# Tautomerism in Barbituric and Thiobarbituric Acids



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The molecular geometry of barbituric and thiobarbituric acid tautomers have been fully optimized using the AM1 method in order to estimate the relative energies of the tautomers. The results are in agreement with available experimental data and indicate that in the vapour the barbiturate ring is essentially planar. In both unsubstituted compounds the trioxo structure is found to be the most stable one, in agreement with experimental findings in the solid. Tautomeric equilibria are sensitive to phase change and to substitution at the $C_5$ position. On passing from the vapour to the water the population of the most polar structure increases, although the order of stability remains unchanged and only for the Br and I derivatives it can be suggested the coexistence of two forms in solution. The substitution at $C_5$ does not alter the order of stability except for the 5-nitro derivatives where the dioxo form predominates, in agreement with experimental results in the solid. Electron affinities and ionization potentials of the tautomers have been evaluated and briefly discussed. It is suggested that gas-phase uv photoelectron spectroscopy should be able in analysing the tautomeric equilibria of barbituric and thiobarbituric acids in the vapour.

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## Introduction.

Tautomerism is a phenomenon of great interest in chemistry [1]. Its energetics is intimately connected with an understanding of the physical nature of the chemical bond. Tautomerism of pyrimidine bases has important consequences in molecular biology being believed, *inter alia*, to play a role in mutagenesis of DNA [1,2]. We are here concerned with the tautomerism of barbituric and thiobarbituric acids by evaluating by means of semiempirical calculations; a) the geometry and relative stability of tautomeric forms showing the lactim-lactam as well as the methylene-methyne tautomerism (Figure 1); b) water-tautomer interaction energies; c) effects of substitution at $C_5$. The chemistry of barbiturates is very rich; a recent review was published by Bojarski *et al.* [3]. We are not aware with molecular structural data in the vapour for the barbituric acids which we are dealing with, although several studies in condensed media are available [3]. Previous molecular orbital calculations are rather sparse [3].

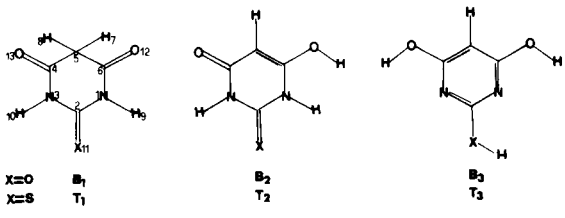


Figure 1.

## Calculations.

All calculations were performed by the AM1 method using the AMPAC program [4]. The molecular geometries of the tautomers were fully optimized with any conformational and symmetry restriction. Starting geometrical parameters of the ring atoms were based on crystallographic X-ray structures of barbituric acid [5], 5,5-diethylbarbituric acid [6,7] and 1,3-diethylthiobarbituric acid [8].

## Results and Discussion.

### Molecular Geometries.

The optimized geometries of the studied tautomers are shown in Figure 2. The calculated figures show some significant difference with experiment [5-8]. In barbituric acid, for example, discrepancies up to 0.05 Å and 5° are found. To test the reliability of the AM1 method in reproducing the geometrical parameters of a related free molecule, we report (Table 1) the AM1 structure of

Table 1

Theoretical and Experimental Structures of Pyrimidine

| | AM1 | STO-3G [a] | 3-21G [a] | gas [b] |
|---|---|---|---|---|
| $N_1$-$C_2$ | 1.356 | 1.354 | 1.329 | 1.340 |
| $N_1$-$C_6$ | 1.356 | 1.354 | 1.332 | 1.340 |
| $C_5$-$C_6$ | 1.407 | 1.386 | 1.382 | 1.393 |
| $C_5$-H | 1.111 | 1.089 | 1.067 | 1.099 |
| $C_5$-H | 1.095 | 1.081 | 1.069 | 1.099 |
| $C_6$-H | 1.104 | 1.088 | 1.070 | 1.099 |
| $N_1$-$C_2$-$N_3$ | 127.5 | 128.0 | 124.6 | 127.6 |
| $C_2$-$N_1$-$C_6$ | 115.6 | 114.6 | 117.7 | 115.5 |
| $N_1$-$C_6$-$C_5$ | 122.2 | 122.6 | 121.5 | 122.3 |
| $C_4$-$C_5$-$C_6$ | 117.0 | 117.5 | 116.9 | 116.8 |
| $N_1$-$C_2$-H | 116.3 | 116.0 | 117.7 | 116.2 |
| $N_1$-$C_6$-H | 116.3 | 116.5 | 117.0 | 115.3 |
| $C_6$-$C_5$-H | 121.5 | 121.3 | 121.6 | 121.6 |

[a] Ref [11]. [b] L. Fernholt and C. Romming, *Acta Chem. Scand.*, **A32**, 271 (1978).

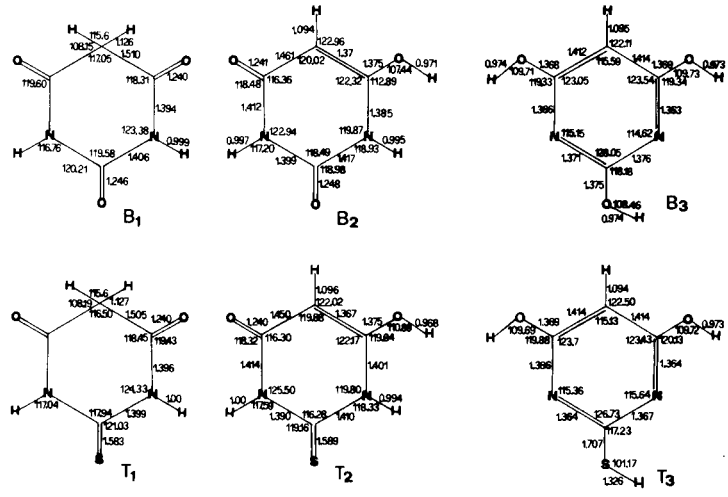


Figure 2. AM1 molecular geometries of barbituric and thiobarbituric acid tautomers.

pyrimidine together with some experimental and theoretical data. The agreement between theory and experiment is fair good. Furthermore it is worth mentioning that MINDO/3 calculations, of which AM1 is a development, reproduce satisfactorily [9] the electron diffraction geometry [10] of the related uracil molecule. Therefore it can be inferred that some part of the discrepancy between calculated and experimental geometry of barbituric acids may be mainly attributed to hydrogen bonding effects in the solid [7].

The **B** and **T** tautomers are very nearly planar molecules. The $\mathbf{B}_1$ and $\mathbf{T}_1$ as well as $\mathbf{B}_3$ and $\mathbf{T}_3$, show $C_{2v}$ symmetry. Changes in the molecular geometry associated with tautomerism are similar in both series of compounds, and in the $\mathbf{B}_1$-$\mathbf{B}_2$ and $\mathbf{T}_1$-$\mathbf{T}_2$ couples they are confined essentially in the O=C-$CH_2$-C=O frame, the urea moiety of the molecule HN-CO-NH being very little affected (Figure 2).

Tables 2 and 3 show the heavy atom geometry of some 5-substituted barbituric and thiobarbituric acids. The ef-

Table 2

Comparison of Calculated Bond Lengths and Bond Angles of 5-Substituted Barbituric ($\mathbf{B}_1$) Acid Derivatives

| | -H | -F | -Cl | -Br | -I | -$CH_3$ | -OH | -$NO_2$ |
|---|---|---|---|---|---|---|---|---|
| $N_1$-$C_2$ | 1.406 | 1.406 | 1.408 | 1.404 | 1.406 | 1.406 | 1.405 | 1.406 |
| $N_1$-$C_6$ | 1.394 | 1.388 | 1.390 | 1.389 | 1.391 | 1.393 | 1.386 | 1.388 |
| $C_5$-$C_6$ | 1.510 | 1.540 | 1.523 | 1.516 | 1.518 | 1.519 | 1.533 | 1.532 |
| $C_2$-O | 1.246 | 1.246 | 1.245 | 1.246 | 1.246 | 1.246 | 1.246 | 1.241 |
| $C_6$-O | 1.240 | 1.237 | 1.238 | 1.239 | 1.240 | 1.241 | 1.238 | 1.237 |
| $N_1$-$C_2$-$N_3$ | 119.6 | 119.0 | 118.3 | 118.7 | 118.1 | 118.6 | 118.9 | 118.8 |
| $C_2$-$N_1$-$C_6$ | 123.4 | 124.1 | 124.0 | 123.9 | 124.2 | 123.9 | 124.0 | 124.1 |
| $N_1$-$C_6$-$C_5$ | 118.3 | 118.9 | 118.8 | 118.8 | 119.0 | 119.0 | 119.0 | 118.8 |
| $C_6$-$C_5$-$C_4$ | 117.1 | 114.9 | 115.4 | 115.8 | 115.2 | 115.5 | 115.3 | 115.2 |
| $H_8$-$C_5$-$C_6$ | 108.1 | 108.8 | 108.9 | 108.2 | 108.1 | 106.7 | 107.7 | |
| $H_8$-$C_5$-$C_6$-$O_{12}$ | -57.8 | -59.4 | -54.6 | -55.6 | -56.7 | -59.9 | -61.5 | |

Substituent

| | |
|---|---|
| -F | $C_5$-F = 1.385, F-$C_5$-$C_6$ = 108.8, F-$C_5$-$C_6$-$O_{12}$ = 57.9 |
| -Cl | $C_5$-Cl = 1.757, Cl-$C_5$-$C_6$ = 108.0, Cl-$C_5$-$C_6$-$O_{12}$ = 71.0 |
| -Br | $C_5$-Br = 1.949, Br-$C_5$-$C_6$ = 109.7, Br-$C_5$-$C_6$-$O_{12}$ = 60.6 |
| -I | $C_5$-I = 2.078, I-$C_5$-$C_6$ = 110.1, I-$C_5$-$C_6$-$O_{12}$ = 58.6 |
| -$CH_3$ | $C_5$-C = 1.516, C-$C_5$-$C_6$ = 109.5, C-$C_5$-$C_6$-$O_{12}$ = 57.6, C-H (mean) = 1.116, H-C-H (mean) = 109.9, H-C-$C_5$-$C_6$ = 69.3, -50.8, -170.8 |
| -OH | $C_5$-O = 1.412, O-$C_5$-$C_6$ = 108.9, O-$C_5$-$C_6$-$O_{12}$ = 58.8, O-H = 0.970, H-O-$C_5$ = 106.7, H-O-$C_5$-$C_6$ = -60.5 |
| -$NO_2$ | $C_5$-N = 1.496, N-$C_5$-$C_6$ = 113.0, N-$C_5$-$C_6$-$O_{12}$ = 53.8, N-O = 1.355, O-N-$C_5$ = 115.9, O-N-$C_5$-$C_6$ = 93.1, 26.9 |

Table 3

Comparison of Calculated Bond Lengths and Bond Angles of 5-Substituted Thiobarbituric ($\mathbf{T}_1$) Acid Derivatives

| | -H | -F | -Cl | -Br | -I | -$CH_3$ | -OH | -$NO_2$ |
|---|---|---|---|---|---|---|---|---|
| $N_1$-$C_2$ | 1.399 | 1.400 | 1.399 | 1.398 | 1.398 | 1.399 | 1.397 | 1.399 |
| $N_1$-$C_6$ | 1.396 | 1.392 | 1.396 | 1.394 | 1.390 | 1.395 | 1.394 | 1.391 |
| $C_5$-$C_6$ | 1.505 | 1.540 | 1.518 | 1.516 | 1.516 | 1.516 | 1.530 | 1.529 |
| $C_2$-S | 1.583 | 1.582 | 1.582 | 1.586 | 1.584 | 1.584 | 1.584 | 1.581 |
| $C_6$-O | 1.240 | 1.236 | 1.238 | 1.239 | 1.240 | 1.240 | 1.237 | 1.238 |
| $N_1$-$C_2$-$N_3$ | 117.9 | 118.2 | 118.2 | 118.4 | 118.6 | 118.1 | 118.3 | 118.3 |
| $C_2$-$N_1$-$C_6$ | 124.3 | 124.9 | 124.1 | 124.1 | 124.1 | 124.3 | 124.5 | 124.3 |
| $N_1$-$C_6$-$C_5$ | 118.5 | 118.7 | 118.8 | 118.7 | 118.8 | 119.0 | 119.2 | 118.9 |
| $C_6$-$C_5$-$C_4$ | 116.5 | 114.6 | 115.4 | 115.3 | 115.3 | 115.3 | 114.6 | 114.9 |
| $H_8$-$C_5$-$C_6$ | 108.2 | 106.7 | 108.4 | 107.5 | 108.1 | 106.6 | 108.0 | 106.4 |
| $H_8$-$C_5$-$C_6$-$O_{12}$ | -58.0 | -61.2 | -52.0 | -52.9 | -51.9 | -60.5 | -60.0 | -56.8 |

Substituent

| | |
|---|---|
| -F | $C_5$-F = 1.380, F-$C_5$-$C_6$ = 109.9, F-$C_5$-$C_6$-$O_{12}$ = 56.4 |
| -Cl | $C_5$-Cl = 1.758, Cl-$C_5$-$C_6$ = 108.7, Cl-$C_5$-$C_6$-$O_{12}$ = 63.4 |
| -Br | $C_5$-Br = 1.937, Br-$C_5$-$C_6$ = 110.5, Br-$C_5$-$C_6$-$O_{12}$ = 61.2 |
| -I | $C_5$-I = 2.086, I-$C_5$-$C_6$ = 109.8, I-$C_5$-$C_6$-$O_{12}$ = 63.3 |
| -$CH_3$ | $C_5$-C = 1.518, C-$C_5$-$C_6$ = 109.7, C-$C_5$-$C_6$-$O_{12}$ = 57.1, C-H (mean) = 1.117, H-C-H (mean) = 110.0, H-C-$C_5$-$C_6$ = 68.7, -51.4, -171.4 |
| -OH | $C_5$-O = 1.405, O-$C_5$-$C_6$ = 110.8, O-$C_5$-$C_6$-$O_{12}$ = 53.6, O-H = 0.967, H-O-$C_5$ = 107.2, H-O-$C_5$-$C_6$ = -58.5 |
| -$NO_2$ | $C_5$-N = 1.496, N-$C_5$-$C_6$ = 113.0, N-$C_5$-$C_6$-$O_{12}$ = 54.4, N-O = 1.354, O-N-$C_5$ = 116.0, O-N-$C_5$-$C_6$ = 93.1, 26.8 |

fect of the substituent is very small in agreement with recent theoretical results on the related uracil molecule [9,11]. The largest change is at the internal $C_6C_5C_4$ and external $H_8C_5C_6$ angles (*ca.* 2°) and at the dihedral angle $H_8C_5C_6O_{12}$. Some distortion from planarity is encountered for some $\mathbf{B}_1$ derivatives, although it is limited to few degrees. On the other hand it does not appreciably influence the calculated physical properties of the molecule, such as charge distribution, sequence and molecular orbital energies, as compared with results in the corresponding planar structure. Thus the puckering phenomenon observed in the solid [7] was not explicitly investigated.

Similar results were obtained for $\mathbf{B}_2$, $\mathbf{B}_3$, $\mathbf{T}_2$ and $\mathbf{T}_3$ tautomers, where planarity is even more effective. A particular interest is offered by $\mathbf{B}_2$, $\mathbf{B}_3$, $\mathbf{T}_2$ and $\mathbf{T}_3$-nitro derivatives owing to the expected presence of an intramolecular hydrogen bonding, which was indeed experimentally observed in anhydrous dilituric acid ($\mathbf{B}_2$-$NO_2$) in the solid state [12]. Actually AM1 calculations predict an intramolecular hydrogen bonding energy of about 8-9 Kcal/mole for $\mathbf{B}_2$-$NO_2$ and $\mathbf{T}_2$-$NO_2$. Changes in the molecular geometry induced by intramolecular hydrogen bonding in the case of $\mathbf{B}_2$-$NO_2$ are shown in Figure 3, where experimental figures are also included. The local symmetry of the $NO_2$ group is clearly lost. As expected, the length of the chelated N-O bond as well as the O-H bond is significantly elongated on H-bond formation, while the N-C, C-C and C-O bond lengths are typically alternately shortened and elongated, indicating that charge rearrangement within the six-membered chelate ring is assisted by polarization effects [13,14]. It is worth noting that the presence of an intramolecular hydrogen bonding is not a necessary requisite for planarity, since non H-bonded structures are also planar.

Relative Tautomeric Stabilities.

Previous experimental work [3] has shown that generally barbiturates exist in the trioxo structure in the solid.

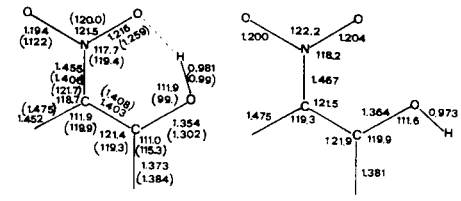

Figure 3. Effect of the intramolecular hydrogen bonding on the geometry of 5-nitro-2,6-dioxo-6-hydroxy barbituric acid.

Dilituric acid (5-nitrobarbituric acid) however exists in the 5-nitro-2,5-dioxo-4-hydroxy configuration [12] with the nitro group coplanar with the pyrimidine ring; the same structure is shown by dialuric acid (5-hydroxybarbituric acid) [15]. In solution hydroxy forms are present and the oxo-hydroxy ratio depends on the solvent and substitution. The calculated heats of formation and relative stabilities of the investigated tautomers are reported in Table 4. The results are on the whole in agreement with the experimental findings in the solid [3], in that the trioxo structure is predicted the most stable one for both barbituric and thiobarbituric acids. In $\mathbf{B}_2$-$NO_2$ and $\mathbf{T}_2$-$NO_2$ the dioxo-hydroxy form prevails, in agreement with experimental data in the solid state [12]. However the experimental results of dialuric acid [15] are not reproduced. The substituent effect on the relative stability of the tautomeric forms is analogous in both the series of compounds; it increases the stability of the hydroxy form relative to the trioxo form. This agrees with the postulated substituent effect on the relative stability of uracil tautomers [1,16].

Solvent Effects.

The relative stabilities of tautomers in solution can be obtained by evaluating solute-solvent interactions by the reaction field continuum model [17,18]. In this model the solute-solvent interaction energy is related to the dielectric constant of the solvent, $\epsilon$, the cavity radius, $a$, and to the

Table 4

Heats of Formation and Relative Energies (Kcal/mole) of 5-Substituted Barbituric and Thiobarbituric Acids

| Compound | -H | $E_R$ | -F | $E_R$ | -Cl | $E_R$ | -Br | $E_R$ | -I | $E_R$ | -$CH_3$ | $E_R$ | -OH | $E_R$ | -$NO_2$ | $E_R$ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| $\mathbf{B}_1$ | -107.8 | 0.0 | -143.0 | 0.0 | -106.0 | 0.0 | -92.7 | 0.0 | -81.0 | 0.0 | -111.5 | 0.0 | -145.4 | 0.0 | 1.8 | 93.1 |
| $E_R$ | 0.0 | | -35.2 | | 1.8 | | 1.5 | | 26.8 | | -3.6 | | -37.6 | | 109.6 | |
| $\mathbf{B}_2$ | -96.4 | 11.4 | -136.0 | 7.0 | -99.3 | 6.7 | -88.1 | 4.6 | -76.6 | 4.4 | -103.2 | 8.3 | -138.1 | 7.3 | -91.5 | 0.0 |
| $E_R$ | 0.0 | | -39.6 | | -2.9 | | 8.3 | | 19.8 | | -6.8 | | -41.7 | | 5.1 | |
| $\mathbf{B}_3$ | -83.0 | 24.8 | -122.2 | 20.8 | -84.4 | 21.6 | -72.9 | 19.8 | -61.7 | 19.3 | -89.3 | 22.2 | -121.2 | 24.2 | -73.2 | 18.1 |
| $E_R$ | 0.0 | | -39.2 | | -1.4 | | 10.1 | | 21.3 | | -6.3 | | -38.2 | | 9.8 | |
| $\mathbf{T}_1$ | -45.0 | 0.0 | -80.3 | 0.0 | -43.1 | 0.0 | -30.0 | 0.0 | -18.8 | 0.0 | -48.7 | 0.0 | -81.9 | 0.0 | 64.6 | 91.0 |
| $E_R$ | 0.0 | | -35.3 | | 1.9 | | 15.0 | | 26.2 | | -3.7 | | -36.9 | | 109.6 | |
| $\mathbf{T}_2$ | -31.7 | 13.3 | -69.7 | 10.6 | -32.8 | 10.3 | -21.4 | 8.6 | -10.3 | 8.5 | -38.1 | 10.6 | -69.7 | 12.2 | -28.8 | 0.0 |
| $E_R$ | 0.0 | | -38.0 | | -1.1 | | 10.3 | | 21.4 | | -6.4 | | -3.8 | | 11.6 | |
| $\mathbf{T}_3$ | -36.7 | 8.3 | -76.2 | 4.1 | -38.3 | 4.8 | -26.5 | 3.5 | -15.2 | 3.6 | -43.1 | 5.6 | -75.6 | 6.3 | -25.4 | 3.4 |
| $E_R$ | 0.0 | | -39.5 | | -1.6 | | 10.2 | | 21.5 | | -6.4 | | -38.9 | | 11.3 | |

solute dipole moment $\mu$. The following relation was used to evaluate $E_{int}$:

$$E_{int} = -0.5\mu^2 f/1\text{-}fa$$

where $$f = 2(\epsilon\text{-}1)/2\epsilon + 1)a^3$$

Table 5 reports $E_{int}$ in water obtained using dipole moment values of Table 6 together with an $\epsilon$ value of 78.5 for water and an assumed spherical cavity radius of 3.3 Å. It must be remarked that the present simple model accounts only for electrostatic solute-solvent interactions leaving out specific interactions such as hydrogen bonding ones; moreover the solute polarizability was taken constant through the series of tautomers. Relative energies of the tautomers in water solution can be easily evaluated by adding together the corresponding figures of Tables 4 and 5. It is found that $\mathbf{B}_2$ and $\mathbf{T}_2$ derivatives are the most stabilized tautomers, owing to their greater dipole moment value. The order of stability remaines unchanged however in both the **B** and **T** series, the most relevant consequence of the water-solute interaction being the probable coexistence in solution of $\mathbf{B}_1$-Br, $\mathbf{B}_1$-I, $\mathbf{T}_1$-Br and $\mathbf{T}_1$-I with the corresponding $\mathbf{B}_2$ and $\mathbf{T}_3$ tautomers.

Table 5

Base-water Interaction Energies, $-E_{int}$ (Kcal/mole), from the Reaction Field Continuum Model

| Compound | -H | -F | -Cl | -Br | -I | $-CH_3$ | -OH | $-NO_2$ |
|---|---|---|---|---|---|---|---|---|
| $\mathbf{B}_1$ | 0.10 | 0.36 | 0.04 | 0.03 | 0.03 | 0.20 | 0.45 | 0.70 |
| $\mathbf{B}_2$ | 3.28 | 2.32 | 2.83 | 3.10 | 3.20 | 3.35 | 1.09 | 4.83 |
| $\mathbf{B}_3$ | 0.36 | 0.93 | 0.59 | 0.70 | 0.70 | 0.37 | 1.24 | 6.18 |
| $\mathbf{T}_1$ | 0.22 | 0.34 | 0.08 | 0.03 | 0.06 | 0.38 | 0.07 | 0.67 |
| $\mathbf{T}_2$ | 4.23 | 4.12 | 4.16 | 4.49 | 4.63 | 4.05 | 4.16 | 4.60 |
| $\mathbf{T}_3$ | 0.34 | 0.91 | 0.58 | 0.64 | 0.67 | 0.35 | 1.21 | 0.73 |

Table 6

Calculated Dipole Moments (Debyes) of 5-Substituted Barbituric and Thiobarbituric Acids

| Compound | -H | -F | -Cl | -Br | -I | $-CH_3$ | -OH | $-NO_2$ |
|---|---|---|---|---|---|---|---|---|
| $\mathbf{B}_1$ | 0.67 | 1.29 | 0.41 | 0.36 | 0.36 | 0.97 | 1.45 | 1.80 |
| $\mathbf{B}_2$ | 3.90 | 3.28 | 3.62 | 3.79 | 3.85 | 3.94 | 2.25 | 4.73 |
| $\mathbf{B}_3$ | 1.29 | 2.08 | 1.66 | 1.80 | 1.80 | 1.31 | 2.40 | 1.71 |
| $\mathbf{T}_1$ | 1.02 | 1.25 | 0.59 | 0.36 | 0.51 | 1.33 | 0.58 | 1.76 |
| $\mathbf{T}_2$ | 4.43 | 4.37 | 4.39 | 4.56 | 4.63 | 4.33 | 4.39 | 4.60 |
| $\mathbf{T}_3$ | 1.26 | 2.05 | 1.64 | 1.72 | 1.76 | 1.27 | 2.37 | 1.84 |

## Ionization Potentials and Electron Affinities.

We are not aware of experimental studies concerning ionization potentials (IPS) and electron affinities (EAs) of barbituric and thiobarbituric acids. In absence of experimental values they may be evaluated from the molecular orbital energies through the Koopmans' theorem. The energy and composition of the lowest vacant (LUMO) and of the three uppermost occupied molecular orbitals of **B** and **T** tautomers are shown in Figure 4. The LUMO of $\mathbf{B}_1$ and $\mathbf{T}_1$ have exclusively $\pi$ C=O and C=S antibonding character, respectively, while in the other tautomers it is essentially localized in the ring, except for $\mathbf{T}_2$, where contributions from the S atomic orbital are consistent. EA is predicted to be positive for all the tautomers, the **T** series displaying higher figures than the **B** series in agreement with the generally higher EA value of sulphur compounds relative to the corresponding oxygen compounds [19-22]. Substitution of sulphur for oxygen leads to important changes also in the energy and composition of occupied orbitals. The highest occupied molecular orbital (HOMO) of $\mathbf{T}_1$, for example, is more stable by about 2 eV with respect to the $\mathbf{B}_1$ HOMO. This is exactly what it was found in the uv gas-phase photoelectron spectra, PES, of urea and thiourea [23,24]. Indeed the uppermost occupied orbitals of $\mathbf{B}_1$ and $\mathbf{T}_1$ can be compared with the molecular orbitals of urea and thiourea and their corresponding photoelectron spectra [23,24]. The PES of urea shows at low binding energy a band at 10.2 eV composed of three overlapping bands originated from the $^2B\text{-}\pi$ (O,N), $^2B\text{-}\sigma$ (O,N) and $^2A\text{-}\pi$ (N) orbital ionizations. A similar situation is predicted by AM1 calculations, as $\mathbf{B}_1$ shows three accidentally degenerate MOs as the highest occupied orbitals with composition very reminescent of the lowest energy MO structure of urea. The PES of thiourea shows

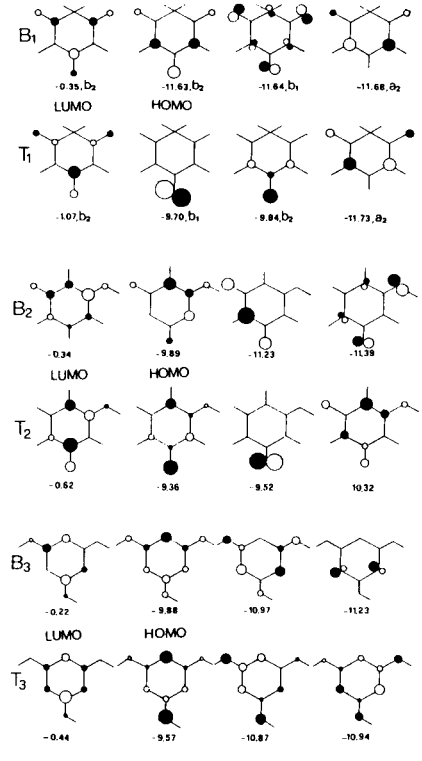


Figure 4. Lowest unoccupied (LUMO) and the three uppermost occupied molecular orbitals of barbituric (**B**) and thiobarbituric (**T**) acid tautomers.

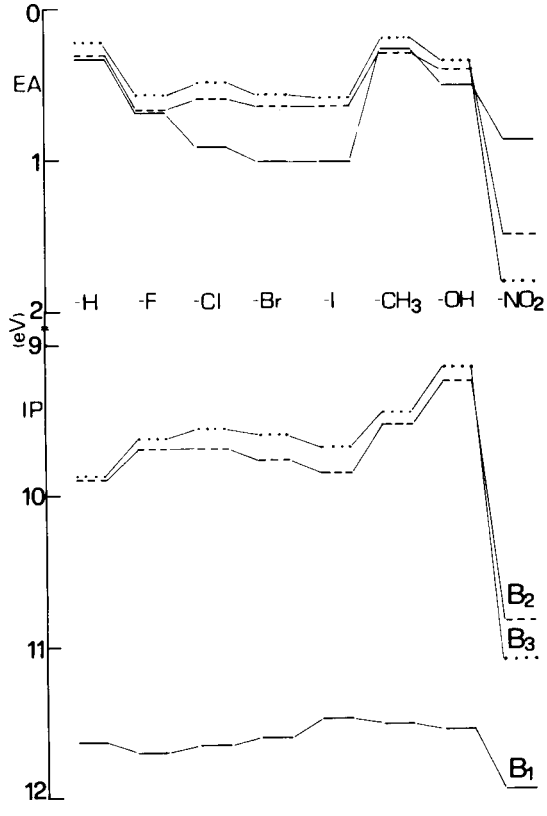


Figure 5. Effect of substitution at $C_5$ on the first electron affinity (EA) and first ionization potential (IP) of barbituric acid tautomers.

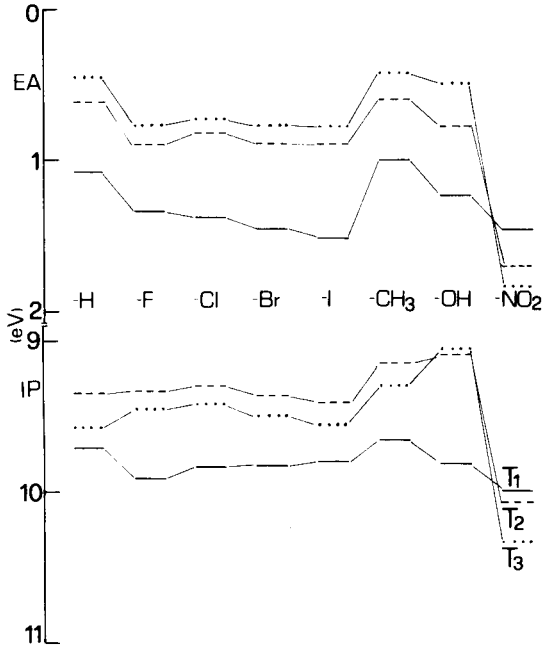


Figure 6. Effect of substitution at $C_5$ on the first electron affinity (EA) and first ionization potential (IP) of thiobarbituric acid tautomers.

two bands with a 2:1 intensity ratio [23,24]. The first band at 8.5 eV results from two ionizations of $^2B_2$-$\pi$ (S) and $^2B_1$-$\sigma$ (S) type. The second band at 10.5 eV represents the ionization from the $^2A_2$ $\pi$-MO antisymmetric combination of the two $\pi_N$ MOs. Here again the AM1 calculations reproduce this situation well (Figure 4). It can be concluded that the lower-energy PES of barbituric and thiobarbituric acids ($\mathbf{B}_1$ and $\mathbf{T}_1$) should be very similar to the PES of urea and thiourea, respectively. The HOMO of $\mathbf{B}_2$ and $\mathbf{B}_3$ are stabilized by about 1.7 eV relative to the $\mathbf{B}_1$ HOMO (Figure 4). This should make easy to reveal the presence of $\mathbf{B}_2$ and/or $\mathbf{B}_3$ tautomers in the vapour by means of uv UPS [25]. On the basis of the AM1 results it should be somewhat more difficult to investigate on **T** tautomerism by PES, although the third highest occupied MO of $\mathbf{T}_2$ at 10.32 eV seems to be sufficiently separated from the neighbour $\mathbf{T}_1$ and $\mathbf{T}_3$ MOs to serve as a diagnostic MO. The effect of substitution at $C_5$ on LUMO and HOMO of **B** and **T** tautomers is shown in Figures 5 and 6. Introduction of an electron withdrawing group ($NO_2$) increases considerably EA of **B** and **T** tautomers. Methyl substitution has practically no effect on EA of $\mathbf{B}_2$, $\mathbf{T}_2$, $\mathbf{B}_3$ and $\mathbf{T}_3$ or it little decreases EA of $\mathbf{B}_1$ and $\mathbf{T}_1$. Alkyl substitution generally slightly decreases EA [26,27]. Substitution with OH decreases slightly EA of **B** and **T** tautomers. A similar effect is observed in substituted benzenes [26,27] as the result of opposite stabilizing field effects and destabilizing effects of $\pi$ donation. As found in substituted benzenes [27] and aromatic compounds [28] the halogen substitution leads to an increase of EA in the order F < Cl < Br < I in $\mathbf{B}_1$ series and F $\cong$ Br $\cong$ I > Cl in $\mathbf{B}_2$ and $\mathbf{B}_3$ series. Essentially the same trend is predicted for the **T** series. The inversion in the effect of halogen substitution may be probably attributed to a somewhat greater electron donation of Cl, Br and I relative to F in $\mathbf{B}_2$, $\mathbf{T}_2$, $\mathbf{B}_3$ and $\mathbf{T}_3$, where LUMO has finite population at $C_5$. The population analysis supports this view.

The $b_2$ and $b_1$ HOMOs of $\mathbf{B}_1$ and $\mathbf{T}_1$ have no population at $C_5$ and the effect of substituent at this position is that expected for a purely inductive mechanism. On the contrary, interactions with the substituent MOs are operative in the $\mathbf{B}_2$, $\mathbf{T}_2$, $\mathbf{B}_3$ and $\mathbf{T}_3$ series leading to a large stabilization in the nitro derivatives and to a consistent destabilization in the OH and $CH_3$ derivatives, especially in the **B** series.

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