The Tautomeric Equilibria of Thio Analogues of Nucleic Acid Bases, Part 3.[1] Ultraviolet Photoelectron Spectra of 2-Thiouracil and its Methyl Derivatives

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The photoelectron spectra of 2-thiouracil and four monoalkyl and four dimethyl derivatives were recorded using He(I) and He(II) excitations. The assignments of the photoelectron bands were based on relative band intensity variations, on the results of AM1 calculations, and by comparisons with uracil and its methyl derivatives. The photoelectron spectrum of 2-methyl-2-thiouracil gave evidence of two forms in tautomeric equilibrium in the gas phase.

The electronic structure of biological pyrimidines has been the subject of extensive theoretical investigations.[2] However, the ordering and spacing of energy levels predicted by theoretical calculations vary depending upon the method employed. UV photoelectron spectroscopy can supply useful information which helps to provide an accurate description of the electronic structure in such molecules.[3]

The photoelectron spectra, PE, arising from the most accessible orbitals of uracil and thymine do not contain strongly overlapping bands and a relatively simple interpretation of the low energy region is possible.[3] The first, third, and fifth bands in the spectra have been assigned to π orbitals, while the second and fourth bands were assigned to lone-pair orbitals associated with oxygen atoms.[3c] A comparison of the uracil and thymine spectra indicates that they are qualitatively similar. However, the ionisation potential of thymine is significantly lower (by 0.4 eV) than that of uracil, due to the effect of methylation. The assignment of PE spectra of related molecules by comparisons within series of related molecules and by recourse to MO calculations is now well established.[4]

In the present paper, the gas phase UV photoelectron spectra of 2-thiouracil, of representatives of all four classes of its monoalkyl derivatives, and of four of the six possible classes of dialkyl derivatives, are studied. The structures in the gas phase of the most stable tautomer of 2-thiouracil, and of its four monoalkyl derivatives have recently been determined from IR spectra,[5] and results deduced from proton affinity E_{pa} values, both experimental[6] and as determined by AM1 calculations,[1] agree well.

Experimental

Photoelectron spectra were recorded on a Perkin–Elmer PS-18 spectrometer with He(I) and He(II) sources (21.21 and 40.8 eV, respectively). They were calibrated by using the ${}^2P_{\frac{1}{2}}$ and ${}^2P_{\frac{3}{2}}$ doublets of argon (15.755 and 15.93 eV) and of xenon (12.13 and 13.43 eV). The ionisation potentials recorded are accurate to within 30 meV,§ with the exception of the superimposed peaks. The pressure in the ionisation chamber was *ca.* 10^{-2} Torr* and samples were heated up to 150 °C.

The AM1 calculations[7] were performed using the MOPAC program[8] on a MicroVAX II; for details see ref. 1.

The syntheses and physical constants of the compounds used are described in Part 1.[6]

Results

Predominant gas-phase tautomeric structures of the five compounds investigated, (**1**), (**2**), (**3**), (**6**), (**9a**), and/or (**9b**), which have been determined from their vapour-phase IR spectra,[5] and confirmed by E_{pa} data,[1] are shown overleaf. The UV photoelectron spectra of these five tautomeric compounds, and of four model compounds of fixed structure [(**4**), (**5**), (**7**), and (**8**)], are given in Figures 1–4 and 7–11. The calculated vertical ionisation potentials and assignments for all the six cyclically conjugated 2-thiouracil tautomers, as calculated by the AM1 method, are listed in Table 1. All of the experimental and calculated potentials are listed in Table 2 and are plotted in Figures 5 and 12. In Table 3 the calculated vertical ionisation potentials of uracil and its *N*-methyl derivatives are compared with the experimental data. The photoelectron spectra interpretations are based on (*i*) comparisons with the spectra of uracil, its methyl derivatives, and 5-halouracils, (*ii*) the variation of the intensity observed by the use of He(I) and He(II) radiation taking account of the localisation energies calculated for various orbitals, and (*iii*) the theoretical values of the various orbital energies.

Discussion

2-Thiouracil and its N-*Methyl and* N,N-*Dimethyl Derivatives.*—Figures 1–4 show the photoelectron spectra of compounds (**1**)–(**4**) which contain bands arising from the five highest energy orbitals. The spectra contain only four bands, owing to the superposition of the first and second bands. The comparison between He(I) and He(II) spectra is of great utility for assignment purposes in compounds containing third-row atoms, since a PE band related to a MO localised on such an atom shows a marked decrease in relative intensity on going from He(I) to He(II) radiation.[9]

The He(II) PE spectra of (**1**)–(**4**) when compared with the He(I) spectra (Figures 1–4) show a decrease in the relative intensity of the first band relative to the second one, indicating a greater contribution of s atomic orbitals to the first of these bands. Figure 5(*a*) shows the experimental ionisation potentials

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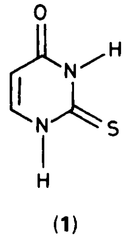
§ 1 Torr = 133.322 Pa; 1 eV ≈ $1.602\,18 \times 10^{-19}$ J.

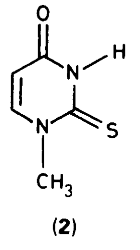
Table 1. AM1 vertical ionisation potentials (eV) and assignments of six 2-thiouracil tautomers.

H[a]	$-\varepsilon_1$	$-\varepsilon_2$	$-\varepsilon_3$	$-\varepsilon_4$	$-\varepsilon_5$	$-\varepsilon_6$	$-\varepsilon_7$
1,3	9.63 π_1	9.48 n_s	10.68 π_2	11.70 $n(0)$	12.94 π_3	14.25 σ_s	14.79 π_4
1,2	9.71 π_1	10.23 $n_{N-3} + n(0)$	10.76 π_2	12.43 $n_{N-3} - n(0)$	12.53 π_3	13.92 σ_s	14.05 π_4
1,4	9.08 π_1	9.32 n_s	11.33 π_2	11.51 n_{N-3}	12.32 π_3	13.83 σ_s	14.91 π_4
2,3	9.62 π_1	11.28 π_2	11.34 $n(0)$	11.89 n_{N-1}	12.22 π_3	13.64 σ_s	14.16 π_4
2,4	9.80 π_1	10.99 π_2	11.01 $n_{N-1} - n_{N-3}$	11.84 π_3	12.35 $n_{N-1} + n_{N-3}$	13.65 σ_s	14.39 π_4
3,4	9.04 π_1	9.39 n_s	11.42 π_2	11.61 n_{N-1}	12.58 π_3	13.47 σ_s	14.78 π_4

[a] Indicates positions to which hydrogen atoms attached.



(1)



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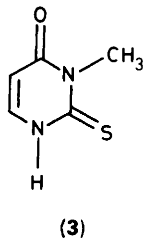

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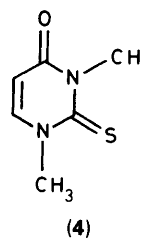

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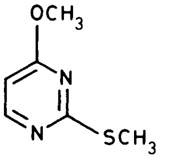

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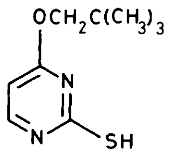

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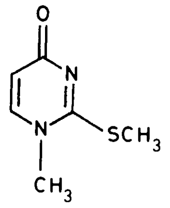

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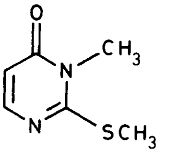

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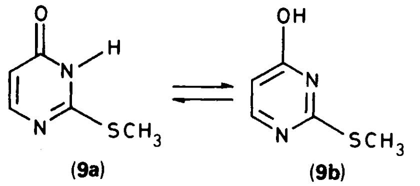

(9a) **(9b)**

of 2-thiouracil and its *N*-methyl derivatives. Figure 5(*b*) shows the corresponding ionisation potentials calculated by the AM1 method, assuming Koopmans' theorem[10] for the same compounds. Because electron correlation energy and zero-point energy effects are only partly included in the AM1 method (within the parametrisation), the experimental and theoretical energy scales are not in agreement. However, the energy shifts predicted by the AM1 calculations are remarkably similar to those obtained experimentally.

Comparison of the experimental and calculated ionisation potentials obtained for *N*-methyl substituted uracils and 2-thiouracils indicate the *N*-methylation effect differs in the two series. In the uracil series the energy of the π_1 orbital is most increased by substitution of *N*-methyl at the 1-position and is relatively unperturbed by substitution in the 3-position. 2-Thiouracil is less perturbed by *N*-methylation. The differences between the ionisation potentials of the oxygen lone pairs at the 2-position of the uracils and the sulphur lone pairs of the corresponding 2-thiouracil derivatives are *ca.* 2.2 eV. The differences between 1-methylpyridin-4- and -2-ones and their thio analogues are 1.7 and 1.0 eV, respectively.[11] The π_1 orbital in 2-thiouracil and its *N*-monomethyl derivatives is shifted *ca.* 0.6–0.8 eV to lower energy in comparison with the uracil analogues. The difference between 1-methylpyridin-1-one and its thio analogue is 0.7 eV.[11]

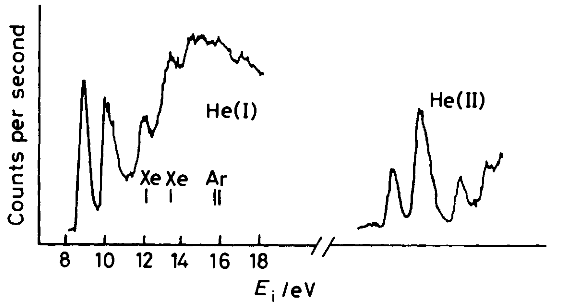

Figure 1. Photoelectron spectrum of 2-thiouracil (**1**).

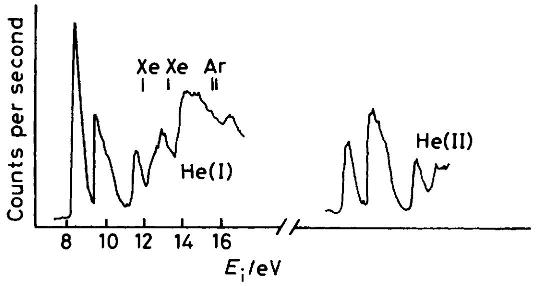

Figure 2. Photoelectron spectrum of 1-methyl-2-thiouracil (**2**).

Using Koopmans' theorem, we correlate the calculated energy directly with the PE spectra. Good correlations between the experimental E_i and the calculated orbital energy for the first five bands of uracils [Figure 6(*a*); $E_i(\text{exp}) = -0.314 + (-0.929\ \varepsilon_{\text{AM1}})$; $r = 0.954$, $N = 20$] and 2-thiouracils [Figure 6(*b*); $E_i(\text{exp}) = 0.245 + (0.902\ \varepsilon_{\text{AM1}})$; $r = 0.960$, $N = 20$] are found. Other work leads to similar correlations.[4] This makes us rather confident with the given assignment.

2-Thiouracils Methylated on Sulphur and/or Oxygen.—The spectrum of compound (**7**) is given in Figure 7. The two first high ionisations of the system correspond to the bands observed at 8.80 and 9.1 eV. This peak also covers one of the combinations of the lone pairs attached to oxygen or N-3 (effect of polarisation noted by agreement with Koopmans' theorem), whereas the other combination is associated with the band at 10.15 eV. The bands at 11.20 and 11.85 eV correspond to the ionisation of the third and fourth π orbitals of a ring. This last band also incorporates the ionisation of the sulphur σ-electron pairs [strong diminution of the intensity with He(II)].

The spectrum of compound (**8**) is given in Figure 8. The first two bands, at 8.55 and 9.45 eV, correspond to the ionisation of the first two π orbitals of the ring (the diminution of the intensity of the second is interpreted as indicating some localisation on the sulphur atom). On the high energy side, fine structure is observed corresponding to the ionisation of the lone pair of the oxygen and probably of the N-1. The band at 10.80 eV corresponds to the third π-ionisation of this system. The following peak covers the ionisation of the σ-electron pair of the sulphur

Table 2. Experimental and AM1 vertical ionisation potentials (eV) and assignments of 2-thiouracil and its monomethyl and dimethyl derivatives.

Compound	Experimental						Calculated						
(1)	8.80	9.90	10.15	12.00	—	—	9.63	9.83	10.68	11.70	12.94	—	—
(MO type)	π_1,$n(2)$	π_2	$n(4)$	π_3			π_1	$n(2)$	π_2	$m(4)$	π_3		
(2)	8.65	9.65	9.90	11.75	—	—	9.50	9.71	10.50	11.62	12.62	—	—
(MO type)	π_1,$n(2)$	π_2	$n(4)$	π_3			π_1	$n(2)$	π_2	$n(4)$	π_3		
(3)	8.60	9.55	9.75	11.35	—	—	9.51	9.69	10.40	11.55	12.12	—	—
(MO type)	π_1,$n(2)$	π_2	$n(4)$	π_3			π_1	$n(2)$	π_2	$n(4)$	π_3		
(4)	8.40	9.35	9.60	11.10	—	—	9.40	9.55	10.22	11.47	11.97	—	—
(MO type)	π_1,$n(2)$	π_2	$n(4)$	π_3			π_1	$n(2)$	π_2	$n(4)$	π_3		
(5)	8.35	9.35	9.70	10.75	11.45	12.10	9.50	10.48	10.74	11.49	12.05	12.61	12.78
(MO type)	π_1	$n(1) - n(3)$	π_2	π_3,$n(1) + n(3)$	σ_s	π_4	π_1	π_2	$n(1) - n(3)$	π_3	$n(1) + n(3)$	σ_s	π_4
(6)	8.80	9.40	9.75	11.00	11.45	12.10	9.69	10.84	10.90	11.74	12.20	12.81	13.9
(MO type)	π_1	$n(1) - n(3)$	π_2	π_3,$n(1) + n(3)$	σ_s	π_4	π_1	π_2	$n(1) - n(3)$	π_3	$n(1) + n(3)$	σ_s	π_4
(7)	8.80	9.10	10.15	11.20	11.85	—	9.39	10.06	10.28	11.98	12.17	12.87	12.98
(MO type)	π_1,$n(3) + n(4)$	π_2	$n(3) - n(4)$	π_3	σ_s,π_4		π_1	$n(3) + n(4)$	π_2	$n(3) - n(4)$	π_3	σ_s	π_4
(8)	8.55	9.45	10.00	10.80	11.75	12.20	9.35	10.58	11.10	11.49	11.54	12.80	13.65
(MO type)	π_1	π_2	$n(4)$,$n(1)$	π_3	σ_s	π_4	π_1	π_2	$n(4)$	$n(1)$	π_3	σ_s	π_4
(9a)	8.70	9.80	10.10	11.30	12.10	12.30	9.50	10.79	11.21	11.73	12.05	13.04	13.81
(MO type)	π_1	π_2	$n(4)$,$n(1)$	π_3	σ_s	π_4	π_1	π_2	$n(4)$	$n(1)$	π_3	σ_s	π_4
(9b)	8.70	9.80	—	10.80	—	12.75	9.57	10.70	10.89	11.59	12.19	12.89	13.67
(MO type)	π_1	$n(1) - n(3)$,π_2		π_3,$n(1) + n(3)$		π_4	π_1	π_2	$n(1) - n(3)$	π_3	$n(1) + n(3)$	σ_s	π_4

Table 3. Comparison of AM1 vertical ionisation potentials (eV) with experiment for uracil and its *N*-methyl derivatives.

Compound	$E_i(1)$	$-\varepsilon_1$	$E_i(2)$	$-\varepsilon_2$	$E_i(3)$	$-\varepsilon_3$	$E_i(4)$	$-\varepsilon_4$	$E_i(5)$	$-\varepsilon_5$
(1) Uracil[a]	9.59	9.97 π_1	10.12	11.16 *n*	10.56	11.37 π_2	11.00	12.05 *n*	12.63	13.42 π_3
(2) 1-methyluracil[b,c]	9.2	9.72 π_1	9.9	11.10 *n*	10.3	11.29 π_2	10.75	11.98 *n*	12.13	12.60 π_3
(3) 3-methyluracil[b,c]	9.4	9.88 π_1	10.0	10.50 *n*	10.1	11.26 π_2	10.75	11.88 *n*	12.10	13.03 π_3
(4) 1,3-dimethyluracil[a]	9.00	9.64 π_1	9.70	10.45 *n*	9.85	11.20 π_2	10.55	11.79 *n*	11.85	12.45 π_3

[a] Ref. 3(*b*). [b] Ref. 3(*c*). [c] Experimental values estimated from plot. E_i(exp) = 0.2452 + 0.9022 E_i(calc.; r = 0.9595, N = 20.

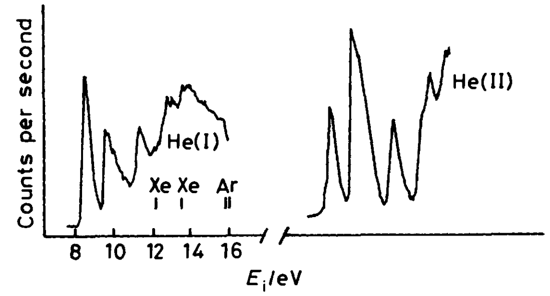

Figure 3. Photoelectron spectrum of 3-methyl-2-thiouracil (**3**).

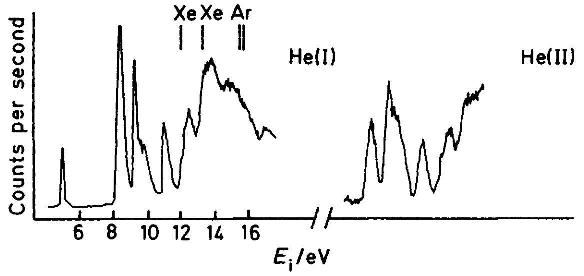

Figure 4. Photoelectron spectrum of 1,3-dimethyl-2-thiouracil (**4**).

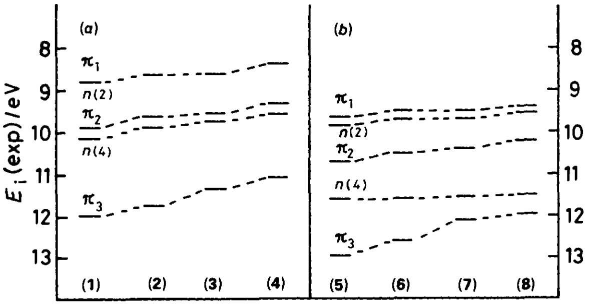

Figure 5. (*a*) The experimental photoelectron spectrum energy-level diagram for the five highest occupied molecular orbitals in 2-thiouracil and its *N*-mono- and *N,N'*-di-methyl derivatives; (*b*) The AM1 energy-level diagram for the five highest occupied molecular orbitals in 2-thiouracil and its *N*-mono- and *N,N'*-di-methyl derivatives.

atom, which gives a very noticeable diminution of the intensity of a π-ionisation of the ring.

The spectrum of compound (**5**) is recorded in Figure 11. The first band at 8.35 eV is associated with the first π orbital. Its diminished intensity under the He(II) radiation is caused by the strong localisation on the sulphur orbital. The second band is broad and unsymmetrical and covers two ionisations (π orbital and the σ-electron pairs of the nitrogens N-1 and N-3). The band at 10.75 eV is associated with the fourth molecular orbital with an important localisation on the sulphur. Its intensity is not diminished with He(II) radiation and it is reasonable to assign the ionisation of the lone pairs on the nitrogens in the same region.

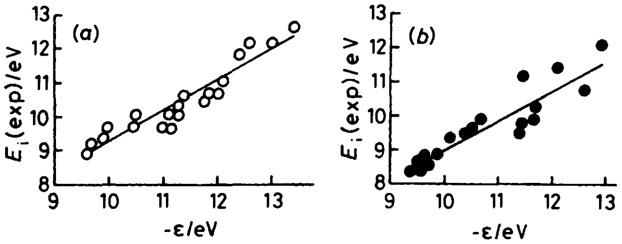

Figure 6. (*a*) Plot of the experimental E_i values of uracil and its *N*-methyl derivatives against the corresponding calculated orbital energies ($-\varepsilon_i$); (*b*) Plot of the experimental E_i of 2-thiouracil and its *N*-methyl derivatives against the corresponding calculated orbital energies ($-\varepsilon_i$).

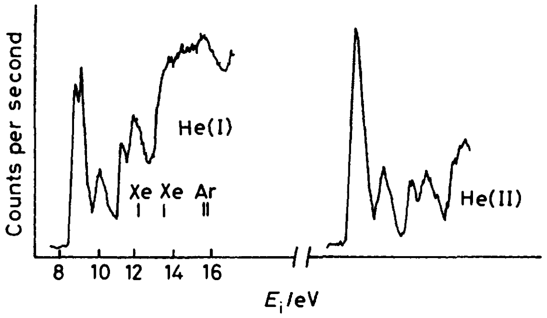

Figure 7. Photoelectron spectrum of 1,2-dimethyl-2-thiouracil (**7**).

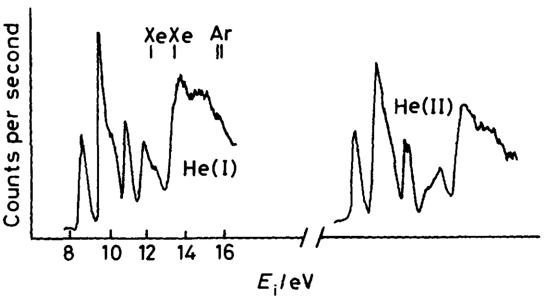

Figure 8. Photoelectron spectrum of 2,3-dimethyl-2-thiouracil (**8**).

The spectrum of compound (**9**) given in Figure 9 shows an appearance similar to that found for compound (**11**) and different from that of compound (**5**); in particular, the invariance of the intensity of the first band with He(II) indicates the predominance in the vapour phase of the form N_3H [(**9a**)]. The presence of feeble intensity at 10.80 eV indicates the simultaneous presence of some of the OH-tautomer [(**9b**)].

The IR spectrum[4] of 2-methyl-2-thiouracil showed the existence of a prototropic equilibrium in the vapour state between (**9a**) and (**9b**) tautomers. Tautomer (**9a**) is more stable

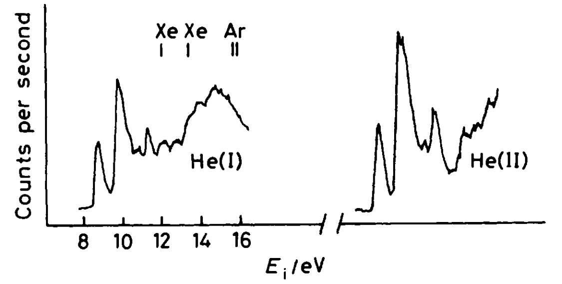

Figure 9. Photoelectron spectrum of 2-methyl-2-thiouracil (**9**) and (**10**).

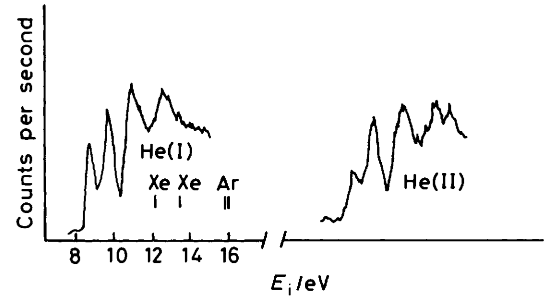

Figure 10. Photoelectron spectrum of 4-neopentyl-2-thiouracil (**6**).

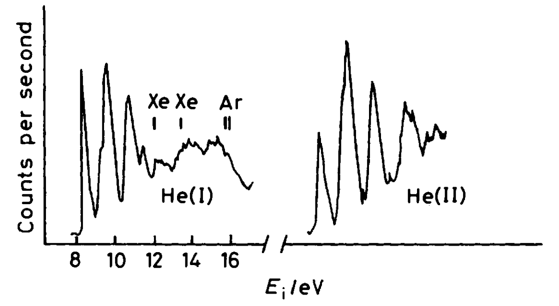

Figure 11. Photoelectron spectrum of 2,4-dimethyl-2-thiouracil (**5**).

than (**9b**) by 1.64 kcal mol^{-1} * according to *ab initio* calculations using the 6-31G** basis set.[1]

By contrast, the spectrum of compound (**6**) (Figure 10) is very similar to that of (**5**). The band at 8.80 eV corresponds to that observed at 8.35 eV in the dimethyl derivative (Figure 11). It is expected, given the strong participation of sulphur in this orbital, that it should be more stable in the SH-derivative. The band at 9.75 eV shows a shoulder at 9.40 eV, which is found at the same position in the two spectra. The band at 11 eV corresponds to that observed at 10.75 eV for the compound (**5**). The photoelectron spectroscopy confirms the structure of (**6**) as an SH form.

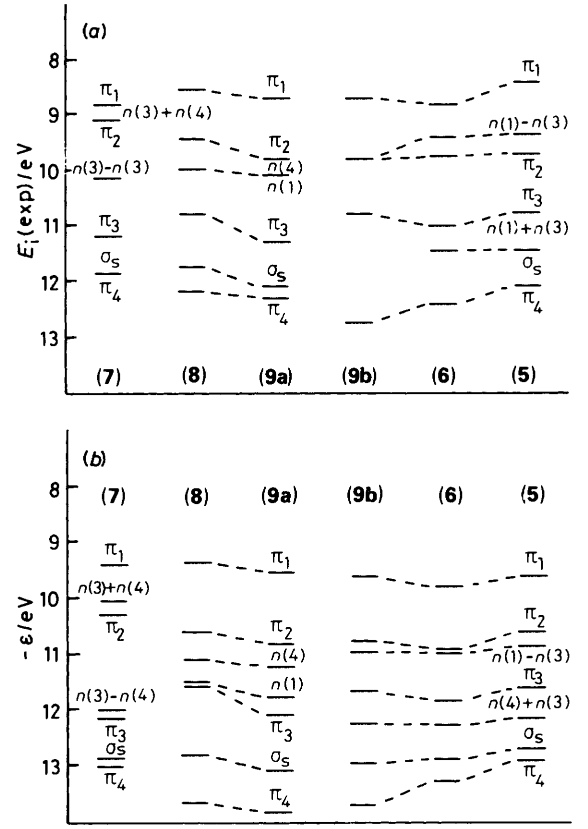

Figure 12. The experimental photoelectron spectrum (*a*) and the AM1 (*b*) energy-level diagram for the seven highest occupied molecular orbitals in 1,2-dimethyl-2-thiouracil (**7**), 2,3-dimethyl-2-thiouracil (**8**), 2-methyl-2-thiouracil (**9**) and (**10**), 4-neopentyl-2-thiouracil (**6**), and 2,4-dimethyl-2-thiouracil (**5**).

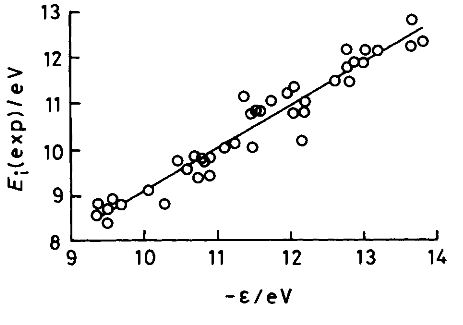

Figure 13. Plot of the experimental E_i values of *S*-methyl and/or *O*-methyl derivatives of 2-thiouracil against the corresponding calculated orbital energies ($-\varepsilon_i$).

Figures 12(*a*) and 12(*b*) show, respectively, experimental and calculated (AM1 method) ionisation potentials of compounds (**5**)–(**9**). The theoretical energy scale is shifted in comparison with that of the experimental. For structures (**5**) and (**6**), the AM1 method predicts the reverse order of π_c and $n(1)$–$n(3)$ orbitals to that found by experiment. Except in this respect, there is again a good correlation between experimental E_i and calculated orbital energy for the first seven bands [Figure 13; $E_i(\text{exp}) = -0.333 + (0.935\,\varepsilon_{AM1})$; $r = 0.974$, $N = 41$].

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* 1 cal = 4.184 J.

References

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