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# 5-Oxo and 7-oxo derivatives of [1,2,4]triazolo-[1,5-a]pyrimidine: characterization and theoretical study

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**Abstract**

4,5-Dihydro-5-oxo-[1,2,4]triazolo-[1,5-a]pyrimidine (5HtpO) and 4,7-dihydro-7-oxo-[1,2,4]triazolo-[1,5-a]pyrimidine (7HtpO) have been synthesized by the condensation of 3-amino-[1,2,4]triazole with a reagent bearing the three carbon atoms that close the six-membered ring in a strongly acidic (7HtpO) or strongly basic (5HtpO) medium. The crystal structures of these compounds have been determined by X-ray diffraction, exhibiting the N4–H tautomer, as expected from the RHF/AM1 calculations. The different possibilities for binding metal ions are discussed from the MO results. 

*Keywords:* Triazolopyrimidines; RHF/AM1 calculations

## 1. Introduction

This article continues the work of our research group about [1,2,4]-triazolo-[1,5-a]-pyrimidine derivatives and their interaction with metal ions; we have recently made a review about this subject [1]. The work collected in this revision is mainly focused in the derivatives that are commercially available (from Aldrich Chemical Co.): unsubstituted 1,2,4-triazolo-[1,5-a]-pyrimidine (tp), 5,7-dimethyl-1,2,4-triazolo-[1,5-a]-pyrimidine (dmtp) and 4,7-dihydro-5-methyl-7-oxo-1,2,4-triazolo-[1,5-a]-pyrimidine (HmtpO). These ligands display a broad versatility to bind metal ions through different positions, the nitrogen atom in position 3 being however the main binding site in most cases.

Recently, we have started to extend these studies to other derivatives, synthesizing and characterizing that with carbonyl groups both at position 5 and 7 [2] and studying its interaction with divalent cations of the first transition series [3]. In this ligand, coordination through N1–O7 is preferred to coordination through N3.

Following this line, we present in this article two new ligands of this series, the isomers 4,5-dihydro-5-oxo-[1,2,4]triazolo-[1,5-a]pyrimidine (5HtpO) and 4,7-dihydro-7-oxo-[1,2,4]triazolo-[1,5-a]pyrimidine (7HtpO), which are also isomers of the purine base hypoxanthine. A comparison of the coordination behaviour of these compounds may yield important information about the possible different role played by the exocyclic oxygen atom when it changes from position 5 to 7.

Prior to study the interaction of these compounds with metal ions, we present here their synthesis,

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characterization, X-ray determined crystal structure and theoretical MO study.

## 2. Experimental

### 2.1. Materials

3-Amino-[1,2,4]-triazole and ethyl 3,3-dietoxypropionate were purchased from Aldrich Chemical Co. and malic acid from Sigma Chemicals and they were used as received. Other chemical reagents were supplied by commercial sources. All preparative manipulations were carried out in an open atmosphere.

### 2.2. Synthesis of 4,5-dihydro-5-oxo-[1,2,4]triazolo-[1,5-a]pyrimidine (5HtpO)

The synthesis was done as described by Levin et al. [4,5]: 3.7 g of sodium were dissolved in 150 ml of absolute ethanol; 13.3 g of 3-amino-[1,2,4]-triazole and 30.0 g of ethyl 3,3-diethoxypropionate were then added and the resulting solution was refluxed for 20 h. After cooling down, the resulting precipitate was filtered and dissolved in distilled water. Concentrated hydrochloric acid was then added until a heavy precipitate appeared, which was filtered, washed with water, ethanol and ether and recrystallized from a mixture of water:acetonitrile (2:1). Overall yield: 37%. Elemental analysis, found: C, 44.0; H, 2.8; N, 40.9%. $C_5H_4N_4O$ requires C, 44.12; H, 2.94; N, 41.18%. Most intense IR bands: 3103, 1736, 1715, 1683, 1510, 1348, 1179, 831, 526 $cm^{-1}$.

### 2.3. Synthesis of 4,7-dihydro-7-oxo-[1,2,4]triazolo-[1,5-a]pyrimidine (7HtpO)

The synthesis was carried out by modifying the procedure described by Makisumi and Kano [6]. $H_2SO_4$ (80 ml) was cooled in an ice bath and 25.2 g of 3-amino-s-triazole were added with good stirring at such a rate that the temperature kept close to 0°C. After this, 45 g of malic acid were added, also very slowly and with continuous stirring to prevent the temperature from rising: $CO_2$ bubbles are released during this procedure. The mixture was allowed to warm spontaneously to room temperature and to stand overnight. It was then heated on a water bath with vigorous stirring for an hour, cooled to room temperature and poured on ice. The resulting solution was adjusted to pH 6 with concentrated ammonia and the product was obtained by leaving the solution overnight; it was filtered and recrystallized as white needles from water. Overall yield: 22%. Elemental analysis, found: C, 41.5; H, 3.5; N, 38.6%. $C_5H_5N_4O_{1.5}$ requires C, 41.38; H, 3.45; N, 38.62%. Most intense IR bands: 3139, 3097, 1702, 1635, 1596, 1315, 1170, 815, 749, 642, 626 $cm^{-1}$.

Caution: Concentrated sulphuric acid is a strongly corrosive substance, especially when heated. Extreme care should be taken during all manipulations.

### 2.4. Physical measurements

Microanalysis of C, H and N were performed in a Fison Instruments EA-1008 analyzer, $^1H$ and $^{13}C$ NMR spectra were recorded in a Bruker AM300 equipment using dmso-$d_6$ as solvent, thermal behaviour was studied in a Shimadzu DSC-50 calorimeter and a Shimadzu TGA-50 thermobalance provided with a mass spectrometer and a FTIR to analyze the evolved gases: all this instrumentation is at the Centre of Scientific Instrumentation of the University of Granada. Infrared spectra were obtained in a Perkin Elmer 983G spectrophotometer with samples dispersed in KBr pellets.

### 2.5. MO calculations

Semiempirical molecular orbital calculations type RHF/AM1 [7] have been performed for different tautomeric forms of 5HtpO and 7HtpO and their conjugated anions $5tpO^-$ and $7tpO^-$ by means of the SPARTAN program [8]. Full geometry optimization was performed autoconsistently with the MO calculations. Net charges on the atoms were calculated according to fits to the molecular electrostatic potential as implemented in the SPARTAN program.

### 2.6. Potentiometric titrations

For the determination of the $K_a$ value of each compound, $2.5 \times 10^{-3}$ mol of it were dissolved in the stoichiometric amount of 0.25 M NaOH and distilled water was added to get 25 ml. of a 0.1 M solution of the sodium salt. This was titrated at 18°C with 0.1 M HCl and the results were fitted by a

Table 1
Atomic coordinates and equivalent isotropic thermal parameters for 5HtpO and 7HtpO·$\frac{1}{2}H_2O$

| | $x$ | $y$ | $z$ | $B$ (Å$^2$) |
|---|---|---|---|---|
| 5HtpO | | | | |
| N1 | 0.45517(7) | 0.2989(6) | 0.0084(5) | 3.78(4) |
| C2 | 0.44848(9) | 0.1376(8) | 0.2077(7) | 3.92(5) |
| N3 | 0.39829(7) | 0.1532(6) | 0.3087(5) | 3.60(4) |
| C3A | 0.37161(8) | 0.3451(6) | 0.1610(5) | 2.86(4) |
| N4 | 0.31908(7) | 0.4486(5) | 0.1639(4) | 3.08(4) |
| C5 | 0.29750(8) | 0.6468(6) | − 0.0077(5) | 2.96(4) |
| O5 | 0.24937(6) | 0.7369(5) | 0.0077(4) | 3.89(4) |
| C6 | 0.33406(9) | 0.7369(7) | − 0.1980(5) | 3.32(4) |
| C7 | 0.38597(9) | 0.6334(6) | − 0.2008(5) | 3.19(4) |
| N8 | 0.40390(7) | 0.4352(5) | − 0.0211(4) | 3.06(4) |
| 7HtpO·1/2$H_2O$ | | | | |
| N1 | 0.0974(1) | 0.5717(4) | 0.1766(1) | 2.84(1) |
| C2 | 0.0588(1) | 0.6824(5) | 0.0886(2) | 3.16(1) |
| N3 | 0.0616(1) | 0.6352(4) | − 0.0212(1) | 3.08(1) |
| C3A | 0.1053(1) | 0.4835(5) | 0.0022(2) | 2.45(1) |
| N4 | 0.1288(1) | 0.3737(4) | − 0.0714(1) | 2.92(1) |
| C5 | 0.1744(1) | 0.2234(5) | − 0.0249(2) | 3.24(1) |
| C6 | 0.1974(1) | 0.1778(5) | 0.0914(2) | 3.08(1) |
| C7 | 0.1754(1) | 0.2932(5) | 0.1751(2) | 2.53(1) |
| O7 | 0.1922(1) | 0.2756(3) | 0.2821(1) | 3.32(1) |
| N8 | 0.1280(1) | 0.4396(4) | 0.1194(1) | 2.37(1) |
| O1W | 0 | 0.9654(6) | − 0.2500 | 4.58(1) |

Table 2
Interatomic distances (Å) and bond angles (°) for 5HtpO and 7HtpO·$\frac{1}{2}H_2O$

| | 5HtpO | 7HtpO·1/2$H_2O$ |
|---|---|---|
| N1–C2 | 1.320(4) | 1.320(3) |
| N1–N8 | 1.380(2) | 1.382(2) |
| C2–N3 | 1.359(3) | 1.372(3) |
| N3–C3A | 1.317(3) | 1.319(3) |
| C3A–N4 | 1.352(3) | 1.350(3) |
| C3A–N8 | 1.356(3) | 1.358(3) |
| N4–C5 | 1.370(3) | 1.363(3) |
| C5–O5 | 1.236(3) | – |
| C5–C6 | 1.454(4) | 1.349(3) |
| C6–C7 | 1.338(3) | 1.429(3) |
| C7–O7 | – | 1.223(3) |
| C7–N8 | 1.372(3) | 1.412(3) |
| C2–N1–N8 | 100.8(2) | 102.2(2) |
| N1–C2–N3 | 117.1(2) | 115.7(2) |
| C2–N3–C3A | 101.8(2) | 102.2(2) |
| N3–C3A–N4 | 130.2(2) | 129.9(2) |
| N3–C3A–N8 | 111.0(2) | 111.3(2) |
| N4–C3A–N8 | 118.8(2) | 118.9(2) |
| C3A–N4–C5 | 122.6(2) | 118.6(2) |
| N4–C5–O5 | 119.2(2) | – |
| N4–C5–C6 | 116.3(2) | 123.2(3) |
| O5–C5–C6 | 124.5(2) | – |
| C5–C6–C7 | 121.1(2) | 121.7(3) |
| C6–C7–O7 | – | 128.7(2) |
| C6–C7–N8 | 118.4(2) | 111.3(2) |
| O7–C7–N8 | – | 119.9(2) |
| N1–N8–C3A | 109.3(2) | 108.6(2) |
| N1–N8–C7 | 127.8(2) | 125.1(2) |
| C3A–N8–C7 | 122.9(2) | 126.3(2) |

least-squares procedure that yielded the values $K_a = 1.3 \times 10^{-6}$ (p$K_a = 5.9$) for 5HtpO and $K_a = 2.1 \times 10^{-6}$ (p$K_a = 5.7$) for 7HtpO.

### 2.7. Crystal structure determination

Crystal data for 5HtpO: $C_5H_4N_4O$, orthorhombic, space group $Pna2_1$, $a = 24.483(3)$, $b = 4.0272(3)$, $c = 5.7096(4)$ Å, $V = 562.95(9)$ Å$^3$, $Z = 4$, $M = 136.11$, $D_c = 1.607$ g cm$^{-3}$, $\mu$(CuK$\alpha$) = 10.4 cm$^{-1}$, crystal dimensions $0.01 \times 0.36 \times 0.88$ mm.

Crystal data for 7HtpO·1/2$H_2O$: $C_5H_5N_4O_{1.5}$, monoclinic, space group $C_2/c$, $a = 28.836(3)$, $b = 3.6902(2)$, $c = 12.116(1)$ Å, $\beta = 109.763(3)°$, $V = 1213.3(5)$ Å$^3$, $Z = 8$, $M = 145.12$, $D_c = 1.589$ g cm$^{-3}$, $\mu$(MoK$\alpha$) = 1.3 cm$^{-1}$, crystal dimensions $0.01 \times 0.10 \times 0.10$ mm.

Diffraction data were taken on a Nonius CADH diffractometer with CuK$\alpha$ radiation for 5HtpO and MoK$\alpha$ for 7HtpO. 607 ($\Theta < 73°$) and 1279 ($\Theta < 27°$) independent reflections were measured respectively; of these, 569 and 681 with $F > 6\sigma(F)$ were used for structure solution and refinement. The intensity data were corrected for Lorentz and polarization effects; the absorption was empirically ($\psi$ scans) corrected for 5HtpO (transmission range, 0.780–0.999) but not for 7HtpO. The structures were solved by direct methods by means of the MULTAN program [9] and non-hydrogen atoms were refined anisotropically by full matrix least-squares using weighting schemes $w = F_o^2[\sigma^2(F_o^2) + (0.10F_o^2)]^{-1}$ (5HtpO) and $\sigma^{-1}(F_o^2)$ (7HtpO). Hydrogen atoms were refined isotropically. The final residues for 5HtpO are $R = 0.055$, $R_w = 0.069$, goodness-of-fit = 1.41, maximum residual peak = 0.35 e Å$^{-3}$; for 7HtpO, the values are $R = 0.036$, $R_w = 0.037$, goodness-of-fit = 1.42, maximum residual peak = 0.18 e Å$^{-3}$. The refinement was performed using the Enraf–Nonius SDP system [10]. Atomic positional parameters are listed in

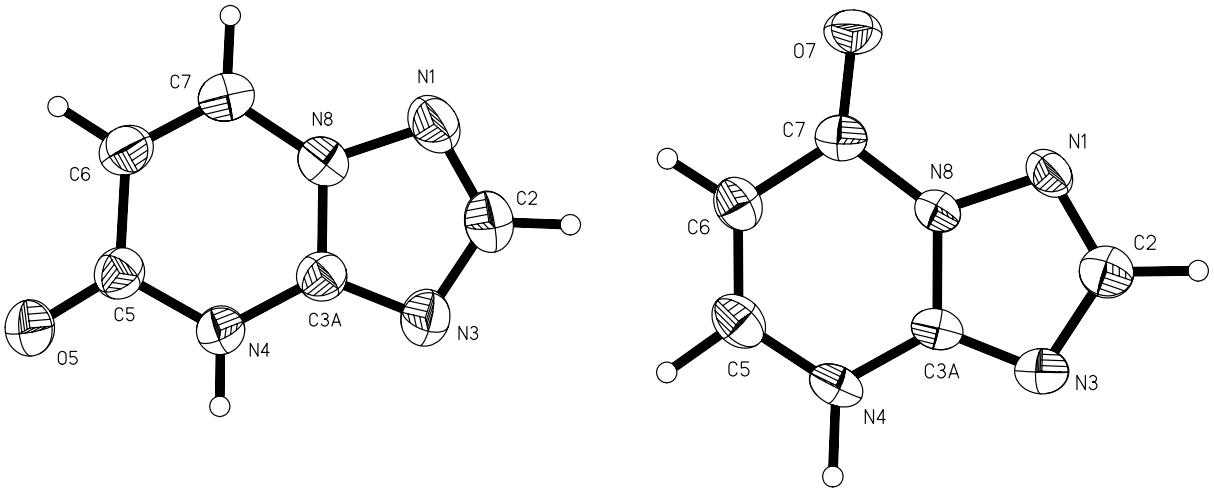


Fig. 1. Molecular structure of 5HtpO (left) and 7HtpO (right) as deduced from X-ray diffraction data. Atoms are represented as thermal ellipsoids at the 50% probability level.

Table 1 and interatomic distances and angles are listed in Table 2.[1]

## 3. Results and discussion

### *3.1. Synthesis and characterization*

The synthesis of the two compounds was described as early as 1964 for 5HtpO [4,5] and 1959 for 7HtpO [6]. The procedure followed by us is essentially the same described there for 5HtpO whereas for 7HtpO we have changed the order of addition of the reagents avoiding in this way the use of fuming sulphuric acid (concentrated sulphuric acid is used instead). A later reference for these synthesis [11] clearly gave worst results.

The assignment of the $^{1}H$ and $^{13}C$ NMR spectra is straightforward with the help of the DEPT spectra. The signal due to N4–H in the spectrum of 7HtpO is not observed (possibly it is too broad). The data (in ppm) are:

5HtpO, $^{1}H$ NMR: 6.16 (d,H6), 8.11 (s,H2), 8.62 (d,H7), 13.03 (s,H4), $J$(H6–H7) = 7.9 Hz. $^{13}C$ NMR: 108.0 (C6), 136.9 (C7), 150.0 (C3A), 152.6 (C2), 161.0 (C5).

7HtpO, $^{1}H$ NMR: 5.96 (d,H6), 8.02 (d,H5), 8.25 (s,H2), $J$(H5–H6) = 7.5 Hz. $^{13}C$ NMR: 99.1 (C6), 141.0 (C5), 151.0 (C3A), 151.8 (C2), 156.6 (C7).

The acidity constants of the compounds have been determined as indicated in the experimental section. The p$K_a$ values are very similar for both compounds: 5.9 for 5HtpO and 5.7 for 7HtpO, these values being appreciably lower than those found for analogous purines [13]; for example, the p$K_a$ value for hypoxanthine, a compound very similar to 7HtpO, is 8.9. This enhanced acidity of triazolopyrimidines if compared with purines can be attributed to better delocalization of the negative charge in their conjugated anions.

TG and DSC diagrams of 5HtpO show the anhydrous nature of this compound, which melts at 266.7°C, just prior to decomposition. On the contrary, the dehydration of 7HtpO·1/2$H_2O$ takes place in two well separated steps, in the first one only 1/3 mole of water per mole of compound (4.0%) is lost, with an associated enthalpy change of 31.4 kJ $mol^{-1}$ of water (endothermic peak centred at 83.0°C), and an apparently definite phase of composition 7Htpo·1/6$H_2O$ is generated. The remaining water is very tightly bound and is eliminated at quite a high temperature, a very broad weight loss effect appearing in the range

[1] Supplementary material: hydrogen coordinates, anisotropic thermal parameters and structure factor tables are available from the authors on request.

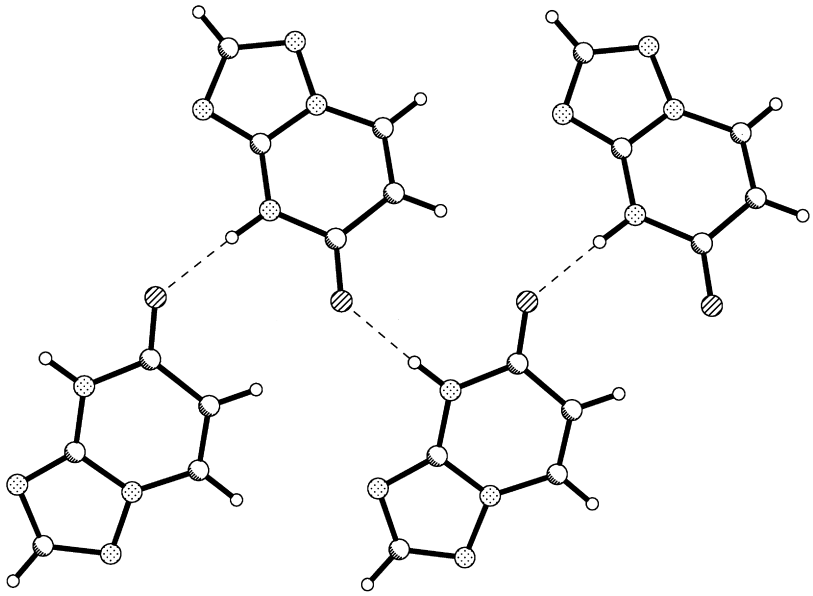

Fig. 2. Hydrogen-bonded chain along the ⟨011⟩ direction in the crystal structure of 5HtpO.

180–280°C. The IR analysis of the evolving gases confirms that only water is eliminated until the temperature reaches 280°C. The anhydrous compound melts at 300.6°C, prior to decomposition.

### *3.2. Description of the crystal structures*

Fig. 1 displays the molecular structure of 5HtpO and 7HtpO, as deduced from X-ray diffraction. Both ligands are present in the solid state as the expected

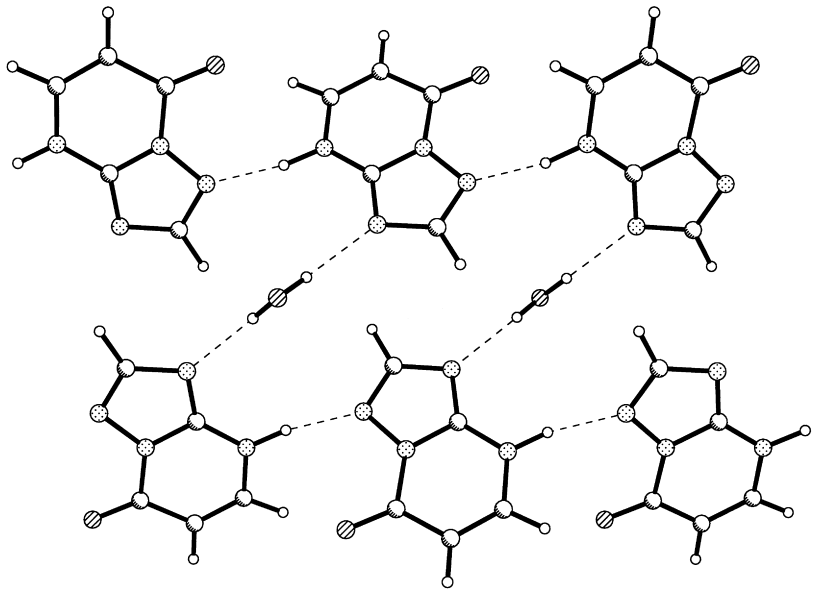

Fig. 3. Hydrogen-bonded double chain along the *c* axis in the crystal structure of 7HtpO·\,{\textstyle{1\above {} 2}}\,$H_2O$.

Table 3
Heats of formation (in kJ mol$^{-1}$) calculated for the different possible tautomeric forms of 5HtpO and 7HtpO

| | 5HtpO | 7HtpO |
|---|---|---|
| N1–H | 433.5[a] | 380.2 |
| N3–H | 377.0 | 332.5 |
| N4–H | 320.5 | 329.8 |
| O–H | 370.4 | 348.8 |
| Anion | 177.3 | 126.8 |

[a] Non-planar geometry: see text.

N4–H tautomer: this hydrogen atom has been found in the $\Delta F$ maps and refined and its presence is confirmed by the formation of hydrogen bonds (distances: N4···O5 $(-x+1/2, y-1/2, z+1/2)$ in 5HtpO, 2.718(4) Å; N4···N1 $(x, -y+1, z-1/2)$ in 7HtpO, 2.883(2) Å).

Bond distances and angles are collected in Table 2. There is no unexpected value in this table: changing the carbonyl group from position 5 to 7 translates the bond with less double-bond character from C5–C6 to C6–C7. The endocyclic angle at C5 or C7 becomes about 7° smaller when the carbonyl is placed at that position. The C7–O7 bond is appreciably bent towards N1 (see Fig. 1 and Table 2). Endocyclic atoms are coplanar within 0.015 Å, with the carbonyl oxygen atom included in the plane for 5HtpO and 0.035 Å deviated from it in 7HtpO.

In the crystal network, the molecules associate themselves in rows along the ⟨011⟩ (5HtpO, see Fig. 2) or ⟨001⟩ (7HtpO) directions. In the latter case, a solvation water molecule is present for each two 7HtpO moieties, placed on a binary axis and hydrogen-bonded to the nitrogen atom in position 3 (distance O1W···N3, 3.000(2) Å), which generates double rather than single chains (Fig. 3).

Partial stacking is observed in the structure of 5HtpO with N3 of one molecule falling over the centre of the hexagonal ring of one neighbour in the *b* direction (staking distance 3.28 Å). More definite stacking (along the *b* direction) is observed in the structure of 7HtpO with the C3A–N8 bond of one molecule placed over the centre of the hexagonal ring of another (staking distance 3.34 Å).

### 3.3. Molecular orbital calculations

These two compounds have in their molecules an acidic proton with several hypothetically possible attachment positions for it, leading to different tautomeric forms, namely N1–H, N3–H, N4–H and O–H. Calculations have been performed for all these forms as indicated in the experimental section, leading to the

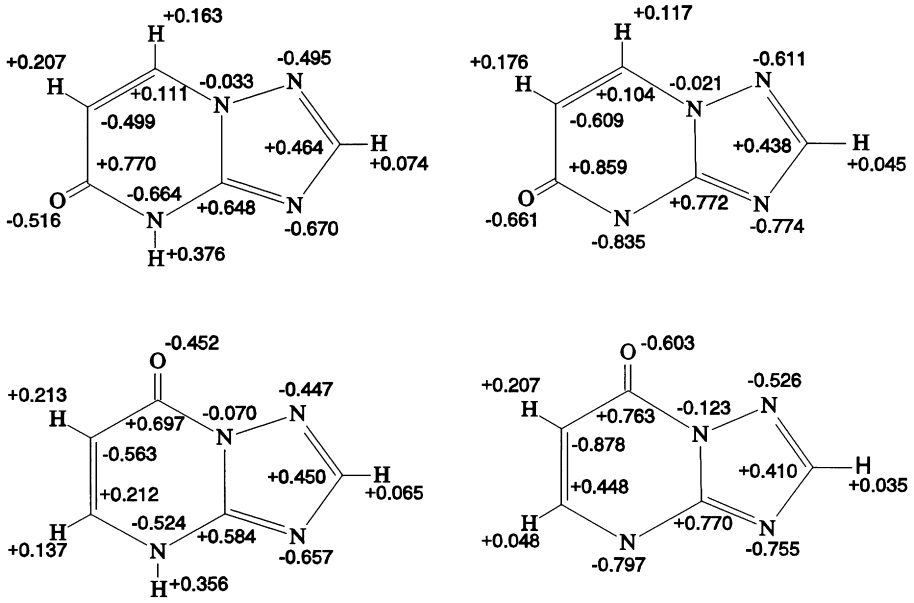


Fig. 4. Calculated net charges for 5HtpO (top) and 7HtpO (bottom) in neutral (left) and anionic (right) forms.

Table 4
Contributions of atomic orbitals of N and O atoms to the molecular orbitals of the species 5HtpO, $5tpO^-$, 7HtpO and $7tpO^-$. The contribution for one atom is calculated as the sum of the squared coefficients of that atom AO's in the linear combination that defines the MO

| Orbital | N1 | N3 | N4 | N8 | O5/O7 | Symmetry[a] | $E$ (eV) |
|---|---|---|---|---|---|---|---|
| 5HtpO | | | | | | | |
| $\psi_{20}$ | 0.017 | 0.172 | 0.204 | 0.116 | 0.042 | π | −13.327 |
| $\psi_{21}$ | 0.161 | 0.048 | 0.157 | 0.029 | 0.213 | π | −12.310 |
| $\psi_{22}$ | 0.258 | 0.441 | 0.010 | 0.040 | 0.077 | σ | −12.177 |
| $\psi_{23}$ | 0.012 | 0.078 | 0.093 | 0.013 | 0.600 | σ | −11.676 |
| $\psi_{24}$ | 0.170 | 0.298 | 0.108 | 0.105 | 0.003 | π | −10.514 |
| $\psi_{25}$(HOMO) | 0.167 | 0.043 | 0.152 | 0.146 | 0.116 | π | −9.735 |
| $\psi_{26}$(LUMO) | 0.067 | 0.006 | 0.065 | 0.000 | 0.034 | π | −8.632 |
| $5tpo^-$ | | | | | | | |
| $\psi_{20}$ | 0.051 | 0.370 | 0.094 | 0.084 | 0.237 | σ | −7.433 |
| $\psi_{21}$ | 0.205 | 0.196 | 0.197 | 0.021 | 0.231 | σ | −7.212 |
| $\psi_{22}$ | 0.248 | 0.013 | 0.163 | 0.397 | 0.220 | π | −7.130 |
| $\psi_{23}$ | 0.276 | 0.191 | 0.059 | 0.161 | 0.015 | π | −5.635 |
| $\psi_{24}$ | 0.015 | 0.013 | 0.323 | 0.044 | 0.352 | σ | −5.498 |
| $\psi_{25}$(HOMO) | 0.181 | 0.163 | 0.263 | 0.102 | 0.160 | π | −4.160 |
| $\psi_{26}$(LUMO) | 0.054 | 0.011 | 0.092 | 0.007 | 0.008 | π | 4.020 |
| 7Htpo | | | | | | | |
| $\psi_{20}$ | 0.278 | 0.272 | 0.016 | 0.131 | 0.048 | σ | −13.258 |
| $\psi_{21}$ | 0.308 | 0.222 | 0.004 | 0.050 | 0.204 | σ | −12.126 |
| $\psi_{22}$ | 0.084 | 0.208 | 0.002 | 0.104 | 0.444 | σ | −11.438 |
| $\psi_{23}$ | 0.095 | 0.318 | 0.001 | 0.184 | 0.163 | π | −11.436 |
| $\psi_{24}$ | 0.076 | 0.053 | 0.045 | 0.178 | 0.000 | π | −10.722 |
| $\psi_{25}$(HOMO) | 0.181 | 0.102 | 0.238 | 0.046 | 0.086 | π | −9.491 |
| $\psi_{26}$(LUMO) | 0.001 | 0.014 | 0.072 | 0.026 | 0.095 | π | −5.394 |
| $7tpo^-$ | | | | | | | |
| $\psi_{20}$ | 0.209 | 0.386 | 0.015 | 0.044 | 0.150 | σ | −7.558 |
| $\psi_{21}$ | 0.053 | 0.361 | 0.002 | 0.256 | 0.165 | π | −6.787 |
| $\psi_{22}$ | 0.139 | 0.186 | 0.402 | 0.048 | 0.096 | σ | −6.763 |
| $\psi_{23}$ | 0.004 | 0.106 | 0.116 | 0.130 | 0.482 | σ | −6.626 |
| $\psi_{24}$ | 0.157 | 0.003 | 0.004 | 0.142 | 0.001 | π | −5.768 |
| $\psi_{25}$(HOMO) | 0.111 | 0.128 | 0.253 | 0.023 | 0.121 | π | −4.092 |
| $\psi_{26}$(LUMO) | 0.078 | 0.072 | 0.018 | 0.140 | 0.005 | π | 4.380 |

[a] σ = Molecular plane is a symmetry plane for the MO. π = Molecular plane is a nodal plane for the MO.

values for their heats of formation that have been indicated in Table 3.

According to this, the most stable tautomeric form is the N4–H, as it happens with the 5-methyl-7-oxo derivative (HmtpO) [12], and it is the one found in solid state (see above). Nevertheless, the $\Delta H_f$ value for the N3–H tautomer of 7HtpO is quite close to that of the N4–H tautomer, so we may expect that this isomer could play a role in the chemistry of 7HtpO: the calculated proportion of the N3–H tautomer in equilibrium with the N4–H one is around 25%. Such equilibrium has been indeed observed by means of $^{15}N$ NMR for HmtpO and several of its derivatives substituted at position 2 or 6 [12].

The geometry optimization yielded planar results in all cases except for the N1–H tautomer of 5HtpO, the nitrogen atoms at positions 1 and 8 which become clearly of $sp^3$ nature: if planarity is forced for this molecule, a very unstable (heat of formation, 859.0 kJ $mol^{-1}$) species is obtained. This does not happen with the N1–H tautomer of 7HtpO, with N8 still keeping its $sp^2$ nature surely due to the influence of the neighbouring carbonyl group.

Fig. 4 displays the calculated net charges on the atoms of the theoretically most stable tautomers of both triazolopyrimidine derivatives as well as those on their anionic forms. The results are very similar to those obtained for the 5,7-dioxo derivative ($H_2tpO_2$)

[2] (obviously, in the portion of the molecules that are comparable), some of the C–C bonds being also quite polar though not as much as in $H_2tpO_2$. According to these data, the most basic positions are N3 or N4, respectively, for the compounds in the molecular or anionic form.

In order to predict the behaviour of a compound as a ligand, we have shown [14] that it is not enough to consider just charge densities and that it is a better approach to consider the molecular orbitals more likely to form bonds with atomic orbitals of metal ions. In Table 4, the contribution of atomic orbitals of N and O atoms to the highest occupied molecular orbitals (including also the LUMO) of 5HtpO and 7HtpO in neutral and anionic forms is indicated. The MO's more likely to combine with metal atomic orbitals are those occupied with higher energy and $\sigma$ symmetry and we can check in Table 4 that the oxygen atom is in all cases the main contributor to these orbitals. Nevertheless, as a difference with $HtpO_2^-$ [2], the endocyclic nitrogen atoms N1, N3 and N4 (the latter in the anionic forms) also make appreciable contributions to these MO, which do not let us to clearly predict the preferred binding sites although we can expect that the oxygen atom is more likely to participate in binding metal ions than in related ligands such as the 5-methyl-7-oxo derivative [15].

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