CHAPTER 4

Designing Organic Molecules for Non Linear Optics
4.1. Introduction

Nonlinear optical (NLO) properties arise as the result of the interactions of electromagnetic fields in various media. They produce new fields altered in phase, frequency, amplitude, or other propagation characteristics from the incident fields. Electromagnetic radiation can be regarded as an oscillating electrical field. When a light beam (a form of electromagnetic radiation) is incident on, for example, an inorganic crystal, the ions in the crystal lattice are polarized and oscillate with the radiation. This polarization of ions in turn induces a small electrical field. This induced electrical field alters the direction of the electrical field of the incident light. In linear optics the polarization is proportional to the incident radiation and is responsible for phenomena such as refraction and reflection of the light. However, a laser beam may have a peak field strength of $10^7$ V/m which is comparable to the forces binding the ions together in a crystal lattice. Thus polarization induced by laser can induce highly nonlinear oscillations. In other words the polarization is not proportional to the field strength of the incident radiation. This gives rise to the nonlinear phenomena such as optical mixing and harmonic generation.

The traditional linear optics are based on optical phenomena arising from the interaction between light and materials. The optical properties like refractive index, of these materials are independent of the intensity of incident light intensity. But in nonlinear optics the optical properties of the material are a function of the electric field strength of high intensity light (i.e. a laser) or an externally applied electric field. These materials are useful for applications in nonlinear optics such as second-harmonic generation (SHG, i.e. doubling the frequency of laser radiation) and electro optic phase modulation. The important second order nonlinear optical effects are the frequency doubling (or second harmonic generation, SHG), optical rectification and Pockels effect. SHG is the conversion
of coherent light of frequency $\omega$ into light of frequency $2\omega$. Optical rectification is the ability to induce a direct current (DC) voltage between electrodes placed on the surface of the crystal when an intense laser beam is directed into the crystal. Pockels effect (or linear electro optic effect) is manifested when a DC field is applied to a medium through which an optical wave propagates. All these effects arise through the hyperpolarisability, $\beta$ of a crystal. The degree to which a material exhibits macroscopic second order nonlinear optical properties is dependent upon the microscopic nonlinear polarizabilities of the constituent molecules.

The origin of macroscopic NLO phenomena is given by the familiar equation 1. The bulk polarization $P$ of the material can be expressed as a power series of the applied electric field strength $E$.

$$P = \chi_1 E + \chi_2 E^2 + \chi_3 E^3 + \ldots \quad 1$$

The coefficients $\chi_i$, $\chi_2$, $\chi_3$ in the above equation are the first-, second- and third-order susceptibilities. The IJKL, refer to the coordinate system of the bulk material.

On a microscopic level, a similar expression can be written for the polarizability of a molecule in an applied electric field $^2$.

$$\rho_j = \alpha_j E_j + \beta_{jk} E_j E_k + \gamma_{jkl} E_j E_k E_l + \ldots \quad 2$$

The coefficients $\alpha$, $\beta$, $\gamma$ are the first-, second- and third-order polarizabilities and $E_{jkl}$ refer to the components of the applied field. Like macroscopic susceptibilities, the molecular hyperpolarizabilities are also tensorial quantities and they are determined by the geometry and electronic structures of the molecule.

The two state model expresses hyperpolarizability $\beta$ in terms of measurable spectroscopic and photophysical parameters. This model has been shown to give reasonable estimates of $\beta$ for a number of organic molecules $^3$.

$$\beta = \frac{3\Delta \mu m^2}{2\hbar^2} \cdot \frac{\omega_i^3}{(\omega_i^2 - 4\omega^2) (\omega_i^2 - \omega^2)} \ldots \quad 3$$
In this expression, $\omega_1$ is the energy gap between the ground state and excited state. $\omega$ is the frequency of the incident (laser) light beam, $\Delta\mu_1$ is the dipole moment change between the ground state and excited state and $m_1$ is the transition moment for the optical transition between the two states. From the equation 3 it is evident that the hyperpolarizability ($\beta$) is a function of excited state properties of the molecule. In order to maximize $\beta$, it is necessary to maximize the absolute value of the induced dipole moment $\Delta\mu_1$.

**Origin of optical nonlinearity in organic materials**

Interest in organic materials has steadily grown since the 1980s. This is due to their potentially superior properties over inorganic compounds. In inorganic crystals the optical nonlinearity originates from oscillations of positive and negative ions. These ions have relatively large masses, hence the speed of oscillation and displacement are restricted. The origin of nonlinear optical phenomena in organic materials lies in their conjugated $\pi$-electrons. This phenomenon involves the complete transport of electrons. It is well known that the electron density of a $\pi$-bond is mobile. Hence the electron distribution can be perturbed very easily by the interaction with a radiation field produced by a laser. Therefore the NLO responses of organic molecules are both fast and large in magnitude compared to the inorganic solids. Virtually all organic NLO molecules contain $\pi$ bonds such as the single short polar $\pi$-bond of the carbonyl as in urea or a more extended series of $\pi$-bonds as in benzene and substituted benzene.

**Molecular Engineering:** Molecular engineering can be defined as the planned synthesis of materials providing the simultaneous optimization of molecular and crystal properties responsible for SHG. The first step involved is the design of an active molecule with high hyperpolarizability. The second step is to get an optimized crystal packing of the active molecule, *i.e.* the crystal should have a non centrosymmetric structure.

**4.2. Results**

The synthesis of thiophene derivatives from N-nitrothioacetylpyrroolidine and phenacyl bromide or bromoacetone was discussed in the second chapter. Similar reaction
with N-nitrothioacetylproline ethyl ester and phenacyl bromide or bromoacetone afforded 2-(ethyl N-prolinyl)-3-nitro-4-alkyl/aryl thiophenes.

SCHEME-1

\[
\begin{align*}
\text{O}_2\text{N-} & \quad \text{N} \\
\text{S} & \quad \text{N} \\
\text{CO}_2\text{R} & \quad \text{CO}_2\text{R} \\
1 & \quad + \\
\text{Br} & \quad \text{Br} \\
\text{R'} & \quad \text{R'} \\
\end{align*}
\]

\[
\text{DBU,} \quad \text{Benzene,} \quad 60^\circ \text{C}
\]

\[
\begin{align*}
\text{NO}_2 & \quad \text{N} \\
\text{CO}_2\text{R} & \quad \text{CO}_2\text{R} \\
3 & \quad \text{R'} \\
\end{align*}
\]

\begin{align*}
a) & \quad R = \text{Et} \quad , \quad R' = \text{Ph} \quad c) \quad R = \text{Et} \quad , \quad R' = \text{Me} \\
b) & \quad R = \text{Bz} \quad , \quad R' = \text{Ph} \quad d) \quad R = \text{Et} \quad , \quad R' = \text{Ph} - \text{NO}_2
\end{align*}

i) 2-(Ethyl N-prolinyl)-3-nitro-4-phenylthiophene (3a): The experimental procedure for the synthesis of this compound is described in the experimental section (Scheme 1). It was obtained as a gum in 65% yield, \([\alpha]_\text{D}^\text{MeOH} = -250.93^\circ\). In the infrared spectrum of this compound a peak at 1740cm\(^{-1}\) was observed for the ester carbonyl of proline moiety and a weak peak was seen at 1680\(^{-1}\) corresponding to olefinic CH stretching frequency. The peaks corresponding to nitro group stretching frequencies were seen at 1550 and 1380cm\(^{-1}\). In the ultraviolet absorption spectrum, the compound showed an intense absorption band at \(\lambda_{\text{max}} = 405\text{nm}\) (\(\epsilon: 1.94 \times 10^5\)). This intense broad low energy transition of the donor-acceptor thiophene derivative was assigned to the intramolecular charge transfer (ICT) resulting from the donor (proline moiety nitrogen) to the acceptor (nitro) group. In addition to this broad ICT band, an intense transition at \(\lambda_{\text{max}} = 234\text{nm}\) (\(\epsilon: 1.56 \times 10^6\)) was also observed and this was assigned to a \(\pi - \pi^*\) transition. The \(n - \pi^*\) transition band was not observed for
this compound. In the \(^1\)H NMR spectrum (Spectrum No. 1), a triplet at 1.22\(\delta\) was assigned for the protons of the methyl group, a multiplet at 2.13\(\delta\) was assigned to the four protons on \(\beta\) and \(\gamma\) carbons of proline ring; the multiplet at 3.58\(\delta\) was assigned to NCH\(_2\) group protons and a quartet at 4.11\(\delta\) to the OCH\(_2\) group protons. The NCH proton showed up as a multiplet at 4.60\(\delta\). A sharp singlet was seen at 6.24\(\delta\) for the lone proton of thiophene ring. The five protons of phenyl ring occurred as a multiplet at 7.31\(\delta\). In the \(^{13}\)C NMR spectrum in CDCl\(_3\) (Spectrum No. 2), the signal assignment was made on the basis of chemical shift values and the results of an INEPT experiment. The signal at 13.74ppm was assigned to the methyl group carbon, and the signals at 23.81 and 30.96 were assigned to the \(\beta\) and \(\gamma\) carbons of the proline moiety. The signals at 53.68 and 63.83 were assigned to the \(\alpha\) and \(\delta\) carbons. The signal at 61.19 was assigned to the OCH\(_2\) group carbon and the signal at 106.61 for the C-5 carbon of the thiophene ring. The signals at 127.44, 127.82, 128.12, 128.45 were assigned to the phenyl ring carbons. The signals at 135.42, 137.64 and 154.62 were assigned to C-2, C-4 and C-3 carbons of the thiophene ring. The ester carbonyl was seen at 171.23ppm. The structure of the compound was further confirmed by its mass spectrum, in which the molecular ion peak was observed at 346(m/e); MS(m/e): 273, 212, 142, 141, 139 (100%). The compound analysed for C\(_{13}\)H\(_{18}\)N\(_2\)O\(_4\)S.

ii) 2-(Benzyl N-prolinyl)-3-nitro-4-phenylthiophene (3b):

This compound was synthesized as described in the experimental section. The product was obtained as a thick gum in 60% yield; \([\alpha]\)^{MeOH}_{D} = -262.35\(^\circ\). In the infrared spectrum of this compound, a peak was seen at 1740cm\(^{-1}\) for the ester carbonyl group and the peaks at 1510 and 1370cm\(^{-1}\) corresponding to the nitro group stretching frequencies were observed. In the \(^1\)H NMR spectrum (Spectrum No. 3),
Spectrum No. 2

[Chemical structure image]

160 140 120 100 80 60 40 20 0 PPM

160 140 120 100 80 60 40 20 0 PPM
the multiplet at 2.07δ was assigned to the four protons on β and γ carbons on the proline ring. The multiplet at 3.53δ was assigned to the NCH₂ group protons, the multiplet at 5.07δ for the OCH₂ group protons and a sharp singlet at 6.16δ for the olefinic proton of the thiophene ring. The multiplet at 7.22δ was assigned for the protons of two phenyl rings; In the ¹³C NMR spectrum, the signals at 23.76, 30.03, 53.64 and 63.79 were assigned to the β, γ, α and α carbons of the proline moiety respectively and the signal at 66.93 was assigned to the benzylic carbon. The signal at 106.50 was assigned to the C-5 carbon of the thiophene ring. The signals at 127.40, 127.77, 127.84, 128.04, 128.25 and 128.39 were assigned to the carbons of phenyl rings. The signals at 135.07, 137.53 and 135.26 were assigned to the C-2, C-3 and C-4 carbons of the thiophene ring. The signal at 171.06 was assigned to the carbon of the ester carbonyl group. The structure was further confirmed by the observation of molecular ion peak at 408 in the mass spectrum. MS(m/e): 346, 332, 273 (100%), 237, 135, 105, 91, 77. The compound analysed for C₂₂H₂₀N₂O₄S.

iii) 2-(Ethyl N-prolinyl)-3-nitro-4-methylthiophene (3c):

The synthesis of the compound is discussed in the experimental section. The compound was obtained as an orange coloured liquid in 70% yield; In the infrared spectrum, the peaks were seen at 2900-3000, 1750, 1560, 1530, 1380cm⁻¹; [α]ᵣₑₒ₉ = -556.48°. In the ultraviolet absorption spectrum, the broad intense band at λₑₓₐ₅ 416nm (ε 4.1 x 10⁵) was assigned to the donor to acceptor intramolecular charge transfer transition and another band at 256nm (ε 0.97 x 10⁶) was assigned to the π - π⁺ transition. In the ¹H NMR spectrum (Spectrum No. 4),

the triplet at 1.16δ was assigned to the methyl group protons. A set of multiplets at 2.108, 2.138 and 2.44δ were assigned to the four protons on the β and γ carbons of the proline moiety. A doublet at 2.35δ was assigned to =C-CH₃ protons, the coupling between these protons and the proton on C-5 carbon of thiophene ring was observed. The multiplets at 3.40 and 3.65δ were assigned to the two protons of NCH₂ group. The quartet at 4.09δ was assigned to the OCH₂ group protons. The multiplets at 4.65 and 6.04δ were assigned to
the protons of NCH and \( =\text{CH} \) groups respectively. In the \( ^{13}\text{C NMR} \) spectrum (Spectrum No. 5), the signals at 13.50 and 17.30 were assigned to the carbons of two methyl groups, the latter one being attached to the thiophene ring. The signals at 23.74, 30.39, 54.02 and 60.96 were assigned to the \( \beta, \gamma, \alpha \) and \( \delta \) carbons of the proline moiety. The signal at 63.64 was assigned to the carbon of OCH\(_2\) group. The signals at 132.89, 156.58, 63.76 and 104.25 were assigned to the C-2, C-3, C-4, C-5 carbons of the thiophene moiety. The structure of the compound was confirmed by the observation of molecular ion peak at 284. MS(m/e) : 284(M\(^+\)), 211(100%), 193, 177, 165, 151, 139, 126 and 71. The compound analysed for C\(_{12}\)H\(_{16}\)N\(_2\)O\(_4\)S.

iv) 2-(Ethyl N-prolinyl)-3-nitro-4-(4'-nitro phenyl)thiophene (3d):

The compound was synthesized by following the procedure discussed in the experimental section. The compound was obtained in 81% yield, m.p. 132\(^\circ\)C, \([\alpha]_D^{\text{MeOH}} = -320.83^\circ\). In the infrared spectrum, the peaks were seen at 1750, 1610, 1560, 1450, 1380\(\text{cm}^{-1}\). In the \( ^1\text{H NMR} \) spectrum (Spectrum No. 6), the triplet at 1.24\(\delta\) was assigned to the methyl group protons. A set of multiplets at 2.09, 2.17 and 2.48\(\delta\) were assigned to the four protons on the \( \beta \) and \( \gamma \) carbons of the proline ring and another set of multiplets at 3.48 and 3.71\(\delta\) were assigned to the NCH\(_2\) group protons. The quartet at 4.17\(\delta\) was assigned to the OCH\(_2\) group protons and a multiplet at 4.67\(\delta\) was assigned to the NCH proton. The olefinic proton of the thiophene ring was seen as a sharp singlet at 6.35\(\delta\). A set of multiplets at 7.43 and 8.21\(\delta\) was assigned to the protons of the phenyl ring. The structure of the compound was confirmed by observing the molecular ion peak at 391. The other fragment ion peaks were seen at 345, 142, 113. The compound analysed for C\(_{17}\)H\(_{17}\)N\(_3\)O\(_2\)S.
Spectrum No. 6

The spectrum shows a series of peaks at different δ values (parts per million), indicating the chemical shifts of various protons in the molecule. The peaks are labeled with δ values ranging from 2.0 to 4.8. The structure below the spectrum corresponds to the molecules probed in the NMR experiment, with specific functional groups indicated such as nitro (NO₂) and ethoxy (OEt) groups. The δ values are specific to the different chemical environments of the protons in the molecule, providing insights into the molecular structure and its conformations.
4.3. Discussion

The reaction of ethyl N-nitrothioacetyl proline with phenacyl bromide resembles the classical Hantzsch synthesis of pyrrole. From our methodology it is possible to synthesize chiral thiophene derivatives. Apart from the chiral centre there is a strong push pull system in these thiophene derivatives.

The donor-acceptor charge transfer interactions are very strong in these compounds. This is evident from the significant spectral shifts as a result of low lying charge transfer interactions. Hence it was anticipated that such donor-acceptor charge transfer interactions can lead to anomalously large nonlinear optical susceptibilities and thereby molecular hyperpolarizabilities. Among these thiophene derivatives the compound 3d was a solid. This compound also satisfied the necessary conditions for a molecule to be active in showing second order nonlinear optical properties; i) the crystal must be non-centrosymmetric: the chirality was used as an efficient strategy for achieving this condition. As the thiophene derivative is chiral the product has to crystallize in an acentric crystal structure. Because of push-pull interactions the C-N bond has the partial double bond character. Hence the rotation around C-N bond is restricted and is expected to contribute to make the crystal noncentrosymmetric. ii) The molecule has loosely bound electrons that can be displaced by the optical field. It is clear that the $\pi$-electrons of the push-pull ethylenes can be perturbed very easily. It is also proved that the magnitude of second order hyperpolarizability ($\beta$) increases with strong donor-acceptor combinations. The most dramatic effect is found when both a donor and an acceptor interact in mesomeric fashion. Moreover for a fixed donor group, the nitro group is found to be the strongest acceptor group and for a fixed acceptor, the dialkyl amine group is found to be the strongest donor. Since this thiophene derivative has the combination of strongest donor and strongest acceptor groups, it is anticipated to increase the hyperpolarizability. Moreover the other acceptor nitro group on phenyl ring and the donor sulfur atom of thiophene ring are in conjugation. This forms another push-pull system. The dipoles arising from these two
push-pull systems are parallel and pointing in the same direction. Hence it is likely to increase the ground state dipole moment of the molecule. It was of interest to us to see the impact of parallel dipoles on the magnitude of $\beta$.

But to our surprise, the molecule did not show any second harmonic generation\(^7\). In spite of the compound's high dipole moment and crystallization in a noncentrosymmetric space group it shows no second order NLO property. There are two possible reasons this. It is clear that as the ground state molecular dipoles become larger, the electrostatic interaction between adjacent molecules will increase and the net molecular dipole alignment required to achieve the maximum crystal anisotropy becomes more energetically unfavorable. To avoid this the molecule adopts the quasi-antiparallel molecular packing in the unit cell\(^8\). As a result no second harmonic generation signals will be observed. The second reason is, the second harmonic efficiency depends on the change in dipole moment between an excited state and the ground state. It is likely that the difference in dipole moment of the excited and the ground state of this molecule is not significant.

As a final comment on the molecular engineering, it is important to point out the value of an unprejudiced and objective approach. The molecule 4-nitrobenzonitrile breaks all the rules, and with a strict dogmatic approach one would reject the compound out of hand. But the molecular alignment is quite good and although electronically the molecule is not ideally substituted, \textit{i.e.} two acceptor groups are disposed at para positions on the aromatic ring, it has a powder efficiency ($2 \times$ urea) which is larger than many other well intended and well engineered donor-acceptor molecules.

4.4. Conformational studies

The thiophene derivatives (3a-d) have a strong push-pull system in which the strong electron withdrawing nitro group is in conjugation with strong electron donating prolinyl group. This push-pull system is a part of an aromatic ring system. Because of the push-pull interaction between the nitro and prolinyl group the C$_2$-N bond will have a partial double
bond character as shown in structures 4C and 4D (Scheme 2). As a result these molecules (3a-d) can exist in two conformations.

**SCHEME - 2**

In one conformation the ester group on proline moiety is nearer to the nitro group on thiophene ring. In the second conformation the ester group is away from the nitro group.

Mannschreck observed that the two Me groups attached to the nitrogen in the nitro vinylamine, 1-dimethylamino-2-nitroethylene are nonequivalent. This magnetic nonequivalence is ascribed to a barrier to free rotation around N-C bond. The barrier to rotation around N-C bond in this compound is found to be 16.5 kcas/mol. Similarly the
magnetic nonequivalence of two NCH₂ protons in 1-pyrrolidino-2-nitroethylene is ascribed to a barrier to free rotation around N-C₁ bond. In general the barrier to rotation around C-N bond is more than 9kcal/mol.

In the ¹H NMR spectrum (Spectrum No. 4) of the compound 3c only one set of signals is observed. Hence, of the two possible conformers (4A and 4B) only one conformer is present. The two protons of the methylene group adjacent to the nitrogen atom of the proline unit in compound 3c are differentiated in their chemical shift value. These protons show two multiplets at 3.4 and 3.65δ. The proton in the vicinity of the nitro group is deshielded and appears downfield compared to the other proton. Similarly, the two protons on the γ carbon of the proline moiety are also magnetically nonequivalent. One which is nearer to the nitro group appeared downfield (2.44δ) compared to the other proton (2.14δ). Hence the conformer present in CDCl₃ solution is 4B. Similar observations were made in the ¹H NMR spectrum of compound 3d (Spectra No. 6 and 7).

This preference for conformer 4B of the two possible conformers indicates that this conformer might have lower energy than the other. There are two possible factors which could be responsible for this: i) Non-bonded attraction involving sulfur of thiophene ring and oxygen of ester group, ii) steric reasons.
1) **Non-bonded attractive interaction**: Previously, $^1$H NMR studies on similar push-pull system (i.e. nitromethylene thiazolidine) had been carried out by our group$^{11}$. Nitromethylene thiazolidine (8) exists in hydrogen bonded (E)-configuration in pure CDCl$_3$ (Scheme 3). Only one set of signals is seen corresponding to a single isomer. As DMSO-$d_6$ is added to the solution, the hydrogen bonds are broken and a second set of signals is observed. The second set of signals has been assigned to the Z-isomer. Other tautomeric forms are ruled out by its $^{15}$N NMR spectrum. In pure DMSO-$d_6$, 40% of the compound exists in Z-form. The preference for Z-configuration is due to the non-bonded attractive interaction between oxygen of the nitro group and sulfur atom of thiazolidine ring. The role of non-bonding attractive interaction was proved by carrying out similar $^1$H NMR experiments on compound 9. In this molecule the sulfur atom is replaced by a methylene
group, hence the possibility of S..O attractive interaction is ruled out. This compound exists only in hydrogen bonded form in both polar and nonpolar solvents. These observations support the argument that the non-bonded attractive interaction between sulfur of thiazolidine ring and the oxygen of nitro group is responsible for the presence of Z-isomer of compound 5. These results prompted us to think of the role of similar attractive interactions for the relative preference for conformer 4B (Scheme 4). In order to determine the possible role of non-bonded attractive interactions 2-(ethyl N-prolinyl) nitrobenzene (7) was synthesized and its conformation studied. In this molecule the sulfur atom is absent, hence there is no possibility for non-bonded interaction (Scheme 5). However, the environment (both electronic and steric) around nitro group and prolinyl group is the same as in the thiophene derivatives.

**Scheme 4**

\[
\begin{align*}
\text{Cl} & \quad \text{HN} \quad \text{CO}_2\text{Et} \\
\text{NO}_2 & \quad \text{TEA,} \\
\text{CH}_3\text{CN} & \quad 60^\circ\text{C} \\
5 & \quad 6 \\
\text{NO}_2 & \quad \text{CO}_2\text{Et} \\
\end{align*}
\]

**Scheme 5**

\[
\begin{align*}
\text{O}_2\text{N} & \quad \text{CO}_2\text{Et} \\
\text{N} & \quad \text{CO}_2\text{Et} \\
\text{NO}_2 & \quad \text{CO}_2\text{Et} \\
7a & \quad 7b
\end{align*}
\]
2-Ethyl N-prolinyl nitrobenzene (7): The experimental procedure for the synthesis of this compound is discussed in the experimental section. It was obtained as a gum in 35% yield. In the infrared spectrum peaks at 1750, 1610, 1570, 1520 and 1380 cm\(^{-1}\) are observed. In the \(^1\)H NMR spectrum (Spectrum No. 8) only one set of signals are seen corresponding to one conformer. The triplet at 1.19 δ is assigned to the methyl group protons and a set of multiplets at 1.95, 2.17 and 2.43 δ are assigned to four protons on β and γ carbons of proline ring. The two multiplets at 3.18 and 3.49 δ are assigned to the two protons of the \(\text{NCH}_2\) group. The proton nearer to the nitro group is observed down field compared to the other proton. Hence the conformation 7b is present. A quartet at 4.13 is assigned to OCH\(_3\) group protons. The multiplet at 4.40 δ is assigned to the proton of the α-NCH group. A set of multiplets at 6.85, 7.40 and 7.69 δ are assigned to the four protons on the aromatic ring. In the mass spectrum, the molecular ion peak is seen at 264 and other fragment ions are seen at 247, 191 (100%), 91 and 77. The compound analysed for C\(_{13}\)H\(_{16}\)N\(_2\)O\(_4\). Though there is no sulfur atom in the molecule, the CO\(_2\)Et group prefers to stay away from the nitro group. Obviously it is not because of non-bonded attractive interactions, but because of the steric interaction between the nitro group and CO\(_2\)Et group.

ii) Steric reasons: It is reasonable to extend the same logic to thiophene derivatives (3a-d). Hence it is concluded that the steric interaction between the nitro group and CO\(_2\)Et group is responsible for forcing the molecule 3c to adopt the conformation 4B.
4.5. Experimental Section

Synthesis of 2-(ethyl N-prolinyl)-3-nitro-4-phenylthiophene (3a):

N-nitrothioacetylproline ethyl ester (492 mg) was taken in benzene (8 ml) and DBU (340 mg) was added to the solution. The contents were kept under nitrogen atmosphere and stirred for 10 minutes. Phenacyl bromide (438 mg) in benzene (7 ml) was added to the flask. The reaction mixture was stirred at 60°C for 12 h. The solvent was removed under reduced pressure. The mixture was chromatographed on a silica gel column (benzene: petroleum ether 3:1) to get 450 mg of the pure product. Gum; yield: 65%; [α]D^25° = -250.93; IR(neat): 2900 - 3100, 1740, 1680 (weak), 1550, 1480 and 1380; $^1$H NMR(CDCl$_3$): 1.22(t, 3H, Me), 2.13(m, 4H, 2NCCH$_2$), 3.58(m, 2H, NCH$_2$), 4.11(q, 2H, OCH$_2$), 4.60(m, 1H, NCH), 6.24(s, 1H, =CH), 7.31(m, 5H, Ph); $^{13}$C NMR(CDCl$_3$): 13.74, 23.81, 30.96, 53.68, 61.19, 63.83, 106.61, 127.44, 127.82, 128.12, 128.45, 135.42, 137.64, 154.62, 171.23; MS(m/e): 346(M$^+$), 273, 212, 142, 141, 139 (100%), 105, 85, 83, 77, 70; UV(MeOH): $\lambda_{max}$ 405 nm ($\varepsilon$ 1.94 x 10$^5$), 234 nm ($\varepsilon$ 1.56 x 10$^4$). Found, C, 59.03, H, 5.32, S, 9.12, calculated for C$_{17}$H$_{19}$N$_2$O$_4$S, C, 58.96, H, 5.20, S, 9.25, N, 8.09%.

Synthesis of 2-(benzyl N-prolinyl)-3-nitro-4-phenylthiophene (3b):

This compound was synthesized by following the same experimental procedure as described above. Thick gum; yield: 60%; [α]D^25° = -262.35°; IR(nujol): 2950-3100, 1740, 1510, 1370, 1300, 1160 cm$^{-1}$; $^1$H NMR(CDCl$_3$): 2.07(m, 4H, 2NCCH$_2$), 3.53(m, 2H, NCH$_2$), 4.58(m, 1H, NCH), 5.07(s, 2H, OCH$_2$), 6.16(s, 1H, =CH), 7.22(s, 5H, Ph); $^{13}$C NMR(CDCl$_3$): 23.76, 30.03, 53.64, 63.79, 66.93, 106.58, 127.40, 127.77, 127.84, 128.04, 128.25, 128.39, 135.07, 135.26, 137.53, 171.06.; MS(m/e): 408(M$^+$), 346, 332, 273, 237, 221, 165, 135, 105, 91, 77. Found, C, 64.95, H, 4.97, S, 7.92, N, 6.95, calculated for C$_{22}$H$_{20}$N$_2$O$_4$S, C, 64.71, H, 4.90, S, 7.84, N, 6.86%.
Synthesis of 2-(ethyl N-prolinyl)-3-nitro-4-methylthiophene (3c)

N-nitrothioacetylproline ethyl ester (492 mg) was dissolved in benzene (dry, 10ml). Bromoacetone (275 mg) was added to the solution followed by K₂CO₃ and phase transfer catalyst (TEBA) was used in this reaction. The reaction mixture was stirred at 50°C for 3h. under nitrogen atmosphere. The solvent was removed under vacuum and the product was purified by the chromatography on the silica gel column (benzene : petroleum ether 3:1). Orange coloured liquid, yield: 70%; [α]_D^MeOH = -556.48°; IR(neat): 2900-3000, 1750, 1560, 1530 and 1380; ^1H NMR(CDCl₃): 1.16(t, 3H, Me), 2.108, 2.138 and 2.44(m, 4H, 2NCCH₂), 2.35(d, 3H, =C-Me), 3.40 and 3.65(m, 2H, NCH₂), 4.09(q, 2H, OCH₂), 4.65(m, 1H, NCH), 6.04(m, 1H, =CH); ^13C NMR(CDCl₃): 13.58, 17.30, 23.74, 30.89, 54.02, 60.96, 63.64, 63.76, 104.25, 132.89, 156.58, 171.01; MS(m/e): 284(M⁺), 211(100), 193, 177, 165, 151, 139, 126, 71, 66; UV(MeOH): λ_max 416nm, (ε 4.1 × 10⁵), 256nm (ε 0.97 × 10⁵).


Synthesis of 2-(ethyl N-prolinyl)-3-nitro-4-(4' nitro phenyl)thiophene (3d):

The N-nitrothioacetylproline ethyl ester (492 mg) was taken in dry benzene (15ml) and p-nitrophenacyl bromide (385 mg), K₂CO₃ (280 mg) and 25mg of phase transfer catalyst (TEBA) were added to the solution. The contents were stirred at 80°C for 4h. under nitrogen atmosphere. The product formation was not observed in the absence of phase transfer catalyst. The solvent was evaporated and the product was purified by the chromatographic separation using silica gel column. Yield: 81%, m.p.: 132°C, [α]_D^MeOH = -320.83°, IR(nujol): 1750, 1610, 1560, 1450, 1380cm⁻¹; ^1H NMR(CDCl₃): 1.24(t, 3H, Me), 2.09, 2.17 and 2.48(m, 4H, 2NCCH₂), 3.48 and 3.71(m, 2H, NCH₂), 4.17(q, 2H, OCH₂), 4.67(m, 1H, NCH), 6.37(s, 1H, =CH), 7.43 and 8.21(m, 4H, C₆H₄NO₂); Found, C,64.95, H,4.97, S,7.92, N,6.95%, calculated for C₂₂H₂₀N₂O₄S, C,64.71, H,4.90, S,7.84, N,6.86%.
Synthesis of 2-(ethyl N-prolinyl) nitrobenzene (7)

The proline ethyl ester (910mg) and ortho chloronitrobenzene (788mg) and excess triethylamine (4eq.) were taken in acetonitrile (20ml) and stirred at 60°C for 2 days. Even after 2 days the reaction was not complete. The solvent was evaporated and the product was purified by the chromatography on silica gel column (benzene as an eluent). The product was obtained in 35% yield (calculated from the amount of consumed starting material). Gum; IR(neat): 1750, 1610, 1570, 1520, 1380, 1360 and 1190. $^1$H NMR(CDCl$_3$): 1.19(t, 3H, CH$_3$), 1.95, 2.17 and 2.43(m, 4H, 2NCCH$_2$), 3.18 and 3.49(m, 2H, NCH$_2$), 4.13(q, 2H, OCH$_2$), 4.40(m, 1H, NCH), 6.85, 7.40 and 7.69(m, 4H, Ph); MS(m/e): 264(M$^+$), 247, 191(100%), 144, 131, 117, 104, 91 and 77. Found, C, 59.21, H, 6.25 and N, 10.82%, calculated for C$_{13}$H$_{16}$N$_2$O$_4$, C, 59.09, H, 6.06, N, 10.61%. 
4.6. References

7. Personal communication from Dr.P.K. Das, IISc. Bangalore.