

**INFRARED STUDY OF THE ASSOCIATION AND CONFORMATIONS
OF THIAZOLE 2-CARBOXYLIC ACID AND 2-AMINOTHIAZOLE**

**ESTUDIO INFRARROJO DE LA ASOCIACION Y CONFORMACIONES
DEL ACIDO TIAZOL 2-CARBOXILICO Y DEL 2-AMINOTIAZOL**

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ABSTRACT

The $\nu(\text{OH})$, $\nu(\text{C}=\text{O})$ bands of thiazole 2-carboxylic acid in solid state and DMSO solutions and the NH_2 bands of solid and solutions in inert and proton-donor solvents for 2-aminothiazole have been studied. The i.r. spectra of the acid show bands in the $\nu(\text{OH})$ region which arise from $\text{O}-\text{H}\cdots\text{N}_c$ strong intermolecular association, where N_c is the thiazolinic nitrogen atom, and well resolved doublets in the $\nu(\text{C}=\text{O})$ region which arise presumably from rotational isomers. Solutions of 2-aminothiazole show NH_2 stretching bands corresponding to the free and associated molecules which arise from $\text{N}-\text{H}\cdots\text{N}_c$ intermolecular associations.

RESUMEN

Se ha procedido al estudio de las bandas correspondientes a los grupos OH y CO del ácido tiazol 2-carboxílico sólido y en disoluciones de dimetilsulfóxido y las del grupo NH_2 del 2-aminotiazol sólido y disoluciones en disolventes inertes y donadores de protones. Los espectros i.r. del ácido muestran tres bandas anchas en la región correspondiente a las tensiones del grupo OH que se explican tentativamente en términos de una asociación intermolecular tipo $\text{O}-\text{H}\cdots\text{N}_c$, donde N_c es el nitrógeno tiazolínico, así como dobletes bien resueltos en la región $\nu(\text{C}=\text{O})$ debidas a la presencia de isómeros rotacionales. Las disoluciones del 2-aminotiazol muestran las bandas de tensión del grupo NH_2 correspondientes a las moléculas libres y asociadas, explicadas en términos de asociaciones intermoleculares tipo $\text{N}-\text{H}\cdots\text{N}_c$.

1. INTRODUCTION

Investigations of the conformations and associations in heterocyclic compounds have been carried out using various techniques. For esters, aldehydes and amines, it has been observed that the study by i.r. spectroscopy is more effective than by n.m.r. spectrometry (1-5). With the alkyl furan- and thiophen 2-carboxylates the relative merits of the n.m.r. and i.r. methods for detecting rotational isomerism are reversed (2). For thiphen-, furan-, thiazole- and pyrrole 2-carboxylate esters, the presence of rotational isomers was detected by examining their $\text{C}=\text{O}$ stretching bands (1-5) while

the study of the associations was carried out by various authors through analysis of the OH stretching band (6,7) for the acid compounds and of the NH stretching bands for the amine (6,8).

The aim of the present work was to examine the inter- and intramolecular associations for both 2-aminothiazole ($\text{C}_3\text{H}_4\text{N}_2\text{S}$) and thiazole 2-carboxylic acid ($\text{C}_4\text{H}_3\text{NO}_2\text{S}$), as well as the possible existence of rotational isomers in this acid derivative, by i.r. spectroscopy. However, as it was expected, the spectra of the acids lacking N-substituents would be complicated by the occurrence of associations through hydrogen-bonding between the carboxylic acid and the

basic cyclic nitrogen. Although 2-aminothiazole is soluble in different solvents, which makes the study easier (9), the thiazole 2-carboxylic acid is insoluble, except in DMSO, and thus the analysis of the acid was carried out using the information provided by the i.r. spectra in solid state.

The i.r. bands of the acid in the 2700–1900 cm^{-1} and 1800–1700 cm^{-1} regions and the i.r. bands of the aminothiazole in the 3500–3200 cm^{-1} region are recorded in Table I.

2. EXPERIMENTAL

The samples used were 2-aminothiazole over 98% purity from Merck and thiazole 2-carboxylic acid synthesized by Palle E. Iversen (10), and kindly sent to us by Dr. Henning Lund, University of Aarhus, Denmark, and were used without further purification.

Infrared spectra were recorded on a Perkin Elmer 783 spectrophotometer in the region 4000–200 cm^{-1} . Results for the solutions from 0.002 M to 0.1 M of 2-aminothiazole in CCl_4 , HCCl_3 , C_2Cl_4 and CS_2 were obtained with cells of 0.025 mm and 0.050 mm path-lengths fitted with CsI and KBr windows. For thiazole 2-carboxylic acid, the i.r. spectra of KBr and CsI pellets and nujol mull were recorded. As this acid does not dissolve in ordinary solvents, the i.r. spectrum

on a diluted solution of dimethylsulfoxide was carried out. Standards for wavenumber determinations were polystyrene film and indene + camphor + cyclohexanone mixtures as described in ref. (11).

3. DISCUSSION

3.1. Thiazole-2-carboxylic acid

Few thiazole 2-carboxylic acid derivatives are described in the literature (12), the first complete assignment of the fundamental vibrations of the acid having been made in a previous work (13). In the present work the study of the $\nu(\text{OH})$ and $\nu(\text{C}=\text{O})$ bands was carried out in order to obtain information about the possible existence of associations and rotational isomers for the acid.

In the region 3700–1800 cm^{-1} , the most important feature due to the $-\text{COOH}$ group is the presence of an absorption characteristic of the stretching vibration of the $-\text{OH}$ bond. The shape of said band will give us information about the possible existence of molecular associations. Claydon and Sheppard (14) explained the bands called A, B, C, and D in the spectrum of systems bonded by hydrogen bonding assuming that the region of greatest intensity within the band system as a whole is approximately the main value

TABLE I

OH and C=O bands of KBr pellets and 0.1 M DMSO solutions of Thiazole-2-carboxylic acid and N-H bands of KBr pellets and C_2Cl_4 0.1 M solutions of 2-aminothiazole

	Thiazole-2-carboxylic acid			2-aminothiazole		
	Solid	Solution		Solid	Solution	
$\nu(\text{OH})$	2750	N.D. ^a	$\nu_{\text{as}}(\text{NH}_2)_{\text{free}}$	N.D.	3485.7	
	2495	N.D.		$\nu_{\text{as}}(\text{NH}_2)_{\text{assoc.}}$	3409	3411.2
	1880	N.D.	$\nu_{\text{s}}(\text{NH}_2)_{\text{free}}$		N.D.	3385.7
$\nu(\text{C}=\text{O})$	1736	1712.9		$\nu_{\text{s}}(\text{NH}_2)_{\text{assoc.}}$	3291	3280.7
	1703	1692.3				

^a non-detected.

of $\nu(\text{OH})$, and postulated that these bands are the consequence of the subdivision of the one which would be a simple, continuous and broad $\nu(\text{OH})$ band, owing to a strong Fermi resonance between $\nu(\text{OH})$ and $2\delta(\text{OH})$ and $2\gamma(\text{OH})$.

In the i.r. spectrum of thiazole 2-carboxylic acid in solid state (Fig. 1), three bands can be seen, at 2750 cm^{-1} , 2495 cm^{-1} , and 1880 cm^{-1} respectively which have been tentatively interpreted as corresponding to the "A", "B" and "C" bands of the $\nu(\text{OH})$ mode, on the basis of the shape and frequency of the bands reported by Claydon and Sheppard for different acid derivatives (14). The presence of "transmission windows" can be observed at the same frequency where the $2\delta(\text{OH})$ and $2\gamma(\text{OH})$ overtones would be expected.

In other sense, through the study of the net charge on the thiazole ring for each atom, by different methods, a negative charge on the nitrogen is always observed (12). So, some evidence for proton transfer and the presence of $\text{O}^- \cdots \text{H} \cdots \text{N}^+$ species can be expected and reflected in the spectrum with the presence of a broad band near 3050 cm^{-1} due to the $\nu(\text{NH}^+)$ and another broad D-type band centered about 800 cm^{-1} due to the anion $(\text{RCO}_2\text{HO}_2\text{CR})^-$, although explained also on the basis of intermolecular bond through the ring nitrogen (14-16). Neither of this features is found in our i.r. spectrum of the acid (see Fig. 1 and ref. 13). It is very difficult to postulate the complete proton transfer to the thiazolinic nitrogen in this case.

Based on the above considerations and taking into account similar phenomena in some imidazoles, triazoles and hydantoins (18-21), a very strong intermolecular

association by hydrogen bonding between the acid center of one molecule and the basic one of the another (in our case the thiazolinic nitrogen), has been assumed (Fig. 2).

Moreover, in the region $1800\text{--}1700\text{ cm}^{-1}$, where the $\nu(\text{C}=\text{O})$ fundamental appears, the i.r. spectrum of thiazole 2-carboxylic acid shows a doublet at 1736 cm^{-1} and 1703 cm^{-1} in the solid state and the corresponding bands at 1712.9 cm^{-1} and 1692.3 cm^{-1} in DMSO solutions. In the thiazole 2-carboxylic acid, where a planar form is assumed, the rotation of the acid group locates the CO group in the proximity of either

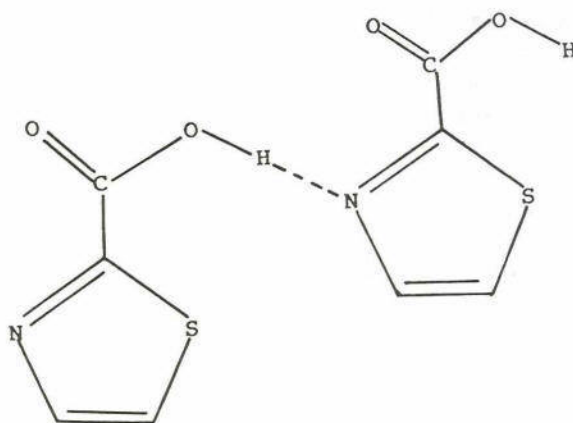


Fig. 2.— Intermolecular association of thiazole-2-carboxylic acid.

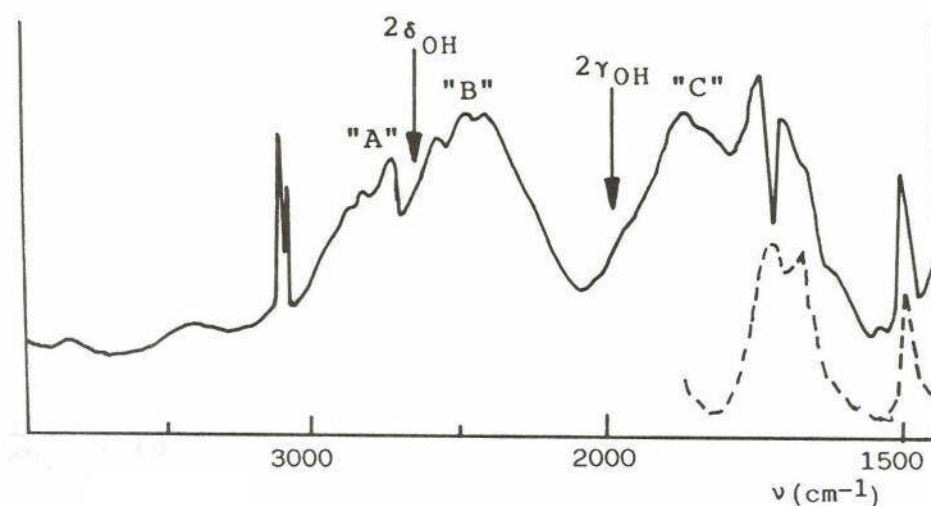


Fig. 1.— Infrared spectra of thiazole-2-carboxylic acid in the $4000\text{--}1400\text{ cm}^{-1}$ region.
 ——— solid - - - solution in DMSO.

the nitrogen or the sulphur atom of the heterocyclic system, and thus it must be considered that this might lead to doublet absorptions. Therefore, given that the doublet persists in a solvent of very high polarity like DMSO, we can conclude that this doublet arises from rotational isomers. By the reasoning set out earlier, the rotamers generating the doublet may be considered to be the carbonyl *O,S-anti-s-trans* and the carbonyl *O,S-syn-s-trans* form (Fig. 3).

From the frequency values given in Table I, it is observed that both the higher- and lower-wavenumber components of the doublet move toward lower wavenumbers when the acid is dissolved in a highly polar solvent, but the displacement is greater for the higher frequency band. In this way, the rotamer which causes the band at 1736 cm^{-1} is the most polar form. Dipole considerations, even at the simple level illustrated in Figure 3, suggest that the anti-rotamer (3a) is the most polar form and gives the band at higher frequency.

3.2.—aminothiazole

The primary amines are characterized in the i.r. spectrum by the two vibration bands ν_{as} and ν_s of the free NH_2 group which, in the case of the aromatic or heterocyclic amines, are manifested by two bands close to 3500 cm^{-1} and 3400 cm^{-1} , respectively. However, amines are compounds which undergo hydrogen bonding causing a small fall in frequency, which is usually less than 100 cm^{-1} . In some cases a third band is shown in this region due to hydrogen bonding effects (6).

With the aim of determining which type of association could exist in the 2-aminothiazole molecule, we have studied the modifications that the inert and

proton-donor solvents exert upon the frequency at which the bands appear in the solid spectrum.

The study of the spectra in very diluted solutions (0.002 mol l^{-1}) in inert solvents (CCl_4 , CS_2 , C_2Cl_4) (Fig. 4,5) allows us to assign the free $\nu_{as}(\text{NH}_2)$ and the free $\nu_s(\text{NH}_2)$ vibrations at 3485.7 cm^{-1} and 3385.7 cm^{-1} , respectively (9).

Besides these two bands, a band at 3280.7 cm^{-1} is observed whose intensity increases with concentration, while the corresponding free $\nu_s(\text{NH}_2)$ band decreases. This allows us to assign this band to the $\nu(\text{NH}_2)$ stretching of the associated species, a vibration which is observed in the solid spectrum at 3291 cm^{-1} . Another band is observed at lower frequency both in solid and solution spectra at 3142.7 cm^{-1} and 3161.9 cm^{-1} , respectively. This band could be tentatively interpreted as the overtone of the NH_2 deformation vibration, which was assigned at about 1620 cm^{-1} (9). This band appears increased in intensity and shifted in frequency owing to a Fermi resonance between the NH_2 stretching vibrations and $2\delta(\text{NH}_2)$ (22). It must be noted that no absorption appears at a frequency below 3100 cm^{-1} which could be due to strongly associated NH groups.

Concerning the free $\nu_{as}(\text{NH}_2)$, which in diluted solution is of lesser intensity than the free $\nu_s(\text{NH}_2)$, it becomes more intense in concentrated solutions and in solid state, decreasing in frequency and increasing in width. This broad band represents the enveloping of the free $\nu_{as}(\text{NH}_2)$ and the associated $\nu_{as}(\text{NH}_2)$ vibrations. In C_2Cl_4 solutions, these two bands are clearly resolved at 3485.7 cm^{-1} and 3411.2 cm^{-1} respectively, the latter corresponding to the one observed in the solid spectrum at 3409 cm^{-1} .

In a proton-donor solvent like HCl_3 (Fig. 4), it is possible that the nitrogen of amino groups acts as a

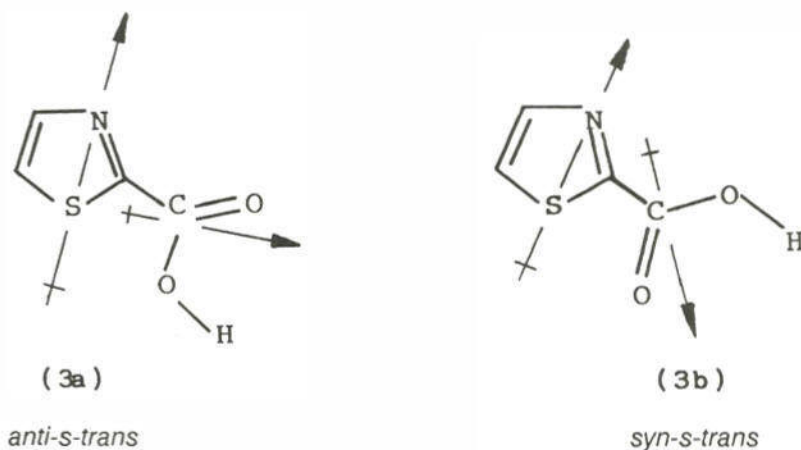


Fig. 3.— Rotational isomers of thiazole-2-carboxylic acid.

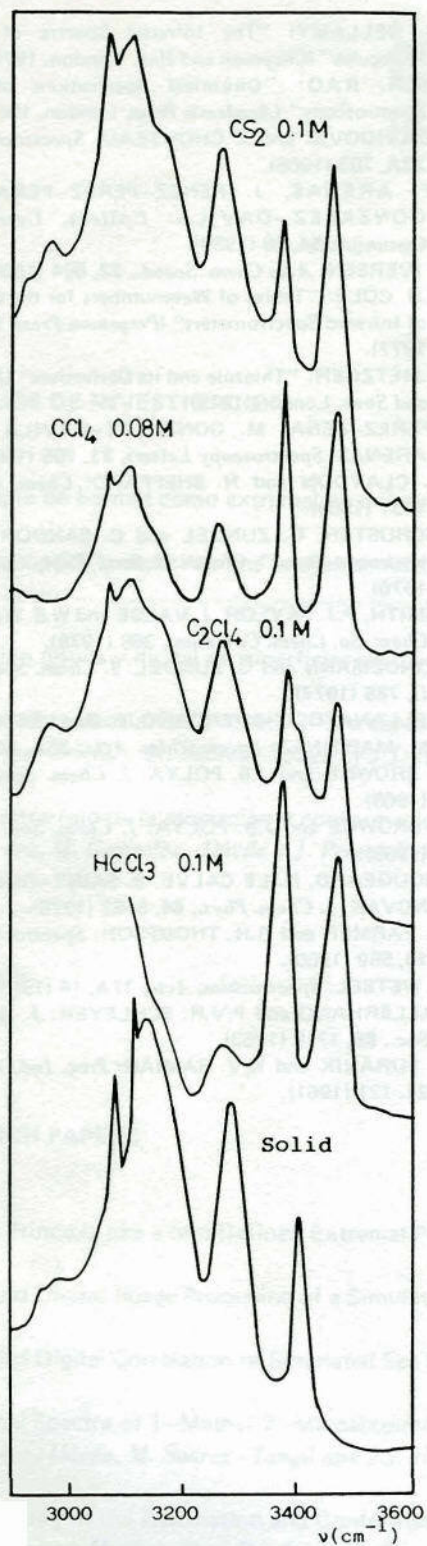


Fig. 4.— Infrared spectra of 2-aminothiazole in the 3600–3000 cm⁻¹ region.

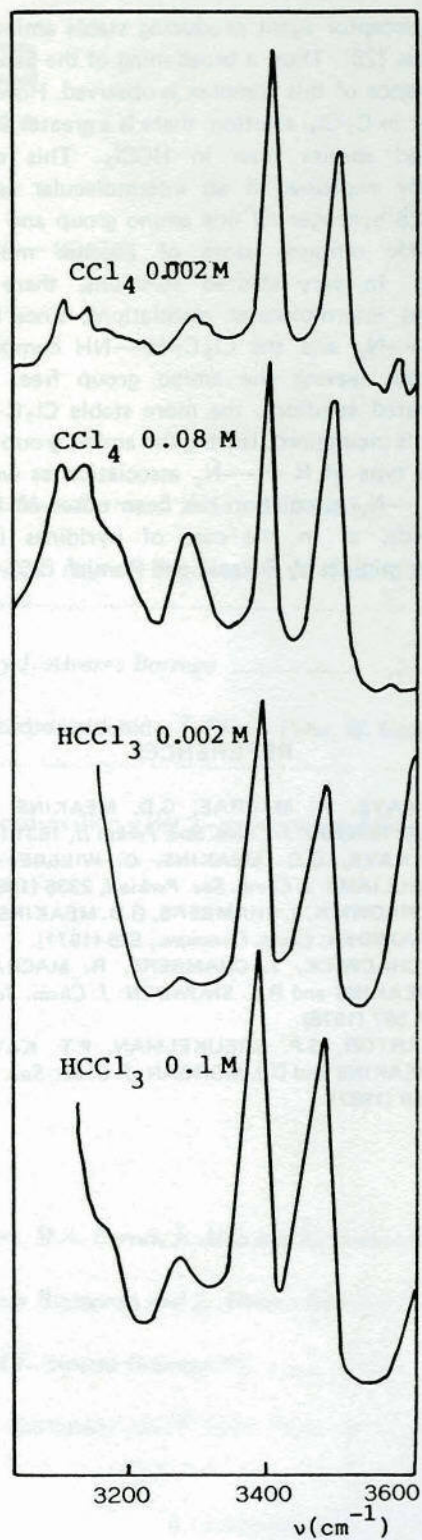


Fig. 5.— Infrared spectra (3600–3000 cm⁻¹) of 2-aminothiazole in CCl₄ and HCCl₃ solutions.

proton-acceptor agent producing stable amino-HCCl₃ complexes (23). Thus, a broadening of the bands due to the existence of this complex is observed. However, it is seen that in C₂Cl₄ solution, there is a greater amount of associated species than in HCCl₃. This could be tentatively explained if an intermolecular association between a hydrogen of one amino group and the basic thiazolinic nitrogen atom of another molecule is assumed. In very diluted solutions, there are no significant intermolecular associations, since both the Cl₃C-H—N_C and the Cl₃C-H—NH complexes are maintained, leaving the amino group free. In more concentrated solutions, the more stable Cl₃C-H—N_C complex is maintained, leaving the amino group free.

This type of N-H—N_C association as well as the Cl₃C-H—N_C association has been observed for other compounds, as in the case of pyridines (24) and aminopyrimidines by Puranik and Ramiah (25).

REFERENCES

1. P.T. KAYE, R. MACRAE, G.D. MEAKINS and C.H. PATTERSON: *J. Chem. Soc. Perkin II*, 1631 (1980).
2. P.T. KAYE, G.D. MEAKINS, C. WILLBE and P.R. WILLIAMS: *J. Chem. Soc. Perkin I*, 2335 (1981).
3. D.J. CHADWICK, J. CHAMBERS, G.D. MEAKINS and R.L. SNOWDEN: *Chem. Commun.*, 625 (1971).
4. D.J. CHADWICK, J. CHAMBERS, R. MACRAE, G.D. MEAKINS and R.L. SNOWDEN: *J. Chem. Soc. Perkin II*, 597 (1976).
5. A. BARTON, S.P. BREUKELMAN, P.T. KAYE, G.D. MEAKINS and D.J. MORGAN: *J. Chem. Soc. Perkin II*, 159 (1982).
6. L.J. BELLAMY: "The Infrared Spectra of Complex Molecules" (*Chapman and Hall*, London, 1975).
7. C.N.R. RAO: "Chemical Applications of Infrared Spectroscopy" (*Academic Press*, London, 1963).
8. G. DAVIDOVIC and J. CHOUTEAU: *Spectrochim. Acta*, 22A, 703 (1966).
9. J.F. ARENAS, J. PEREZ-PEREZ-PEÑA and M. GONZALEZ-DAVILA: *Collect. Czech. Chem. Commun.*, 54, 28 (1989).
10. P.E. IVERSEN: *Acta Chem. Scand.*, 22, 694 (1968).
11. A.R.H. COLE: "Tables of Wavenumbers for the Calibration of Infrared Spectrometers" (*Pergamon Press*, New York, 1977).
12. J.V. METZGER: "Thiazole and its Derivatives" (*John Wiley and Sons*, London, 1979).
13. J. PEREZ-PEÑA, M. GONZALEZ-DAVILA and J.F. ARENAS: *Spectroscopy Letters*, 21, 795 (1988).
14. M.F. CLAYDON and N. SHEPPARD: *Chem. Commun.*, 1431 (1969).
15. P. SCHUSTER, G. ZUNDEL and C. SANDORFY: "The Hydrogen Bond" (*North Holland Publ. Co.*, Holland, 1976).
16. D. SMITH, P.J. TAYLOR, J. VAUSE and W.S. WARING: *J. Chem. Soc. Chem. Commun.*, 369 (1978).
17. R. LINDEMANN and G. ZUNDEL: *J. Chem. Soc. Faraday II*, 788 (1977).
18. J. BELLANATO, C. AVENDAÑO, P. BALLESTEROS and M. MARTINEZ: *Spectrochim. Acta*, 35A, 807 (1979).
19. E.J. BROWNE and J.B. POLYA: *J. Chem. Soc. (C)*, 824 (1968).
20. E.J. BROWNE and J.B. POLYA: *J. Chem. Soc. (C)*, 1056 (1969).
21. D. BOUGEARD, N. LE CALVE, B. SAINT-ROCH and A. NOVAK: *J. Chem. Phys.*, 64, 5152 (1976).
22. V.C. FARMER and R.H. THOMPSON: *Spectrochim. Acta*, 16, 559 (1960).
23. K.B. WETSEL: *Spectrochim. Acta*, 17A, 14 (1961).
24. A. ALLERHAND and P.V.R. SCHLEYER: *J. Am. Chem. Soc.*, 85, 1715 (1963).
25. P.G. PURANIK and K.V. RAMIAH: *Proc. Ind. Acad. Sci.*, 21, 121 (1961).

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