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FULL PAPER

Silver complexes with triazolopyrimidine ligands containing an exocyclic oxygen atom: X-ray evidence for an unusual tautomeric form

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The crystal structures of the silver complexes $[Ag_2(5HtpO)_2][NO_3]_2$ **1**, $[Ag_2(5HtpO)_2][ClO_4]_2\cdot 2H_2O$ **2** and $\{[Ag(7HtpO)]ClO_4\}_n$ **3**, where the ligands are the triazolopyrimidine derivatives 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), are described. **1** and **2** are binuclear compounds, with two ligands bridging two silver atoms through their nitrogen atoms at positions 3 and 4. The ligand in these compounds is in an unusual tautomeric form with its acidic proton attached to the exocyclic oxygen atom, which influences its geometric and spectroscopic (infrared) properties. On the other hand, the ligand 7HtpO in compound **3** is in its usual tautomeric form and binds two different silver atoms through its nitrogen atoms in positions 1 and 3, building infinite –Ag–7HtpO–Ag–7HtpO– chains.

Introduction

Tautomerism plays an important role in the chemical properties of heterocyclic bases which contain exocyclic electronegative atoms such as oxygen, nitrogen or sulfur. For these compounds, two or more tautomeric forms are conceivable, depending on the position to which the acidic protons are attached. Nevertheless, one of these forms usually is much more stable than the others and, thus, accounts for the vast majority of the molecules present in any given sample. If the exocyclic atom is oxygen or sulfur, the amido (or thioamido) tautomer is usually preferred to the iminophenolic (or iminothiophenolic) form whereas exocyclic nitrogen atoms invariably appear as exocyclic amino groups.

Minority tautomers may, however, influence the chemistry and biochemistry of these compounds. For example, it has been proposed that mispairing of non-complementary bases in the nucleic acids and, thus, mutagenic effects may be caused by the presence of such minority species.[1] This "mispaired" kind of interaction has been observed between two thymine bases, one of them present as the enolic tautomer.[2]

One way to force the formation of unstable tautomers is to displace one acidic hydrogen atom from its "usual" position by a metal atom that is able to bind strongly to that position and, at the same time, keep the medium acid enough so that the "unusual" position becomes protonated.[3] This strategy has led to the stabilization of tautomers of heterocyclic bases with a protonated exocyclic oxygen atom (iminophenolic tautomer). This tautomer has been identified in solution[4] and in the solid state; crystal structures have been solved for 2-hydroxypyridine[5] and a few pyrimidine bases.[6] Likewise, the migration of a proton of the exocyclic amino group to an endocyclic position has been observed for adenine[7] and the displacement from one endocyclic position to another has been observed for 9-methylguanine.[8]

This is not the only way to stabilize unusual tautomers and, for example, the iminophenolic form of a pyrimidine derivative has been found to exist in the solid state stabilized by strong intermolecular interactions that are only possible for that particular tautomer.[9]

The present work follows that by our research group about the interaction of metal ions with triazolopyrimidine ligands,[10] which may be regarded as mimetic compounds of purines. Their reaction with silver(I) usually leads to compounds in which the basic unit comprises two metal atoms bridged by two ligands through the nitrogen atoms in positions 3 and 4 (see, for example, Fig. 1 for the numbering scheme; these positions are equivalent, respectively, to positions 9 and 3 in the biochemical numbering scheme of purines).[11]

The ligands chosen for this work are 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), the latter being a mimic for the also isomeric hypoxanthine. The most stable tautomer is that with the acidic proton attached to N(4), according to X-ray data and also to theoretical calculations.[12] If a silver atom is strongly bound to this position and the medium is acidic enough to keep the ligand in neutral form, an unusual tautomeric form could be generated. This has been achieved for 5HtpO, for which the iminophenolic form has been found in two silver compounds, but not for 7HtpO for reasons that are clear from the crystal structures of the compounds, described below.

Results and discussion

Description of the structures

Selected distances and angles for the three compounds are displayed in Table 1. The molecular structures of compounds $[Ag_2(5HtpO)_2][NO_3]_2$ **1** and $[Ag_2(5HtpO)_2][ClO_4]_2\cdot 2H_2O$ **2** are shown in Figs. 1 and 2. Both consist in dinuclear centrosymmetric units with two silver atoms bridged by two 5HtpO ligands through the nitrogen atoms at positions 3 and 4. Nitrate (**1**) or perchlorate (**2**) ions balance the charge and non-coordinated water molecules (**2**) complete the crystal structures.

Such dinuclear structures are common for silver complexes

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Table 1 Selected distances (Å) and angles (deg) for compounds **1**–**3**

	1	**2**	**3**
Ag–Ag	3.1393(11)	3.0559(13)	—
Ag–N(3)	2.177(5)	2.144(4)	2.226(8)
Ag–N(1,4)	2.190(5)	2.167(4)	2.262(7)
Ag–O(7)	—	—	2.760(7)
Ag–O(anion)	2.603(6)	2.997(12)	2.772(10)
	2.763(7)		2.78(2)
C(5,7)–O(5,7)	1.301(8)	1.304(6)	1.213(9)
N(4)–C(5)	1.338(8)	1.329(7)	1.383(12)
N(3)–Ag–N(1,4)	160.5(2)	162.54(16)	156.1(3)
N(4)–C(3A)–N(8)	122.1(6)	122.4(4)	119.9(8)
C(3A)–N(4)–C(5)	116.8(5)	116.6(4)	117.3(8)
N(4)–C(5)–O(5)	115.4(5)	114.4(4)	—
N(4)–C(5)–C(6)	121.5(6)	122.3(4)	122.8(8)

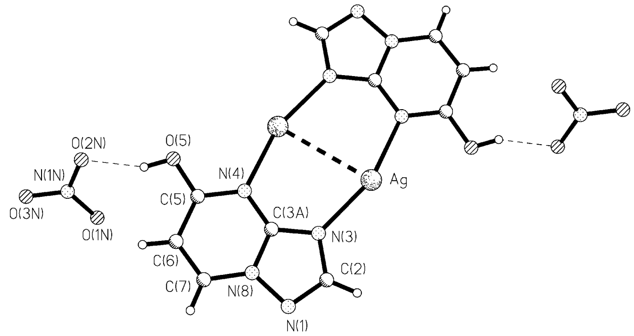

Fig. 1 View of the molecular structure of compound **1**.

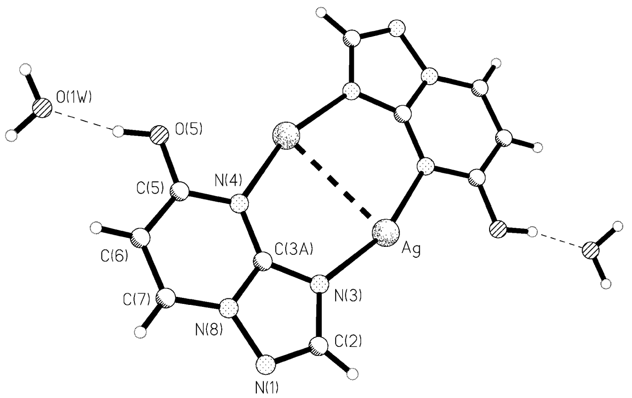

Fig. 2 View of the molecular structure of compound **2**.

of triazolopyrimidine ligands[11] and one example has also been described for protonated adenine.[13] The Ag–Ag distance (Table 1) is within the range found in these references. Bridging binding through N(3) and N(4) atoms of triazolopyrimidine derivatives has also been observed for Cu(I),[14] Pd(II),[15] Pt(II)[16] and heterometallic Pt(II)–Pd(II) compounds.[17]

The most outstanding feature of these structures is, however, the tautomeric form of the ligand 5HtpO. The usual position for acidic protons in heterocycles with endocyclic nitrogen atoms and exocyclic oxygen atoms is bound to the former and the acidic proton of 5HtpO is placed at N(4) in the crystal structure of the "free" ligand.[12] Nevertheless, the strength of the Ag–N(4) bond makes the dimer stable (or inert) enough to withstand the strongly acidic medium. The proton has to move to another position and the other endocyclic nitrogen atom, N(1), is ruled out because the corresponding tautomer would be non-aromatic and rather unstable according to theoretical calculations.[12] The only choice is, then, O(5), generating the unusual iminophenolic tautomer. As far as we know, these are the first examples of crystal structures including a purine-like ligand with an exocyclic OH group.

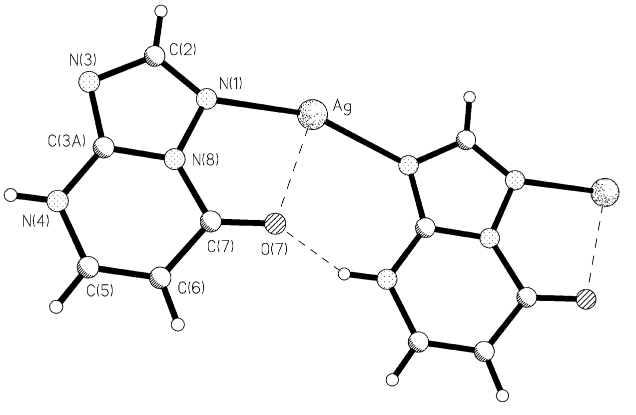

Fig. 3 View of two monomeric units of the polymeric structure of compound **3**.

The presence of the proton attached to O(5), clearly located in the ΔF maps, is confirmed by the very strong hydrogen bonds in which it is involved, towards a nitrate ion in **1** and towards a water molecule in **2**, the corresponding O···O distances being 2.588(8) and 2.514(6) Å respectively. In any hydrogen bond, it must be assumed that a certain proportion of D···H–A is in equilibrium with D–H···A but, in our case, the percentage of O(5)···HNO_3 or O(5)···H_3O^+ appears to be negligible, since the corresponding N–O distance in the nitrate anion of **1** is almost equal to the N–O distance for the oxygen that interacts with the silver atom; and the water molecule in **2** forms, as a donor, two rather long hydrogen bonds with perchlorate ions (O···O distances, 2.924(6) and 2.837(9) Å), much weaker than should be expected for a H_3O^+ ion.

The change in the tautomeric form induces important changes in the geometry of the ligand. As expected, the C(5)–O(5) bond is considerably longer than in the N(4)–H tautomer (1.236(3) Å for free 5HtpO),[12] though the distance is still shorter than the expected one for a typical single bond; this COH group may be regarded perhaps as a "protonated carbonyl" instead of an "hydroxyl". Other geometric changes are the shortening of the N(4)–C(5) bond (1.370(3) Å for free 5HtpO)[12] and the changes in the angles in which N(4) is involved, with the opening of N(4)–C(3A)–N(8) and N(4)–C(5)–C(6) (118.8(2) and 116.3(2)° respectively for free 5HtpO)[12] and the closing of C(3A)–N(4)–C(5) and N(4)–C(5)–O(5) (122.6(2) and 119.2(2)° respectively for free 5HtpO).[12]

The N(4)–Ag–N(3) angle deviates appreciably from linearity due to the presence of the other metal atom and to the steric requirements of the donor orbitals of the nitrogen atoms. Apart from the two strong Ag–N bonds and the interaction with the other Ag atom, weaker links are present with oxygen atoms of the anions. These interactions, together with the above mentioned hydrogen bonds, link the dimeric units to one another.

On the other hand, the structure of compound $\{[Ag(7HtpO)]ClO_4\}_n$ **3**, which has been obtained under the same experimental conditions using the ligand 7HtpO, is rather different. In this case, the acidic medium is able to prevent the silver atom from binding to N(4). Instead, it binds to N(1) of another 7HtpO molecule generating in this way polymeric chains along the *a* axis (see Fig. 3). The ligand analogous to 7HtpO with a methyl group at position 5 has been found to bind silver in the same way when it is in neutral form whereas it combines the formation of N(3)–N(4) dimers like those in **1** and **2** with polymers through N(1) like **3** when it is in anionic form.[18]

The coordination to N(1) is reinforced by the weak chelating interaction of the metal atom with O(7) and the presence of the proton attached to N(4) stabilizes the polymer by means of the hydrogen bond formed with the carbonyl oxygen of the adjacent monomeric unit (distance N(4)···O(7), 2.753(10) Å).

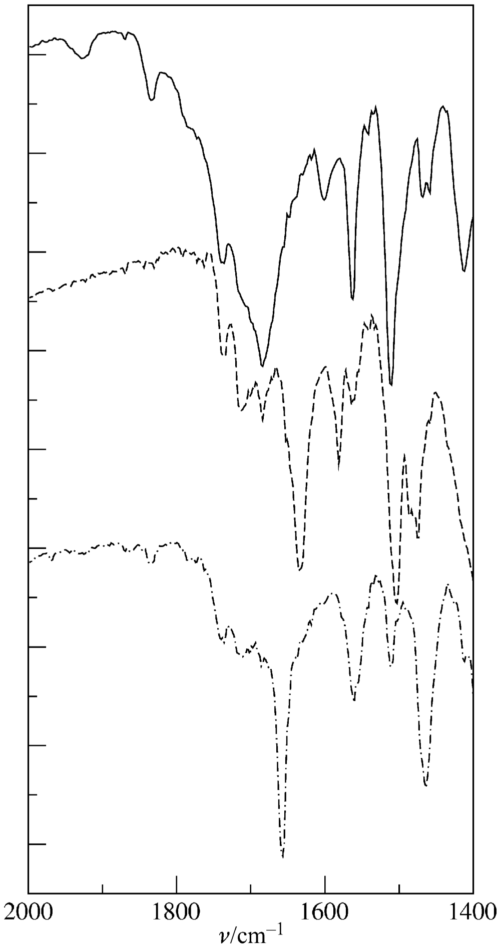

Fig. 4 2000–1400 cm^{-1} region of the infrared spectra of 5HtpO (———), compound **1** (-----) and compound **2** (-·-·-·-).

Obviously, these two effects are not possible if the oxygen atom is in position 5, which easily explains the structural differences with **1** and **2**.

The geometry around the silver atom is more deviated from linearity than in compounds **1** and **2**, which may be attributable to the geometric demands of the N(4)–H···O(7) hydrogen bond. The geometric parameters within the ligand do not show any significant change with respect to free 7HtpO,[12] bond distance and angle changes being below 0.02 Å and 1.5° respectively. Consecutive 7HtpO ligands in the polymer are parallel, the distance between the corresponding average planes being 1.03 Å.

Infrared spectroscopy

The 1400–1700 cm^{-1} region of the infrared spectra of compounds **1** and **2** (see Fig. 4) is very different to that of other analogous compounds, probably reflecting the tautomeric form of the ligand. Heterocycles with an exocyclic carbonyl oxygen atom invariably present one (or more than one) strong, usually broad, band in the 1600–1750 cm^{-1} range, attributable to ν(C=O), the exact position of it depending on whether the compound is in its neutral, cationic or anionic form, the possible coordination to a metal atom and the possible hydrogen bonds with neighbouring species. This band has disappeared (or become very weak) in the spectra of **1** and **2** and, in its place, an acute band of medium intensity appears at 1635 (**1**) or 1657 (**2**) cm^{-1}, with a number of accompanying low intensity sharp bands at higher wavenumber (up to *ca.* 1750 cm^{-1}). On the other hand, the spectrum of **3** displays the usual features, with two strong bands, a broad one at 1682 cm^{-1} and a sharp one at 1728 cm^{-1}.

The presence of the hydrogen-bond associated N–H group in the "free" ligand is reflected in its IR spectrum as a number of bands in the 3100–2700 cm^{-1} region; for the O–H group in **1** and **2**, the corresponding bands are considerably weaker and more spread out (3200–2400 cm^{-1}). Apart from this, the most intense bands in the spectra are those due to the stretching vibrations within the anions. At least two bands are present for NO_3^- and three for ClO_4^-, around 1370 and 1100 cm^{-1} respectively, showing the lack of symmetry of the anions in the structure.

Experimental

Synthesis of the compounds

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) were synthesized as indicated in a previous work.[12] Silver salts, other reagents and solvents were obtained from standard commercial suppliers.

Each of the three compounds described in this work was synthesized by mixing two solutions, 10 ml each, one containing 2 mmol of the ligand (5HtpO or 7HtpO) and the other 2 mmol of the appropriate silver salt ($AgNO_3$ or $AgClO_4$). The solvent was 5 M HNO_3 or 5 M $HClO_4$. For the solutions containing 5HtpO and silver nitrate or perchlorate, colourless crystals of the product (**1** or **2**) appeared after one week. For the solution containing 7HtpO and silver perchlorate, a greyish precipitate immediately appeared which was filtered off, showing an unclear analysis. From the mother liquor, a very small amount of colourless crystals of the final product (**3**) was obtained. $[Ag_2(5HtpO)_2][NO_3]_2$, **1**: C, 19.4; H, 1.3; N, 22.7%. Calculated for $C_{10}H_8Ag_2N_{10}O_8$: C, 19.63; H, 1.32; N, 22.89%. $[Ag_2(5HtpO)_2][ClO_4]_2\cdot 2H_2O$, **2**: C, 16.4; H, 1.7; N, 15.3%. Calculated for $C_{10}H_{12}Ag_2Cl_2N_8O_{12}$: C, 16.62; H, 1.67; N, 15.50%. $\{[Ag(7HtpO)]ClO_4\}_n$, **3**: C, 17.5; H, 1.2; N, 16.2%. Calculated for $C_5H_4AgClN_4O_5$: C, 17.49; H, 1.17; N, 16.31%.

Instrumentation

Microanalyses of C, H, and N were performed in a Fisons Instruments EA-1008 analyser at the Centre of Scientific Instrumentation of the University of Granada. IR spectra were obtained in an FT MIDAC Prospect 1 spectrophotometer with samples dispersed in KBr pellets.

Crystallography

X-Ray work was carried out at room temperature on a Siemens P4 (**1** and **3**) or Nonius KappaCCD (**2**) diffractometer with Mo-Kα radiation. Data collections were performed in 2θ–ω scan mode for **1** and **3**. The number of independent reflections collected were, after averaging, 2227, 2580 and 1716 for **1**, **2** and **3** respectively. Data were corrected for Lorentz and polarization effects and analytically (integration) for absorption for compound **3**. The structures were solved by standard Patterson methods and refined by full-matrix least squares using the SHELXL 97[19] program. All non-hydrogen atoms were refined anisotropically. Hydrogen atoms of the organic residues were introduced in their ideal positions; those of water molecules and O5–H were clearly found in the ΔF maps and refined with fixed O–H distance (0.86 Å). An isotropic thermal parameter was applied to all hydrogen atoms, 1.2 times those of their parent atoms. Crystal data are summarized in Table 2.

CCDC reference numbers 157473–157475.

See http://www.rsc.org/suppdata/dt/b1/b100869m/ for crystallographic data in CIF or other electronic format.

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Table 2 Crystal and refinement data for compounds **1**, **2** and **3**

	1	**2**	**3**
Chemical formula	$C_{10}H_8Ag_2N_{10}O_8$	$C_{10}H_{12}Ag_2Cl_2N_8O_{12}$	$C_5H_4AgClN_4O_5$
Formula weight	612.00	722.92	343.44
Crystal system	Monoclinic	Triclinic	Monoclinic
Space group	$P2_1/c$	$P\bar{1}$	Cc
a/Å	5.3881(7)	5.6419(11)	6.6046(10)
b/Å	18.245(2)	8.6644(17)	14.487(2)
c/Å	8.7100(8)	11.136(2)	9.9594(12)
α/°	—	74.07(3)	—
β/°	97.946(9)	81.49(3)	93.379(10)
γ/°	—	76.53(3)	—
V/Å^3	848.04(17)	507.02(17)	951.3(2)
Z	2	1	4
μ/mm^{-1}	2.381	2.277	2.413
R_1 (F) ($F_o^2 > 2\sigma(F_o^2)$)	0.0617	0.0499	0.0450
R_w (F_o^2) (all data)	0.1759	0.1335	0.1388

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