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Vibrational spectra of 5-halogenouracils: Part I

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Abstract

The N–H, C=O and C=C stretching modes of 5-halogenouracils are analyzed in Ar matrices. FTIR spectra with the support of ab initio (HF, MP2) and DFT (B3P86, B3PW91) calculations using the 3-21G** basis set are presented. The influence of the halogen substituent on the normal modes is discussed. © 1997 Elsevier Science B.V.

Keywords: Ab initio calculations; DFT; 5-Halogenouracils; IR matrix; MP2

1. Introduction

The bioactivity of 5-halogenouracils (5-XU) induces exceptional interest in their biochemistry and pharmacology. The substitution of uracil or thymine in RNA or DNA by 5-XU perturbs the replication of nucleic acids. 5-Fluorouracil (5-FU) has been used as an antitumor drug (EFUDIX, EFUDEX) and all 5-XU compounds are presently tested against HIV [1–3].

Previously, we have investigated the influence of halogen substituents on the electron system of benzoic acid by NMR, IR, and Raman spectroscopy and we found that changes of vibrational frequencies and intensities of some modes were correlated with changes of the halogen ionization potential [4,5].

Here, we are studying the influence of the halogen substituent on some selected vibrational modes of the pyrimidinodione ring. Since the vibrational spectra of 5-XU in the crystalline state are complex [6], we have

decided to use the IR matrix isolation technique in order to minimize the intermolecular interactions. Although the IR matrix isolation spectra have been interpreted for similar compounds [7–17], the interpretation has been only partial for 5-XU [14,17].

2. Experimental and computational methodology

Sigma 99% w/w 5-halogenouracils were used. The Ar matrices were prepared within a Displex (Air Products) closed cycle He refrigerator. After cooling down to 19 K, the Ar gas (Aldrich, 99.998%) was passed over 5-XU crystals, placed in a heated tube (370–450 K) close to the CsI cold window. The spectra were measured using a Nicolet 170SX FTIR instrument (KBr beam splitter, resolution 1 cm⁻¹).

All calculations were performed using the Gaussian

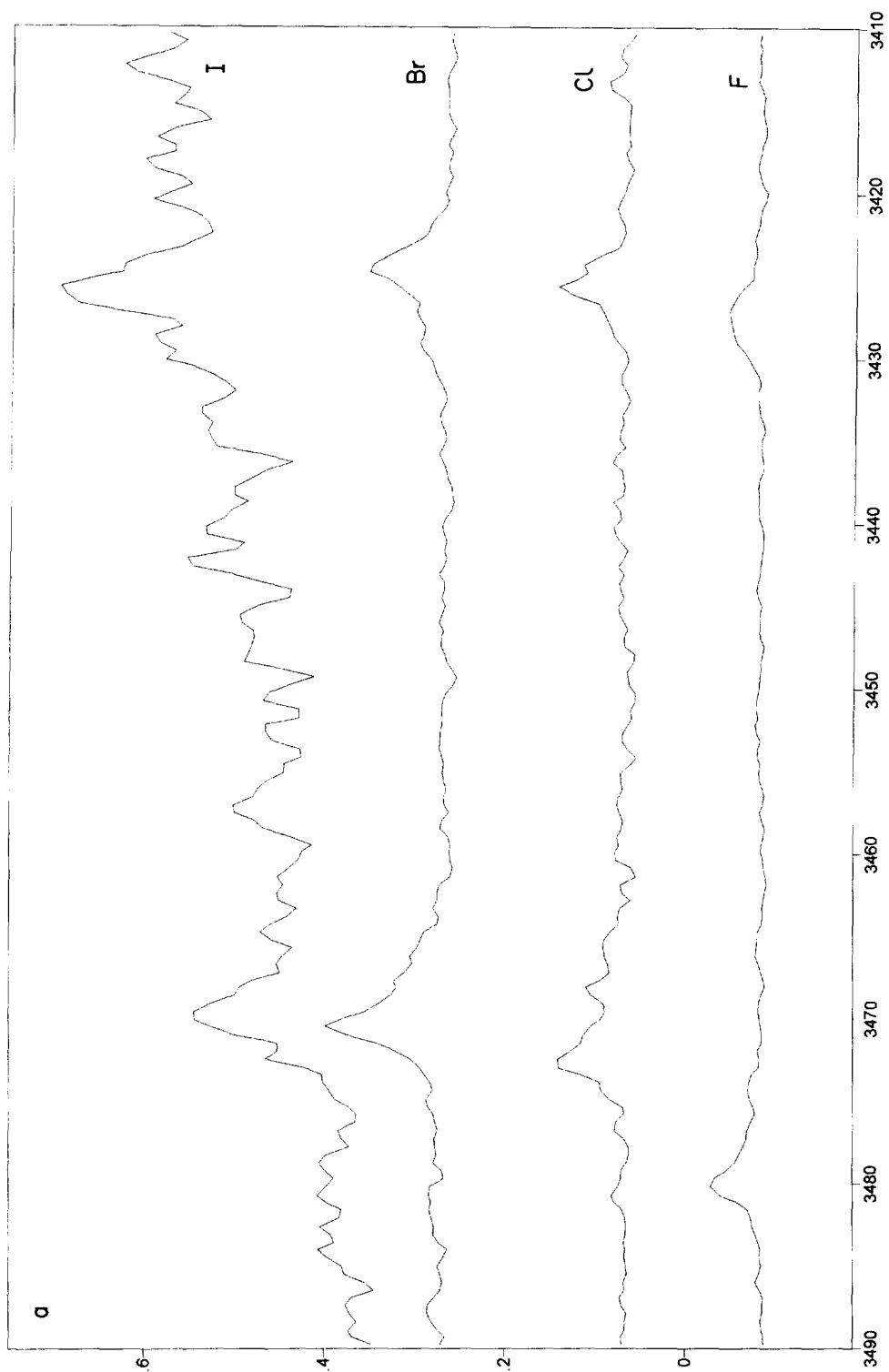


Fig. 1. The Ar matrix FTIR spectra of 5-halogenouracils: (a) $\nu(\text{N-H})$, (b) $\nu(\text{C=O})$ stretching vibration regions.

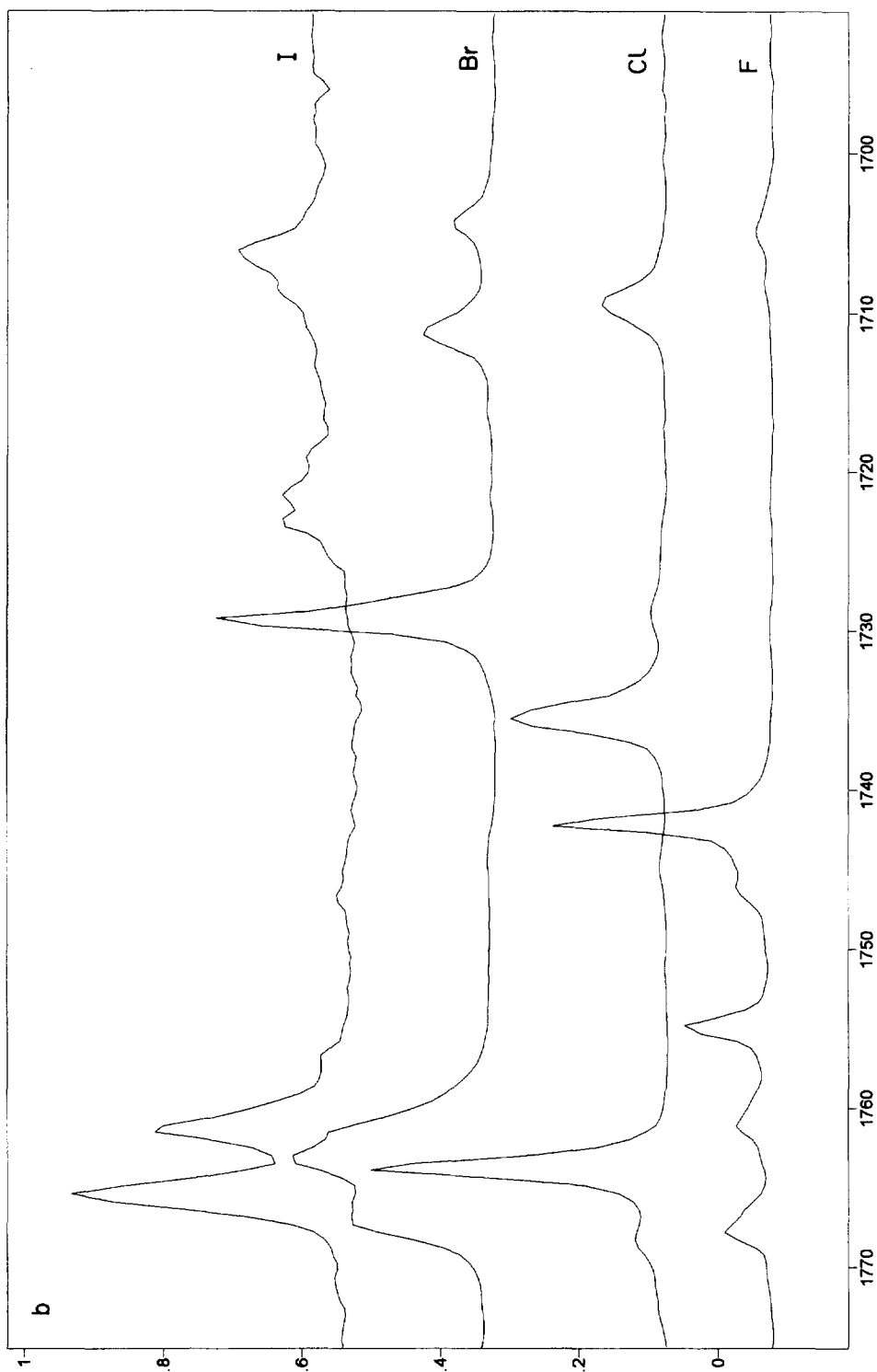


Fig. 1. Continued.

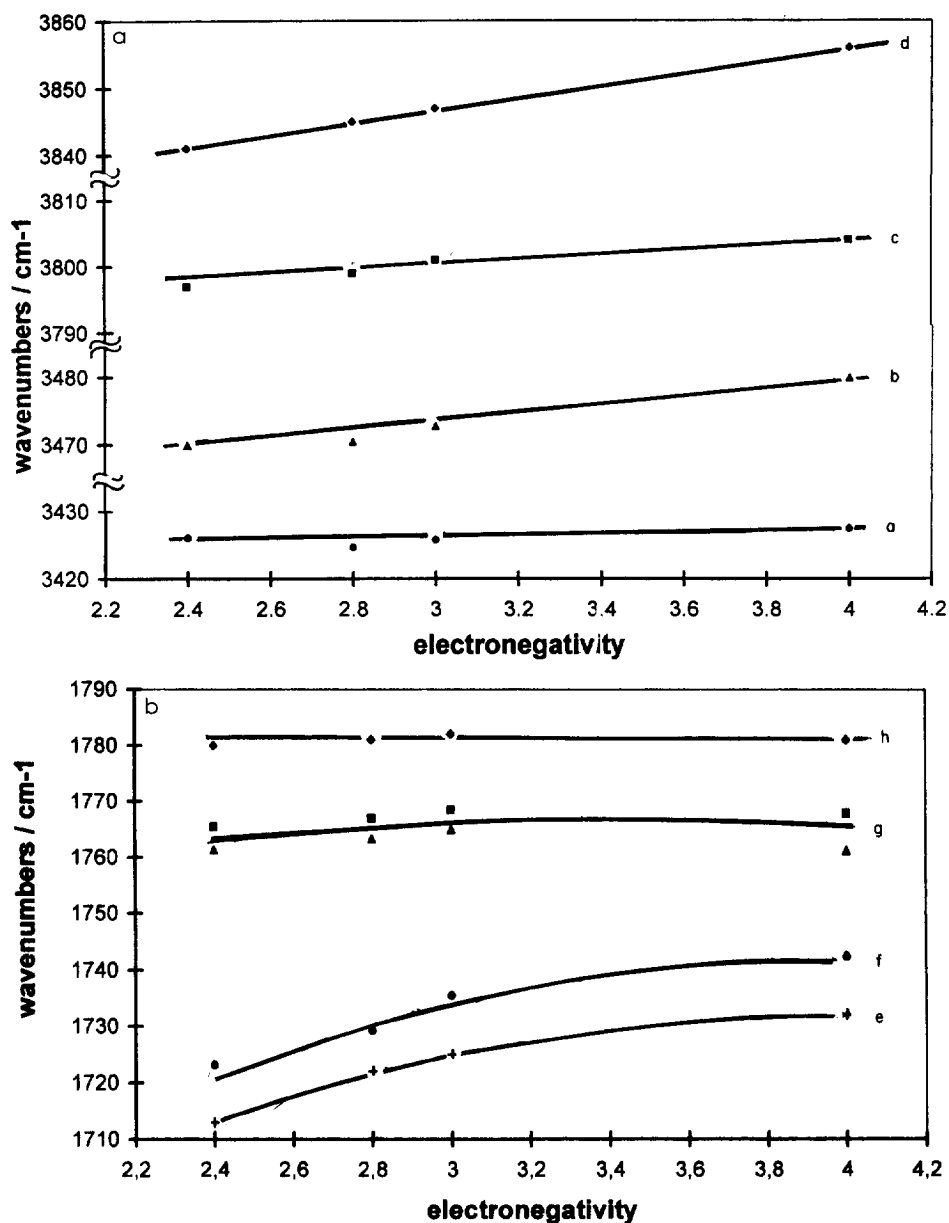


Fig. 2. The dependence of: (a) $\nu(\text{N}_3-\text{H})_{\text{exp}}$, (b) $\nu(\text{N}_1-\text{H})_{\text{exp}}$, (c) $\nu(\text{N}_3-\text{H})_{\text{MP2}}$, (d) $\nu(\text{N}_1-\text{H})_{\text{MP2}}$, (e) $\nu(\text{C}_4=\text{O})_{\text{MP2}}$, (f) $\nu(\text{C}_4=\text{O})_{\text{exp}}$, (g) $\nu(\text{C}_2=\text{O})_{\text{exp}}$, and (h) $\nu(\text{C}_2=\text{O})_{\text{MP2}}$ on the halogen electronegativity.

94 program [18] on an SGI Power Challenge computer. The Hartree–Fock (HF), second order of Møller–Plesset (MP2) and density functional (DFT) (B3P86, B3PW91) methods with the 3-21G** basis set were used. The 3-21G** was the largest standard

basis set available in the GAUSSIAN 94 program that included parametrization for all halogen substituents. The frequencies were obtained analytically. The potential energy distributions were obtained using a special PED program [19].

Table 1
Selected frequencies (cm^{-1}) of 5-halogenouracils observed in FTIR Ar-matrix spectra and calculated theoretically using the 3-21G** basis set

Mode	Ar matrix	HF	MP2	DFT B3P86	DFT BP3W91	PED (%) (MP2)
<i>5-fluorouracil</i>						
$\nu(\text{N}_1\text{--H})$	3480.1	3987	3856	3743	3738	100 $\nu(\text{N}_1\text{--H})$
$\nu(\text{N}_3\text{--H})$	3427.4	3941	3804	3694	3691	100 $\nu(\text{N}_3\text{--H})$
$\nu(\text{C}_2=\text{O})$	1767.8	1955	1781	1815	1809	62 $\nu(\text{C}_2=\text{O})$
	1761.1					
$\nu(\text{C}_4=\text{O})$	1742.3	1944	1733	1770	1765	40 $\nu(\text{C}_5=\text{C}_6)$, 23 $\nu(\text{C}_4=\text{O})$
$\nu(\text{C}_5=\text{C}_6)$	–	1904	1696	1741	1736	50 $\nu(\text{C}_4=\text{O})$, 23 $\nu(\text{C}_5=\text{C}_6)$
<i>5-chlorouracil</i>						
$\nu(\text{N}_1\text{--H})$	3472.1	3979	3847	3735	3731	100 $\nu(\text{N}_1\text{--H})$
$\nu(\text{N}_3\text{--H})$	3425.7	3940	3801	3695	3691	100 $\nu(\text{N}_3\text{--H})$
$\nu(\text{C}_2=\text{O})$	1768.4	1956	1782	1814	1809	63 $\nu(\text{C}_2=\text{O})$
	1764.9					
$\nu(\text{C}_4=\text{O})$	1735.5	1940	1725	1778	1773	61 $\nu(\text{C}_4=\text{O})$, 10 $\nu(\text{C}_5=\text{C}_6)$
$\nu(\text{C}_5=\text{C}_6)$	–	1834	1667	1686	1681	54 $\nu(\text{C}_5=\text{C}_6)$, 15 $\nu(\text{C}_4=\text{O})$, 13 $\delta(\text{C}_6\text{--H})$
<i>5-bromouracil</i>						
$\nu(\text{N}_1\text{--H})$	3470.5	3979	3845	3736	3731	100 $\nu(\text{N}_1\text{--H})$
$\nu(\text{N}_3\text{--H})$	3424.6	3941	3799	3695	3691	100 $\nu(\text{N}_3\text{--H})$
$\nu(\text{C}_2=\text{O})$	1766.9	1954	1781	1813	1808	63 $\nu(\text{C}_2=\text{O})$
	1763.2					
$\nu(\text{C}_4=\text{O})$	1729.2	1936	1722	1773	1768	63 $\nu(\text{C}_4=\text{O})$
$\nu(\text{C}_5=\text{C}_6)$	–	1823	1657	1679	1674	56 $\nu(\text{C}_5=\text{C}_6)$, 12 $\nu(\text{C}_4=\text{O})$, 13 $\delta(\text{C}_6\text{--H})$
<i>5-iodouracil</i>						
$\nu(\text{N}_1\text{--H})$	3469.9	3977	3841	3733	3730	100 $\nu(\text{N}_1\text{--H})$
$\nu(\text{N}_3\text{--H})$	3426.0	3940	3797	3695	3691	100 $\nu(\text{N}_3\text{--H})$
$\nu(\text{C}_2=\text{O})$	1765.4	1954	1780	1813	1808	63 $\nu(\text{C}_2=\text{O})$
	1761.3					
$\nu(\text{C}_4=\text{O})$	1723.1	1926	1713	1766	1756	63 $\nu(\text{C}_4=\text{O})$
$\nu(\text{C}_5=\text{C}_6)$	–	1807	1647	1667	1661	55 $\nu(\text{C}_5=\text{C}_6)$, 12 $\nu(\text{C}_4=\text{O})$, 15 $\delta(\text{C}_6\text{--H})$

3. Results and discussion

3.1. The N–H stretching vibrations

The N–H stretching vibration region of 5-XU crystals exhibits a very broad, structured band originating from the hydrogen-bonded network, which cannot be simply interpreted in terms of halogen electronegativity [6]. In the Ar matrix, the hydrogen bonds between 5-XU molecules do not

exist and the N–H stretching vibration region exhibits only two bands (Fig. 1a) located at 3480–3470 cm^{-1} ($\nu(\text{N}_1\text{--H})$) and ca. 3426 cm^{-1} ($\nu(\text{N}_3\text{--H})$), respectively. The halogen substituent effect is manifested mainly in the $\nu(\text{N}_1\text{--H})$ mode, and this is illustrated by the correlations between $\nu(\text{N}_1\text{--H})$ and the X-atom electronegativity (Fig. 2a–d). These correlations demonstrate that the $\nu(\text{N}_1\text{--H})$ changes are determined by the X-atom inductive effect.

3.2. The C=O stretching vibrations

In the C=O stretching vibration region of the Ar matrix spectra, many bands occur (Fig. 1b) and this is due to Fermi resonance [7,11,17]. However, one can select bands of significant intensity, which are associated with the $\nu(\text{C}_2=\text{O})$ and $\nu(\text{C}_4=\text{O})$ modes. According to Refs. [7–17] and our own calculations (Table 1) the higher frequency band is assigned to the $\nu(\text{C}_2=\text{O})$ mode and the lower frequency band to the $\nu(\text{C}_4=\text{O})$ mode. The results of the calculations suggest the former to be insensitive to the X-atom change, whereas the latter should shift to lower frequency from F- to I-derivatives. Indeed, the Ar matrix frequency of the $\nu(\text{C}_2=\text{O})$ mode varies from F- to I-derivatives by only a few cm^{-1} , while the $\nu(\text{C}_4=\text{O})$ frequency decreases in parallel with the decrease in halogen electronegativity (Fig. 2e-h). Since the $\text{C}_2=\text{O}$ group is distanced from the C–X group, the insensitivity of $\nu(\text{C}_2=\text{O})$ to the X-atom nature is easy to understand.

3.3. The C=C stretching vibrations

Since the $\text{C}_5=\text{C}_6$ bond is adjacent to the X-substituent, a significant effect of the halogen atom nature on the $\nu(\text{C}_5=\text{C}_6)$ frequency is expected. Indeed, our calculations show a large increase of the $\nu(\text{C}_5=\text{C}_6)$ frequency with the X-atom electronegativity. However, the $\nu(\text{C}_5=\text{C}_6)$ Ar matrix FTIR bands are too weak to be observed, but the Raman frequencies discovered for polycrystalline samples [6] confirm the predicted trend.

4. Conclusions

The correlation of the $\nu(\text{N-H})$ and $\nu(\text{C=O})$ stretching vibration frequencies with X-atom electronegativity proves that the effect of the halogen substituent is manifested mainly by an increase of the $\nu(\text{N}_1-\text{H})$ and the $\nu(\text{C}_4=\text{O})$ frequency. The $\nu(\text{C}_5=\text{C}_6)$ bands are too weak to be observed in Ar matrices, but the Raman $\nu(\text{C}_5=\text{C}_6)$ frequencies of polycrystalline 5-halogenouracil samples satisfy a similar correlation.

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