Lim (University of Akron) for helpful discussions. The X-ray crystallographic data were provided by Dr. Scott R. Wilson of the University of Illinois at Urbana—Champaign. The Pittsburgh Supercomputing Center, the National Center for Supercomputing Applications at the University of Illinois at Urbana—Champaign, and the Cornell National Supercomputer Facility provided access time on CRAY X-MP/48 and IBM 3090/600 VF computers.

Registry No. 1,9-DMG, 42484-34-4; O^6,9-DMG, 61580-66-3; 9-MG, 5502-78-3.

Tautomerism and Infrared Spectra of Thiouracils. Matrix Isolation and ab Initio Studies[†]

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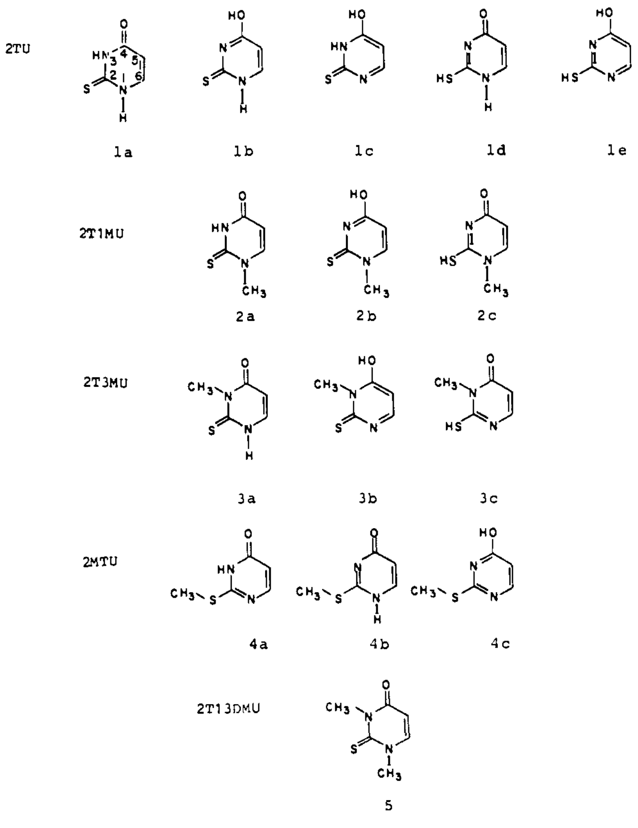
Abstract: A study of the infrared (IR) spectra of a variety of thiouracils isolated in low-temperature inert matrices demonstrated that 2- and 4-thiouracils together with their N1- and N3-methylated derivatives as well as 2,4-dithiouracil exist under these conditions only in the oxothione or dithione tautomeric forms. In contrast, S2- and S4-methylated derivatives under the same conditions exist as a mixture of hydroxy and oxo tautomeric forms. The ratio of concentrations of the tautomers $K(\text{o/h}) = ([\text{oxo}]/[\text{hydroxy}])$ and the free energy differences, ΔG, were experimentally estimated from the ratio of the absorbances of the NH and OH stretches. The values obtained are $K(\text{o/h}) = 1.5$ and $\Delta G = -1.7$ kJ/mol for 2-(methylthio)uracil and $K(\text{o/h}) = 0.5$ and $\Delta G = +2.5$ kJ/mol for 4-(methylthio)-6-methyluracil. An assignment of the observed infrared bands, particularly those related to the C=S stretching vibrations, is proposed on the basis of the comparison of the matrix spectra from different derivatives and of the spectra calculated by using ab initio methods (3-21G* basis set).

Chart I



Thio derivatives of nucleosides are of interest because of their biological and pharmacological activities; e.g., as minor components of tRNA or as anticancer drugs (refs 2–8 and references therein). In particular, when 4-thiothymidine is substituted for thymidine, anomalous properties appear which are inconsistent with a Watson–Crick structure but instead agree with a left-handed double helix structure build up from Haschemeyer–Sobell (reversed Hoogsteen) base pairs.[2,5-8] Since the C_4=O group of thymidine is involved in base pairing in the Watson–Crick structure of DNA, substitution of O_4 by sulfur (in 4-thiothymidine) is expected to cause perturbation of base-pair hydrogen bonding and also of other interactions (e.g., stacking or surface interactions) of the nucleic bases.

Although thiopyrimidines identified as minor components of tRNA have been extensively studied,[9] only a few systematic investigations have been devoted to the tautomerism of thiouracils (e.g., refs 14–19 and references therein). Little attention has been given to the tautomerism of thiouracils in an inert environment,[1,15] although it is well-known that tautomeric equilibria of a number of pyrimidine bases depend strongly on intermolecular interactions of the bases (e.g., 16–21). Such inert local environments, although infrequent, might occasionally be expected to occur in the vicinity of a base or its fragment.

Even if a direct biological significance of the matrix isolation studies of biological molecules such as thiouracils might be questionable because of the "unrealistic" conditions in which molecules exist in the low-temperature inert matrix, such studies *are* necessary for testing the reliability of theoretical calculations of the properties of these molecules including their stabilities. The most reliable theoretical calculations (ab initio with good basis sets) can be performed at present only for molecules in vacuum,

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[†] This is Part 2 of a series of studies of thiouracils. Part 1 is ref 1.

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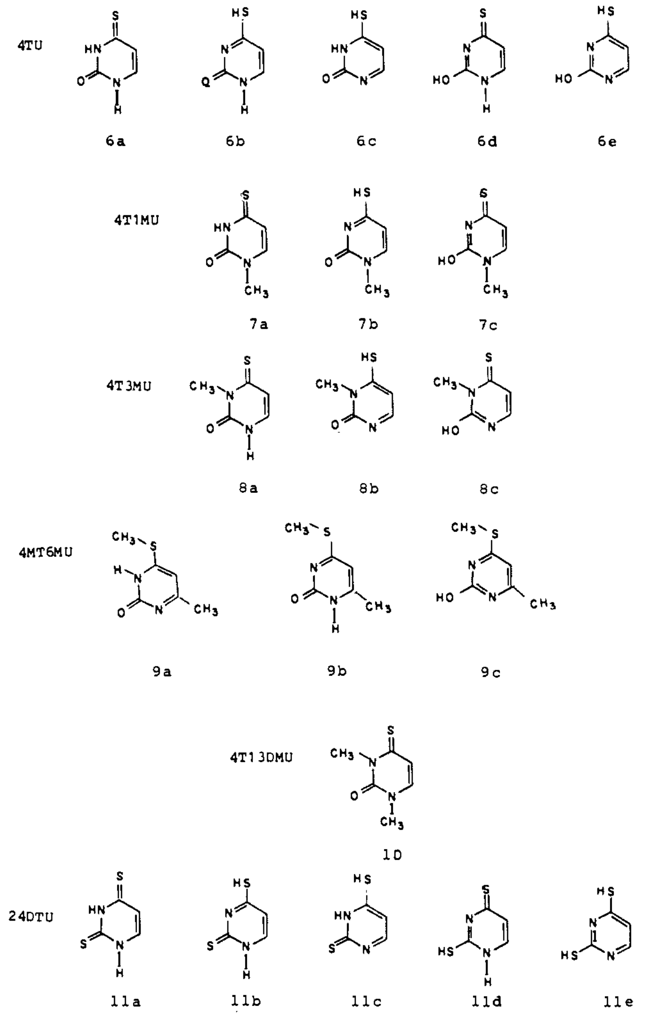
Chart II



and their predictions are applicable strictly only to isolated molecules. Until recently such theoretical calculations were usually compared with experimental results from solutions (most often aqueous) or crystals, because of the absence of experimental data for molecules in the vapor phase or in inert solvents. Such data are difficult or impossible to obtain because of thermal decomposition, in the case of vapor, or low solubility, in the case of inert solvents. Matrix isolation studies provide results for isolated, practically noninteracting, molecules for comparison with results from calculations to test the reliability of theoretical methods to predict properties of larger biomolecules.

One of the aims of this work is to analyze and to interpret the IR spectra of isolated thiouracils unperturbed by intermolecular interactions, in order to obtain necessary reference data for the spectral studies of molecular interactions.

In the present investigation we have examined the tautomerism of 2- and 4-thiouracil and of the various derivatives methylated at the N1-, N3-, S2-, and S4-atoms and also of 2,4-dithiouracil all isolated in inert low-temperature matrices.

The compounds studied include several which may adopt different tautomeric forms (see structures **1–4**, **6–9**, and **11**) and also some which have only one fixed tautomeric form (see structures **5** and **10**) and which serve as models for particular tautomers.

Experimental Section

The compounds which were studied were kindly made available by Professor D. Shugar (Warsaw). (Abbreviations used here for these compounds are as follows: uracil = U; 2-thiouracil = 2TU; 4-thiouracil = 4TU; 2,4-dithiouracil = 24DTU; 1-methyl-2-thiouracil = 2T1MU; 3-methyl-2-thiouracil = 2T3MU; 1,3-dimethyl-2-thiouracil = 2T13DMU; 2-(methylthio)uracil = 2MTU; 1-methyl-4-thiouracil = 4T1MU; 3-methyl-4-thiouracil = 4T3MU; 1,3-dimethyl-4-thiouracil = 4T13DMU; 4-(methylthio)-6-methyluracil = 4MT6MU; and 4-thio-6-methyluracil = 4T6MU.) The methods of synthesis are described elsewhere (refs 10a,b, 22, and references cited therein). All compounds were checked for thermal decomposition by comparison of the ultraviolet spectra in solution (methanol or water) and infrared spectra in KBr pellets of the samples before and after heating (to the same temperature as that for matrix study) supplemented occasionally, by chromatographic study.

The infrared spectra were recorded with a Perkin-Elmer Model 580B spectrometer. Matrix-isolated samples were prepared according to the procedure described in ref 23. A continuous-flow helium cryostat (cooled to about 5–7 K) was used as a cooling system. N_2 and Ar (spectral purity, VEB Technische Gase Leipzig, GDR) were used as matrix gases.

Studies of the infrared spectra of a number of pyrimidine and purine bases isolated in low-temperature inert matrices published in the recent years have established the usefulness of this method for determination of the structure and tautomeric equilibria as well as for study of spectroscopic and other properties of these molecules without the interfering

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Table I. Comparison of the Experimental and Calculated Frequencies (ν) and Relative Intensities (a, A) of the N1H and N3H Stretching Modes of Different Thiouracil and Uracil

	experiment				calculation (this work)			
compd	ν(N1H)[b]	ν(N3H)[b]	$\Delta\nu$[b]	a(N3H)/a(N1H)	ν(N1H)[b]	ν(N3H)[b]	$\Delta\nu$[b]	A(N3H)/A(N1H)
2TU	3439	3399	40	0.71	3425	3395	30	0.83
2T1MU		3400						
2T3MU	3445							
4TU	3463	3401	62	0.43	3432	3392	40	0.51
4T1MU		3398						
4T3MU	3456							
24DTU	3434	3379	55	0.46	3418	3379	39	0.49
uracil[a]	3470	3423	47	0.72	3440	3410	50	0.72

[a] Experimental data for uracil in N2 matrix from ref 23 and calculated data obtained recently in our laboratory using an ab initio method with 3-21G basis set[38] (see also ref 40). [b] Measured in cm^{-1}.

effects of stronger intermolecular interactions [e.g., refs 18–21, 23, and 24].

Method of Calculation

Ab initio LCAO-MO methods were used for the theoretical study of the tautomers of thiouracils. The calculations have been carried out by using the GAUSSIAN 86 program[25] with a split valence, 3-21G* basis set.[26] The geometry was optimized by the gradient procedure.[27a] For all tautomers the planar, C_s, structure was assumed. The optimized geometry was not significantly different from that obtained from X-ray studies, with the exception of the bonds involving atoms participating in hydrogen bonding in the crystal. In particular, the use of polarization functions in the 3-21G* basis set allows a prediction of the C=S bond length that agrees with the experimental value within 0.014 Å.[34] All optimized structures were checked by analysis of the harmonic vibrational frequencies obtained from diagonalization of force constant matrices to verify whether they are minima, saddle points, or stationary points of higher orders. Only positive eigenvalues of the Hessian matrix were obtained, proving that the calculated geometry is a minimum on the potential energy surface.

The ab initio vibrational frequencies were calculated analytically at the optimized geometry. The force constant matrices $\mathbf{F}_x$ for the in-plane and out-of-plane Cartesian displacements were obtained from the analytical gradient at the equilibrium geometries. The normal coordinate transformation matrix $\mathbf{l}$ and vibrational frequencies were calculated by diagonalizing the resulting force constant matrix $\mathbf{F}_q$ in mass-weighted Cartesian coordinates. These procedures are standard in the GAUSSIAN 86 program.[25] Transformation of $\mathbf{F}_x$ to the force constant matrix in internal symmetry coordinates for in-plane vibrations and for out-of-plane vibrations (nonredundant symmetry coordinates were defined as recommended by Pulay et al.[27b,c]) allowed ordinary normal coordinate calculations to be carried out as described by Schachtschneider.[27d]

Calculation of normal mode vibrational frequencies at the HF/3-21G* level of theory is expected to be as successful as similar calculations by using the larger 6-31G* basis.[26] Vibrational frequencies calculated at the 3-21G* level are, in general, 11% higher[28] than experimental (anharmonic) values. Errors in frequencies corresponding to related motions are relatively similar from one molecule to another. The magnitude of the error is reduced by about half when the comparison between values from theory is made with experimental values of harmonic frequencies. Hence corrections for anharmonicity and for the basis set limitation are made to the calculated frequencies by multiplying them by scaling factors of 0.9 for in-plane modes and 0.81 for out-of-plane modes (see footnote under Table II). The calculated force constants and the definition of symmetry coordinates are given in the Supplementary Material (Tables 7–10).

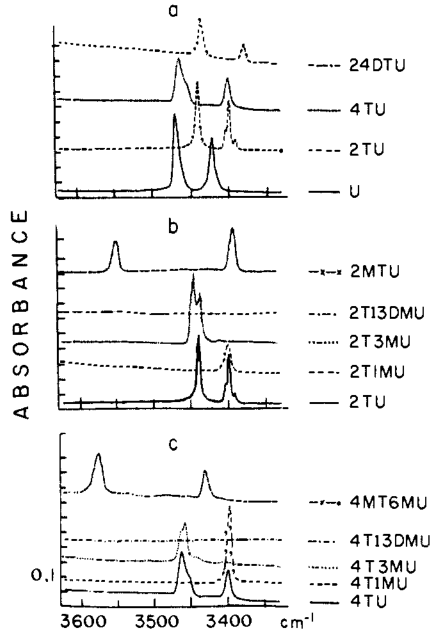

Figure 1. Comparison of the IR spectra in the NH and OH stretching (in-plane) region (3650–3350 cm^{-1}) of different thiouracils isolated in a nitrogen matrix at about 6–7 K: (a) unmethylated compounds 2TU, 4TU, 24DTU, and, for a comparison, U (uracil); (b) series of 2-thiouracils; and (c) series of 4-thiouracils.

Results and Discussion

This section is divided into two parts. In the first part results from the spectral region corresponding to the most characteristic vibrations of the NH, OH, and SH groups involved in tautomeric transitions are presented and discussed, and the oxo–hydroxy tautomeric equilibrium is examined. The second part presents an analysis of other spectral regions, with special attention to those corresponding to the stretching vibrations of the C=O, C=C, and C=S groups.

Frequencies, intensities, and assignments of absorption bands for all the studied compounds are presented in Tables I–VI.

The NH, OH, and SH Stretching Region (3650–2000 cm^{-1}). Figure 1a shows the spectral region related to the OH and NH stretching modes for 2TU, 4TU, and 24DTU. For comparison the spectrum of matrix-isolated uracil is also included. Figure 1b shows the spectra of all methylated 2-thiouracils compared with the parent 2TU. Figure 1c presents the same comparison of the spectra for the analogous series of 4-thiouracils.

As seen in Figure 1a for 2TU, 4TU, and 24DTU, two bands are observed in the characteristic NH stretching region just as

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Table II. Experimental and Calculated Infrared Frequencies, ν, Intensities, A, and Potential Energy Distributions, PEDs, of 2TU Monomers

	calculation					
	ν, cm^{-1}				experiment (in N2)[c]	
normal coord	unscl[a]	scl[a]	A, km/mol	PED[b]	ν, cm^{-1}	A rel
1	3805	3425	135	N1H str(99–)	3439	280
2	3772	3395	112	N3H str(100–)	3399	198
3	3453	3108	2	C5H str(94+)		
4	3409	3068	3	C6H str(94+)		
					1737	119
5	1948	1753	623	C4O str(72+)	1732	237
				C4C5 str(7–)	1727	49
				N3H bend(6+)	1715	152
					1703	30
					1688	13
					1673	10
6	1832	1649	41	C5C6 str(61+)	1635	26
				C6H bend(12+)		
				N1H bend(8+)	1615	10
				C4O str(6–)	1597	40
7	1718	1546	744	N1H bend(43+)	1541	482
				N3H bend(23–)		
					1531	23
					1525	40
8	1601	1441	7	N3H bend(49+)	1432	33
				N1H bend(25+)		
9	1558	1402	8	C6H bend(42+)	1417	26
				C5H bend(30+)		
10	1505	1354	233	N1C2 str(32+)	1396	63
				C2N3 str(29+)		
					1380	50
					1372	30
					1353	16
11	1366	1229	6	C5H bend(43+)	1225	50
				C6H bend(20–)		
				C5C6 str(10+)		
					1218	6
					1209	13
					1205	43
12	1313	1182	402	C2N3 str(33–)	1197	155
				N3C4 str(21+)		
				C6H bend(13+)		
				N1H bend(10–)		
					1176	49
					1162	43
13	1250	1125	183	ring def I(35–)	1148	227
				C2S str(26+)		
				N1C2 str(14–)		
14	1193	966	8	C6H opl wag(78+)	906	6
				C5H opl wag(38+)		
15	1150	1035	6	C6N1 str(39+)	1062	3
				C5H bend(14+)		
16	1086	977	28	ring def I(33+)	994	20
				N1C2 str(23–)		
				C6N1 str(19–)		
				C2N3 str(10–)		
17	1012	819	297	N3H opl wag(47–)	811	85
				C4O opl wag(40+)		
				C5H opl wag(11–)		
18	961	865	5	N3C4 str(32+)	or 906?	6
				C4C5 str(27+)		
				C2S str(16–)		
19	954	772	24	C5H opl wag(43+)	744	23
				N3H opl wag(25–)		
				C6H opl wag(14–)		
				C2S opl wag(12+)		
				N1H opl wag(12–)		
20	862	698	41	N1H opl wag(52+)	717	30
				N3H opl wag(26–)		
				opl ring def I(13+)		
				C2S opl wag(11–)		
21	812	658	90	opl ring def I(33–)	655	56
				C4O opl wag(23+)		
				N1H opl wag(22+)		
22	773	695	11	ring def III(33–)	714	23
				C4C5 str(30–)		
				C2S str(13–)		
23	727	589	20	C2S opl wag(44–)	635	13
				N1H opl wag(16–)		
				C4O opl wat(12+)		
				opl ring def I(10+)		

Table II (Continued)

	calculation				experiment (in N2)[c]	
	ν, cm⁻¹					
normal coord	unscl[a]	scl[a]	A, km/mol	PED[b]	ν, cm⁻¹	A rel
24	591	532	12	ring def II(74−)	531	20
25	536	482	20	C4O bend(62+) ring def III(15−) C2S bend(14+)	492	20
26	487	438	24	C2S str(37+) ring def III(28−)	402	13
27	477	386	11	opl ring def III(56−) opl ring def I(19−) C4O opl wag(16−) opl ring def II(10−)	or 402?	13
28	295	265	11	C2S bend(70−) C4O bend(10+)	271	16
29	196	159	2	opl ring def II(91+) opl ring def I(12−)	*	
30	177	143	1	opl ring def III(51+) opl ring def I(28−) C2S opl wag(20−)	*	

[a] Unsc, unscaled frequencies; sc frequencies scaled by 0.90 in the case of all in-plane normal modes and by 0.81 in the case of out-of-plane modes. [b] PEDs calculated according to the procedure given by the following: Keresztury, G., Jalsovsky, G. *J. Mol. Struct.* **1971**, *10*, 304. Morino, Y.; Kuchitsu, K. *J. Chem. Phys.* **1952**, *20*, 1809. Abbreviations: str, stretching; bend, bending; def, deformation; opl, out-of-plane; wag, wagging. Signs describe phases of the motions. [c] Relative integrated intensities expressed in relative units in which the sum of the experimental integrated intensities was supposed to be equal to the sum of the calculated intensities. Presence in some regions of the experimental spectrum of several bands instead of one predicted by calculation results probably from anharmonicity effects (e.g., Fermi resonance), traces of self-associated molecules, and/or matrix side effect.

for uracil, but the frequencies of the corresponding bands of thiouracils are slightly lower than those of uracil. N1- or N3-methylated derivatives of 2TU (Figure 1b) and 4TU (Figure 1c) each exhibit only one band obviously related to N1H or N3H stretches, but with frequencies also slightly lower than those of the corresponding N-methylated uracils.[29] The comparison shown in Figure 1 (parts a, b, and c) allows the straightforward assignment of the higher frequency band in the NH stretching region to the N1H vibration and the lower frequency band to N3H vibration.

As expected, no absorption is observed in the spectral region discussed here for 2T13DMU and for 4T13DMTU. No absorption was found also in the characteristic SH stretching region (not shown in Figure 1; such absorption was observed at 2601 cm^{-1} for the O4-alkylated derivative of 2TU[1a]) and in the OH stretching region (near 3600 cm^{-1}) for any of the N-methylated thiouracils.

The appearance of the N1H and/or N3H stretches and the absence of the SH and OH stretches in the spectrum of 2TU, 4TU and their N1- and N3-methylated derivatives, and also of 24DTU indicates that these molecules exist only in the oxothione (structures **1a**, **2a**, **3a**, **6a**, **7a**, and **8a**) or dithione (structure **11a**) tautomeric form in an inert matrix. This conclusion is consistent with the results of quantum mechanical calculations of the stabilization energies,[30-34] particularly with the most recent ab initio calculations[32,33] and with our own ab initio calculations for 2TU, 4TU, and 2,4DTU.[34]

The spectra of S-methylated thiouracils (2MTU and 4MT6MU) are drastically different from those for other thiouracils discussed above (see Figure 1 (parts b and c)). In addition to an absorption in the NH stretching range, both these molecules exhibit an absorption near 3570 cm^{-1}, the region characteristic for the OH stretching mode of a number of hydroxypyrimidines isolated in low-temperature matrices or in the vapor phase [e.g., refs 18–21]. The appearance of NH and OH stretches in the spectrum of both S-methylated thiouracils suggests strongly that these molecules exist in this inert matrix as a mixture of both oxo and hydroxy tautomers.

In the oxo form of 2MTU a hydrogen atom is attached to nitrogen N3 (structure **4a**), as indicated by the frequency observed for the NH stretch, which is close to that of the N3H stretch of 2T1MU but different from that of N1H expected for structure **4b**.

The NH stretch of the oxo tautomer of 4MT6MU is located at 3430 cm^{-1}, between the N1H stretch of 4T3MU and the N3H stretch for 4T1MU. We have assigned this NH stretch for 4MT6MU to the N1H vibration (structure **9b**) on the basis of a comparison of the NH stretching frequencies of 4TU with those for its derivative methylated at carbon C6 (4T6MU) shown below:

	N1H str	N3H str
4TU (in Ar)	3483 cm⁻¹	3413 cm⁻¹
4T6MU (in Ar)	3457 cm⁻¹	3417 cm⁻¹

As seen, methylation at C6 decreases the frequency of the N1H stretch (in the position ortho to C6) by 26 cm^{-1}, while the frequency of the N3H stretch (in a para position with respect to C6) increases only slightly. This effect of methylation in an ortho position on the frequency of an NH stretch has also been observed for other compounds (e.g., ref 35). It has been suggested there that intramolecular interaction is responsible for this effect. The frequency of the N1H stretch for 4MT6MU in the N_2 matrix (3430 cm^{-1}) is lower than the frequency of the N1H stretch of 4T6MU in an Ar matrix (3457 cm^{-1}) because the N_2 matrix is more strongly interacting; probably there may also be an effect due to the additional methylation at sulfur S4.

When sulfur is substituted for oxygen at carbon C4, the frequency of the N3H stretch involving the bond in an ortho position with respect to C4 shifts strongly downward, while the frequency of the N1H stretch involving the more distant N1H bond is only slightly lowered (Table I). For 2TU and 24DTU both N1H and N3H stretches are shifted down, but for 24DTU the effect of two

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sulfur substituents is almost additive (Table I). Also the ratio of the intensities of N1H to N3H stretches is affected by the sulfur substitution at C4 and at both C2 and C4 but not by substitution only at C2 (Table I). These changes of the frequencies and relative intensities of N1H and N3H stretches reflect chemical changes (e.g., changes of electron charge on N1 and N3[31,34]) resulting from the replacement of oxygen by sulfur on the properties of these molecules and would suggest a decrease of the proton donor abilities of these groups particularly for the biologically significant N3H group.

Equilibrium Constant and Free Energy Differences of S-Methylated Thiouracils. The ratio of the concentrations of the oxo and hydroxy tautomers "equilibrium constant", K(o/h), of S-methylated derivatives (2MTU and 4MT6MU) can be determined from the ratio of the experimental absorbances of the NH and OH stretching modes, abs(NH)/abs(OH), and the ratio of the absolute integrated molar absorption coefficients of these modes A(NH)/A(OH). For 2MTU, K(o/h) = abs(N3H)/abs(OH) × A(OH)/A(N3H), because in the oxo form the hydrogen atom is attached to the N3 nitrogen (structure **4a**), while for 4MT6MU K(o/h) = abs(N1H)/abs(OH) × A(OH)/A(N1H), because the hydrogen atom in the oxo form is attached to the N1 nitrogen (structure **9b**). The integrated molar absorption coefficients of N1H and N3H stretches are not the same even in the same molecule (as indicated by the ratios the experimental absorbances in Table I), and they are even more likely to be different in the different molecules such as 2MTU and 4MT6MU. The absolute molar absorption coefficients A(OH) and A(N1H) cannot be measured experimentally; hence we have used the ratio A(OH)/A(NH) calculated for the hydroxy and oxo tautomers of 2- and 4-mercaptouracil by ab initio (3-21G)* methods (see Supplementary Material, Tables 11 and 12).

The values used for estimation of K(o/h) of 2MT were abs(N3H)/abs(OH) = 1.2 ± 0.1 (from experiment) and A(OH)/A(N3H) = 1.3 ± 0.1 (from calculations Supplementary Material, Table 11) leading to K(o/h) = 1.5 ± 0.2.

The values used for estimation of K(o/h) of 4MT6MU were abs(N1H)/abs(OH) = 0.5 ± 0.1 (from experiment) and A(OH)/A(N1H) = 1.1 ± 0.1 (from calculation Supplementary Material, Table 12) leading to K(o/h) = 0.55 ± 0.2. The uncertainty of K(o/h) value results from the error in the experimental determination of the absorbances (about 10%, due to the uncertainty of background and bands overlap) and the uncertainty of the ratio of calculated molar absorption coefficients.

The calculated ratios of the molar absorption coefficients and their uncertainties were verified against experimental data by comparing the calculated and experimental ratios (not absolute values) of the intensities of the N_1H and N_3H stretches of 2TU and 4TU (see Table I). It is worthwhile to note that the calculated intensities of the OH and NH stretches of a number of pyrimidine and purine bases that have been studied have been found to be very similar (see e.g., ref 18f,i and 41).

The K(o/h) value can also be obtained from ratios of the intensities of the OH stretch for the hydroxy tautomer and of the C=O stretch for the oxo tautomer, by using again the molar absorption coefficients of these modes calculated for the corresponding tautomers of 2- and 4-mercaptouracils (Supplementary Material). This estimation gives values very close to those obtained by using NH and OH absorptions.

We believe that these K(o/h) values reflect the equilibrium existing in the gas phase at about 500 K just before the gas mixture condenses onto the cold window in the matrix experiment. From these "equilibrium constants" we estimate that the standard Gibbs free energy difference $\Delta G = -RT \ln K$(o/h) for 2MTU at 500 K is about −1.7 ± 0.6 kJ/mol in favor of the oxo form (structure **4a**), while for 4MT6MU it is about +2.5 ±1 kJ/mol in favor of the hydroxy form (structure **9b**). The uncertainty of ΔG results from the uncertainty of the equilibrium constant (about 20%, see above) and the uncertainty of the estimated temperature (we believe not more than about 10%).

We can expect that the entropies of the oxo and hydroxy tautomers are similar so that the entropy difference is not large. Furthermore, we can expect that the difference in the thermal energies for the two tautomers is also small, so that

$$\Delta G^0_{500} + T\Delta S \simeq \Delta G^0_{500} \simeq \Delta H^0_0 = \Delta E^0_0$$

Hence, for 2MTU, $\Delta E^0_0 \cong -1.7 \pm 1$ kJ/mol (in favor of the oxo form), while for 4MT6MU $\Delta E^0_0 = +2.5 \pm 1$ kJ/mol (in favor of the hydroxy form).

The preference of the hydroxy over the oxo tautomer in the case of 4MT6MU is consistent with the results from studies of tautomerism of other pyrimidine bases such as 2- and 4-oxo- (or hydroxy) pyrimidines isolated in an inert environment or in the vapor phase. When an oxygen atom is attached to the C2 carbon, the hydroxy tautomer is predominant (e.g., ref 18a–c). For molecules with an oxygen atom at C4 both oxo and hydroxy tautomers are present at approximately the same concentrations (e.g., ref 18a,b). When oxygen atoms are attached to both C2 and C4, as in the case of uracils, only the oxo tautomer is present in the matrix and in the vapor (according to the infrared studies (e.g., refs 18b, 19, 23, and 29)).

An ab initio calculation of the energy difference between the oxo and hydroxy tautomers of 2-(methylthio)uracil was made recently (3-12G* optimized geometry with a single point 6-31G** calculation of the energies) by Katritzky, Szafran, and Stevens.[32] The calculated energy difference ΔE(SCF) = E(oxo) − E(hydroxy) = −6.9 kJ/mol in favor of the oxo form (structure **4a**). This energy difference was not corrected for the zero point vibrational energy (ZPE). The magnitude of this correction can be estimated on the basis of our ab initio 3-21G* calculations of the vibrational frequencies of the oxo and hydroxy tautomers of 2-mercaptouracil (see Supplementary Material, Table 11) (ZPE,oxo) − (ZPE,hydroxy) = +2.5 kJ/mol. This brings the calculated difference in energies E(o) − E(h) to about −4.4 kJ/mol which is still greater than the experimental value of ΔE^0_0 of −1.7 kJ/mol. However, taking into account limitations of the calculation, the approximation involved in estimating (ZPE), the uncertainty in the experimental estimate of the ΔG^0_0, and the assumption that $\Delta G^0_0 = \Delta E^0_0$, we consider the agreement between experiment and calculation to be very good.

According to our knowledge, ab initio calculations have not been performed for 4-(methylthio)uracil (and for 4-(methylthio)-6-methyluracil). We have carried out ab initio calculations for the oxo and hydroxy tautomers of 4-mercaptouracil model compounds (with H atom instead of CH_3 on the S4 atom) at the SCF(3-21G*) + MP2(correlation) level and with (ZPE) (3-21G*) included.[34] The difference of the energy E(o) − E(h) obtained from this calculation for 4-mercaptouracil is −4.49 kJ/mol in favor of the oxo tautomer (structure **6b**). (For 2-mercaptouracil a similar calculation[34] leads to an energy difference of −5.70 kJ/mol, also in favor of the oxo tautomer (structure **1c**). The prediction of higher stability for the oxo form for 4-mercaptouracil (structure **6b**) does not agree with our experimental findings that the hydroxy form of 4-(methylthio)-6-methyluracil is more stable (by about +1.5 kJ/mol). The most recent calculation by Les and Adamowicz[33] at the 6-31G** + MBPT(2) level predict that for both 2-mercaptouracil and 4-mercaptouracil the hydroxy form is more stable. This prediction agrees with our experimental findings only for S4-methylated thiouracil but not for S2-methylated thiouracil. However, there might be at least two reasons for such disagreement. First, methylation at sulfur and at carbon C6 is expected to have some effect on the relative stabilities of tautomers. Second, calculation at the SCF(3-21G*) + MP2 (and at SCF (6-31G** + MPBT(2)) level is still not sufficiently accurate to predict such small energy differences. It is worth noting that the calculated tautomeric energy difference (E(o) − E(h)) for 4-mercaptouracil is smaller than that for 2-mercaptouracil,[34] hence changing in the direction suggested by experiment.

Infrared Spectra in the 1800–200-cm^{-1} Region. The normal modes in this region are usually strongly coupled. Also Fermi resonance between fundamental modes and their combinations may often produce multicomponent structure of the bands.[23,29]

Matrix site effects might also cause additional splitting of the bands [e.g., ref 23]. All these effects make the interpretation of this spectral region much more difficult and uncertain than for the 3000–4000-cm^{-1} region. In the interpretation of the spectra we have been guided by the comparison of the experimental matrix spectra from different thiouracils and by our recent ab initio calculations of the infrared frequencies and intensities of the fundamental in-plane and out-of-plane modes of 2TU, 4TU, and of 24DTU made by using force constants (see Supplementary Material, Tables 8–10) and intensity parameters calculated with the 3-21G* basis set. All experimental and calculated frequencies and intensities, together with the assignment of the observed bands for 2TU, 4TU, and for 24DTU, are listed in Tables II–IV. Experimental data for the methylated thiouracils are collected in Tables V and VI. The interpretation of the spectra of N-methylated compounds was made by comparison with the assignment of unmethylated molecules and with the assignment for *N*-methyluracils.[29] Although vibrations of the methyl group are well-known in molecules like oxopyrimidines, they are often coupled with the ring and other vibrations of the pyrimidine unit (see e.g., refs 36 and 37), making their assignment more difficult and uncertain. Tables V and VI collect frequencies, intensities, and preliminary assignments, when possible, for N1-, for N3-, and for S2- and S4-methylated derivatives. The assignment for S2- and S4-methylated thiouracils was guided by a comparison of the spectra of these molecules with the IR spectra of S2- and S4-mercaptouracils by the ab initio 3-21G* calculation (see Supplementary Material, Tables 11 and 12).

In the following discussion we will focus most of our attention on the strongest and most characteristic bands related to the C=O, C=C, and C=S stretching modes. Figure 2 shows the part of the spectrum (1900–1600 cm^{-1}) related to the C=O and C5=C6 stretching motions.

For 2TU the C4=O stretch appears as a relatively strong band at 1732 cm^{-1}, while for 4TU the strong C2=O stretch is located at 1752 cm^{-1} (Figure 2a, Tables II and III). In both cases the strong C=O absorption is accompanied by weaker satellites. Superposition of the spectrum of 2TU on that of 4TU gives a result in this C=O stretching region which resembles the spectral pattern observed for uracil in general appearance, although the latter contains some additional satellite bands assigned to Fermi resonance.[23,29]

As expected, no absorption is found in the C=O stretching region for 24DTU.

The C4=O stretching modes for methylated 2-thiouracils are similar to that for 2TU in general appearance (Figure 2b). Methylation at N1 (the para position with respect to C4) does not change the frequency of C4=O stretch strongly, in contrast to the strong lowering of the frequency of this vibration as a result of methylation at N3 (in the ortho position with respect to C4). Some lowering of this frequency is also observed after methylation at S2.

The frequencies of C2=O stretching modes observed in methylated derivatives of 4-thiouracils are lowered by methylation either at N3 or at N1 (both in the ortho position towards C2) as well as by methylation at S4 (Figure 2c and Table III).

The absorption in the spectral region near 1650 cm^{-1} related to the C5=C6 stretch is very sensitive to sulfur substitution. For 2TU and all its derivatives the absorption in this region is relatively weak, similar to that observed for uracil (Figure 2a,b). In contrast, for 4TU and all its derivatives absorption in this range is almost as strong as that of the C2=O stretch (Figure 2a,c). To explain such a drastic change in the intensity of C5=C6 stretch from 2-thiouracils (or uracil) to 4-thiouracils, we note that the PEDs calculated for this mode in 2TU (Table II) and in uracil[23] show that the C5=C6 coordinate is coupled (out-of-phase) with the C4=O coordinate. However, when the S atom is substituted at the C4 position to change C4=O to C4=S, the C5=C6 motion no longer couples with the C4=S stretch. The effect of this coupling of C5=C6 and C4=O is even more pronounced when intensity parameters are analyzed. We will discuss such intensity analyses for the thiouracils and related compounds in a separate paper.[38] (For coupling of C5=C6 and C4=O in uracils see, also: Lewis, Miles, and Becker[39] and Harsanyi, Csaszar, Csaszar, and Boggs[40].) The results observed in this spectral region for thiouracils are consistent with our recent results from matrix studies of cytosines and isocytosines.[20,41,42] For cytosines having the amino group at C4 the intensity of the C5=C6 stretch is relatively high, while for isocytosine (with the C4=O group at C4) the intensity of this vibration is very low. The relatively strong absorption observed for 2MTU and 4MT6MU slightly below 1600 cm^{-1} can be attributed to the aromatic ring C=C stretching mode of the hydroxy tautomer (see Tables V and VI and Supplementary Material). The appearance of this absorption provides additional evidence for the presence of hydroxy tautomer **4c** (and possibly **9c**).

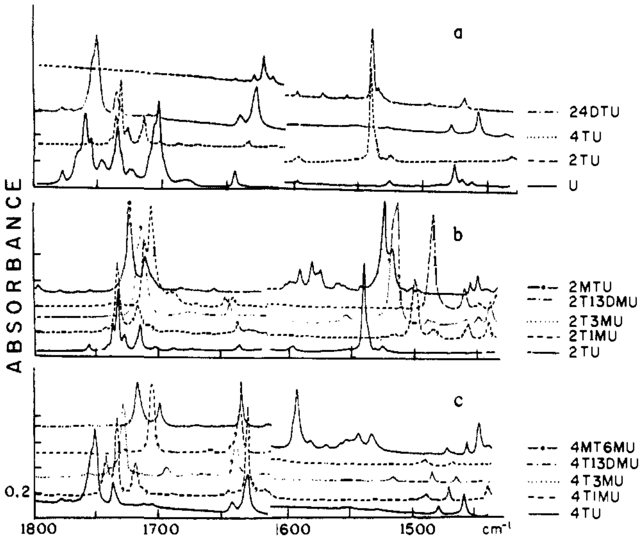

Figure 2. Comparison of the IR spectra in the spectral region (1800–1400 cm^{-1}) related mainly to the C=O, C=C and ring stretching, and NH bending in-plane vibrations of different thiouracils isolated in a nitrogen matrix at about 6–7 K: (a), (b), and (c) the same as in Figure 1.

A drastic difference between the spectral pattern for 2- and 4-thiouracils is also observed near 1500–1600 cm^{-1} (Figure 2a–c). For all 2-thiouracils and for 24DTU a relatively strong absorption is present in this region, while for all 4-thiouracils and for uracil only very weak bands are found.

In agreement with these observations, our calculation predicts strong absorption near 1546 cm^{-1} for 2TU and at 1553 cm^{-1} for 24DTU but only a weak band at 1487 cm^{-1} for 4TU. The PEDs given in Tables II–IV suggest that the main contributions to this intense band near 1550 cm^{-1} come from NH bending vibrations in the case of 2TU and from ring vibrations in the case of N-methylated derivatives (see calculation for 2-mercaptouracils[34]). According to calculations of the contributions to the intensity, different ring atoms contribute strongly to the intensities of these vibrations for different 2-thiouracils.[38] These drastic differences in the intensities of the modes between 1500 and 1600 cm^{-1} observed for different thiouracils are discussed in more detail elsewhere.[38]

One of the goals of this study was to identify the infrared absorption band related to the C=S stretches. A comparison of

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Table III. Experimental and Calculated Infrared Frequencies, ν, Intensities, *A*, and Potential Energy Distribution (PEDs) of 4TU Monomers

	calculation				experiment[c]			
	ν, cm^{-1}				(in Ar)[c]		(in N2)	
normal coord	unscl[a]	scl[a]	*A*, km/mol	PED[b]	ν, cm^{-1} [d]	*A* rel	ν, cm^{-1}	*A* rel
1	3814	3432	183	N1H str(100+)	3483	281	3463	350
					3470			
2	3769	3392	94	N3H str(100-)	3416	108	3401	150
3	3460	3114	6	C5H str(96-)				
4	3408	3067	2	C6H str(96+)				
					2624	3		
					1885	7		
					1862	7		
					1840	31		
					1798	18	1800	4
					1779		1778	14
					1774		1773	7
					1767			
5	1955	1759	840	C2O str(67-)	1757	835	1752	724
				N1H bend(7-)	1740			
				N3H bend(6+)	1734	267	1737	126
					1723			
					1715		1712	21
							1704	24
							1642	77
6	1808	1627	512	C5C6 str(58-)	1634	511	1629	395
				C6H bend(14-)	1630			
				ring def 2(7-)	1610	29		
				C5H bend(6+)	1529	7	1528	10
					1512	25		
					1496	31		
7	1652	1487	100	N3H bend(61+)	1472	39	1479	49
8	1633	1470	124	N1H bend(53+)	1455	215	1459	164
				C6N1 str(16+)	1450			
				C2O str(13-)	1444			
					1442		1436	21
					1421	6		
					1399	3		
9	1561	1405	30	C5H bend(30-)	1389	27	1394	50
				C6H bend(27-)	1386			
				N1H bend(14-)				
				N3H bend(13-)				
					1370			
					1362			
					1357		1350	10
10	1479	1331	123	N1C2 str(22+)	1341	69	1344	10
				N3C4 str(14-)	1338			
				C2N3 str(12-)	1331			
				C4C5 str(12+)				
					1305	4		
					1264	2		
11	1388	1249	3	C5H bend(27-)	1240	40	1240	38
				C6H bend(24+)	1237			
				C5C6 str(15-)				
				N3C4 str(11-)				
					1215	22	1211	10
					1207		1205	24
12	1314	1182	256	C2N3 str(31-)	1196	74	1196	143
				N3C4 str(24+)	1190		1191	
				C6H bend(19+)	1186			
					1166			
					1154		1153	115
					1151	154	1147	17
13	1249	1125	336	C4S str(35-)	1142	211	1140	231
				ring def I(32+)	1137			
					1121	11	1121	7
					1117			
14	1190	964	7	C6H opl wag(70+)	1102	4	998	4
				C5H opl wag(30+)				
15	1178	1060	35	C6N1 str(46+)	1079	14	1085	10
				C5H bend(13+)	1069	2	1064	10
				C5C6 str(11+)	1048	4		
				N3C4 str(11-)				
16	1085	976	68	ring def I(44+)	991	20	987	10
				C4C5 str(26-)				
				N3C4 str(11-)				
					762			
17	999	809	331	N3H opl wag(55-)	755	63	765	95
				C2O opl wag(45+)				

Table III (Continued)

	calculation				experiment[c]			
	ν, cm^{-1}				(in Ar)[c]		(in N2)	
normal coord	unscl[a]	scl[a]	A, km/mol	PED[b]	ν, cm^{-1} [d]	A rel	ν, cm^{-1}	A rel
18	995	895	19	N1C2 str(33–) C2N3 str(28–) C4S str(11+)	922	19	928	10
19	956	774	21	C5H opl wag(64+) C6H opl wag(27–)	792 784	36	794	32
20	866	701	8	N3H opl wag(47–) C2O opl wag(24–) N1H opl wag(21+)	666	17	723	21
21	776	628	53	opl ring def I(52–) C4S opl wag(31+) N1H opl wag(13+)	688	65	675 712	21 17
22	773	696	0	C4C5 str(23–) ring def II(20–) N1C2 str(14–) C4S str(14–) ring def III(10–)				
23	721	584	85	N1H opl wag(61–) C2O opl wag(19–) C4S opl wag(11+)	575 564 550	107	597 592	63
24	624	562	14	ring def III(69–)	558 542		560	17
25	544	489	11	C2O bend(61–) C4S bend(15–) ring def II(11–)	496	9	497	17
26	477	429	21	ring def II(46+) C4S str(21–)	436	21	436	21
27	462	374	17	opl ring def III(45–) opl ring def II(24–) C4S opl wag(21–) opl ring def I(14–)	383	24	393	24
28	301	271	10	C4S bend(72+) C2O bend(10–)	273	3	273	14
29	210	170	3	opl ring def III(58–) opl ring def II(19+)	*		*	
30	167	151	1	opl ring def II(65+) opl ring def I(19–) C4S opl wag(18–)	*		*	

[a–c] The same as in Table II. [d] The brackets show groups of overlapping lines for which the total intensity is given. This sum intensity is placed in the same line as the strongest band of the overlapped group.

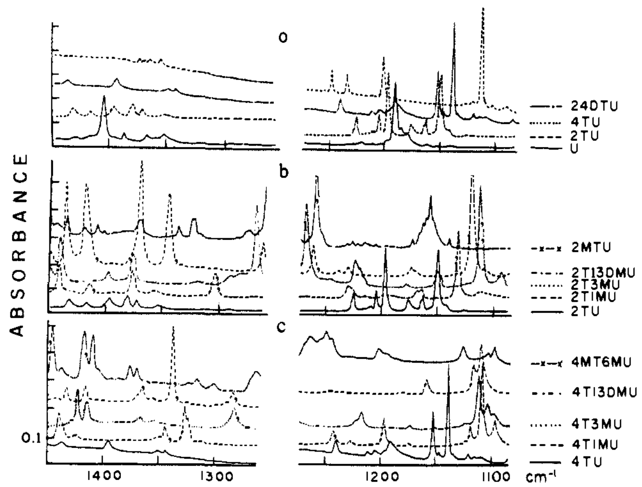

Figure 3. Comparison of the IR spectra in the spectral region (1450–1070 cm^{-1}) related predominantly to the ring stretching, NH bending and CH bending, and C=S stretching in-plane vibrations of different thiouracils isolated in a nitrogen matrix at about 6–7 K: (a), (b), and (c) the same as in Figure 1.

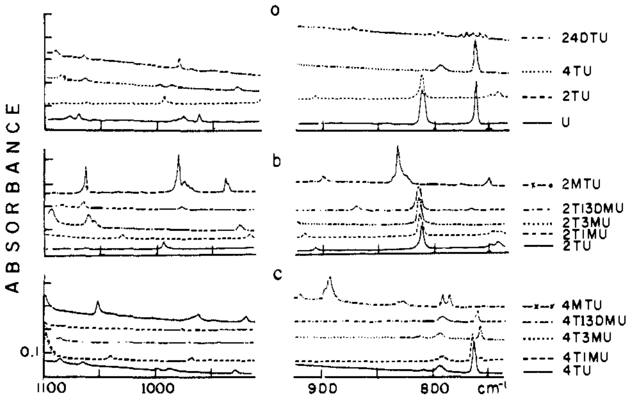

Figure 4. Comparison of the IR spectra in the spectral region (1100–750 cm^{-1}) related mainly to the ring stretching, ring deformation, C=S stretching, and NH and CH bending in-plane and out-of-plane vibrations of different thiouracils isolated in a nitrogen matrix at about 6–7 K: (a), (b), and (c) the same as in Figure 1.

the spectra of thiouracils with the spectra of uracils strongly suggests that the C=S absorption is located in the region near 1100–1150 cm^{-1} (Figure 3a–c). All thiouracils exhibit strong absorption in this range, while uracil does not show any significant absorption there.

According to our calculated PEDs, vibrations associated with stretching the C=S bond are expected to appear as relatively strong bands near 1125 cm^{-1} for 2TU and 4TU and for 24DTU as a strong band near 1070 cm^{-1} with some contribution to the weaker one near 1220 cm^{-1} (see Tables II–IV). In contrast with characteristic C=O stretch (for which the C=O contribution to the normal mode near 1700 cm^{-1} is about 60%), the PED contribution of the C=S stretch to the normal modes in the region

Table IV. Experimental and Calculated Infrared Frequencies, *ν*, Intensities, *A*, and Potential Energy Distributions, PED, of 2,4-Dithiouracil Monomers

	calculation				experiment (in N2)[c]	
	ν, cm^{-1}					
normal coord	unscl[a]	scl[a]	*A*, km/mol	PED[b]	*ν*, cm^{-1}	*A* rel
1	3798	3418	185	N1H str(100−)	3434	374
2	3754	3379	91	N3H str(100+)	3379	174
3	3458	3112	7	C5H str(95−)		
4	3412	3070	3	C6H str(95+)		
					1645	17
					1635	9
					1631	61
5	1810	1629	350	C5C6 str(56−)	1624	304
				C6H bend(13−)	1616	70
				N1H bend(12−)	1598	35
					1578	61
					1560	26
					1555	17
6	1726	1553	1096	N3H bend(46−)	1540	435
				N1H bend(29+)	1535	96
					1496	26
7	1642	1477	57	N3H bend(29+)	1469	148
				N1H bend(28+)		
				C6H bend(11−)		
				C6N1 str(11+)		
					1374	
8	1565	1409	20	C5H bend(33−)	1371	87
				C6H bend(28−)	1365	
				N1H bend(13−)	1361	
				N3H bend(12−)		
9	1476	1328	146	N1C2 str(34−)	1357	43
				C2N3 str(18+)		
					1254	9
10	1384	1246	10	C5H bend(26+)	1248	104
				C6H bend(23−)		
				N3C4 str(15+)		
				C5C6 str(12+)		
11	1355	1220	69	ring def I(41+)	1234	96
				C2S str(14−)		
				C4S str(13−)		
				C2N3 str(11+)		
12	1314	1183	398	C2N3 str(30−)	1202	226
				N3C4 str(27+)		
				C6H bend(17+)		
13	1189	963	7	C6H opl wag(73+)		
				C5H opl wag(42+)		
					1120	17
14	1188	1070	705	N1C2 str(26−)	1114	565
				C4C5 str(18+)	1104	9
				C4S str(15−)		
				C2S str(11+)		
15	1153	1037	29	C6N1 str(45+)	1065	17
				N3C4 str(17−)		
				C5H bend(14+)		
16	1060	954	54	ring def I(36−)	980	43
				C2N3 str(12+)		
				C6N1 str(12+)		
				N1C2 str(10+)		
					775	
17	999	809	216	N3H opl wag(91−)	770	100
				C2S opl wag(14+)	764	
				C4S opl wag(11+)		
18	962	779	7	C5H opl wag(60+)	759	17
				C6H opl wag(27−)	754	17
19	937	844	26	C2S str(22−)	871	17
				C4S str(14+)		
				ring def II(12+)		
				C4C5 str(11+)		
				ring def III(11−)		
20	875	708	85	N1H opl wag(60+)	694	17
				C2S opl wag(17−)		
				N3H opl wag(11−)		
				opl ring def I(10+)		
21	791	641	71	opl ring def I(60−)	662	70
				N1H opl wag(25+)		
				C4S opl wag(15+)		
22	755	679	2	ring def III(37−)	666	10
				C4C5 str(23−)		
				ring def II(13−)		

Table IV (Continued)

	calculation				experiment (in N2)^c	
	ν, cm^{-1}					
normal coord	unscl^a	scl^a	A, km/mol	PED^b	ν, cm^{-1}	A rel
23	694	562	6	C2S opl wag(44−) C4S opl wag(27+) opl ring def III(14−)		
24	503	453	43	rind def II(30+) C2S str(29+) ring def III(27−)	462	35
25	486	438	13	ring def II(28+) C4S str(27−) C2S str(10−)	444	26
26	459	372	15	opl ring def III(52+) opl ring def II(21+) C4S opl wag(20+) opl ring def I(11+)	393	26
27	424	382	0	C4S bend(46+) C2S bend(44+)		
28	236	212	8	C2S bend(42−) C4S bend(40+)	293	9
29	181	147	1	opl ring def II(49+) opl ring def III(37−) C2S opl wag (12+)	*	
30	162	131	1	opl ring def II(34−) opl ring def I(32+) C4S opl wag(17+) opl ring def III(13−)	*	

$^{a-c}$The same as in Table II.

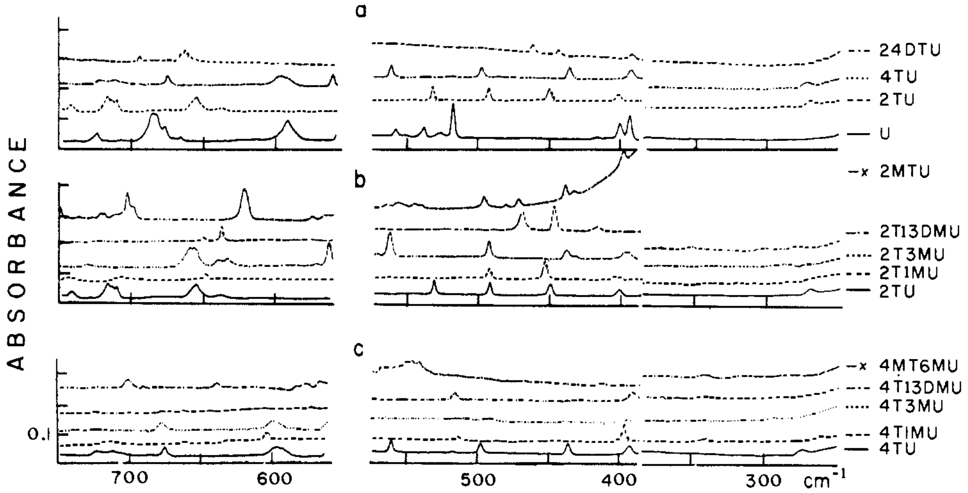

Figure 5. Comparison of the IR spectra in the spectral region (750–250 cm^{-1}) related mainly to the ring stretching and ring deformation in-plane and C═S bending in-plane vibrations and several out-of-plane vibrations of different thiouracils isolated in a nitrogen matrix at about 6–7 K: (a), (b), and (c) the same as in Figure 1.

discussed here is only on the order of 10–25%. Other large contributions to these normal modes in the thiouracils come from the ring stretching and ring deformation motions (Tables II–IV). This coupling of different motions might be responsible for discrepancies in the assignment of the C═S stretching mode to the absorption bands observed in the IR spectra of compounds containing the C═S group.

Our assignment of the absorption near 1070–1150 cm^{-1} to normal modes involving the C═S stretches agrees with assignments made for other compounds containing the C═S group.[9m–o,43–52]

For S-methylated thiouracils no C═S absorption is expected. In agreement with this expectation no strong band is observed (in the 1150–1250 cm^{-1} region) in the matrix spectrum of 4MT6MU (Figure 3c). However, for 2MTU a relatively strong band near 1157 cm^{-1} is present (Figure 3b). This absorption is probably related to the OH bending mode (see Supplementary Material, Table 11) in the hydroxy tautomeric form of that molecule.

Another region of stronger absorption of thiouracils which we shall discuss here is that near 800–750 cm^{-1}. Figure 4a–c shows this part of the spectrum of 2-thio, 4-thio, and 2,4-dithiouracils compared with that of uracil. Two relatively strong bands assigned to out-of-plane modes are present in the spectrum of uracil near 811 and 762 cm^{-1}. For 2-thiouracils a strong absorption near 807 cm^{-1} is observed, while for 4-thiouracils the strong band is found near 765 cm^{-1}. No strong absorption is present in this range for 24DTU. Such a result suggests that absorption near 800 cm^{-1}

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Table V. Infrared Frequencies, ν, Intensities at the Maxima, A_m, and Assignment of the Bands of Monomers of N1- and/or N3- and S2-Methylated Derivatives of 2-Thiouracil Isolated in an N2 Matrix

2T1MU		2T3MU		2T13DMU			2MTU		
ν, cm^{-1}	A_m rel[a]	ν, cm^{-1}	A_m rel[a]	ν, cm^{-1}	A_m rel[a]	assign[b]	ν, cm^{-1}	A_m rel[a]	assign[b]
							3550	72	OH st/H
		3445	110			N1H st			
		3437	77						
3400	128					N3H st	3393	95	N3H st/O
				3100	1	CH st	3100	5	CH st
				3000	4	CH st			
				2960	8	Me st	2950	10	Me st
1733	428	1713	629	1711	189	C=O st	1722	486	C=O st/O
1717	202			1705	441		1711	144	
1636	63	1642	45	1646	27	C=C st	1655	10	
				1640	27				
							1592	83	C=C st/O
							1582	112	RI st/H
							1575	113	RI st/H
		1554	22				1560	36	
							1543	25	
1500	322	1515	450	1487	263	Me de	1525	403	RI st/H
						NH be	1519	201	NH be/O
1485	138	1489	9			CH be	1503	21	CH be
1457	77	1459	16	1461	53	NH be	1462	72	Me de
1441	92	1440	90	1436	124		1450	102	CH be/H
							1434	47	NH be/O
1415	27	1397	16	1418	128		1419	21	RI st
						NH be	1408	26	CH be/O
1376	50	1376	55	1370	218	CH be	1371	26	CH be/H
						RI st	1369	26	RI st
1357	11			1345	113		1336	17	CH be
							1324	43	C-O be/H
1304	72			1303	3		1318	8	
		1268	164	1262	43	RI st	1275	21	
						NH be	1260	149	CH be/O
		1247	4	1239	6		1226	18	CH be/H
1230	38			1230	11		1222	7	
1227	31	1224	47				1215	13	
1164	31	1152	32	1174	13	Me ro	1173	21	Me ro
							1157	94	RI st/H
1132	207	1113	211	1120	227	C2=S st			
		1083	32	1085	5				
		1061	29			RI st	1063	72	RI st/H
		1030	13	1055	16	CH be			
				978	5		980	106	RI/O
916	13	925	11	869	7		938	31	RI st/O
							898	13	RI st/H
812	68	813	54	813	37	C=O opl	831	109	C=O opl/O
746	9			766	3	CH opl	749	21	CH opl/O
							721	11	
							702	56	RI de/H
649	12	660	31	652	4	C=S opl			
		640	11			RI opl			
		634	12	638	17		622	67	RI opl/O
		563	40			RI	574	13	C—S opl
							565	12	RI
							544	13	RI
493	23	493	25	470	21	C=O be	496	23	C=O be/O
						C=S be	481	7	
							472	16	
454	45	439	16	448	31	RI de			
							400	26	OH to/H
404	9	396	12	418	67	C=S st	400	16	RI de/H
						RI de			OH to/H
		310	21	351	4	Me de			
283	4	286	5	279	5	C=S be			

[a] In the experimental spectrum splitting of the band into several components is observed in many spectral regions. This splitting results probably from the anharmonicity effects (e.g., Fermi resonance) and/or matrix site effects and traces of self-associated molecules. A few very weak bands (intensity below 3) are not given in the table. Relative intensities chosen in such a way that the sum of the intensities at the maxima of all components observed in the carbonyl region equals to the calculated intensity of the C=O stretch of unmethylated thiouracil. [b] Description of vibrations: "H" and "O" relate to the hydroxy and oxo tautomers respectively: be, bending; RI, ring; ro, rocking; opl, out-of-plane; de, deformation; Me, methyl. Only the most important contributions of the vibrations of groups are given. For more details about PEDs see Table II with the calculated normal modes. Assignment of the S-methylated derivative was made on the basis of comparison with our ab initio calculations (3-21G*//3-21G*) of the IR spectra of oxo and hydroxy tautomers of mercaptouracils.[34]

is related to the C4=O and that near 760 cm^{-1} to the corresponding mode for the C2=O group. The calculated PEDs shown in Tables II and III suuggest that for 2TU the intense absorption near 819 cm^{-1} is expected for a normal mode which has a large contribution from the out-of-plane C4=O vibration. For 4TU strong absorption with contribution from C2=O out-of-plane

Table VI. Infrared Frequencies, ν, Intensities at the Maxima, A_m, and the Assignment of the Bands of Monomers of N1- and/or N3- and S2-Methylated Derivatives of 4-Thiouracil in an N2 Matrix

4T1MU		4T3MU		4T13DMU			4MT6MU		
ν, cm^{-1}	A_m rel[a]	ν, cm^{-1}	A_m rel[a]	ν, cm^{-1}	A_m rel[a]	assign[b]	ν, cm^{-1}	A_m rel[a]	assign[b]
							3575	200	OH st/H
		3456	168			N1H st	3430	148	N1H st/O
3398	75					N3H st			
3135	4	3120	3	3140	3	CH st			
				3000	5	CH st	3000	12	CH st
		2960	6	2960	13	Me st	2950	28	Me st
1742	216								
1734	426	1729	840	1707	840	C=O st	1717	544	C=O st/O
1719	198						1700	296	
1630	524	1639	489	1641	380	C=C st	1639	556	C=C st/O
							1593	636	C=C st/H
							1544	200	RI st/O
							1533	220	RI st/H
		1515	38	1518	16	Me de			
1489	41	1484	90	1489	56	RI st	1472	72	Me de
1471	83	1468	63	1467	35	NH be	1460	160	CO st/H
1438	88	1445	18	1432	70	CH be	1717	376	CH be/H
1424	14	1422	177	1415	75	Me de	1437	64	Me de
		1413	96				1416	324	CH be
		1366	27				1408	304	NH be/O
1344	48	1354	12	1364	62	NH be	1375	104	
						CH be	1369	92	RI st
1325	108			1335	353		1335	16	CH be/H
							1323	24	CH be
							1315	76	C—O st/H
		1281	102	1289	67	NH be	1300	72	
						CH be	1263	136	OH be/H
1243	43			1246	11		1248	172	
1227	12	1217	72	1236	5		1201	76	
1197	83	1174	15	1188	11				
1175	12			1159	65	Me ro			
1120	57	1112	255	1117	124	C=S st	1126	100	RI st/O
1109	257	1104	120	1110	224	CH be	1103	68	CH be
1097	104	1098	78			RI	1098	96	RI st/O
1039	11					CH be	1051	88	RI st/H
967	9			978	8	RI de	962	52	RI de
							919	40	
							892	176	RI st/H
							832	24	CH be
							827	28	
794	18	793	33	791	27	RI	791	80	opl C=O/O
764	88	757	69	759	54	opl C=O	785	92	opl C=O
714	7			724	8		701	48	
662	3	677	30	661	11	RI de	690	16	
						C=O opl	638	24	NH opl/O
						NH opl			
604	18	599	36	572	8	C=S opl	576	36	NH opl/O
		562	39			RI	548	64	
							545	92	RI
							540	68	
513	9	513	27	515	27	C=S be			
						C=O be			
		426	12	427	11	RI de	413	16	
						C=S st			
396	41	394	18	391	29	RI de			
341	11			345	8				
261	5	292	9	285	11	C=S be			

[a,b] The same as in Table V.

absorption with contribution from C2=O out-of-plane motion is expected at lower frequencies (809 cm^{-1}). (The calculated intensities of both these out-of-plane modes are drastically higher than observed in experiment.)

The appearance of the absorption near 800 cm^{-1} for 2-thiouracils and that near 760 cm^{-1} for 4-thiouracils has been used by us previously as an argument for the assignment of these out-of-plane vibrations of uracils.[23,39]

In the discussion above we have concentrated our attention on the most characteristic and strongest modes observed in the matrix spectra of thiouracils. The frequencies, intensities, and the assignment of the bands, when possible, in other spectral regions and further details of the spectra are given in Tables II–VI and in Figure 5.

The thiouracils discussed here were studied as isolated in a nitrogen matrix. Results from an argon matrix are given for a comparison only for 4TU (see Table III). In general the spectrum observed for the Ar matrix is very similar to that for N_2 matrix, but the frequencies of related bands are slightly different for samples under these different conditions, and the bands are broader and more overlapped in the N_2 matrix spectrum. In Ar matrix spectrum splitting of some bands into several components is observed (possibly resulting from self-associations and/or nonequivalent sites existing in the Ar matrix). The vapor IR spectra of some thiouracils discussed here have been studied by Barski.[1d]

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(53) Les, A.; Adamowicz, L. *J. Am. Chem. Soc.* Submitted for publication.

Some of his results have been presented in our previous paper.[1a] The vapor spectra resemble those from the matrix sample, but the bands are much broader and more strongly overlapped. The similar spectral patterns observed for the matrix and for the vapor spectra of the thiouracils studied, particularly for the S-methylated thiouracils, suggest that the tautomeric forms present in the vapor phase are the same as those present in the matrix.

Conclusions

The main conclusions from this study are as follows.

(1) 2-Thiouracil, and 4-thiouracil and their N1- or N3-methylated derivatives as well as 2,4-dithiouracil all exist predominantly in the oxothione or dithione tautomeric form in an inert matrix environment (and also in the vapor phase).

(2) In contrast, S2- and S4-methylated derivatives of thiouracils adopt both hydroxy and oxo tautomeric forms under the same matrix (and vapor) conditions. For S2-methylated uracil the oxo tautomer predominates, while for 4-(methylthio)-6-methyluracil the hydroxy form dominates.

(3) Substitution of sulfur for oxygen results in a drastic change of almost the entire spectrum in addition to the obvious changes in the C=O and C=S stretching and bending regions. Strong intensity changes are also found for the C=C stretching, the NH bending (?) modes near 1640 and 1550 cm^{-1} respectively.

(4) The effect of sulfur substitution on N1H and N3H frequencies and intensities reflects changes in proton donor abilities of these groups. This is expected to affect the strength of hydrogen bonding in which they participate, particularly that formed by the biologically significant N3H group. This effect should be taken into account in addition to the generally recognized influence on the hydrogen bonding (and on stacking or surface interactions) resulting from the change of the proton accepting group from C4=O or C2=O to C4=S or C2=S.

(5) Our study suggests that C2=S and C4=S stretching modes appear as relatively strong bands in the region near 1070–1150 cm^{-1}, but they are much more strongly coupled with the vibrations of other groups then in the case of the C=O stretches.

(6) Calculations at the SCF(3-21G*) level appear to be useful for interpretation of the general features of the IR matrix spectra of isolated molecules, but they are not good enough to account for the out-of-plane modes.

(7) Finally, calculations at the SCF(3-21G*) + MBPT(2) [or even at the SCF(6-31G**) + MBPT(2) level] level performed for model compounds in which the methyl group was replaced by a hydrogen atom do not predict correctly the tautomeric equilibria for both the S2- and S4-methylated thiouracils. Hence, experimental infrared matrix studies still provide a necessary test of the reliability of the calculations of tautomeric equilibria.

Note Added in Proof. A recent ab initio calculation (HF, MBPT, CC) by Les and Adamowicz[53] for S2 and S4 methylated thiouracils is in much better agreement with our experimental data.

Acknowledgment. We thank Professor D. Shugar (Warsaw) for his suggestion to undertake studies of thiouracils, for valuable discussions, and for supplying us with these compounds from his collection. We are also grateful to Dr. A. Barski for providing us with his unpublished results for the gas phase. This work was supported by the Ministry of National Education Project CPBP 01.12 (in Warsaw) and by NIH Research Grant No. 32988 (in Gainesville). J.L. thanks the Alabama Supercomputer Network for allotment of computer time for the calculations presented here.

Supplementary Material Available: Tables of symmetry coordinates of the thiouracil tautomers and description of vibrational modes (Table 7), force constants of 2-thiouracil, 4-thiouracil, and 2,4-dithiouracil (calculated by the ab initio 3-21G* method) (Tables 8–10), and frequencies, intensities, and potential energy distributions of 2-mercaptouracil and 4-mercaptouracil (calculated by the ab initio 3-21G* method) (14 pages). Ordering information is given on any current masthead page.

A Theoretical Investigation of the Thermal Ring Opening of Cyclopropyl Radical into Allyl Radical. Evidence for a Highly Nonsymmetric Transition State

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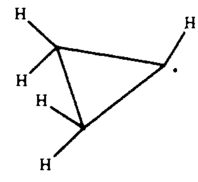
Abstract: An ab initio investigation of the thermal ring opening of cyclopropyl radical (**1**) to give allyl radical (**2**), with geometries optimized at the UHF/3-21G and CASSCF/3-21G levels of theory, predicts a highly nonsymmetric structure for the transition state of such an electrocyclic reaction. Thus, the CASSCF/3-21G-optimized transition structure corresponds to rotation of one of the methylene groups in **1** through 24° while the other remains orthogonal to the plane of the carbon atoms, the length of the CC bond undergoing rupture being 2.066 Å. The present results agree with those of early MINDO/3 calculations by Dewar and Kirschner in the important respect that the minimum-energy reaction path does not involve synchronous rotation of the methylene groups, so that one methylene rotation is almost completed before the other commences. As a consequence, both conrotatory and disrotatory ring-opening modes of **1** involve a common transition state.

The thermolysis of cyclopropyl radical (**1**) leading to ring opening and allyl radical (**2**) formation or, conversely, the cyclization of **2** into **1** is the simplest example of an electrocyclic reaction of a free radical. During the reaction the methylene groups may move in either a disrotatory or conrotatory fashion. Unlike the case of the cyclopropyl cation and anion, no conclusion may be drawn from the Woodward–Hoffmann rules,[1] from the orbital and state correlation diagrams,[2] or from PMO arguments[3]



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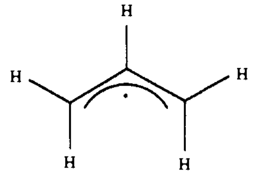

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† On leave of absence from the C.S.I.C.

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