PERKIN 2

Conformational analyses of quinolines substituted with a vinyloxy or vinylthio group at the *ortho* position by means of the NMR selective relaxation method. Experimental verification of the planar conformation in solution

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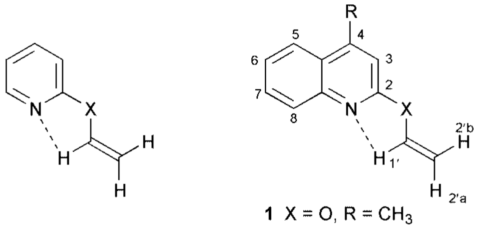
Conformations of 2-vinyloxy-4-methylquinoline (**1**) and 2-vinylthioquinoline (**2**) have been investigated by means of the NMR selective relaxation method where selective non-inversion T_1, T_1^{SNI}, has been used to obtain the cross relaxation terms, σ_{ij}. The interproton distances, r_{ij}, have been estimated using these σ_{ij} values. For the rigid part of the molecule, the values of r_{ij} obtained experimentally give good agreement with the values calculated by the *ab initio* method.

The conformations defined by the rotations about C(2)–X(O or S) and X(O or S)–C(1′) have been analyzed using the equilibrium model, in which the values of σ_{ij} obtained experimentally have been compared with the total average of σ_{ij}, $\sigma_{ij}^{\mathrm{total}}$, and the fractional populations of the pertinent conformers have been determined. The predominance in solution of conformer 1 (see Scheme 2), in which 1′-H is close to the aromatic nitrogen, supporting the planar conformation, has been confirmed for both compounds. Although, for **2**, a small proportion of conformer 3′, with a non-planar conformation, is observed as the second-minimum energy one, the conformational equilibria of **1** lie on the side of the conformer 1.

Introduction

Vinyloxyquinolines and vinylthioquinolines have interesting molecular and electronic properties because of the extra deshielding in NMR chemical shifts[1] observed for one of the vinyl protons. Also these compounds are interesting from the viewpoint of medicinal chemistry since biological activities are reported[2] for some of the derivatives: 6- and 8-vinyloxyquinolines and their metal halide complexes are effective bactericides against microorganisms such as *Staphylococcus aureus*, *E. coli* and others, and 2-vinyloxy- and 2-vinylthioquinolines exhibit effective antitumor activity when copolymerized with maleic acid.



1 X = O, R = CH_3
2 X = S, R = H

Scheme 1 The intramolecular hydrogen bonding proposed for pyridine and quinoline derivatives with a 2-vinyloxy (X = O) or 2-vinylthio (X = S) group.

When ^1H NMR chemical shifts were collected for a variety of pyridine and quinoline derivatives with a vinyloxy or vinylthio group on the aromatic ring, unusual behavior was observed for 2-substituted derivatives:[1] the 1′-H proton shows a specific low field shift, which is unique to the 2-substituted molecules. Such a low field shift is not observed for the 2′-H protons (2′-Ha and 2′-Hb), and intramolecular hydrogen bonding has been proposed between 1′-H and the endocyclic nitrogen as shown in Scheme 1 to explain this specific effect.[1] This proposition means that the conformation which is predominant in solution may be a "planar" one in which 1′-H is directed close to the aromatic nitrogen. For these compounds, the conformational equilibria as shown in Scheme 2 (this Scheme is for quinoline derivatives) are expected, where four conformers are denoted by the two rotational angles about the bonds of C(2)–X (φ = < N(1)–C(2)–X–C(1′)) and X–C(1′) (ϕ = < C(2)–X–C(1′)–C(2′)). From *ab initio* quantum chemical calculations,[3] the global energy minimum for pyridine and quinoline derivatives corresponds to conformer 1 (planar conformation). Furthermore the second energy minimum was found to be around $\varphi = 150 \sim 160°$, and the energy difference between the most stable and the second-minimum energy conformations is 30.5 kJ mol^{-1} for 2-vinyloxypyridine and 10.0 kJ mol^{-1} for 2-vinylthiopyridine. These results from calculation support the specific intramolecular interaction as mentioned above.

In this work, the selective relaxation method which one of the authors proposed previously for conformational analysis in solution[4] has been applied to give experimental support for the above proposition of the planar conformation. This is the prominent method with which to obtain the cross relaxation term and then to provide interproton distances directly. For medium sized molecules, this method can be used as an alternative to 2D NOESY or 1D NOE experiments which provide only relative information on interproton distances. Although, originally in this method, the selective and bi-selective T_1

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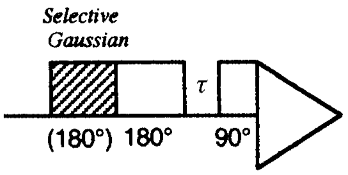
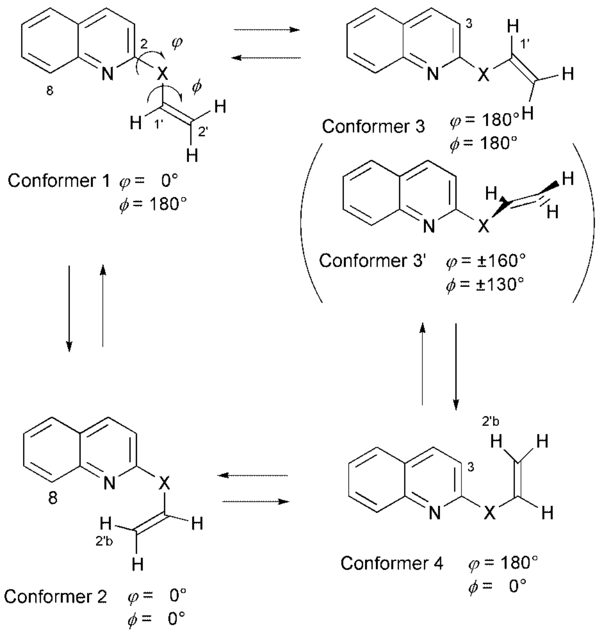


Fig. 1 The pulse sequence for measurement of the selective non-inversion T_1, T_1^{SNI}.



Scheme 2 Conformational equilibria expected for **1** and **2**.

values were used to obtain the cross relaxation term, σ_{ij}, the method has now been modified to make use of the selective non-inversion relaxation time, T_1^{SNI}.[5] The use of the selective non-inversion relaxation time instead of the selective and bi-selective one is beneficial because the decrease in the necessary number of T_1 measurements shortens the experiment time.

Conformations of 2-vinyloxy-4-methylquinoline (**1**) and 2-vinylthioquinoline (**2**) have been investigated by this method.

Experimental

The ^{1}H and ^{13}C NMR spectra were obtained on a Varian VXR-500 instrument (operating at 499.8 MHz for ^{1}H and 125.7 MHz for ^{13}C) at room temperature (23 °C). The non-selective T_1, T_1^{NS}, and the ^{13}C T_1, $T_1(^{13}C)$, were obtained using the conventional inversion-recovery (180°–τ–90°) method. For the measurement of the selective non-inversion T_1, T_1^{SNI}, the pulse sequence shown in Fig. 1 was applied where a Gaussian-shaped selective 180° pulse[6] was used for the achievement of the selective non-inversion condition. The pulse length adopted was 14 μs for the 90°pulse in ^{1}H NMR, 17 μs for the 90° pulse in ^{13}C NMR, and 25 ms for the 180° pulse in the Gaussian-shaped pulse experiment. Also ^{1}H decoupling was achieved by the Waltz sequence when $T_1(^{13}C)$ was measured. For the ^{1}H spectrum of T_1 measurement, the spectral width was 5800 Hz, the number of transients per increment was 4 and the number of data points was 23 040. For $T_1(^{13}C)$ measurement, the spectrum was divided into two parts, a higher field and a lower field region, to get the accurate 90° and 180° pulse, and for each region, the spectral width was 9000 Hz, the number of transients per increment was 192 or 256, the number of data points was 60 032 and a line broadening function of 1.00 Hz was used.

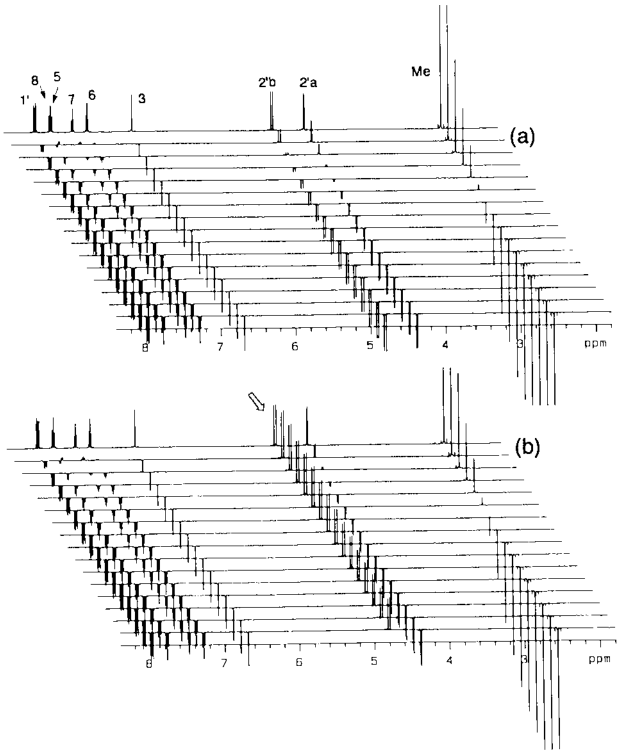


Fig. 2 Series of spectra for (a) the T_1^{NS} measurement and (b) the T_1^{SNI} measurement of **1**, in which the methyl peaks have been clipped. Note that, in (b), the signal for 2′b-H is not inverted.

Fig. 2 illustrates examples of a series of spectra for the measurement of T_1^{NS} and T_1^{SNI}. For both measurements, the waiting times, τ, of 0.05, 0.10, 0.15, 0.20, 0.30, 0.40, 0.60, 0.80, 1.20, 1.60, 2.00, 2.50, 3.00, 4.00, 6.00 and 100 s were used, which were selected to get the initial rate region of a relaxation exponential curve. The error for an exponential curve fitting was less than 3%. All the reported T_1 values are obtained as averages from three or four repeated experiments. The precision for the measurement of ^{1}H T_1 is less than ±2% with careful measurements. Since the value of σ_{ij} is obtained from the difference of the reciprocals of two kinds of ^{1}H T_1 value (as mentioned below), for relatively short T_1 or small cross relaxation, σ_{ij}, values, some problems of precision could arise. Taking into account this precision, the estimated values of σ_{ij} are shown with the range of experimental error, and the allowed ranges of the r_{ij} values also include these errors (Table 4). These errors could be minimized by averaging the repeated measurements.

Compounds **1** and **2** synthesized according to the method reported[7] were dissolved in C_6D_{12} and $CDCl_3$, respectively and the solutions were degassed and sealed under vacuum. The solvent was selected to avoid overlap of signals in the ^{1}H spectrum. The concentration of each solution was *ca.* 10 mM.

Method of analysis

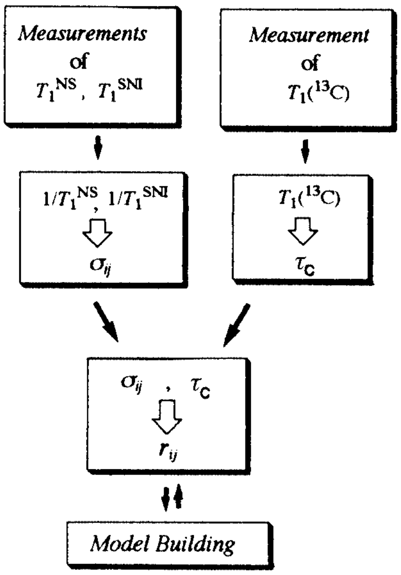
The procedure of the modified selective relaxation method is shown as a flow chart in Scheme 3, where the cross relaxation terms, σ_{ij}, are obtained from two kinds of relaxation times, T_1^{NS} and T_1^{SNI}, and the correlation time for the molecular reorientation, τ_c, is evaluated from the $T_1(^{13}C)$ measurement. The interproton distance, r_{ij}, is estimated by using these σ_{ij} and τ_c values, and the conformation of the molecule can be determined by comparing such estimated r_{ij} values with those calculated under some proposed models of conformation: a suitable model is selected from the proposed models that satisfies well the r_{ij} values derived from the experimental σ_{ij} values.

In a multi-spin system, the non-selective T_1 of proton i, $T_1^{NS}(i)$, is formulated in eqn. (1),[4,8]

$$\frac{1}{T_1^{NS}(i)} = R^i(\text{all}) = \sum_j R^i(ij) = \sum_j N_j\sigma_{ij} + R^i(i) = \sum_j N_j\sigma_{ij} + \sum_j N_j\rho_{ij} + \rho^* \quad (1)$$

Table 1 Observed T_1^{NS} and T_1^{SNI} values and ^1H chemical shifts for **1** in C_6D_{12}

		Observed *i*								
		3	4-Me	5	6	7	8	1′	2′a	2′b
T_1^{NS}/s		16.4	2.88	6.87	8.57	7.32	11.8	14.1	4.13	5.47
	Selected *j*									
T_1^{SNI}/s	3		2.95	6.91	8.53	7.30	11.8	13.9	4.11	5.42
T_1^{SNI}/s	4-Me	19.1		7.81	8.58	7.31	11.9	14.0	4.09	5.47
T_1^{SNI}/s	5	16.5	2.98		10.1	8.69		13.8	4.11	5.45
T_1^{SNI}/s	6	16.2	2.85	7.88		8.21	11.9	13.5	4.09	5.35
T_1^{SNI}/s	7	16.4	2.86	6.80	9.72		14.8	14.1	4.06	5.25
T_1^{SNI}/s	8	16.4	2.93		9.93	8.83		14.3	4.12	5.49
T_1^{SNI}/s	1′	16.4	2.92	6.84	8.60	7.34	12.2		4.54	5.59
T_1^{SNI}/s	2′a	16.5	2.91	6.85	8.52	7.32	11.8	17.0		7.70
T_1^{SNI}/s	2′b	16.2	2.90	6.76	8.54	7.27	11.9	13.5	5.58	
δ_H/ppm		6.691	2.563	7.765	7.288	7.482	7.784	7.984	4.389	4.814



Scheme 3 Flow chart of the modified selective relaxation method for the determination of interproton distance (r_{ij}) leading to the conformational model.

where R means the relaxation rate; R^i(all), $R^i(ij)$, and $R^i(i)$ are the relaxation rates of proton i under the conditions where all protons are inverted, only protons i and j are inverted, and only proton i is inverted, respectively; N_j is the number of magnetically equivalent nuclei for proton j; ρ_{ij} and σ_{ij} are the direct and the cross relaxation terms, respectively, for proton pair i and j; and ρ^* includes the relaxation terms other than the intramolecular dipolar interactions. The selective non-inversion relaxation time, T_1^{SNI}, is defined as the relaxation time observed under the condition in which all spins are inverted except one and then the recovery to thermal equilibrium is monitored for all the spins inverted. So, it is formulated in eqn. (2),[5]

$$\frac{1}{T_1^{SNI}(i,j)} = R^i(\text{all} \neq j) = \sum_{k \neq j} R^i(ik) = \sum_{k \neq j} N_k\sigma_{ik} + R^i(i) = \sum_{k \neq j} N_k\sigma_{ik} + \sum_{k} N_k\rho_{ik} + \rho^* \quad (2)$$

where $T_1^{SNI}(i,j)$ and R^i (all $\neq j$) mean the relaxation time and rate, respectively, of the proton i under the condition where all protons except j are inverted. Furthermore ρ_{ij} and σ_{ij} are represented as in eqns. (3) and (4),[8]

$$\rho_{ij} = \frac{1}{10}\left(\frac{\mu_0}{2\pi}\right)^2 \gamma^4\hbar^2 r_{ij}^{-6}\left\{\tau_c + \frac{3\tau_c}{1+\omega^2\tau_c^2} + \frac{6\tau_c}{1+4\omega^2\tau_c^2}\right\} \quad (3)$$

$$\sigma_{ij} = \frac{1}{10}\left(\frac{\mu_0}{2\pi}\right)^2 \gamma^4\hbar^2 r_{ij}^{-6}\left\{\frac{6_{\tau_c}}{1+4\omega^2\tau_c^2} - \tau_c\right\} \quad (4)$$

where μ_0 is the permeability constant in a vacuum, γ is the proton gyromagnetic ratio, $\hbar$ is the Planck's constant divided by 2π, r_{ij} is the interproton distance between protons i and j, ω is the Larmor precession frequency, and τ_c is the correlation time for molecular reorientation.

This analysis is based on the approximation that the system is a summation of two-spin contributions, which could be limited to the T_1 value obtained from the initial rate region of the relaxation exponential curve. From eqns. (1) and (2) it is easily shown that the cross relaxation term, σ_{ij} is expressed as the difference between the non-selective and the selective non-inversion relaxation rates [eqn. (5)].

$$\frac{1}{T_1^{NS}(i)} - \frac{1}{T_1^{SNI}(i,j)} = R^i(\text{all}) - R^i(\text{all} \neq j) = N_j\sigma_{ij} \quad (5)$$

This difference can remove any contributions from non-dipolar relaxation terms such as paramagnetic oxygen or the quadrupolar effects of nitrogen. And it is seen from eqn. (4) that the interproton distance, r_{ij}, can be estimated from the value of σ_{ij} thus obtained if a reasonable estimation is given for the value of τ_c. To estimate the value of τ_c the experimental value of $T_1(^{13}C)$ can be utilized together with eqn. (6),

$$\frac{1}{T_1(^{13}C)} = N\left(\frac{\mu_0}{2\pi}\right)^2 \gamma_C^2\gamma_H^2\hbar^2 r_{CH}^{-6}\tau_c \quad (6)$$

where N means the number of protons attached to the carbon and r_{CH} is the distance between the carbon and attached proton.

When the molecule takes only one conformation, all of the r_{ij} values experimentally estimated should agree with the corresponding distances calculated for that conformation. In other cases, if the molecule can take different conformations and is undergoing a rapid equilibrium between these conformations, the analysis has to include the contribution from each of these conformations.

When the molecule exists in a conformational equilibrium between two conformers A and B, the average T_1 value of a given nucleus, T_1^{total}, is given by eqn. (7) provided that the rate of interconversion between the two conformers is not faster than the overall molecular tumbling.[8c]

$$\frac{1}{T_1^{total}} = R^{total} = a\frac{1}{T_1(A)} + b\frac{1}{T_1(B)} = aR(A) + bR(B) \quad (7)$$

In eqn. (7) a and b are the fractional populations of the conformers A and B, $T_1(A)$ and $T_1(B)$ are the T_1 values pertaining

Table 2 Observed T_1^{NS} and T_1^{SNI} values and ^{1}H chemical shifts for **2** in CDCl$_3$

		Observed *i*								
		3	4	5	6	7	8	1′	2′a	2′b
T_1^{NS}/s		15.4	9.02	10.7	12.5	9.90	15.0	19.5	6.28	8.13
	Selected *j*									
T_1^{SNI}/s	3		10.9	10.7	12.4	9.88	15.0	19.9	6.20	8.10
T_1^{SNI}/s	4	20.0		12.7	12.1	11.6		19.0	6.18	8.04
T_1^{SNI}/s	5	15.0	10.4		15.4		17.1	18.8	6.05	7.95
T_1^{SNI}/s	6	15.5	8.99	12.5		11.2	15.0		6.62	8.04
T_1^{SNI}/s	7	15.3	9.90		15.6		19.2	19.4	6.24	7.81
T_1^{SNI}/s	8	19.5		12.5	12.1	11.8		19.8	6.06	8.07
T_1^{SNI}/s	1′	16.1	9.05	12.4		11.0	15.4		6.78	8.26
T_1^{SNI}/s	2′a	15.3	9.00	10.7	12.1	9.69	14.9	21.9		
T_1^{SNI}/s	2′b	15.3	9.02	10.7	12.2	9.72	14.9	21.7		
δ_{H}/ppm		7.231	7.955	7.736	7.458	7.671	7.986	7.497	5.582	5.645

Table 3 Observed ^{13}C chemical shifts[a] and $T_1(^{13}\mathrm{C})$[b] and estimated τ_c values

Compounds	Solvent		C(2)	C(3)	C(4)	C(5)	C(6)	C(7)	C(8)	C(9)	C(10)	C(1′)	C(2′)	4-Me
1	C$_6$D$_{12}$	δ_{C}/ppm	159.910	112.874	147.286*	123.628	124.546	129.568	129.198	126.639	147.377*	144.442	94.087	18.676
		$T_1(^{13}\mathrm{C})$/s		3.17		2.85	2.17	2.95	3.07			5.30	2.36	4.04
		$\tau_c/10^{-11}$s		1.47		1.64	2.15	1.58	1.52			0.88	0.99	
3	CDCl$_3$	δ_{C}/ppm	157.351	120.488	136.071	127.627	125.695	129.904	128.253	126.250	148.339	127.757	116.337	
		$T_1(^{13}\mathrm{C})$/s		3.95	4.23	4.37	2.70	3.81	4.35			8.08	3.50	
		$\tau_c/10^{-11}$s		1.18	1.10	1.07	1.73	1.23	1.07			0.58	0.67	

[a] Asterisks imply changeable assignments. [b] Values for quaternary carbons are not listed because of the problem of the accuracy.

Table 4 The obtained σ_{ij} and r_{ij} values[a] compared with the calculated values (r_{ij}^{calc}), for **1** and **2**

		1			**2**			
i	*j*	$\sigma_{ij}/10^{-3}$[b]	$\sigma_{ij}/10^{-3}$[b]	r_{ij}/Å[c]	$\sigma_{ij}/10^{-3}$[b]	$\sigma_{ij}/10^{-3}$[b]	r_{ij}/Å[c]	r_{ij}^{calc}/Å
3	4				15.0 ± 1.2	19.2 ± 2.1	2.3–2.5	2.58
3	4-Me	2.8 ± 1.1		3.3–3.6				3.11
4	5				14.8 ± 2.1	14.3 ± 1.8	2.4–2.5	2.46
4-Me	5		5.9 ± 2.8	2.8–3.4				2.79
5	6	18.7 ± 2.8	17.4 ± 2.2	2.4–2.7	1.34 ± 1.8	14.9 ± 1.5	2.4–2.7	2.54
6	7	13.7 ± 2.2	14.8 ± 2.6	2.5–2.8	15.8 ± 1.5	11.4 ± 1.9	2.5–2.7	2.54
7	8	23.3 ± 2.6	16.8 ± 1.6	2.4–2.6	16.4 ± 1.9	14.3 ± 1.3	2.4–2.5	2.54
1	2′a	12.0 ± 1.3	22.0 ± 4.7	2.2–2.5	5.6 ± 1.0	11.8 ± 3.1	2.3–2.7	2.50
1	2′b		4.0 ± 3.5	2.7–4.3	5.2 ± 1.0	2.0 ± 2.4	>2.6	3.05
2′a	2′b	59.7 ± 4.7	53.2 ± 3.5	1.9–2.0				1.90
3	1′				2.8 ± 1.2	1.1 ± 1.0	3.0–4.8	
8	1′	2.3 ± 1.6	1.0 ± 1.3	>3.2	1.6 ± 1.3	0.8 ± 1.0	>3.1	

[a] Values above the dashed line are those of the rigid part of the molecules and values in the lower part are those depending on the conformation. [b] The estimated values are shown with the ranges of experimental error resulting from the precision for the measurement of T_1. [c] The allowed ranges including the experimental error for the estimated σ_{ij}.

to the conformers A and B, respectively. Combination of eqns. (5) and (7) leads to eqn. (8)

$$N_j\sigma_{ij}^{\mathrm{total}} = \{aR^i(\mathrm{all})(\mathrm{A}) + bR^i(\mathrm{all})(\mathrm{B})\} - \{aR^i(\mathrm{all}\neq j)(\mathrm{A}) + bR^i(\mathrm{all}\neq j)(\mathrm{B})\} \quad (8)$$

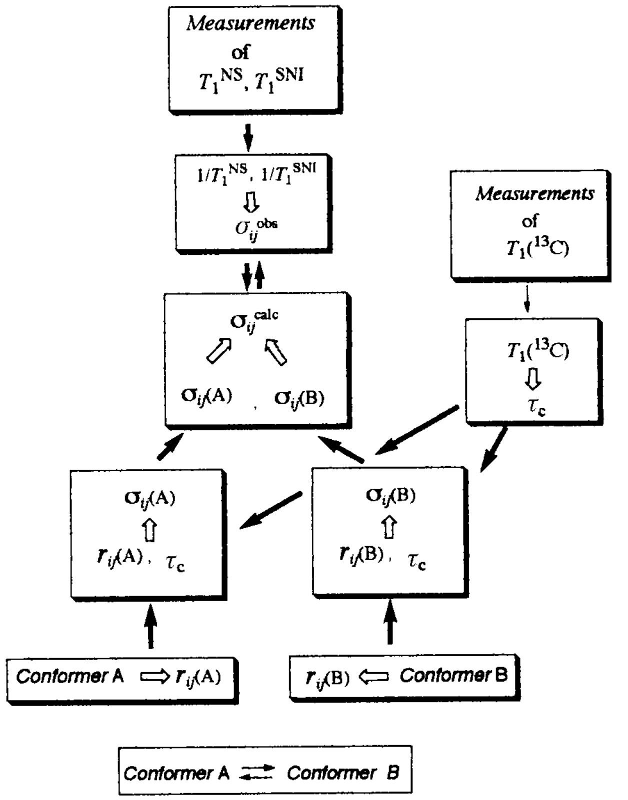
and hence to eqn. (9),

$$\sigma_{ij}^{\mathrm{total}} = a\sigma_{ij}(\mathrm{A}) + b\sigma(_{ij}(\mathrm{B}),\ a + b = 1 \quad (9)$$

where $\sigma_{ij}(\mathrm{A})$ and $\sigma_{ij}(\mathrm{B})$ are the cross relaxation terms between the proton pair of *i* and *j* in conformers A and B, respectively. Eqn. (9) implies that the total value of the cross relaxation term, $\sigma_{ij}^{\mathrm{total}}$, is defined as the sum of terms for individual conformations weighted by their mole fractions. The σ_{ij} value can be calculated according to eqn. (4) when the interproton distance r_{ij} is known together with the correlation time, τ_c^{eff}. Therefore, $\sigma_{ij}(\mathrm{A})$ and $\sigma_{ij}(\mathrm{B})$ can be calculated if the pertinent conformation is assigned and τ_c^{eff} is given. The total flow chart of the analysis is shown in Scheme 4.

Results and discussion

The T_1^{NS} and T_1^{SNI} values obtained experimentally for compounds **1** and **2** are listed in Tables 1 and 2, respectively, in which ^{1}H chemical shifts are also included. The $T_1(^{13}\mathrm{C})$ values are shown in Table 3 together with the ^{13}C chemical shifts. In Tables 1 and 2, it is found that the $T_1^{\mathrm{SNI}}(i,j)$ is significantly longer than $T_1^{\mathrm{NS}}(i)$ for some protons. This larger value of $T_1^{\mathrm{SNI}}(i,j)$ indicates the larger value of σ_{ij} and thus demonstrates the shorter distance between protons *i* and *j*. For example, T_1^{SNI} of 2′-Ha is 5.58 s in **1** when 2′-Hb is selectively non-inverted ($j = 2'$b) (Table 1), which is much larger than the value of T_1^{NS}, 4.13 s, observed for the same proton. This means that σ_{ij} is large and the distance is short for the proton pair of 2′-Ha and 2′-Hb. On the other hand, the enlargement observed on T_1^{SNI} ($j = 8$) of 6-H (9.93 s) of **1** is the effect of the neighbouring



Scheme 4 Total flow chart of the conformational analysis under the equilibrium model.

proton 5-H, the chemical shift of which is very close to 8-H (see Table 1). Similar enhancements are observed on T_1^{SNI} of 7-H ($j = 5$) in Table 1, and 3-H ($j = 8$), 4-H ($j = 7$), 5-H ($j = 8$), 5-H ($j = 1'$), 7-H ($j = 4$), 7-H ($j = 1'$), 8-H ($j = 5$), and 2′-Ha ($j = 6$) in Table 2. The chemical shifts of 4-H and 8-H, and 5-H and 7-H, as well as 6-H and 1′-H are close to each other for **2**.

From the values of T_1^{NS} and T_1^{SNI} in these Tables, the experimental value of σ_{ij} can be estimated through the use of eqn. (5) and these are listed in Table 4. The correlation times (τ_c) are estimated from $T_1(^{13}C)$ together with eqn. (6) and listed in Table 3. Using these σ_{ij} and τ_c values, the allowed ranges of r_{ij} values are obtained from eqn. (4) and are summarized in Table 4, in which the values of r_{ij} calculated from the *ab initio* MO method are also included paying attention to the rigid part only (last column). Despite involving the experimental error ranges, comparison of the values of r_{ij} obtained experimentally with those obtained from the *ab initio* calculation, r_{ij}^{calc}, gives good agreement and gives support for the accuracy of the experiment and the approximations adopted in the analysis.

In contrast to the discussion of the rigid part of the molecules, interpretation of the derived r_{ij} values between protons in the quinoline ring and the vinyl group needs some justified model for the rotations about C(2)–X and X–C(1′). In Scheme 2, in which there are conformational equilibria between four conformers for these compounds, a rather short distance of r_{ij} is predictable for each conformer: $r_{8,1'}$ for conformer 1, $r_{8,2'b}$ for conformer 2, $r_{3,1'}$ for conformer 3 and $r_{3,2'b}$ for conformer 4. In Table 5, these corresponding r_{ij} values calculated from the model for these four conformers are listed, and the calculated values of σ_{ij} from eqn. (4) are also summarized.

By comparing the r_{ij} or σ_{ij} values observed in Table 4 with these calculated values in Table 5, the preferred conformations can be estimated. For **1**, only $\sigma_{8,1'}$ ($\sigma_{1',8}$) and $r_{8,1'}$ are given in Table 4 and the observed values show good agreement with the calculated values in Table 5 for conformer 1 not only on r_{ij} but also on σ_{ij}. This observation means that conformer 1 is predominant for this compound.

Table 5 The calculated values of r_{ij} and σ_{ij} for several conformers of **1** and **2**

Compound	Conformer	$r_{3,1'}$/Å	$\sigma_{3,1'}/10^{-3}$	$\sigma_{1',3}/10^{-3}$	$r_{3,2'b}$/Å	$\sigma_{3,2'b}/10^{-3}$	$\sigma_{2'b,3}/10^{-3}$	$r_{8,1'}$/Å	$\sigma_{8,1'}/10^{-3}$	$\sigma_{1',8}/10^{-3}$	$r_{8,2'b}$/Å	$\sigma_{8,2'b}/10^{-3}$	$\sigma_{2'b,8}/10^{-3}$
1	1 ($\varphi = 0°$, $\phi = 180°$)	4.52	0.49	0.29	4.95	0.28	0.19	3.64	1.84	1.07	6.71	0.05	0.03
	2 ($\varphi = 0°$, $\phi = 0°$)	4.67	0.40	0.24	4.63	0.42	0.28	5.60	0.14	0.08	2.51	17.14	11.23
	3 ($\varphi = 180°$, $\phi = 180°$)	1.49	353.59	231.25	4.46	0.53	0.36	6.43	0.06	0.04	7.22	0.03	0.02
	4 ($\varphi = 180°$, $\phi = 0°$)	3.38	2.78	1.68	0.50	265.41×10^3	179.66×10^3	6.89	0.04	0.02	6.25	0.07	0.05
2	1 ($\varphi = 0°$, $\phi = 180°$)	4.79	0.28	0.14	5.78	0.09	0.05	3.49	1.69	0.91	6.53	0.04	0.03
	2 ($\varphi = 0°$, $\phi = 0°$)	5.40	0.14	0.07	4.58	0.36	0.21	5.47	0.11	0.06	2.65	8.79	5.48
	3 ($\varphi = 180°$, $\phi = 180°$)	1.31	670.33	329.45	4.30	0.53	0.30	6.65	0.04	0.02	8.08	0.01	0.01
	4 ($\varphi = 180°$, $\phi = 0°$)	3.26	2.77	1.36	0.79	13.64×10^3	7.74×10^3	7.61	0.02	0.01	6.16	0.06	0.04
	3′ ($\varphi = \pm 160°$, $\phi = \pm 130°$)	2.25	26.03	12.79	3.71	1.29	0.73	6.69	0.03	0.02	7.98	0.01	0.01

On the other hand, for **2**, there are two r_{ij} values ($r_{3,1'}$ and $r_{8,1'}$) which can be derived and thus suggest a conformational equilibrium between conformer 1 and conformer 3. However, for conformer 3, the calculated distance for $r_{3,1'}$ (1.31 Å) is so short that this conformation seems to be unrealistic. For the *ab initio* calculation using an extended, D95++(α, β), basis set,[3] the second-minimum energy conformer for 2-vinylpyridine is not conformer 3 but the non-planar conformation, conformer 3′ (where $\varphi = \pm 160°$ and $\phi = \pm 130°$). Similarly, in the case of **2**, this conformer 3′ should also be adopted and the possible conformational equilibrium becomes conformer 1 $\rightleftharpoons$ conformer 3′.

According to the flow chart of Scheme 4, the fractional populations of the conformers A and B, *i.e.*, *a* and *b* in eqn. (9), are determined after assuming proper geometries for the two conformers so that the total cross relaxation term, $\sigma_{ij}^{\text{total}}$, coincides well between the calculation and experimental observation. Eqn. (9) is transformed to the eqn. (10),

$$\sigma_{ij}^{\text{total}} = [\sigma_{ij}(1) - \sigma_{ij}(3')]p + \sigma_{ij}(3') \qquad (10)$$

where $\sigma_{ij}(1)$ and $\sigma_{ij}(3')$ are the calculated cross relaxation terms in conformers 1 and 3′ which are listed in Table 5 and *p* is the fractional population of conformer 1. Then, eqns. (11)–(14) are yielded, respectively,

$$\sigma_{3,1'}^{\text{total}} = -2.6 \times 10^{-2} p + 2.6 \times 10^{-2} \qquad (11)$$

$$\sigma_{1',3}^{\text{total}} = -1.3 \times 10^{-2} p + 1.3 \times 10^{-2} \qquad (12)$$

$$\sigma_{8,1'}^{\text{total}} = 1.7 \times 10^{-3} p + 3.4 \times 10^{-5} \qquad (13)$$

$$\sigma_{1',8}^{\text{total}} = 8.9 \times 10^{-4} p + 1.8 \times 10^{-5} \qquad (14)$$

which suggest that $\sigma_{3,1'}$ is the most sensitive to the population, *p*. From these equations and the observed values of $\sigma_{ij}^{\text{total}}$(including errors) in Table 4, the population of conformer 1 (*p*) is estimated; 0.90 ± 0.04 from $\sigma_{3,1'}$, 0.92 ± 0.08 from $\sigma_{1',3}$, 0.94 ± 0.60 from $\sigma_{8,1'}$ and 0.84 ± 0.11 from $\sigma_{1',8}$. Taking into account the sensitivities of these $\sigma_{ij}^{\text{total}}$ to population, the population of conformer 1 is concluded to be 85 ~ 95%. From this result, for **2**, the predominance of conformer 1 is revealed and the second-minimum energy conformer is 3′.

Conclusion

By using the NMR selective relaxation method and a predefined conformational equilibrium model, the predominance in solution of the conformer 1 is confirmed experimentally, in which 1′-H is close to the ring nitrogen supporting the planar conformation as revealed in the *ab initio* calculation. Comparing the second-minimum energy conformation for 2-vinyloxy and 2-vinylthio derivatives, some differences are observed. For **1**, the second-minimum energy conformation is negligible, whereas, for **2**, conformer 3′ is expected to contribute a little.

On *ab initio* quantum chemical calculation,[3] the energy difference between the most stable and the second-minimum energy conformations is larger for 2-vinyloxypyridine (30.5 kJ mol^{-1}) than for 2-vinylthiopyridine (10.0 kJ mol^{-1}). These energy differences correspond to 4×10^{-4}% and 2% of the fractional populations of the minor conformations, respectively. These calculated results are in reasonable agreement with the results observed experimentally for quinoline derivatives.

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