Quantum-chemical interpretation of regioselective coordination in the series of 2-aminoazole—metal complexes

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Relative thermodynamic stabilities and competitive bonding (regioselective coordination) of Pearson acids MCl_2 (hard $BeCl_2$, intermediate $ZnCl_2$, and soft $HgCl_2$) with aminoheterocycles L (2-aminooxazole, 2-aminothiazole, and 2-aminoimidazole) have been calculated by the quantum-chemical MNDO method. It follows from the results of the calculation that in tetrahedral $MCl_2 \cdot 2L$ complexes the coordination bond is formed by the endocyclic pyridine-type nitrogen atom independent of the type of ligands.

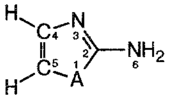
Key words: 2-aminoazoles; Pearson acids; complexes; regioselective coordination; quantum-chemical calculation; thermodynamic stability.

Metal complexes based on derivatives of five- and six-membered nitrogen-containing heterocycles with the NH_2 group are of continuing interest[1—6] due to the ambidentate character of aminoheterocycles and, therefore, their possibility to bind metal atoms with various nucleophilic centers of the ligand systems considered (regioselective competitive coordination).[7—9] In addition, it is important to establish the type of localization of the coordination bond in complexes of aminoheterocycles for understanding the specific character of reactions of metal ions with biologically significant substances, in particular, with nucleotides and nucleosides.[2,10,11]

Quantum-chemical calculations were performed many times to rationalize the regioselective coordination in the series of aminoheterocycles. However, when quantum-chemical methods were used, conclusions about the localization of the coordination bond in complexes were drawn only on the basis of the electron distribution in noncoordinated molecules of aminoheterocycles and, therefore, were often ambiguous (see, *e.g.*, Ref. 12).

Therefore, in the present work, the regioselective coordination of aminoheterocycles has been estimated by the quantum-chemical MNDO method with account of thermodynamic stabilities of coordination compounds. 2-Aminoazoles have been chosen as ligands (L) in these metal complexes: 2-aminooxazole (**1**), 2-aminothiazole (**2**), and 2-aminoimidazole (**3**). The choice of 2-aminoazoles was dictated by different basicities of L, which are determined by the nature of heteroatoms (A) and which increase in the series **1** < **2** < **3**. Metal salts (MCl_2) used in the calculation are represented by hard ($BeCl_2$), intermediate ($ZnCl_2$), and soft ($HgCl_2$) Pearson acids.[7—9,13] These MCl_2 compounds have been selected due to their different hard-soft properties[7—9] and the ability to form complexes of the same composition ($MCl_2 \cdot 2L$) and similar stereochemistry (predominantly tetrahedrons) with 2-aminoazoles.[1,3,14]

Calculations have been performed by the quantum-chemical MNDO method[15] using the MOPAC program.[16] The molecular geometry has been completely optimized, and the *ab initio* parametrization of the following atoms has been used: H,[15] C,[15] N,[15] S,[17] Cl,[18] Be,[19] Zn,[20] and Hg.[21]



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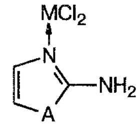

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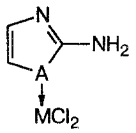

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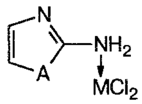

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A = O (**1**), S (**2**), NH (**3**)

When the regioselective coordination in 2-aminoazole—metal complexes **1—3** is considered, three possible types of their binding with aforementioned metal chlorides (MCl_2) should be taken into account[1—3]: with the "pyridine" N atom of the heterocycle (**4**), with the second endocyclic heteroatom as a donor center (**5**), and with the exocyclic nucleophilic center, the N atom

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Table 1. Calculated charges on atoms of molecules **1**—**3**

A	Atom	MNDO	MINDO/3	PM3
O	A	−0.11	−0.39	−0.09
	C(2)	0.12	0.52	−0.03
	N(3)	−0.24	−0.30	−0.18
	C(4)	−0.07	−0.02	−0.12
	C(5)	−0.05	−0.02	−0.11
	N(6)	−0.18	−0.21	0.14
S	A	0.34	−0.26	0.27
	C(2)	−0.07	0.41	−0.22
	N(3)	−0.24	−0.26	−0.15
	C(4)	0.01	0.06	−0.06
	C(5)	−0.32	0.03	−0.36
	N(6)	−0.21	−0.18	0.14
NH	A	−0.20	−0.04	0.35
	C(2)	0.10	0.28	−0.27
	N(3)	−0.24	−0.27	−0.14
	C(4)	−0.06	0.04	−0.12
	C(5)	−0.06	−0.08	−0.34
	N(6)	−0.21	−0.19	0.07

of the amino group, (**6**). However, the analysis of the literature data testifies that aminoazoles are mainly monodentate ligands in which the endocyclic N atom of the pyridine type acts as a donor center.[1—3] There are exceptions from this rule in the case of aminoazoles containing several "pyridine" N atoms in which azole ligands can act as bidentate ones and perform the function of bridges.[22,23]

It is known (see, *e.g.*, Refs. 12 and 24) that the charge on the donor atom is one of the possible factors responsible for the type of coordination in metal complexes of polydentate ligand systems. The atom with the maximum negative charge is considered to be the predominant center that forms the coordination bond. Taking into account this consideration and the possibility of realization of structures **4**—**6**, we have calculated charge distributions in molecules **1**—**3** by the MNDO, MINDO/3, and PM3 methods (Table 1).

As in the case of the Hückel (Ref. 24) and INDO (Ref. 12) methods, the results obtained in the MNDO approximation testify that a large negative charge is localized on the endocyclic "pyridine" N atom of the heterocycle in all of the three ligands (see Table 1). However, the difference in charges of endo- and exocyclic donor N atoms is not high enough to use it for the unambiguous solution of the question concerning the choice between complexes **4** and **6**. According to the calculations (see Table 1), the O (MINDO/3 and INDO[12]), S (MINDO/3), and exocyclic N (MNDO) atoms also possess considerable negative charges.

However, the charge of the S atom calculated by the MNDO and PM3 methods is positive in a molecule of 2-aminothiazole **2**, which should exclude the possibility of the participation of this nucleophilic center in coordination with a metal atom. The ambiguous behavior of the S atom with respect to the coordination bond follows from the experimental data as well: in the majority of cases,[7—9] this nucleophilic center does not possess donor properties; however, complex compounds of thiophene and its derivatives are known in which S → M bonding is observed.[25,26]

Taking into account the aforementioned contradictory results, let us analyze the heats of formation and stabilities of complexes of the type of adducts **4**—**6** (Tables 2 and 3). As can be seen from Table 2, associates $MCl_2 \cdot 2L$ with the coordination with the "pyridine" N atom of the ligands are more thermodynamically stable independently of the nature of 2-aminoazole. This conclusion agrees with the experimental data obtained for complexes of 2-aminoazoles by various physical methods, including X-ray diffraction analysis.[3] It is also seen from Table 2 that, according to the HSAB (hard and soft acids and bases) principle,[7—9,13] the stability of complexes of all ligands considered drops in the series Be > Zn > Hg, *i.e.*, as the hardness of the metal atom bonded to the hardest donor center (the pyridine type N atom) of ligand molecules **1**—**3** decreases, the calculated enthalpy of formation decreases in the series of type **4** complexes.

The use of the quantum-chemical method described above for the estimation of the relative stability of complexes makes it possible to establish the composition of the most stable adducts of types **4**—**6**. Therefore, the calculated energies of formation of $MCl_2 \cdot 2L$ and $MCl_2 \cdot L$ (values in parentheses) complexes of isolated ligands and the corresponding Pearson acids are compared in Table 3. It can be seen that $MCl_2 \cdot 2L$ associates corresponding to form **4** are more stable than adducts $MCl_2 \cdot L$. The exceptions are related to the complex formation between $ZnCl_2$ and **2** ($ZnCl_2 \cdot L$ is somewhat more stable than $ZnCl_2 \cdot 2L$) and to the thermodynamically unfavorable formation of an adduct of $HgCl_2$ with **3**.

Table 2. Enthalpies of formation (kcal mol^{-1}) of complexes **4**—**6** calculated by the MNDO method

Ligand	Type of complex	Metal		
		Be	Zn	Hg
1	**4**	−157.0	−80.3	−41.2
	5	−110.4	*	*
	6	−139.6	−66.7	−33.6
2	**4**	−74.8	2.5	−2.0
	5	−39.9	*	*
	6	−61.8	10.8	0
3	**4**	−79.4	−2.6	36.5
	5	−34.9	*	*
	6	−63.7	10.5	44.9

* An attempt to localize the structure on the potential energy surface was unsuccessful.

Table 3. Energies of formation (kcal mol^{-1}) of $MCl_2 \cdot 2L$ and $MCl_2 \cdot L$ (in parentheses) complexes from MCl_2 and 2L or L, respectively, calculated by the MNDO method

Ligand	Type of complex	Metal		
		Be	Zn	Hg
1	**4**	−49.4 (−32.1)	−13.8 (−11.6)	13.5 (2.5)
	5	−2.8 (−6.1)	*	*
	6	−32.0 (−18.8)	−0.2 (−2.0)	20.9 (8.9)
2	**4**	−44.2 (−30.3)	−8.0 (−9.1)	19.0 (5.3)
	5	−9.3 (−5.2)	*	*
	6	−31.2 (−20.3)	0.3 (−3.3)	20.9 (7.3)
3	**4**	−50.2 (−33.1)	−14.6 (−12.4)	12.8 (2.0)
	5	−5.7 (−10.2)	*	*
	6	−34.5 (−21.8)	−1.5 (−3.9)	21.2 (7.1)

* An attempt to localize the structure on the potential energy surface was unsuccessful.

It follows from the data in Tables 2 and 3 that complex compounds of 2-aminooxazole, $MCl_2 \cdot 2L$, are the most stable associates of type **4** for the same Pearson acid. This result does not allow one to relate directly the stability of the complexes considered and basicity of their ligands, because **1** is the least basic. At the same time, the quantum-chemical MNDO method makes it possible to estimate rather correctly the relative thermodynamic stability and regioselective coordination in the series of adducts of aminoheterocycles.

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