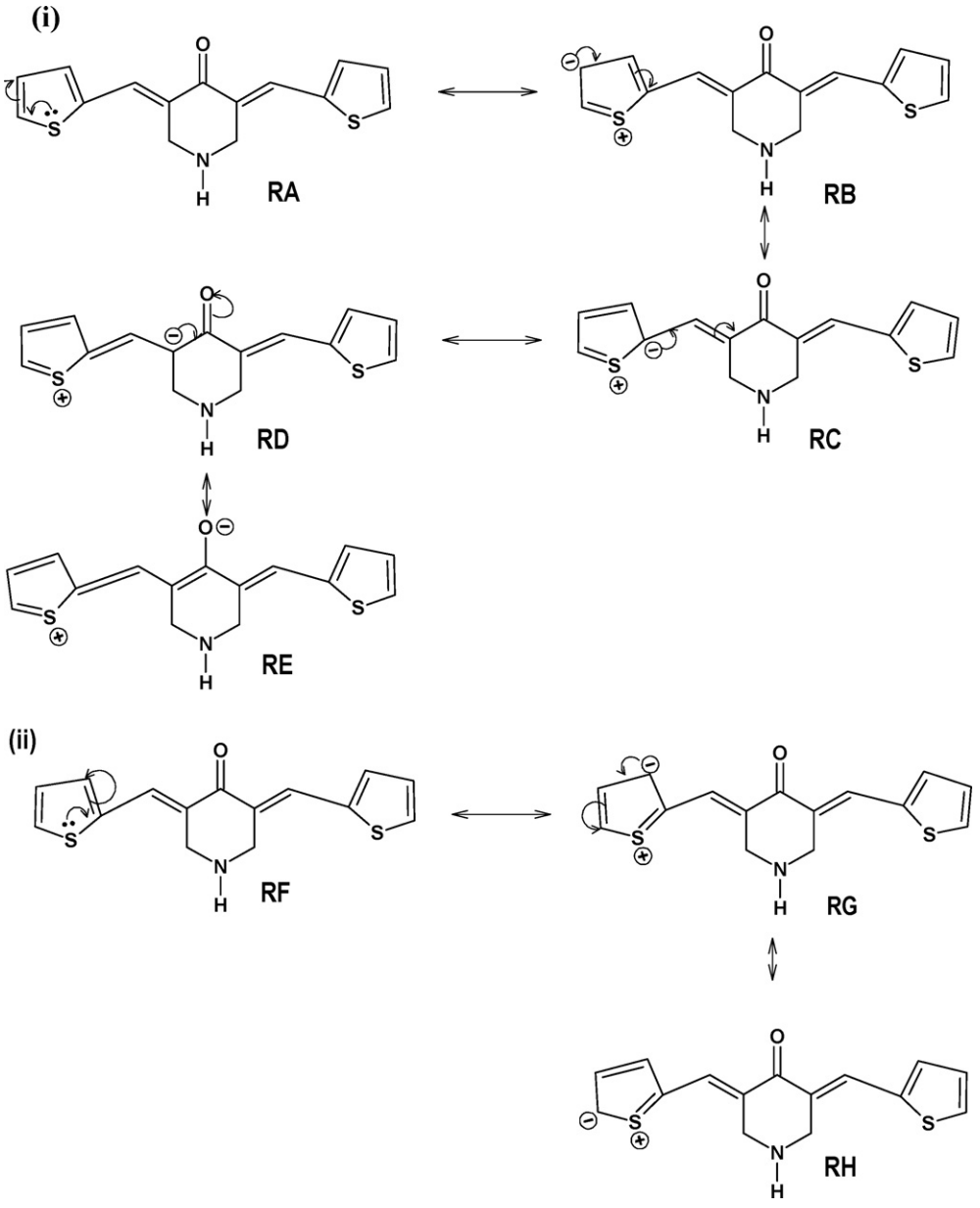
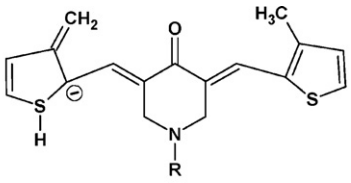


Fig. 4. Possible resonance structures of **1a–c** and **2a–c**.



RI

1b, R = H

2b, R = CH_3

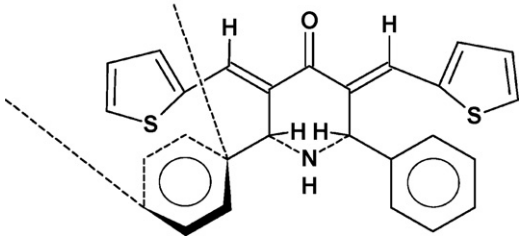


Fig. 5. Anisotropy of phenyl group.

tions **S′N** and **S′N′** should have the phenyl groups in axial positions. Hence, these conformations should be of very high energy and cannot contribute significantly. Thus, **3a** should exist as an equilibrium mixture of conformations **SN** and **SN′** which are not equivalent.

2.5. Analysis of chemical shifts

2.5.1. Chemical shifts of *1a*

In **1a**, the chemical shifts of the protons of the thiophene ring decrease in the order H-(5′,5″) > H-(3′,3″) > H-(4′,4″). This trend can be explained as follows: the possible resonance structures of **1a–c** and **2a-c** are given in Fig. 4. Among the resonance structures **RA**, **RB**, **RC**, **RG** and **RH**, which involve the movement of the lone pair of electrons of the sulphur within the thiophene ring, structures **RB** and **RG**, with a greater charge separation must contribute to a greater extent than structures **RC** and **RH**. Hence, higher negative charges are placed on C-(3′,3″) and C-(4′,4″) than on C-(2′,2″) and C-(5′,5″). Therefore, H-(5′,5″) have a higher chemical shift than H-(3′,3″) and H-(4′,4″). Protons H-(3′,3″) have a higher chemical shift than H-(4′,4″) because they are close to the C=C bond and are deshielded by its magnetic anisotropic effect. However, ^{13}C chemical shifts decrease in the order C-(3′,3″) > C-(5′,5″) > C-(4′,4″). The higher chemical shift of C-(3′,3″) is due to the β-effect of the methyl substituent.

2.5.2. Effects of the C-methyl group

Comparison of **1b** with **1a** suggests that C-(3′,3″) is deshielded by 9.6 ppm by the methyl group. In **2b** this deshielding is 9.7 ppm. These effects are quite comparable to the effect (9.3 ppm) [9] of a methyl group in toluene. In toluene the methyl group has only small effects on *ortho* and *meta* carbons but shields the *p*-carbon by 2.9 ppm [9]. However, the shielding on C-(2′,2″) by the methyl group is 6.3 ppm. In **2b** this shielding is 6.5 ppm. The observed shieldings in **1b** and **2b** suggest that structure **RI** contributes to them significantly.

However, the methyl group shields C-(5′,5″) but deshields C-(4′,4″). This is probably due to a decrease in the contribution of

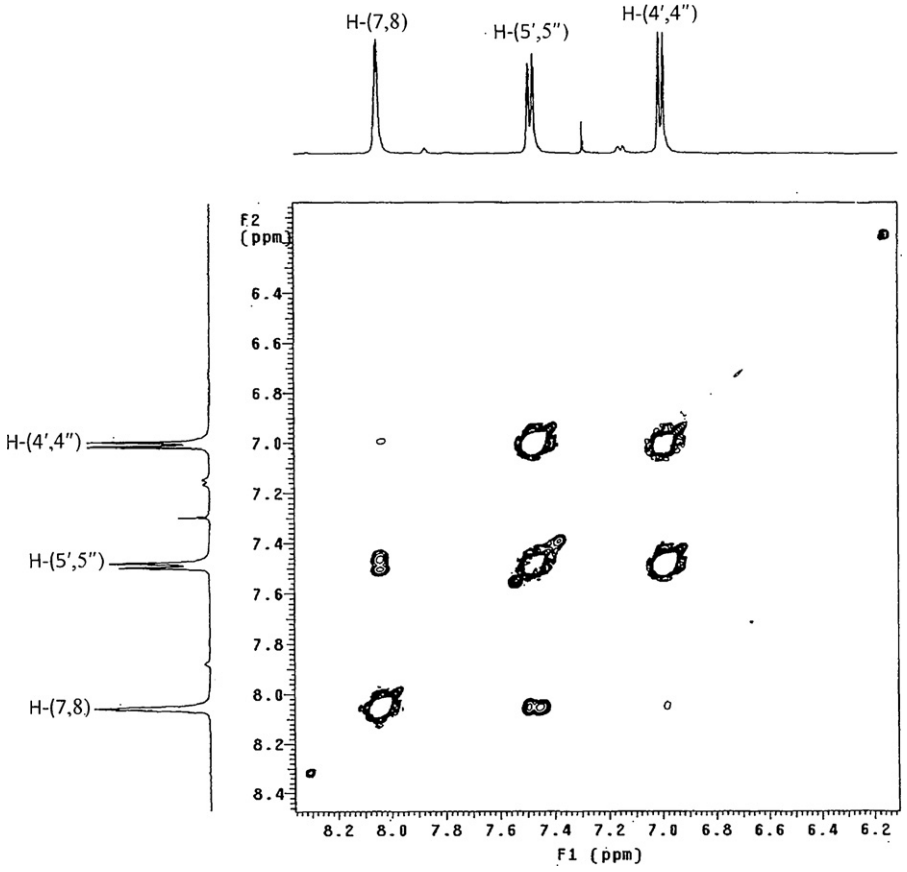


Fig. 6. A part of ^{1}H–^{1}H COSY spectrum of **2b**.

Table 3
^{13}C chemical shift (ppm) of **1a–c**, **2a–c**, **3a**, **2** and **3**.

Compound	C=O	C-(2,6)	C-(3,5)	C-(7,8)	C-(2′,2″)	C-(3′,3″)	C-(4′,4″)	C-(5′,5″)	N–CH_3	(3′,3″)-CH_3
1a	187.0	47.9	132.1	128.2	139.0	133.4	128.2	130.7		
1b	187.4	47.8	131.2	126.3	132.7	143.0	130.9	128.9		14.8
1c	186.0	47.8	133.5	127.7	140.5	132.2	131.1	118.4		
2a	186.3	56.8	130.6	128.1	138.9	133.2	128.5	130.5	46.2	
2b	186.6	56.7	129.4	126.6	132.4	142.9	130.7	128.8	46.1	14.7
2c	185.9	56.7	133.5	128.0	140.3	131.1	130.6	118.4	46.3	
3a[a]	188.3	58.4	133.0	130.1	138.4	133.4	127.9	131.3		
2	208.1	55.3	41.1						45.4	
3[b]	207.8	61.0	50.2							

[a] *ipso* 139.7 ppm, *ortho* 128.9 ppm, *meta* 127.8 ppm, and *para* 126.6 ppm.
[b] *ipso* 142.6 ppm, *ortho* 126.4 ppm, *meta* 128.6 ppm, and *para* 127.7 ppm.

structure **RA** to the resonance. Such a decrease should shield H-(5′,5″) but deshield H-(4′,4″). However, H-(4′,4″) in **1b** is shielded relative to **1a**. Probably, the magnetic anisotropy of the C–CH_3 bond shields it.

2.5.3. Effects of the bromine atom

Comparison of **1a** and **1c** suggests that the bromine atom shields C-(5′,5″) by 12.3 ppm. Though this is due to the well-known heavy atom effect [10] the observed shielding in **1c** is much higher than that (5.4 ppm) [9] observed in bromobenzene. Also, in bromobenzene the *ortho* and *meta* carbons are deshielded by 3.4 and 2.2 ppm, respectively, relative to benzene. Though in **1c** C-(2′,2″) and C-(4′,4″) are deshielded relative to **1a**, C-(3′,3″) are slightly shielded. Also, in bromobenzene the *ortho* protons are deshielded and the other (*meta* and *para*) protons are not influenced by the bromine atom [11]. However, in **1c** the protons of the thiophene rings are shielded by the bromine atom. Similar observations are made in **2c**. All these observations suggest that effects of bromine on the ^{1}H and ^{13}C chemical shifts of the thiophene ring in **1c** and **2c** are much different from those observed in bromobenzene.

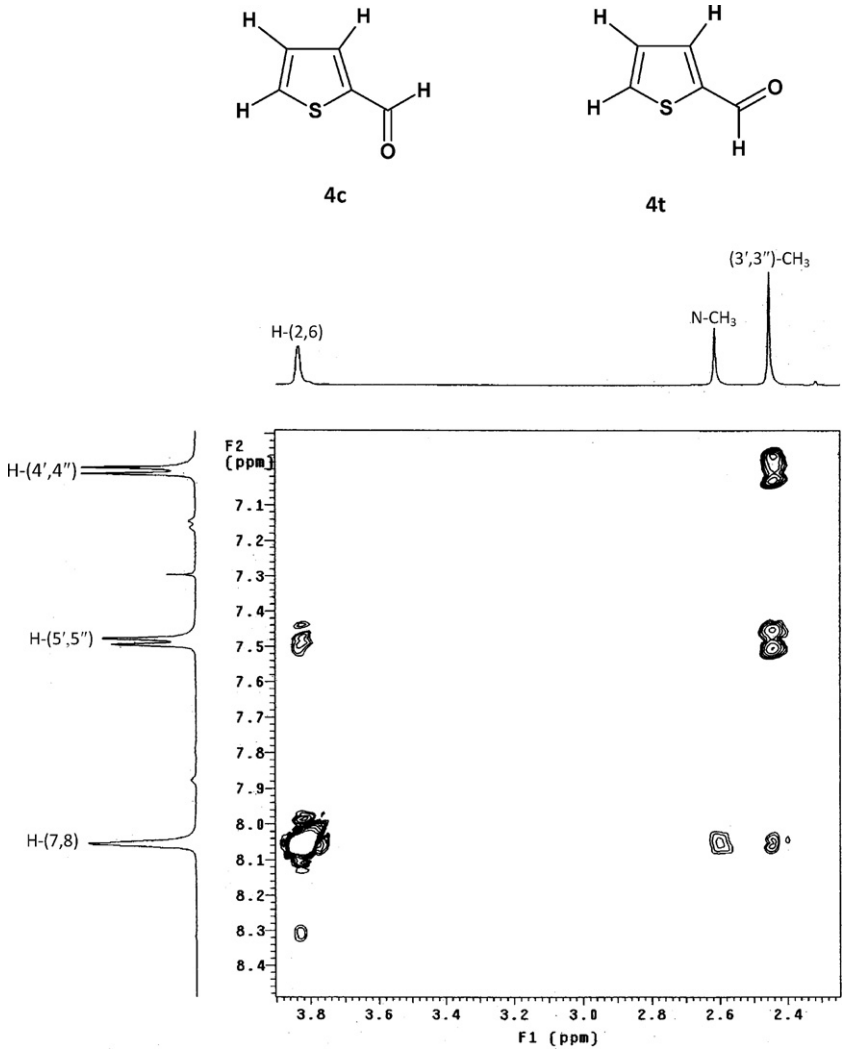


Fig. 7. A part of ^{1}H–^{1}H COSY spectrum of **2b**.

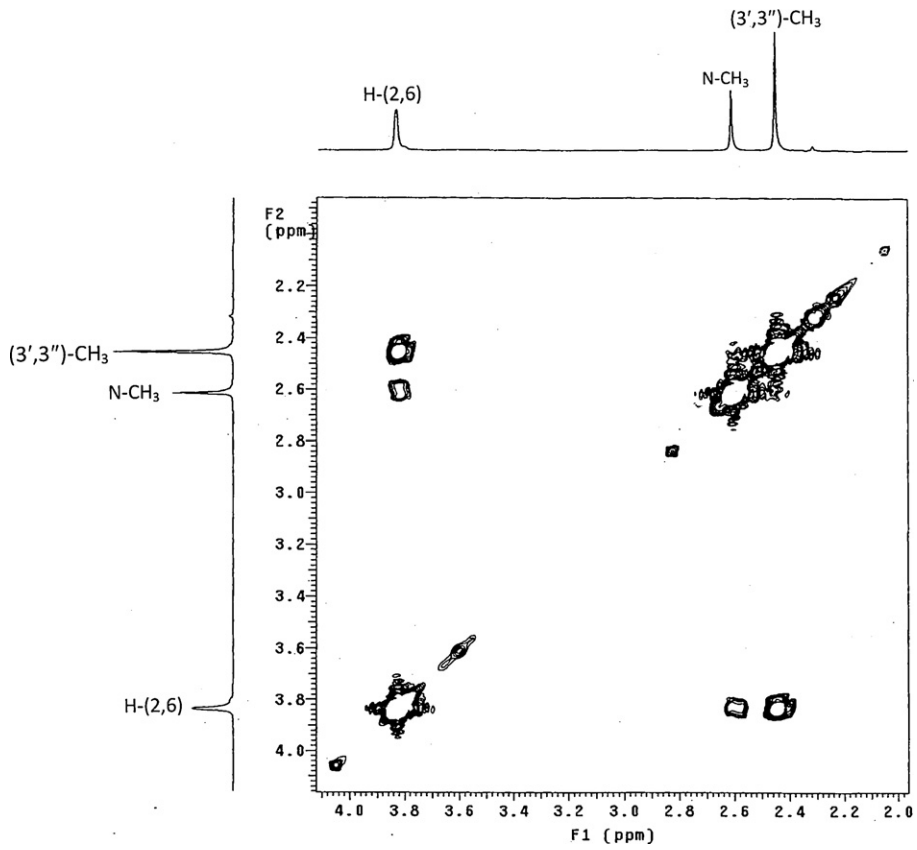


Fig. 8. A part of ^{1}H–^{1}H COSY spectrum of **2b**.

2.5.4. Effects of N-methyl group

Comparison of **1a** and **2a** suggests that N-methylation shields the methylene protons H-(2,6) by 0.38 ppm but deshields the methylene C-(2,6) by 8.9 ppm. These effects are comparable to those (shielding of H-(2,6) by 0.46 ppm and deshielding of C-(2,6) by 9.1 ppm) [12] of N-methyl group in N-methylpiperidine.

2.5.5. Effects of the phenyl group

Comparison of **1a** and **3a** suggests that the phenyl group shields the protons of the thiophene ring but deshields H-(7,8). The phenyl group should be almost parallel to the axial like C–H bond at C-2 (or C-6). It can be seen from Fig. 5, that in such an orientation the protons of the thiophene ring lie in the shielding region of the phenyl group. However, the vinylic proton H-(7,8) lies in the deshielding region and, therefore, is deshielded.

It is also seen that the phenyl group deshields C-(2,6) by 10.5 ppm. This is due to the α-effect of the phenyl group. However, α-effect of the phenyl group in cyclohexane derivatives and saturated six-membered heterocyclic compounds are around 15–17 ppm [13]. Also in these compounds β-effects of phenyl group are around 7–8 ppm [13]. However, the chemical shift of C-(3,5) is not influenced by the adjacent phenyl group. The presence of adjacent exocyclic double bond markedly reduces the α and β-effects of the phenyl group. However, the vinylic carbon which is gamma to the phenyl group, is deshielded by the phenyl group.

2.5.6. Effects of the thienylmethylene group

Comparison of **2** and **2a** suggests that the thienylmethylene group at C-3 deshields the methylene protons by 1.42 ppm. This is a marked effect (about 60% increase). However, the deshielding on the methylene carbon is only 1.5 ppm, which is very small (only about 3%). Obviously, the deshielding on the methylene protons is due to the magnetic anisotropic effect of the thienylmethylene group.

Comparison of **3** and **3a** suggests that the protons of the phenyl group are shielded by the thienylmethylene group. This again is due to the magnetic anisotropic effect of the thienylmethylene group. It is obvious that the phenyl protons lie in the shielding region of the thienylmethylene group. The *ipso* carbon of the phenyl group is shielded whereas the *o*-carbons are deshielded by the thienylmethylene group. The *o*-carbons are at δ-positions with respect to the thienylmethylene group. The *m*-carbons and *p*-carbon are slightly shielded by the thienylmethylene group. Comparison of **3** and **3a** suggests that the thienylmethylene group shields the carbonyl group by 19.5 ppm. This is due to the reduction of positive charge on the carbonyl carbon due to the contribution of resonance structure analogous to **RE** to **3a**.

2.6. Long range couplings

Though there can be allylic coupling between the vinylic proton and the methylene protons, in all cases the signal for vinylic proton appeared as a singlet. In the ^{1}H NMR spectra of **1a**, **1c**, **2a** and **2c** the methylene protons appeared as a doublet with a *J* value of 1.5–2.1 Hz. In order to study the various possible proton–proton couplings ^{1}H–^{1}H COSY spectrum was recorded for **2b**. Three parts of the ^{1}H–^{1}H COSY spectrum are shown in Figs. 6–8.

Fig. 6 shows the correlations among the vinylic proton and the protons of the thiophene ring. In **2b**, the value of $J_{4'5'}$ is 5.0 Hz. There is a strong correlation between H-(4′,4″)and H-(5′,5″) corresponding to this *J* value. There is a moderate correlation between H-(7,8) and H-(5′,5″) indicating a small coupling between them. Also, there is a weak correlation between H-(7,8) and H-(4′,4″) suggesting that

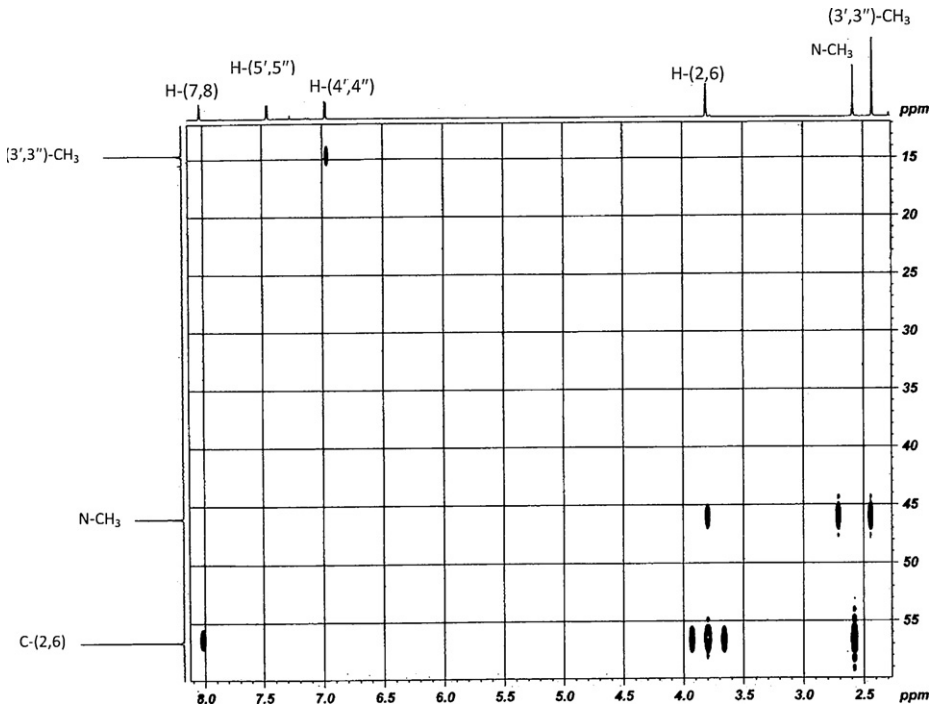


Fig. 9. An expanded part of HMBC of **2b**.

there is a very small coupling between these two protons. Both these couplings involve five bonds but involve different paths. H-(7,8) are anti to the sulphur atoms but, syn to C-(3′,3″). By CNDO/2 calculations it has been shown that [14] in the SO-cis conformation **4c** of thiophene-2-carboxaldehyde the aldehydic proton can have a coupling of 1.286 Hz with H-5 but only a coupling of 0.026 Hz with H-4. In conformation **4t** the coupling between the aldehydic proton and H-5 has been calculated as only about 0.043 Hz whereas that with H-4 has been calculated as 0.884 Hz. In acetone-d_6 the preferred conformation was deduced as **4c** based on the observed long-range coupling between the aldehydic proton and H-5. Since **2b** adopts conformation **A** one should expect the coupling of the vinylic proton with H-(5′,5″) to be higher than that with H-(4′,4″).

In Fig. 7 the strongest correlation is between H-2 and H-7. This corresponds to a J value of around 2.0 Hz. From the observed correlations it is seen that $J_{2,7} > J_{5',3'-CH_3} \approx J_{4',3'-CH_3} > J_{2,5'} \approx J_{7,N-CH_3} > J_{7,3'-CH_3}$. From the observed correlations in Fig. 8, it is seen that $J_{2,3'-CH_3} > J_{2,N-CH_3}$. The coupling between H-2 and H-5′ involves seven bonds.

2.7. Magnetic nonequivalence

In the HMBC spectra, one bond ^{13}C–H couplings are detected as studded peaks instead of cross peaks. An expanded part of the HMBC spectrum of **2b** is shown in Fig. 9. It is seen that the methylene carbons C-(2,6) have studded peaks as well as cross peaks with H-(2,6). This can be explained as follows: though C-2 and C-6 are chemically equivalent, they are not magnetically equivalent. Thus, C-2 is involved in a one-bond coupling with H-2, whereas it is involved in a three-bond coupling with H-6. Similarly, C-6 is involved in a one-bond coupling with H-6 but is involved in a three-bond coupling with H-2. However, H-2 and H-6 have same chemical shift. Thus, a direct correlation due to three-bond coupling and studded peaks due to one-bond coupling are observed between C-(2,6) and H-(2,6) in the HMBC spectrum of **2b**. This observation illustrates the magnetic nonequivalence of C-2 and C-6 and that of H-2 and H-6.

3. Conclusion

In compounds **1a–c**, **2a–c** and **3a** the configuration about C=C bond is E and thiophene group adopts conformation **A**. Piperidine ring in all the seven compounds adopts sofa conformation. The analysis of chemical shifts is done in terms of steric, electronic and magnetic anisotropic effects. The observance of long-range coupling involving seven bonds in ^1H–^1H COSY spectrum of **2b** is interesting. Magnetic nonequivalence of C-2 and C-6 and their corresponding protons are displayed in the HMBC spectrum of **2b**.

4. Materials and methods

4.1. Materials

Piperiridin-4-one hydrochloride, N-methylpiperidin-4-one, thiophene-2-carboxaldehyde, 3-methylthiophene-2-carboxaldehyde and 5-bromothiophene-2-carboxaldehyde were purchased from Sigma–Aldrich. The aldehydes were used after distillation.

4.2. Preparation of compounds

4.2.1. 3,5-Bis[(E)-thienylmethylene]piperidin-4-ones (*1a–c*)

To a solution of piperidin-4-one hydrochloride (0.01 mol) in ethanol (20 mL) appropriate thiophene-2-carboxaldehyde (0.02 mol) and sodium hydroxide solution (20%, 5 mL) were added. The mixture was warmed on a water bath with stirring for 45 min. Then it was allowed to cool to room temperature. The solid obtained was recrystallized from 95% ethanol. The yield and melting points are as follows: **1a**, 82%, 226 °C; **1b**, 80%, 172 °C; **1c**, 70%, 224 °C.

4.2.2. 1-Methyl-3,5-bis[(E)-thienylmethylene]piperidin-4-ones (*2a–c*)

These were prepared by following the literature [6,7] procedures.

4.2.3. 3,5-Bis[(E)-thienylmethylene]-2r,6c-diphenylpiperidin-4-one (**3a**)

To a solution of **3** (0.01 mol) prepared by following the procedure of Baliah et al. [15] in ethanol (20 mL) thiophene-2-carboxaldehyde (0.02 mol) and sodium hydroxide solution (20%, 20 mL) were added. The mixture was warmed on a water bath for 20 min. The solid separated on cooling was filtered and recrystallized from 95% ethanol. Yield 75%; mp 260 °C.

4.3. Methods

The melting points were determined in open capillaries and are uncorrected. IR spectra were recorded on an AVATAR 330 FT-IR Thermo Nicolet spectrometer in KBr pellets. Mass spectra were recorded on JEOL GCmate mass spectrometer.

^{1}H NMR spectra were recorded for **1a**–**c**, **2a**, **2c**, **3a** and **2**, on a Bruker AMX-400 spectrometer operating at 399.88 MHz and for **2b**, on a Bruker DRX-500 NMR spectrometer operating at 500.13 MHz. The spectral parameters are as follows: acquisition time = 1.5–2.0 s, number of scans = 16, number of data points = 32 K and spectral width = around 10,000 Hz.

Proton decoupled ^{13}C NMR spectra were recorded for **1a**–**c**, **2a**, **2c**, **3a** and **2**, on a Bruker AMX-400 spectrometer operating at 100.6 MHz and for **2b**, on a Bruker DRX-500 NMR spectrometer operating at 125.77 MHz. The spectral parameters are as follows: acquisition time = 0.5–1.2 s, number of scans = 1000, number of data points = 32 K and spectral width = around 30,000 Hz.

^{1}H–^{1}H COSY spectrum of **2b** was recorded on a Bruker AMX-400 spectrometer, using standard parameters. HSQC spectra of **1a**, **2b**, **3a** and **3**, HMBC spectra of **1a**, **1b**, **2b**, **3a** and **2**, and phase-sensitive NOESY spectrum of **2b** were recorded on a Bruker DRX-500 NMR spectrometer using standard parameters. The number of data points was 1 K. For NOESY spectrum the mixing time was 800 ms.

All NMR measurements were made in 5 mm NMR tubes using solutions made by dissolving about 10 mg of the material in 0.5 mL of $CDCl_3$.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.saa.2010.12.062.

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