



**Budapest University of Technology and Economics**

**Department of Physical Chemistry**

**Vibrational Spectroscopic Study of  
Nitrogen Heterocycles**

Ph. D. Theses

by

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## Introduction

Nitrogen heterocycles can be found in several biologically active compounds. Their better identification and the discovering of their effects in living organisms need the high level knowledge of their structure and spectroscopic properties.

The investigation of the N-heterocycles builds a traditional project of the Department of Physical Chemistry of the Budapest University of Technology and Economics. I would have been like to continue and extend this tradition. At first, I investigated five membered N-heterocycles (pyrrole, pyrazole, imidazole, triazoles and tetrazole). Later I studied pyrazine and its methyl and chloro substituted derivatives, the substituent effect on the pyrazine structure and vibrational spectra. Similarly, I dealt with isotopic effect of chlorine. On the request of the Babes-Bolyai University in Cluj (Romania) I studied the 10-methyl-(10H)-phenothiazines and 10-methyl-(10H)-phenothiazine-5-oxides. These compounds are promising medicament materials. I investigated the vibrational spectroscopic behaviour of the phenothiazine skeleton and dealt with the aldehyde and the alcohol substituent effect on the vibrational spectroscopic and structural properties of these skeletons.

## **Aim of the work and applied methods**

The aim of the study of the investigation of the N-heterocyclic compounds was to build a comprehensive idea on the vibrational and structural properties of these compounds. For these purpose I worked both experimentally and theoretically.

In the frame of the experimental work I recorded both the infrared and the Raman spectra of the investigated N-heterocycles. A part of the compounds were deuterated. The spectra were evaluated by computer programs. The Raman spectra were measured without polarization and using both parallel and perpendicular polarizations of the scattered light.

In the frame of the theoretical work I carried out quantum chemical calculations. I calculated the optimized geometrical parameters, the vibrational force fields and the fundamental vibrational frequencies of the investigated molecules. The HF/6-31G\*\* method was used for the phenothiazine calculations, while the density functional theory with the Becke3P86 functional and the 6-311G\*\* basis set for the five and six membered heterocycles. The results of the calculations were applied to the assignment of the vibrational fundamentals. The measured fundamental frequencies were used to refine the vibrational force constants. The relative mean deviations between the measured and the calculated frequencies were about 1% or less for every investigated molecule.

## New scientific results

### *Five membered N-heterocyclic compounds* (pyrrole, pyrazole, imidazole, 1,2,3-triazole, 1,2,4-triazole and tetrazole)

1. *Tautomerism.* I calculated the  $r_e$  geometries and the molecular energies of all the tautomeric forms of the 1,2,3-triazole, the 1,2,4-triazole and the tetrazole using the DFT Becke3P86/6-311G\*\* method. On the basis of my calculations the 1H-1,2,3-triazole, the 2H-1,2,4-triazole and the 1H-tetrazole were found the most stable conformers.

2. *Association.* I supposed that the broad band system in the 2500-3400  $\text{cm}^{-1}$  region in the infrared spectra of the five membered N-heterocyclic molecules is the result of the intra- and intermolecular interactions. The association decreases the frequency of the NH and CH band stretchings and increases the frequency of the CH and NH in-plane and out-of-plane bendings and causes the broadening and strengthening of the bands.

3. *Deuteration.* I tried to reduce the effect of the NH---N interactions in the infrared spectra and therefore prepared deuterio derivatives. I found that not only the hydrogen on the nitrogen were changed to deuterium but also partly other hydrogen, that on the vicinal carbon atom to this nitrogen atom. This finding is supported by the appearance of the very sharp 2342  $\text{cm}^{-1}$  band in the Raman spectrum of the deuterioimidazole.

4. *Interpretation of the spectra.* The NH in-plane bendings appear in the 1600-1400  $\text{cm}^{-1}$  region of the infra and Raman spectra, those of CH in-plane bendings are found in the 1500-900  $\text{cm}^{-1}$  one. I established that the  $\beta\text{NH}$  and  $\beta\text{CH}$  bendings are mixed

with one other and also with the ring stretchings and in-plane bendings. I proved that the region of the NH out-of-plane bendings is  $500\text{-}600\text{ cm}^{-1}$  and the same for the CH out-of-plane ones is  $700\text{-}900\text{ cm}^{-1}$ . The  $\gamma\text{NH}$  deformations are sometimes mixed with the ring out-of-plane bendings, while the CH out-of-plane deformations build group frequencies.

The ring stretching modes appear in the  $1000\text{-}1500\text{ cm}^{-1}$  region of the infrared and the Raman spectra. The characteristic region of the ring in-plane bending modes is  $800\text{-}900\text{ cm}^{-1}$ . The ring out-of-plane modes appear in the  $600\text{-}700\text{ cm}^{-1}$  region of the spectra.

*Six membered N-heterocyclic compounds*

(pyrazine, 2-chloropyrazine, 2,6-dichloropyrazine, 2-methylpyrazine, 2,3-dimethylpyrazine, 2,5-dimethylpyrazine, 2,6-dimethylpyrazine)

5. *Substituent effects.* The  $-I/+M$  effect of the chlorine and the  $+I/-M$  one of the methyl substituents acts not only on the near environment of the place of the substitution but also on the other parts of the ring, through the  $\pi$  electron system. As result of the chlorine substitution the force constants of the vicinal CC stretchings decrease and those of the NC stretchings increase, the NC bond lengths decrease. The methyl substitution causes above all the lengthening of the ring NC bonds and decreases the ring angles at the carbon atoms. The second substituent increases for the most part the effect of the first substitution but sometimes does not cause important changes to the first one. The second chlorine substitution equalizes the CC force constants; they are close to that of the pyrazine. The equalization effect is in the case of the 2,6-dimethylpyrazine similar but this force constant is essentially greater than that of the pyrazine. The NC stretching force constants of the methylpyrazines are greater than that of the parent molecule.

6. *Spectrum assignment.* I found that the pyrazine C-H stretchings are group frequencies and appear in the  $3060\text{-}3010\text{ cm}^{-1}$  region of the infrared and Raman spectra. The monochloro or

methyl substitutions shift the CH stretching frequencies about 20-40  $\text{cm}^{-1}$  to the high ones. In the infrared spectrum of the 2,6-dichloropyrazine the CH stretching bands appear at 3104 and 3099  $\text{cm}^{-1}$ . However, the CH stretching frequencies of the dimethylpyrazines show low frequency shift to these values of about 25-40  $\text{cm}^{-1}$ .

The CH in-plane deformations mix both with the stretchings and in-plane bendings of the ring and also with the same type motions of the substituents. The appropriate bands are found in the 1600-1000  $\text{cm}^{-1}$  region. The CH out-of-plane deformations build group frequencies and appear below 1000  $\text{cm}^{-1}$ .

Increasing the number of either the methyl or the chlorine substituents, the ring stretching frequencies shift to higher ones. The ring in-plane and out-of-plane frequencies show low frequency shift to the corresponding pyrazine ones.

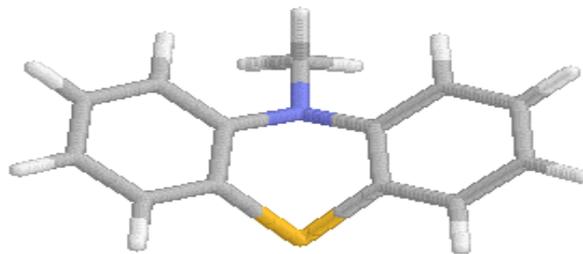
The C-Cl and the C-CH<sub>3</sub> stretchings, in-plane bendings and out-of-plane bendings are mixed with the ring stretchings, in-plane and out-of-plane bendings. Exceptionally, the low frequency out-of-plane deformations build group frequencies.

7. *Isotopic effect.* The  $^{35}\text{Cl}$ - $^{37}\text{Cl}$  isotopic effect was not observable directly in the spectra. The model calculations, however, gave possibility for the estimation of these effects. The calculated isotopic shifts in the C-Cl in-plane and out-of-plane deformations were about 10  $\text{cm}^{-1}$ .

#### *Phenothiazines*

(10-methyl-(10H)-phenothiazine, 10-methyl-(10H)-phenothiazine-13-carbaldehyde, 10-methyl-(10H)-phenothiazine-13-yl-methanol, 10-methyl-(10H)-phenothiazine-5-oxide, 10-methyl-(10H)-phenothiazine-13-carbaldehyde-5-oxide, 10-methyl-(10H)-phenothiazine-13-yl-methanol-5-oxide)

8. *Substitution and molecular structure.* The alcohol and the aldehyde substituents influence the butterfly form of the parent molecule only to a little extent.



10-methyl-(10H)-phenothiazine

The alcohol substituent affect hardly on the phenothiazine ring, while the aldehyde substituent lengthens the N-C bond and shortens the S=O bond. The aldehyde substitution increases the CNC and the CSC valence angles and decreases the CCNC and CCSC torsion angles.

9. *Spectrum assignment.* The vibrational modes of the two aromatic rings of 10-methyl-(10H)-phenothiazine, 10-methyl-(10H)-phenothiazine-5-oxide and their alcohol substituted derivatives are coupled, while the same modes are decoupled in the aldehyde substituted molecules. This decoupling is a consequence of the  $-I/+M$  effect of the aldehyde group.

Comparing the spectra of the parent molecules and their aldehyde substituted derivatives I concluded that the CHO group decreases the CH out-of-plane bending frequencies by  $5-15\text{ cm}^{-1}$ , while the  $\text{CH}_2\text{OH}$  substitution decreases the  $\gamma\text{CH}$  frequencies of the parent molecule (10-methyl-(10H)-phenothiazine) by further  $5-10\text{ cm}^{-1}$ .

The aliphatic CH stretching motions of the N-methyl and aldehyde, and N-methyl and alcohol groups, respectively, do not mix. The N- $\text{CH}_3$  stretching modes appear in  $2980-2850\text{ cm}^{-1}$  region of the investigated molecular spectra.

The ring stretching and bending motions are mixed with the substituent stretching and bending ones. The ring stretching modes with in-plane C-H bending participation are good precedents for this effect. I found lower frequencies for the 10-methyl-(10H)-

phenothiazine aromatic ring in-plane and out-of-plane bendings than for 10-methyl-(10H)-phenothiazine-5-oxide ring ones. The  $\beta$ ring and  $\gamma$ ring frequencies of the aldehyde and the alcohol substituted molecules are lower than those of the parent molecules, which I explained with the mesomeric and inductive effects of the substituents.

According to my calculations the in-plane and out-of-plane deformations of the S=O group are mixed with one another and also with the out-of-plane ring ones.

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