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**ABSTRACT**

The Raman spectra of the iodine derivatives of tyrosine and thyronine in the form of compressed crystalline powders have been excited by 4880 Å Argon laser on rotating samples at room temperature. The strong peaks in the low frequency $\lesssim 400\ cm^{-1}$ region may be described by analogous vibrations of benzene as

i the C-I out-of-plane bendings of $E_{1g}$ mode from 100 $cm^{-1}$ to 180 $cm^{-1}$,

ii the C-I in plane bendings of $E_{2g}$ and $A_{2g}$ mode from 190 $cm^{-1}$ to 330 $cm^{-1}$ and

iii the C-I stretchings of $E_{2g}$ mode from 330 $cm^{-1}$ to 400 $cm^{-1}$.

In 3,3',5 - triiodo-derivatives, the number of both the C-I in-plane bendings and C-Istretchings on the inner phenyl ring approximately doubles from that of diiodo-derivatives. This doubling in number of peaks is presumbly due to the modulation caused by the libration, which is associated with the C-I out-of-plane bending at position 3', of the outer phenyl ring.

## I INTRODUCTION

The iodine derivatives of tyrosine and thyronine have iodine(s) as ring substituent(s) and are closely related to the biochemically important thyroid hormones. Various physical measurements have been made on these compounds. Their ultraviolet absorption band[1] generally shows red shift, which increases with the number of substituted iodines, in solutions of acidic or basic. The crystal structure of some of these compounds have also been determined[2] by x-ray diffraction. Recently, the Mössbauer effect of $^{129}I$ in L-3,5-diiodo tyrosine and L-thyroxine at liquid helium temperature has been measured[3] and shows that the iodine sites in each compound are indistinguishable with the Mössbauer effect. We report here the Raman spectra of the iodine-sensitive vibrations, which are usually strong in Raman intensity due to the large polarizability of heavy atoms, in the iodine derivatives. The samples are pressed crystalline solids at room temperature. Their spectra are distinguishable among all the six derivatives measured and show peaks characterizing the iodine-sensitive vibrations between 100$^{-1}$ and 400 $cm^{-1}$. Our interpretation on the strong peaks is mainly based on the compiled data in the literature, since it is not possible to make rigorous assignment on the vibrational peaks of complicated molecules based solely on the unpolarized Raman spectra of powder samples with limited types of substitutions.

## II. EXPERIMENTALS AND DISCUSSION

The Raman spectra were excited by Argon laser at 4880 Å on the rotating samples in order to avoid the burning of the pressed crystallines at room temperature. The spectra of the iodine derivatives are shown in Fig 1. The Raman spectra of tyrosine and thyronine with no iodine substitution are shown in Fig 2 and serve as the reference spectra for the samples in Fig 1. The strong peaks in the low frequency ≲ 150 cm⁻¹, region of Fig 2 are due to the intermolecular (or external) librations[4] of the molecules and are expected to shift to even lower frequencies after the substitution of heavy atom such as iodine. This means that the strong Raman peaks in the iodine derivations in the same region of Fig 1 are due to iodine sensitive internal vibrations, instead of external librations of the molecules. The iodine sensitive vibrations which appear as strong Raman peaks in Fig 1 may be approximately characterized[5] by

(1) C-I out of plane bendings from 100 cm⁻¹ to 180 cm⁻¹
(2) C-I in plane bendings from 190 cm⁻¹ to 330 cm⁻¹ and
(3) C-I stretchings from 330 cm⁻¹ to 400 cm⁻¹

(1) C-I out of plane bendings, 100 cm⁻¹ to 180 cm⁻¹

The strong peak at 160 cm⁻¹ in 3-iodo-tyrosine, curve 1 in Fig 1, may be assigned as the C-I out of plane bending with benzene ring librating[5] at frequency[6] $\nu_{11}$ in $E_{1g}$ mod (or 10a reference 5,7). The weak peak at 105 cm⁻¹ could be the other component[5,6] of $E_{1g}$ (or 10b). Here we approximate the 3-iodo-tyrosine by either i a meta disubstituted benzene with H at positons 1 and 3 substituted by C and I, respectively, or ii an ortho disubstituted benzene with 3 and 4 positions substituted by I and OH, respectively. Both approximations i and ii yield the same mode[5] of C-I out of plane bendings, $E_{1g}$ (or 10 a and 10 b), and the similar frequency ranges[5], i.e. 170 cm⁻¹ to 270 cm⁻¹ for 10 a and 120 cm⁻¹ to 200 cm⁻¹ for 10 b.

In higher iodine derivatives, the $E_{1g}$ peaks shift slightly to higher frequencies as shown by curves 3 to 6 in Fig 1 and also summarized in Table I in the column of out of plane bendings. For phenyl ring carrying two iodine substituents at meta positons, we use meta diheavy substituted benzene as an approximated molecule, which again gives[5] the same mode and similar frequency ranges for the strong Raman peaks as i an ii mentioned above.

(2) *C-I in plane bendings, 190 cm⁻¹ to 330 cm⁻¹*

The double peak at 190 cm⁻¹ and 195 cm⁻¹ in 3,5-diiodo-L-thyronine, curve 2 in Fig 1, may be assigned as the C-I in plane bendings[5] of $E_{2g}$ mode (or 9 a and 9 b). We approximate the molecule by a meta tetra substituted[5] benzene with H at positons 1,3,4 and 5, Fig 3 substituted by C,I,O and I, respectively.

This double peak moves for ~20 cm⁻¹ toward higher frequencies, i.e. to 206 cm⁻¹ and 219 cm⁻¹, respectively, in 3,5-diiodo-L-tyrosine, curve 3 in Fig 1. This upshift in Raman frequencies form thyronine derivative to the tyrosine derivative is presumbly due to some intramolecular hydrogen bonding between the OH at *position 4* and the bulky iodines at positons 3 and 5 on the same phenyl ring in tyrosine. While in the 3,5-diiodo thyronine, the OH at 4′ of the outer phenyl ring is not likely to form intramolecular hydrogen bonding with the distant iodines at 3 and 5 positions on the inner ring, Fig.3. In curve 3 of Fig 1, a weak peak at 293 cm⁻¹, which may be identified with the double peak 290 cm⁻¹ and 318 cm⁻¹ in curve 5 for 3,3′, 5-triiodo-thyronine, may be assigned as another C-I in-plane bending[5] of $A_{2g}$ mode at $\nu_3$ (or 3).

As we proceed to the triiodo derivatives, curves 4 and 5, the number of peaks in the region of C-I in-plane bendings approximately doubles, which may be attributed to the interaction between the libration, which is associated[5] with the C-I out-of-plane bending of $E_{1g}$ mode at $\nu_{11}$ (or 10 a), of the outer phenyl ring and the C-I in-plane bendings on the inner ring. The molecular conformation[2] of triiodo-L-thyronine is shown in Fig 3 and consists of two nearly mutually perpendicular, bisecting phenyl rings with the outer ring almost coplanar with the C-O-C plane, while the inner ring is almost perpendicular to the C-O-C plane. The C-O-C ether is 122°. With this molecular conformation between two phenyl rings, the libration of the outer ring at $\nu_{11}$ (or 10a) around the axis connecting posistions 2' and 5' has a large oscillating component imparting to the in-plane vibrations of the inner ring and hence will modulate (or split) the inplane bendings, $E_{2g}$ (or 9 a and 9 b) and $a_{2g}$ (or 3), in the region 190 cm$^{-1}$ to 330 cm$^{-1}$ as demonstrated by curves 4 and 5 for triiodo-derivatives.

In both the diiodo-derivatives, curves 2 and 3, and triiodo derivatives, curves 4 and 5, the low energy peak (or 9a) is usually stronger than its high energy partner (or 9b), since the 9a mode is more symmetric[5] than 9b.

The gross feature in the spectrum of thyroxine, which has two iodines on both the inner and outer phenyl ring, appears to be simply the superposition of the in-plane bendings of 3,5-diiodo-L-thyronine, curve 2, and that of 3,5-diiodo-L-tyrosine, curve 3. The main features of thyroxine, curve 6, are: (a) shoulder at ~188 cm$^{-1}$ and peak at 199 cm$^{-1}$ corresponding to 3,5-diiodo-thyronine as the inner ring and (b) shoulder at 207 cm$^{-1}$ and strong peak at 220 cm$^{-1}$ corresponding to 3,5-diiodo-tyrosine as the outer ring. In thyroxine the C-I out-of-plane libration $\nu_{11}$ (or 10a) is around the axis passing either position 1-4 or 1'-4', which has no modulating component projected on the inplane vibration of the other ring and hence does not split the in-plane bendings on the other ring as in the case of triiodo derivatives, curves 4 and 5.

It is interesting to note, that contrary to most of the other iodine derivatives, the thyroxine has stronger high-frequency components (or 9b), i.e. 199 cm$^{-1}$ peak versus 188 cm$^{-1}$ shoulder and 220 cm$^{-1}$ peak versus 207 cm$^{-1}$ shoulder, in the C-I in-plane bending region of curve 6. We speculate that the Raman active C-I out-of-plane bending $\nu_{11}$ (or 10a), which corresponds to the ring libration around the 1-4 or 1'-4' axes in thyroxine, couples better to the high frequency (or 9b) component than to the low frequency (or 9a) one on the other ring. This is because that the amplitudes of the C-O in-plane bending at positions 1' or 4, which are involved (Fig. 3) in coupling with the above ring librations, are zero[5] in mode 9a and non-zero[5] in mode 9b.

The C-I in-plane bendings of the six iodine derivatives are also summarized in Table I.

(3) C-I stretchings, 330 cm$^{-1}$ to 400 cm$^{-1}$

The peaks at 393cm$^{-1}$ and 378 cm$^{-1}$ of 3,5-diiodo-L-tyrosine, curve 3 of Fig.1, may be assigned as the C-I stretchings of $E_{2g}$ mode at $\nu_{15}$ (or 7b and 7a). We approximate the molecule by a vicinal trisubstituted benzene with substituents I, OH and I at positions 3,4 and 5, respectively. Similar results will be obtained, if a meta-diiodo-benzene used as the approximated molecule. Although a meta-tetra-substituted benzene with two light substituents C and OH at 1,4-para positions and two iodines at 3,5 meta positons is the most correct approximation, but there is no existing data[7] for this particular form of substitutions

As we proceed to the triiodo derivatives, curves 4 and 5, the above peaks multiply in number in the region between 330 $cm^{-1}$ and 400 $cm^{-1}$ This splitting is again due to the modulation by the libration on the outer ring, as in the case of the splitting of C-I in-plane bendings, on the C I stretchings on the inner ring The C-I stretchings in Fig.1 are sumarized in Table I

## CONCLUSION

Based on the compiled vibrational assignments on benzene derivatives[5], we assign the low frequency Raman peaks between 100 $cm^{-1}$ and 180 $cm^{-1}$ as C-I out-of-plane bendings in $E_{1g}$ mode and that between 190 $cm^{-1}$ and 330 $cm^{-1}$ as C I inplane bendings of $E_{2g}$ and $A_{2g}$. The strong C I stretching Raman peaks are of $E_{2g}$ in the region from ~330 $cm^{-1}$ to 400 $cm^{-1}$.

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## CAPTIONS OF FIGURES AND TABLE

Figure 1 Raman spectra of iodine derivatives of tyrosine and thyronine
Curve 1 -- 3 iodo-L-tyrosine
Curve 2 -- 3,5 diiodo L thyronine
Curve 3 -- 3,5 diiodo L-tyrosine
Curve 4 -- 3,3',5 triiodo L thyropropionic acid
Curve 5 -- 3,3',5 triiodo L thyronine
Curve 6 -- D thyroxine

Figure 2 Raman spectra of thyronine and tyrosine
Curve 7 -- thyronine
Curve 8 -- DL tyrosine

Figure 3 Sketch of the molecular conformation of 3,3',5 triiodo-L-thyronine

Table I - C I vibration Frequencies ($cm^{-1}$) in Iodine-Derivations of tyrosine and thyronine.

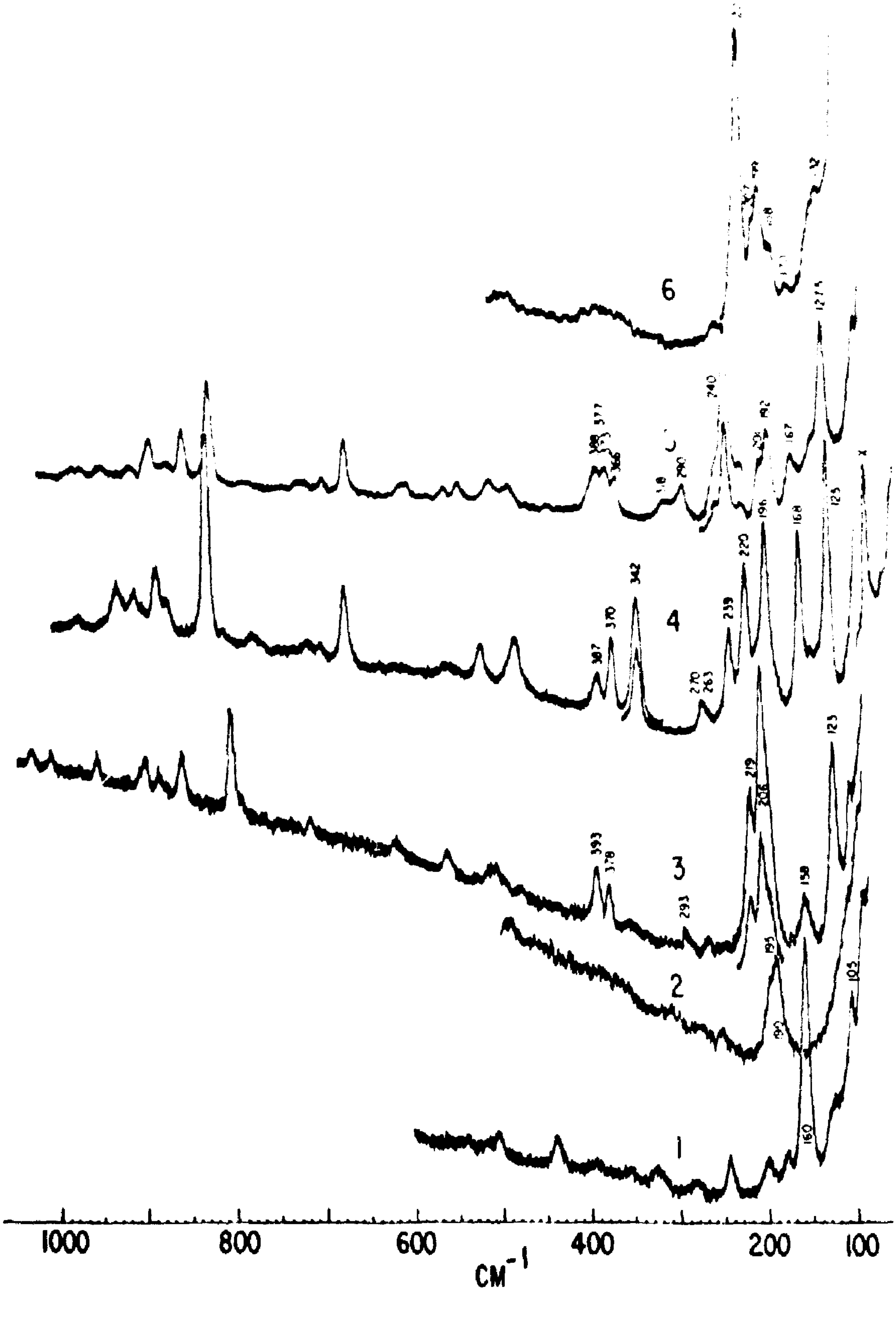


Fig. 1

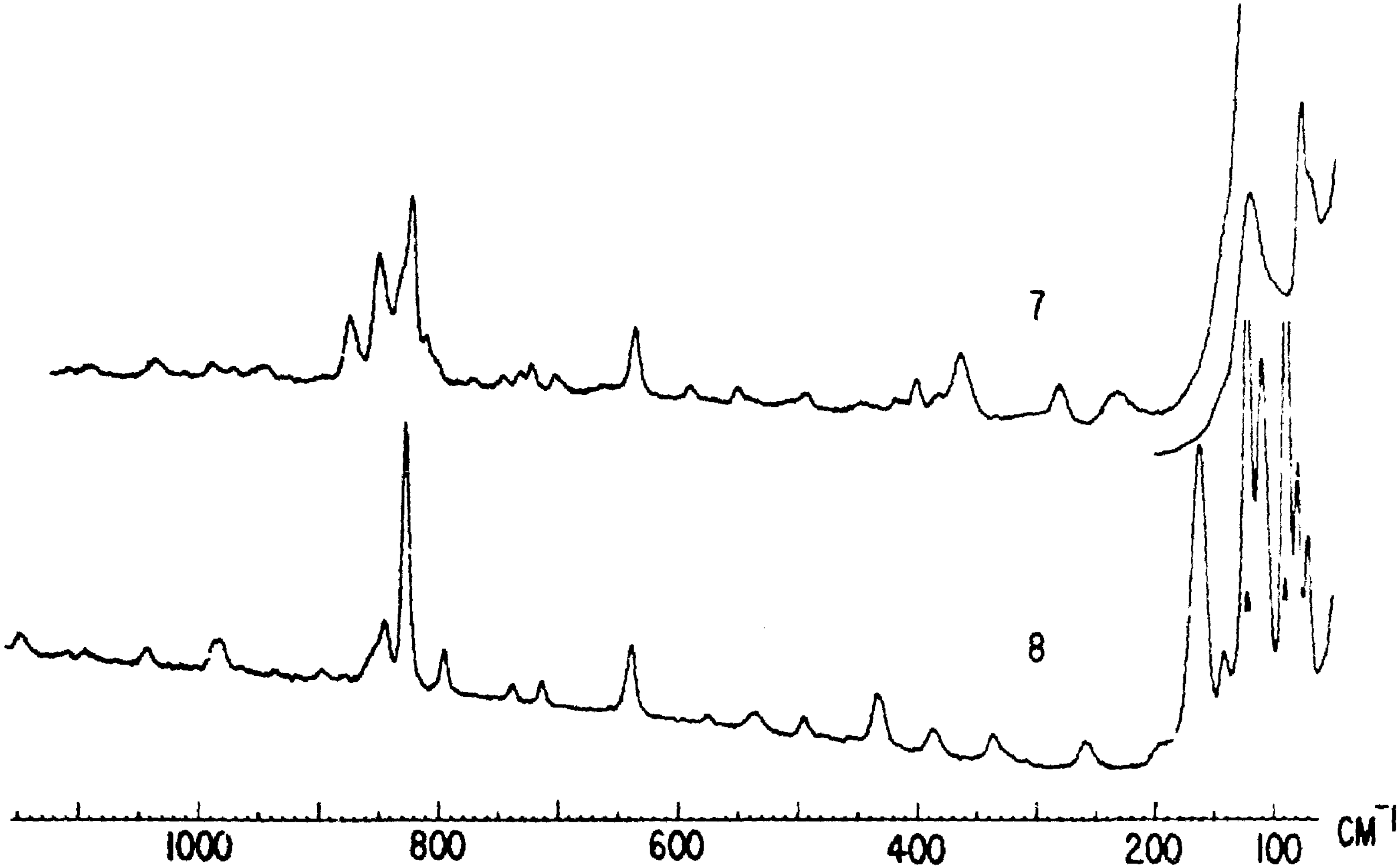


Fig. 2

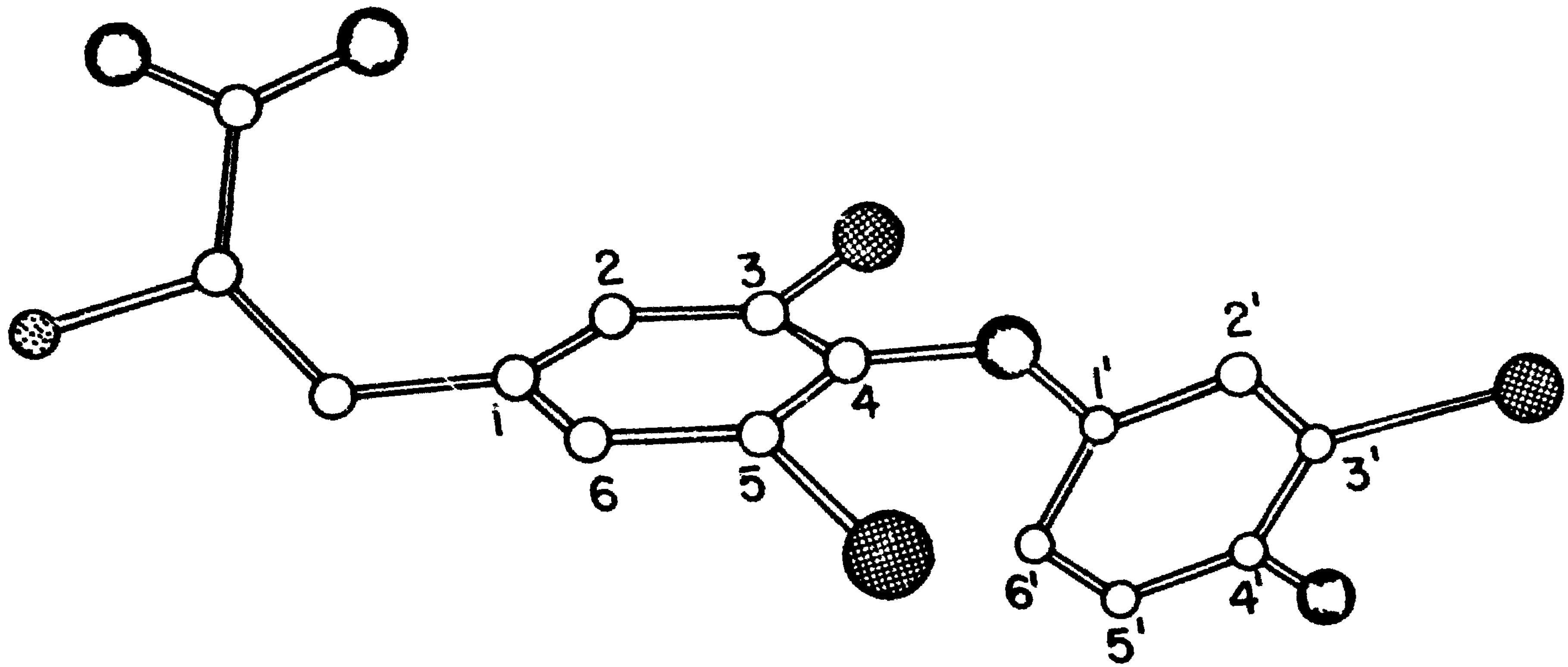


Fig. 3

**Table I**

**C I vibration Frequencies (cm[illegible]) in Iodine Derivatives of Tyrosine and Thyronine**

| Normal Vibrations of Benzene — Herzberg[6] / Varsayni[5] | out of plane bendings | | In plane bendings | | | Stretchings | |
|---|---|---|---|---|---|---|---|
| | $E_{1g}$ | $E_{1g}$([illegible]) | $E_{2g}$([illegible]) | $E_{2g}$ | $A_{2g}$([illegible]) | $E_{2g}$ | $E_{2g}$([illegible]) |
| | 10 b | 10 a | 9 b | 9 a | 3 | 7 a | 7 b |
| 3 iodo tyrosine | 105 | 160 | | | | | |
| 3,5 diiodo tyrosine | 123 | 158 | 206 | 219 | 293 | 378 | 393 |
| 3,5 diiodo thyronine | | | 190 | 195 | | | |
| 3,3',5 triiodo thyropropionic acid | 125 | 168 | 196<br>220 | 239 | 263<br>270 | 342<br>370 | 387 |
| 3,3',5 triiodo thyronine | 127.5 | 167 | 192<br>240 | 201 | 290<br>318 | 366<br>377 | 373<br>388 |
| thyroxine | 132 | 170 | 188<br>207 | 199<br>220 | | | |

## RESUMO

Os espectros Raman dos derivados iodados de tirosina e tironina na forma de pó cristalino comprimido foram excitados com laser de Argônio de 4880 Å em amostras em rotação, a temperatura ambiente. Os picos intensos em frequências baixas 400 $cm^{-1}$ podem ser descritos por vibrações análogas de benzeno do seguinte modo

i. as curvaturas C–I do modo $E_{1g}$ fora do plano, desde 100 $cm^{-1}$ a 180 $cm^{-1}$,

ii. as curvaturas C-I dos modos $E_{2g}$ e $A_{2g}$ no plano desde 190 $cm^{-1}$ a 330 $cm^{-1}$ e

iii. os estiramentos do modo $E_{2g}$ desde 330 $cm^{-1}$ a 400 $cm^{-1}$

Nas derivadas triiodo 3,3',5 o numero das curvaturas C-I no plano e dos estiramentos C-I no anel interno de fenil é aproximadamente o dobro do das derivadas diiodo. Esta duplicação em numero de picos é possivelmente devido à modulação causada pela libração, que esta associada com a curvatura C-I fora do plano na posição 3', do anel externo de fenil

## RÉSUMÉ

Les spectres Raman des derivées iodées de la tyrosine et tyronine sous la forme de poudres cristallines comprimés sont été excités avec le laser d'argonne de 4880 Å sur les echantillons en rotation, à la température ambiente. Les pics intenses dans la region des basses frequences, ≤400 $cm^{-1}$, peuvent être décrits par les vibrations analogues du benzène de la maniere suivant.

i. les curvatures C-I du mode $E_{1g}$, hors du plan des 100 $cm^{-1}$ jusqu'à 180 $cm^{-1}$,

ii. les curvatures C-I des modes $E_{2g}$ et $A_{2g}$, dans le plan, dès 190 $cm^{-1}$ jusqu'à 330 $cm^{-1}$,

iii. les allongements du mode $E_{2g}$ dès 330 $cm^{-1}$ jusqu'à 400 $cm^{-1}$.

Dans les derivées iodées triiode 3,3',5, le nombre des curvatures C-I dans le plan et des allongements C-I dan l'anneau interne du phénil est d'environ le double de celui des derivées diiode. Cette duplication dû à la modulation causée par la libration, que est associée avec la curvature C-I hors du plan, à la position 3', de l'anneau du phénil.


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