Carbon-13 Chemical Shifts of Methanolic Carbon and Electron Reorganization induced by Hydrogen Bonding for Methanol–Base Complexes

Marie-Christine Moreau Descoings, Gérard Goethals, and Jean-Paul Seguin *
Laboratoire de Chimie Organique Physique, Université de Picardie, 33 rue Saint Leu, 80039 Amiens Cedex, France
Jean-Pierre Doucet
Institut de Topologie et de Dynamique des Systèmes de l'Université de Paris VII, associé au CNRS, 1 rue Guy de la Brosse, 75005 Paris, France

Hydrogen-bonding effects in seven complexes between methanol and *n* or π bases have been studied by ^{13}C n.m.r. spectroscopy and CNDO/2 calculations. Methanol–pyridine associations involve only a transfer of σ electrons from aromatic bases to the hydroxy compound, but in methanol an increase of electron population on the carbon atom is observed along an axis perpendicular to the plane of complex. This suggests a reorganization of in-plane and out-of-plane complex electrons in the methanolic moiety. Linear relationships are established, between i.r. frequency shifts ($\Delta\nu_{OH}$) and semi-empirical quantum parameters, but with different slopes depending on the nature of the substituent. This behaviour is attributed to the method of calculation since a unique linear correlation is obtained when $\Delta\nu_{OH}$ is compared with an experimental parameter such as the ionization potentials of pyridines. Associations induce a shielding effect in the methanol carbon atom whereas the corresponding electron population decreases. A good linear relationship with a negative slope is established between ^{13}C chemical shifts and $\Delta\nu_{OH}$ values. Therefore, the sensitivity of the sp^3 carbon chemical shift to electron population is reversed relative to sp^2 carbon behaviour in neutral molecules or in phenol complexed with bases.

The influence of hydrogen-bonding associations in biological processes, *e.g.* anaesthetic potency,[1] sugar transport through cell membranes,[2] or antitumour activity[3] has been often invoked. Increasing interest therefore focuses on the identification of privileged association sites in polyfunctional systems. An i.r. study[4] established that for 3-methyl-4-pyrimidone the sites of complexation vary depending on the proton-donor acidity. Further extension of this work to other bases indicates that the protonation and complexation positions may differ.[5]

^{13}C Chemical shifts give information for each carbon atom and is an attractive probe for determining association sites. Indeed, for associations between phenols and triethylamine, Ratajczak *et al.*[6] have shown that hydrogen-bond formation can shift the C-1 signal of phenols by up to 15 p.p.m. for the more acidic cases. Maciel and his co-workers[7] measured the equilibrium constant for phenol–acetone complex from the variation of the carbonyl carbon chemical shifts. Recently we proposed that analysis of the dilution curves (δ *versus* concentration of 4-substituted phenol) makes it possible to distinguish between homofunctional (X–Ph–OH ••• HO–Ph–X) and heterofunctional (X–Ph–OH ••• X–Ph–OH) associations.[8] In a previous study, we also established that there is a linear relationship between the C-1 chemical shift of phenol bonded to various bases and the corresponding $\Delta\nu_{OH}$ values.[9]

As biomolecules very often contain hydroxy groups bonded to either sp^2 or sp^3 carbons, we report here the behaviour of an sp^3 carbon bearing a hydroxy group involved in hydrogen bonding. Various complexes of methanol with *n* and π bases have been selected as model systems. The perturbations induced by hydrogen bonding have been investigated by ^{13}C n.m.r. and analysed by semi-empirical CNDO/2 calculations.

Experimental

^{13}C Spectra were recorded on a Bruker WP 80 spectrometer operating at 80 MHz, using tetramethylsilane as internal standard. The magnetic field was locked on the ^2D signal of D_2O (capillary inserted in the sample tube); the probe temperature was 35 °C. All spectra were sampled in a 8 K memory block (digital resolution 0.05 p.p.m.) for a 4 000 Hz spectral width, with complete ^1H noise decoupling. Methanol and the various bases were of spectroscopic grade and used without further purification.

Results

Geometry of the Complexes.—First, the favoured geometries of these complexes were sought by energy minimization using the GEOMO program of Rinaldi *et al.* at the CNDO/2 level.[10] In agreement with recent work,[11] the geometry for the methanol–pyridine complexes corresponds to association with the nitrogen lone pair. The OH bond is in the pyridine plane with H, O, and N atoms lying on the symmetry axis of the pyridine ring. The same geometry was found for all associated or free pyridine molecules with the geometrical parameters determined by Bak *et al.*[12]

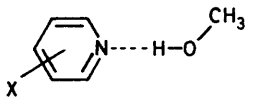
For complexed methanol molecules the C–H bond length was fixed to 1.09 Å with valence angles of 105°, a methyl hydrogen atom being placed *anti* to the hydroxy hydrogen for the methyl carbon, two positions were considered, with the carbon either in the pyridine plane or in a plane perpendicular to the ring, the corresponding energies being very similar. We used the conformation with a methyl carbon coplanar with the ring for subsequent calculations.

Optimized bond lengths for O–H, C–O, and N••• H bonds are in Table 1 for three substituted pyridines. From these results it appears that substitution by electron-withdrawing (CN) or -releasing (Me) groups in the *para* position does not significantly affect the geometrical parameters (Table 1). Therefore, the various substituted pyridine–methanol complexes have been described using the interatomic distances for methanol–pyridine association.

For the methanol–benzene complex, methanol was located outside the plane of the aromatic ring since this association

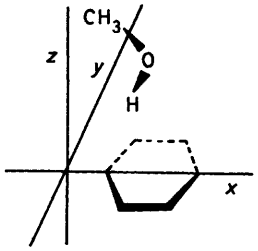
Table 1. Geometrical parameters (Å) for bases associated with methanol

(a) Optimized bond lengths (Å) for pyridines associated with methanol



X	d_{O-H}	$d_{N\cdots H}$	d_{C-O}
4-CN	1.0552	1.521	1.369
H	1.0561	1.514	1.369
4-Me	1.0567	1.510	1.369

(b) Co-ordinates of hydrogen, oxygen, and carbon atoms for methanol associated with benzene



$x_H = 1.92$ $x_O = 2.01$ $x_C = 1.4$

$y_H = 0.95$ $y_O = 0.8$ $y_C = 1.86$

$z_H = 1.63$ $z_O = 2.67$ $z_C = 3.26$

involves the benzene π electrons. A full optimization calculation (performed for all bond lengths and angles for methanol and for the position of the hydroxy proton relative to the benzene ring) gives a geometry for the complex in which the methanolic proton is near one aromatic carbon (Table 1). This result is in agreement with our recent ^{1}H n.m.r. work.[13]

Localized Electron Populations for Complexed Molecules.—For various methanol–base associations, localized electron populations on the associated methanol hydrogen, oxygen, and carbon atoms are summarized in Table 2. The association energies in Table 2 were calculated as the difference between the total energies for the complex and the isolated components). It should be noted that these calculated values are much greater than the measured ones. For the methanol–pyridine complex the calculated value is 11.7 kcal mol^{-1} compared with experimental values of *ca.* 4 kcal mol^{-1}.[14] It is now clearly recognized that such differences are largely due to comparing the gas with the liquid phase.[15]

Hydrogen-bonding Effect on the Methanol Shifts.—Carbon-13 shifts of the methyl carbon have been measured using various bases as solvents, with a methanol concentration of 0.15M (Table 3). For this concentration nearly all the methanol can be considered as hydrogen-bonded to the base. Owing to the small variations observed in the chemical shifts in these various base media, it was necessary to eliminate all contributions to the chemical shifts variations except those induced by hydrogen-bond formation.

Particular attention was therefore to be devoted to non-specific solvent effects resulting from the various media investigated. In a previous study[9] using a variety of bases and phenol as a common proton donor, the specific behaviour of 2-fluoropyridine was interpreted on the basis of a different refractive index (inducing different van der Waals effects). To evaluate such medium effects, the chemical shifts of the methyl carbon, extrapolated to infinite dilution, have been measured in five solvents (pentane, hexane, heptane, di-iodomethane, and carbon tetrachloride). This experimental procedure avoids susceptibility measurements, but allows only 'apparent' medium shifts (relative to Me_4Si) to be formed.[16] A plot of the observed chemical shift *versus* the Rummens g^2 parameter[17] leads to a linear relationship of slope −10. This small value indicates that the resulting chemical shifts corrections could be neglected for all the investigated media (<0.05 p.p.m.).

Magnetic anisotropy corrections have also been evaluated from the complex geometries determined by CNDO optimizations using Bovey diagrams.[18] This model leads to a correction term of −0.3 p.p.m. for the methyl carbon in methanol–pyridine association (planar complex) and of 0.48 p.p.m. when the base is benzene or prehnitene (out-of-plane association).

Table 3 gathers the chemical shifts corrected for these anisotropy effects and the corresponding i.r. association shifts for the various systems investigated ($\Delta\nu_{OH}$ defined as the difference of the stretching ν_{OH} frequencies for free and associated methanol).

Discussion

Association-induced Electron Reorganization.—When methanol is complexed to pyridine, an important electron reorganization occurs on the hydroxy group: the hydrogen atom loses 486 × 10^{-4} electron whereas oxygen gains 740 × 10^{-4} σ electron but loses 37 × 10^{-4} electron in the direction of an axis perpendicular to the plane of the complex (q^z) (Table 4). For each hydrogen atom of the methyl group of methanol the electron population increases by *ca.* 150 × 10^{-4} e. The total carbon electron population decreases by 65 × 10^{-4} e: decreases of 0.0152 e in the *z* direction and increases of 0.0087 σ electron.

Methanol–pyridine association induces an electron transfer of 617 × 10^{-4} e. This reorganization involves only σ electrons since electron populations in orbitals out of plane of the complex (summed over atoms of each moiety) remain nearly constant ($\Delta\Sigma q^z$ 0) (see Table 5). For the associated methanol molecule the total charge increases compared with free methanol ($\Delta\Sigma q^t$ 0.0620). In contrast to the behaviour observed for the pyridine moiety of the complex, the total electron population on the oxygen and carbon atom (sum of the q^z-charges) decreases by 189 × 10^{-4} e. A significant electron reorganization therefore occurs within the methanol molecule, involving a modification of the participation of the out-of-plane hydrogens resulting in the formation of a pseudo π orbital. This behaviour can be explained by a reduction of the hyperconjugation phenomena in the complexed form due to the increase of σ population on the oxygen atom.

When the pyridine ring is substituted by electron-withdrawing groups, q_H values increase compared with that observed in the methanol–pyridine complex. With electron-releasing groups, q_H values decrease, but the reverse behaviour is observed for the oxygen atom: q_O^t is greater for association with collidine.

Comparison between q_H and q_O^t leads to a linear correlation between these two parameters when substituted pyridines are used as base. However, the point corresponding to methanol–benzene clearly deviates from the correlation line (Figure 1).

I.r. Frequency Shifts $\Delta\nu_{OH}$ *and Semi-empirical Quantum Parameters.*—The q_H and q_O^t values have been compared with the methanol frequency shifts ($\Delta\nu_{OH}$), an experimental parameter which may be considered to reflect the relative association strengths. Linear relationships are observed but with different slopes depending of the nature (electron donor or acceptor) of the substituents on the pyridine ring (Figure 2). Stronger intermolecular bonding corresponds to decreased electron population on the hydrogen and an increase on oxygen. In previous work we observed a similar break in the slopes of the correlations when the association shifts were compared with semi-empirical parameters calculated for the free pyridine

Table 2. Localized electron populations on the carbon, oxygen, and hydroxy hydrogen for free or associated methanol and calculated energies of complex formation

Base	q_H	q_O^t	q_O^z	q_C^t	ΔH/kcal mol^{-1}
None	0.8673	6.2293	1.9685	3.8544	
2-Fluoropyridine	0.8209	6.2999	1.9654	3.8483	−11.16
4-Cyanopyridine	0.8211	6.2975	1.9649	3.8483	−11.24
3-Cyanopyridine	0.8218	6.2972	1.9650	3.8485	−11.12
Pyridine	0.8187	6.2996	1.9648	3.8479	−11.75
4-Picoline	0.8168	6.3018	1.9647	3.8476	−12.06
3,5-Lutidine	0.8176	6.3007	1.9647	3.8479	−11.84
2,4,6-Collidine*	0.8130	6.3051	1.9645	3.8480	−12.92
Benzene	0.8221	6.2934		3.8492	

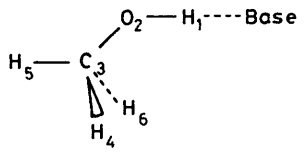
* Calculated for a perpendicular *n* complex owing to steric hindrance for planar association.

Table 3. Observed and corrected ^{13}C chemical shifts of methanol bonded with *n* or π bases and corresponding i.r. association shifts ($\Delta\nu_{OH}$) (from ref. 19)

Bases	δ_{obs}	δ_{corr}	$\Delta\nu_{OH}$/cm^{-1}
Benzene (**1**)	50.2	50.68	31
Prehnitene (**2**)	50.1	50.58	54
2-Fluoropyridine (**3**)	50.1	49.83	162
3-Chloropyridine (**4**)	49.76	49.49	238
Pyridine (**5**)	49.61	49.34	286
4-Picoline (**6**)	49.32	49.05	296
2,4,6-Collidine (**7**)	49.03	48.76	344

Chemical shift of free methanol, δ50.57 p.p.m. Chemical shift in p.p.m. from internal Me_4Si.

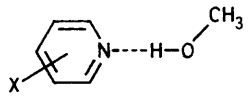
Table 4. Electron population variations for methanol atoms in methanol–pyridine and methanol–benzene associations (10^4 Δq)



	Methanol–pyridine		Methanol–benzene	
Atoms	Δq^t	Δq^σ	Δq^z	Δq^t
H-1	−486	−486		−452
O-2	703	740	−37	641
C-3	−65	87	−152	−52
H-4	162	162		135
H-5	144	144		95
H-6	162	162		135

For the methanol–benzene complex, q^z values are not reported since they do not directly correspond to orbitals contributions. A negative sign corresponds to a decrease of electron population induced by association.

Table 5. Electron transfer (10^4 q) induced by hydrogen bonding for methanol–pyridine association



$\Delta\Sigma q^t$	−617		+620
$\Delta\Sigma q^z$	0		−189
$\Delta\Sigma q^\sigma$	−617		+809
Total transfer		617	
z Transfer		0	
σ Transfer		617	

A negative sign expresses a decrease in electron population. $\Delta\Sigma q^t = \Sigma q^t$ free moiety − Σq^t associated moiety.

substrates (with either electron donor or acceptor groups). It is likely that this behaviour is related to the calculation method used. Indeed a unique linear relationship was obtained when Δν was compared with an experimental parameter such as the ionization potential of pyridines.[20] This observation is also in agreement with the work of Bloor *et al.*[21] suggesting that the effects of electron-attracting substituents are being underestimated.

When the electron donor is a π base, variations in charge are smaller but the same trends are observed. All these results focus on the important observation that when methanol associates with an electron donor, the electron population decreases on the hydroxy hydrogen but increases on the oxygen atom.

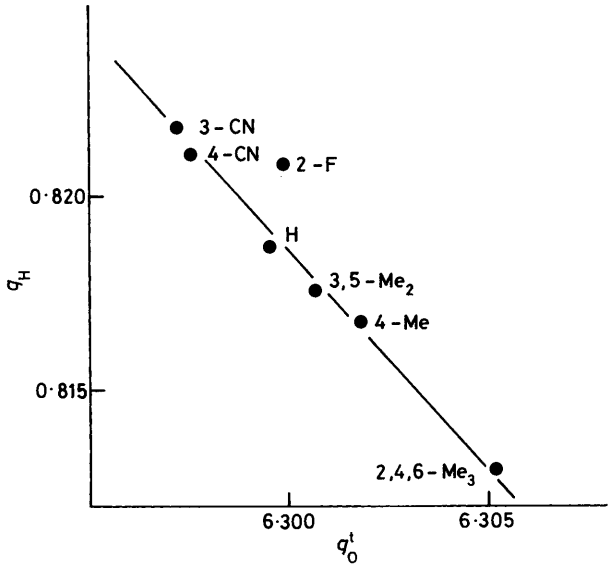


Figure 1. Methanol–pyridine associations: correlation between electron population for hydroxy hydrogen and oxygen atom of bonded methanol

Association-induced Chemical Shifts.—For the methyl carbon, the formation of an hydrogen bond, in all the systems investigated, induces an upfield (shielding) shift (Table 3). This observation contrasts with the results observed for phenol association since complexation leads here to a deshielding of the *ipso*-carbon with respect to hydroxy group. However, CNDO calculations indicate that in the case of association with both pyridine and benzene the electron population on the methyl carbon decreases. The same is true for the *ipso* carbon of phenol

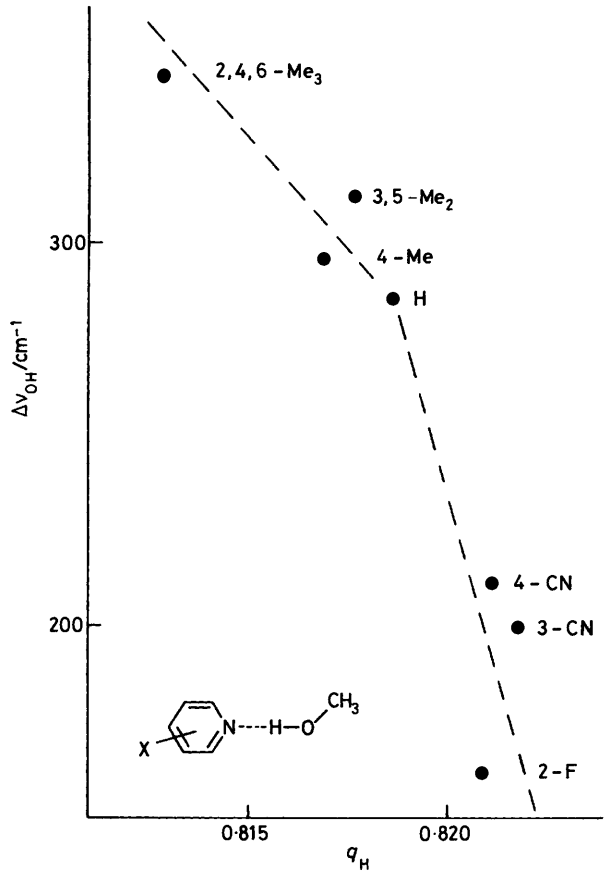


Figure 2. Methanol–pyridine associations: correlation between i.r. frequency shifts and electron population on the associated methanol hydrogen

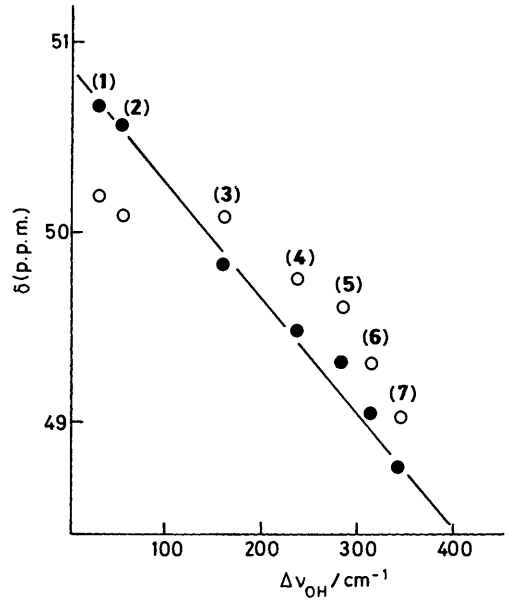


Figure 3. Correlation between methanolic carbon chemical shifts and i.r. frequency shifts for associations with *n* and π bases; ○ experimental values, ● corrected values. Key in Table 3

in similar systems. As the strength of the association increases, the corrected chemical shift values decrease for methanol association whereas they become larger for the *ipso* carbon of

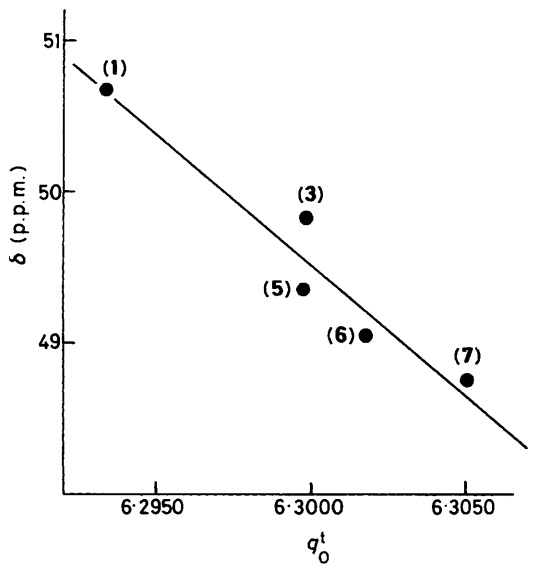


Figure 4. Correlation between carbon chemical shift and electron population of oxygen atoms for methanol–base association. Key in Table 3

phenol. This results in a negative sign for the slope of the δ–$\Delta\nu_{OH}$ relationship (Figure 3) [equation (1)]. With non-corrected

$$\delta = -0.0059\Delta\nu_{OH} + 50.87 \quad (1)$$

mean deviation 0.06; r 0.993

chemical shifts it is not possible to establish a single linear correlation.

These observations are in apparent conflict with the simple rationale of common δ–q relationships often quoted in the literature, especially for sp^2 carbon atoms. Indeed the sp^3 carbon atom of methanol exhibits a reverse sensitivity of the chemical shift to electron reorganization effects. However, this observation seems in line with the recent work of Fliszar [22] who established that (shift–charge) correlations can correspond to positive or negative slopes according to the hybridization state of the resonating nuclei.

The electron organization on neighbouring atoms has been shown to have a non-negligible influence on ^{13}C shifts. We established recently that the ^1H chemical shifts of substituted phenols depend significantly on the electron population on both the hydrogen and oxygen atoms.[13] In the methanol–pyridine complex, the oxygen atom gains 700×10^{-4} e. Such variations in the electron population are much larger than those calculated for the carbon atom and their influence may prevail for variations in carbon shifts. A definite trend can be observed when the electron populations on the oxygen atom are compared with the methanol carbon shifts (Figure 4).

Conclusions

Although methanol–pyridine association involves only a transfer of σ electron from the base, the increase of z electron population on the methanol is greater than expected, suggesting a σ–z reorganization for methanol.

Associations with n or π bases induce shielding shifts for the methanol carbon, whereas the corresponding electron population decreases. However, when phenol is used as a proton donor in similar systems the reverse trend has been observed for the *ipso* carbon (deshielding *ipso* carbon and decreasing electron population). This difference in behaviour suggests that

^{13}C shifts not only reflect the electron population but clearly depend on the hybridization character of the resonating site (sp^2 or sp^3).

An extension of this study to more complex hydroxy systems involving both sp^2 and sp^3 sites is in process.

References

1 R. H. Davies, R. C. Mason, D. A. Smith, D. J. McNellie, and R. James, *Int. J. Quant. Chem., Quant. Biol. Symp.*, 1978, **5**, 221; R. Massuda and C. Sandorfy, *Can. J. Chem.*, 1977, **55**, 3211; P. Hobza, F. Mulder, and C. Sandorfy, *J. Am. Chem. Soc.*, 1981, **103**, 1360; 1982, **104**, 925; R. Buchet and C. Sandorfy, *J. Phys. Chem.*, 1983, **87**, 275; R. Buchet, L. S. Lussier, P. Ménassa, and L. Wilson, *Pure Appl. Chem.*, 1986, **58**, 1115.

2 R. J. Naftalin and G. D. Holman, 'Membrane Transport in Red Blood Cells,' Academic Press, New York, 1981, p. 257.

3 R. Mathis, M. Wilson, F. Mathis, J. F. Labaue, G. Guerch, R. Lahana, A. Mahmoun, and F. Sournies, *Spectrochim. Acta*, 1985, **41A**, 573.

4 O. Kasende and Th. Zeegers-Huyskens, *J. Mol. Struct.*, 1981, **75**, 201.

5 O. Kasende and Th. Zeegers-Huyskens, *J. Phys. Chem.*, 1984, **88**, 2636.

6 M. Ilczyszyn, Z. Latajka, and H. Ratajczak, *Org. Magn. Reson.*, 1980, **13**, 132.

7 T. Nakashima, D. D. Traficante, and G. E. Maciel, *J. Phys. Chem.*, 1974, **78**, 124.

8 F. Guillaume-Vilport, J. P. Seguin, L. Nadjo, R. Uzan, and J. P. Doucet, *J. Mol. Struct.*, 1984, **112**, 163.

9 M. C. Moreau Descoings, F. Guillaume Vilport, J. P. Seguin, R. Uzan, and J. P. Doucet, *J. Mol. Struct.*, 1985, **127**, 297.

10 D. Rinaldi and J. L. Rivail, *C. R. Acad. Sci. Paris*, 1972, **274**, 1664.

11 S. Warycha and I. Wawer, *Adv. Mol. Relax. Inter. Process.*, 1979, **14**, 29; R. C. Phutula, P. S. Arora, and P. P. Singh, *Z. Phys. Chem. (Leipzig)*, 1976, **257**, 945; B. Blaskiewicz and Z. Pajak, *Adv. Mol. Relax. Inter. Process.*, 1978, **13**, 83.

12 B. Bak, L. Hansen-Nygaard, and J. Rastrup-Andasen, *J. Mol. Spectrosc.*, 1958, **2**, 361.

13 J. P. Seguin, F. Guillaume Vilport, R. Uzan, and J. P. Doucet, *J. Chem. Soc., Perkin Trans. 2*, 1986, 773.

14 T. Gramstad, *Acta Chem. Scand.*, 1962, **16**, 807; C. N. R. Rao, P. C. Dwivedi, H. Ratajczak, and J. Orville-Thomas, *J. Chem. Soc., Faraday Trans. 2*, 1975, **71**, 955; Th. Zeegers-Huyskens, *Bull. Soc. Chim. Belg.*, 1977, **86**, 823.

15 S. G. W. Ginn, *J. Mol. Struct.*, 1978, **49**, 137.

16 M. C. Moreau Descoings, G. Goethals, J. P. Seguin, and J. P. Doucet, *Spectrochim. Acta*, 1987, **43A**, 17.

17 F. H. A. Rummens, *J. Chim. Phys.*, 1975, **72**, 448; *Chem. Phys. Lett.*, 1975, **31**, 596; *Can. J. Chem.*, 1976, **54**, 254.

18 C. E. Johnson and F. A. Bovey, *J. Chem. Phys.*, 1958, **29**, 1012.

19 J. P. Seguin, Ph.D Thesis, University of Picardie, 1981.

20 J. P. Seguin, R. Uzan, and J. P. Doucet, *Adv. Mol. Relax. Inter. Process.*, 1981, **19**, 179.

21 J. E. Bloor and D. L. Breen, *J. Am. Chem. Soc.*, 1967, **89**, 6835.

22 S. Fliszar, *Can. J. Chem.*, 1976, **54**, 2839; S. Fliszar, G. Cardinal, and M. Th. Beraldin, *J. Am. Chem. Soc.*, 1982, **104**, 5287.

Received 20*th October* 1986; *Paper* 6/2042