

# Iron(III) complexation by hydroxyurea in acidic aqueous perchlorate solution

---

**Bedrica, A.; Biruš, M.; Kujundžić, N.; Pribanić, M.**

*Source / Izvornik:* **Croatica Chemica Acta, 1988, 61, 21 - 31**

**Journal article, Published version**

**Rad u časopisu, Objavljena verzija rada (izdavačev PDF)**

*Permanent link / Trajna poveznica:* <https://um.nsk.hr/um:nbn:hr:163:866907>

*Rights / Prava:* [In copyright](#)/[Zaštićeno autorskim pravom.](#)

*Download date / Datum preuzimanja:* **2025-03-13**



*Repository / Repozitorij:*

[Repository of Faculty of Pharmacy and Biochemistry University of Zagreb](#)



CCA-1776

YU ISSN 0011-1643

UDC 547.72

Original Scientific Paper

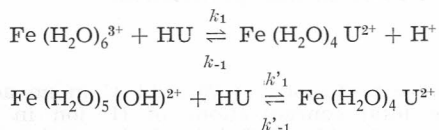
## Iron(III) Complexation by Hydroxyurea in Acidic Aqueous Perchlorate Solution\*

A. Bedrica, M. Biruš, N. Kujundžić, and M. Pribanić

Department of Chemistry, Faculty of Pharmacy and Biochemistry, University of Zagreb, Zagreb, Croatia, Yugoslavia

Received October 19, 1987

Equilibrium and kinetic studies were performed to investigate the complexation of aqueous high spin iron(III) by hydroxyurea  $\text{H}_2\text{NC(O)NH(OH)}$  in acidic solutions at  $25^\circ\text{C}$  and  $I = 2.0 \text{ mol dm}^{-3}$  (maintained by  $\text{NaClO}_4$ ). Complexation has been interpreted in terms of coordination of the N—O oxygen atom and the  $\text{NH}_2$  nitrogen atom of the ligand to the iron(III) ion with concomitant loss of a proton yielding the complex of the molar ratio 1 : 1. The equilibrium quotient for the formation of mono(hydroxyureato)iron (III) complex is found to be  $K_1 = 1.4$ . The kinetic results suggest a parallel path mechanism involving substitution on  $\text{Fe}(\text{H}_2\text{O})_6^{3+}$  and  $\text{Fe}(\text{H}_2\text{O})_5\text{OH}^{2+}$  by the hydroxyurea, HU:



The formation of the complex occurs by the rate constants  $k_1 = 16.8 \text{ M}^{-1} \text{ s}^{-1}$  and  $k'_1 = 5450 \text{ M}^{-1} \text{ s}^{-1}$ . The analogous rate constants for the reverse hydrolysis reactions were obtained as  $k_{-1} = 11.8 \text{ M}^{-1} \text{ s}^{-1}$  and  $k_{-1}' = 6.3 \text{ s}^{-1}$ . The results are compared with kinetic data previously reported for the different mono(hydroxamato)iron(III) complexes.

### INTRODUCTION

Hydroxamic acids,  $\text{R}_1\text{—C(O)N(OH)—R}_2$ , have a wide variety of application in industry, pharmacy and chemistry. They have been used as flotation reagents in extractive metallurgy, inhibitors for copper corrosion, food additives, therapeutic agents and analytical reagents. They are biologically active as antibiotics, growth factors, tumor inhibitors, pigments and chelating agents.<sup>1-3</sup>

The most important feature of hydroxamic acids is their ability of iron(III) sequestration which classifies them in a group of compounds commonly called siderophores which are intimately associated with iron transport in living organisms.<sup>4</sup> The interaction between iron(III) and synthetic,

\* Taken, in part, from the Master Thesis of A. B.

as well as naturally occurring, hydroxamic acids appears to be a very important bioinorganic reaction currently stirring wide interest.<sup>5-12</sup>

Hydroxyurea, ( $\text{H}_2\text{N}-\text{CONHOH} = \text{HU}$ ), is one of hydroxamic acids which shows antitumor activity and is introduced into cancer therapy.<sup>13</sup> It has been shown that HU inhibits enzyme ribonucleotide reductase.<sup>14</sup> Since some of ribonucleotide reductase contain non-heme iron(III), the complex formation reaction of HU with iron(III) may be of importance for an understanding of antitumor activity, as well as the HU side effects.

#### EXPERIMENTAL

##### Materials

Iron(III) perchlorate was prepared by dissolving freshly obtained iron(III) hydroxide in concentrated (70%) perchloric acid and recrystallized from dilute perchloric acid. A stock solution of iron(III) perchlorate (0.15 M in 0.1 M  $\text{HClO}_4$ ) was prepared and standardized as described previously.<sup>6</sup>

The hydrogen ion concentration in the stock solution was determined by passing an aliquot through a Dowex cation exchange resin in the acid form. The  $\text{H}^+$  ion concentration was determined by titration with NaOH and corrections were made for the iron(III) present.

Sodium perchlorate was prepared by neutralization of dry  $\text{Na}_2\text{CO}_3$  by concentrated  $\text{HClO}_4$ , and was recrystallized from water. A stock solution of  $\text{NaClO}_4$  was used to maintain constant ionic strength.

Hydroxyurea was purchased from Sigma Chem. Co. and its reagent solution was prepared by dissolving the solid immediately before the measurements were made.

All solutions were prepared using water which was double distilled from alkaline  $\text{KMnO}_4$  in an all-glass apparatus. All other chemicals were of analytical grade and were used without further purification.

##### Methods

All experiments were performed at  $25 \pm 0.1^\circ\text{C}$  in an aqueous solution of 2.00 M ionic strength. The total concentrations of  $\text{H}^+$  ion in the experiments were calculated by summation of added  $\text{HClO}_4$  and the proton released from the iron species present in solutions.

The spectrophotometric and kinetic measurements were performed on a Unicam SP 800 spectrophotometer, Durrum D-110 stopped-flow spectrophotometer and a Dionex stopped-flow apparatus linked with a Harrick rapid-scan monochromator, all equipped with a thermostated cell compartment. A modified version of an originally published non-linear least square procedure was applied on a UNIVAC 1100 computer at the University Computing center, Zagreb, for the data reduction analysis.<sup>15</sup>

The pseudo-first order conditions were ensured by holding one reactant in excess over the other.

#### RESULTS AND DISCUSSION

By mixing the iron(III) solution with hydroxyurea, a blue colored complex is formed which quickly decomposes. Therefore, the rapid-scan stopped-flow technique was used to record the spectra of mono(hydroxyureato)-iron(III) complex (Figure 1). Essentially the same spectra ( $\lambda_{\text{max}} = 560 \text{ nm}$ ) were recorded both in molar excess of iron(III) over the ligand and *vice versa*. This suggests that in solution of  $[\text{H}^+] > 0.01$  in the first stage a complex of 1:1 iron(III):ligand is formed. This is confirmed by the method of continuous variation applied to the iron(III)-hydroxyurea system at  $\text{pH} = 2.0$ . The plot of the absorbance *vs.* iron(III) fraction, X, where  $\text{X} = [\text{Fe(III)}]/$

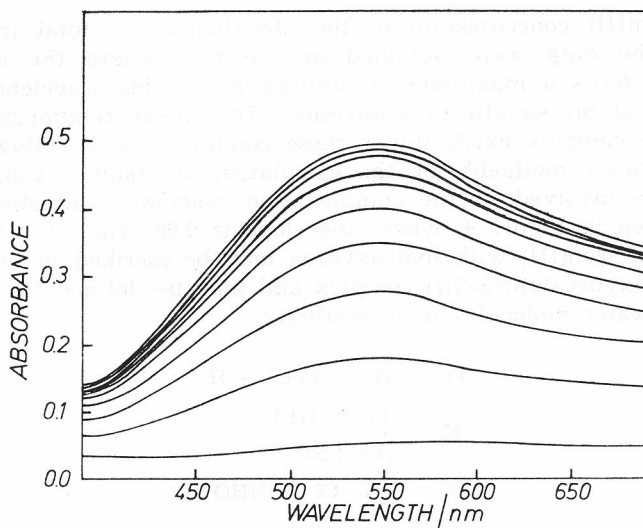


Figure 1. Visible spectra of mono(hydroxyureato)iron(III) complex during the formation of the complex. All 11 spectra were taken in 0.3 s (each spectrum after 0.03 s). Conditions:  $[\text{Fe(III)}]_{\text{tot}} = 5.65 \times 10^{-4}$ ,  $[\text{HU}]_{\text{tot}} = 7.5 \times 10^{-3}$ ,  $[\text{HClO}_4] = 0.4$ ,  $I = 2.0$  M ( $\text{HClO}_4/\text{NaClO}_4$ ).

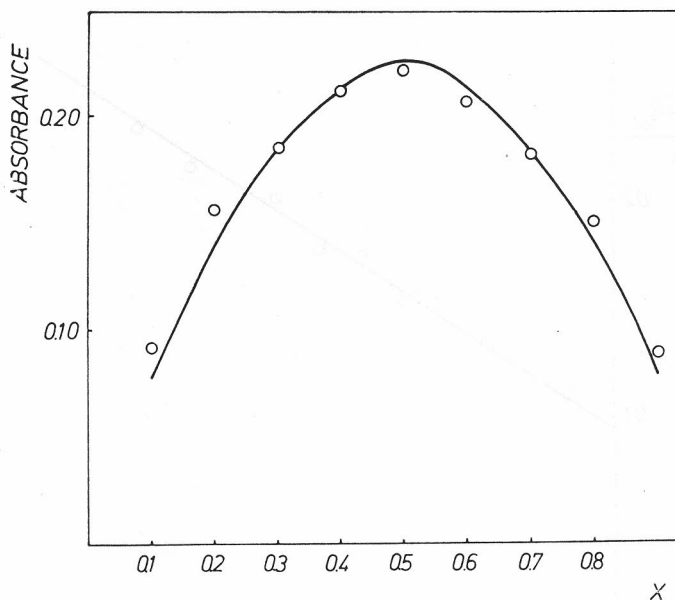


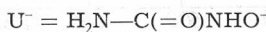
Figure 2. Continuous variation curve at  $\text{pH} = 2.0$ ,  $I = 2.0$  M ( $\text{HClO}_4/\text{NaClO}_4$ ),  $[\text{Fe(III)}]_{\text{tot}} + [\text{HU}]_{\text{tot}} = 1 \times 10^{-2}$  M. The solid line represents the theoretical curve calculated using the values for  $K_1$  and  $\varepsilon_1$  listed in the Table.  $t = 25^\circ\text{C}$ ,  $\lambda = 560$  nm.

$/([\text{Fe(III)}] + [\text{HU}])$ , showed a maximum at 0.5 indicating  $\text{Fe(III)}:\text{HU} = 1:1$  complex stoichiometry (Figure 2). Figure 3 shows the plot of the ratio of

the total iron(III) concentration to the absorbance, *vs.* total iron(III) concentration. The data were obtained at 560 nm, where the spectrum of the complex shows a maximum of absorption. At this wavelength iron(III) ions do not exhibit significant absorption. The linear relationship confirms that only one complex exists under these conditions as it follows from the Benesi-Hildebrand method<sup>16</sup> for the calculation of stability constants. That one H<sup>+</sup> ion is involved in the complexation reaction is illustrated by the Hill plot shown in Figure 4, where the slope is 0.98. Thus, the first step in the reaction of iron(III) with hydroxyurea may be ascribed to the formation of mono(hydroxyureato)iron(III) complex and may be defined by equation (1) (coordinated water molecules were omitted):



$$K_1 = \frac{[\text{FeU}^{2+}][\text{H}^+]}{[\text{Fe}^{3+}][\text{HU}]} \quad (2)$$



Therefore, under the conditions studied the formation of other Fe(III)-hydroxyurea complexes, such as the bis(hydroxyureato)iron(III) complex, have not been recorded, at least, not to a measurable extent.

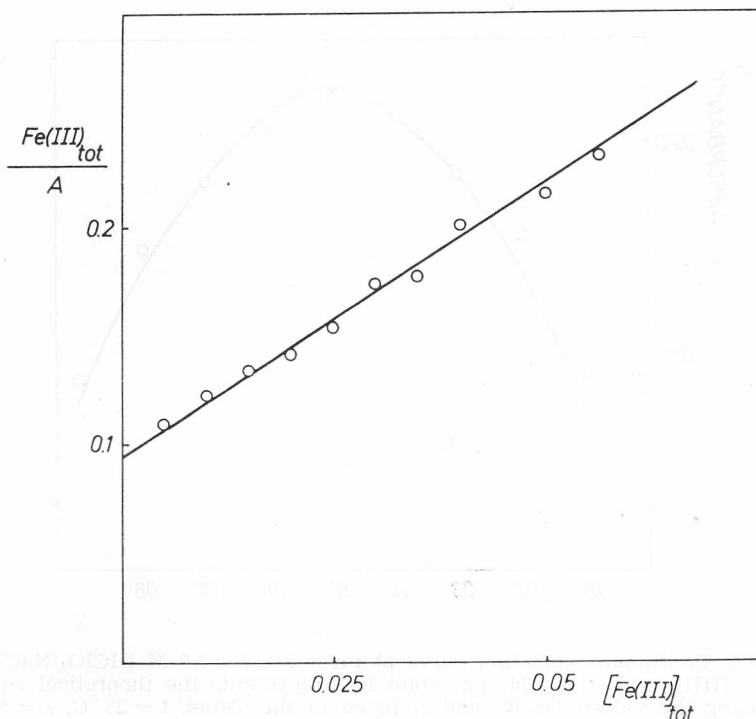


Figure 3. The ratio of total iron(III) concentration to absorbance *vs.* total iron(III) concentration at 560 nm. Conditions: [HU] =  $1 \times 10^{-3}$ , [HClO<sub>4</sub>] =  $1 \times 10^{-2}$ , I = 2.0 M (HClO<sub>4</sub>/NaClO<sub>4</sub>), 25 °C.

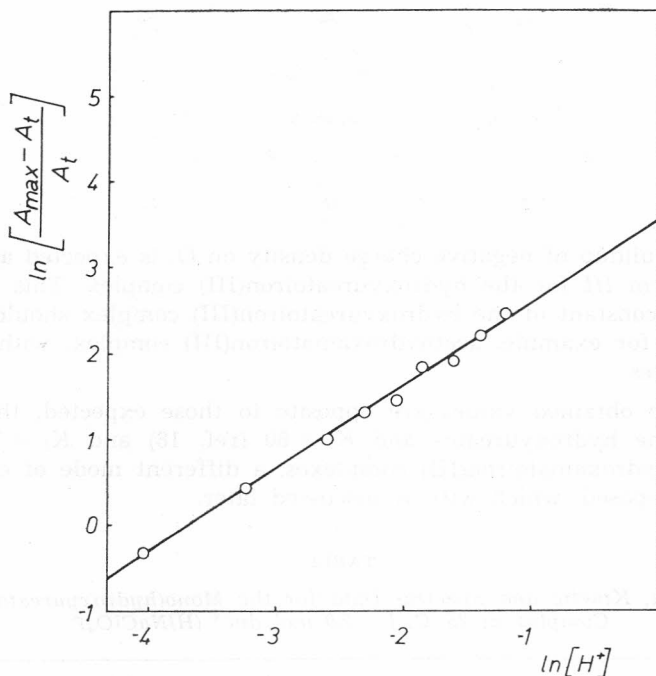


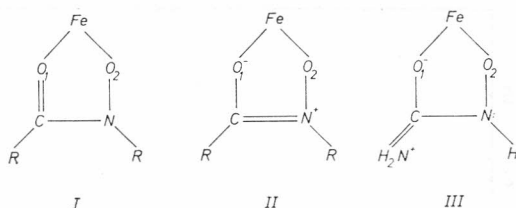
Figure 4. Determination of the number of hydrogen ions involved in the equilibrium. Conditions:  $[\text{Fe(III)}]_{\text{tot}} = 2 \times 10^{-2}$ ,  $[\text{HU}]_{\text{tot}} = 1 \times 10^{-3}$ ,  $I = 2.0 \text{ M}$  ( $\text{NaClO}_4/\text{HClO}_4$ ),  $25^\circ\text{C}$ . Molar absorptivity used in calculation of  $A_{\text{max}}$  is obtained from the plot depicted in Figure 3.

The absorbance data from Figures 1—4 were treated all together using a non-linear least square procedure to fit the function

$$A(\lambda) = \varepsilon_i(\lambda) c_i \quad (3)$$

where  $A$  is the absorbance at  $\lambda = 560 \text{ nm}$ , and  $c_i$  and  $\varepsilon_i$  are concentrations and molar absorptivities at  $560 \text{ nm}$  of each species present in the solutions. Concentrations  $c_i$  are dependent on the experimental total concentrations of iron(III), hydroxyurea, proton, and refined value of  $K_1$ . Since the molar absorptivities of non-chelated iron(III) species, HU and proton at  $560 \text{ nm}$  are negligible, only the molar absorption coefficient of the mono(hydroxyureato)iron(III) complex and  $K_1$  had to be refined during the calculations. The calculated values of  $K_1$  and  $\varepsilon_1$  are given in the Table.

The influence of the electron donor-acceptor ability of the —C and —N substituent of the hydroxamate functionality on the stability of mono(hydroxamato)iron(III) complexes has been thoroughly discussed by Crumbliss *et al.*<sup>5,9,11</sup> They found that increasing inductive electron donor strength of  $R_2$ , for example, when  $R_2 = \text{CH}_3$ , enhanced the relative contribution of resonance form *II* by delocalization of the N atom lone pair of electrons into the carbonyl functionality and thereby increased the negative charge density on  $O_1$ , which would be expected to enhance the iron(III)—carbonyl oxygen bond strength



(Fe—O<sub>1</sub>). A buildup of negative charge density on O<sub>1</sub> is expected also through resonance form *III* for the hydroxyureatoiron(III) complex. This means that the stability constant of the hydroxyureatoiron(III) complex should be higher than that of for example, acethydroxamatoiron(III) complex, with R<sub>2</sub> = H in both complexes.

Since the obtained values are opposite to those expected, that is  $K_1 = 1.42$  for the hydroxyureato- and  $K_1 = 80$  (ref. 18) and  $K_1 = 109$  (ref. 5) for the acethydroxamatoiron(III) complexes, a different mode of coordination should be proposed, which will be discussed later.

TABLE

*Equilibrium, Kinetic and Spectral Data for the Mono(hydroxyureato)iron(III) Complex at 25 °C, I = 2.0 mol dm<sup>-3</sup> (H/NaClO<sub>4</sub>)<sup>a</sup>*

pK <sub>a</sub> <sup>b</sup>	$K_1$	$k_1$ M <sup>-1</sup> s <sup>-1</sup>	$k'_1$ s <sup>-1</sup>	$k_{-1}$ M <sup>-1</sup> s <sup>-1</sup>	$k'_{-1}$ s <sup>-1</sup>	$\epsilon(\lambda_{\max})$ M <sup>-1</sup> cm <sup>-1</sup>
9.0°	1.42	16.78	5450	11.82 <sup>d</sup>	6.33 <sup>d</sup>	400 (560)
8.52°	1.3 <sup>f</sup>					

<sup>a</sup> Estimated values of standard deviations are not shown throughout this Table since they do not exceed 10% of the reported parameters.

<sup>b</sup> For the following reaction:  $\text{HU} \rightleftharpoons \text{U}^- + \text{H}^+$

<sup>c</sup> Determined potentiometrically under the same experimental conditions.

<sup>d</sup> Hydrolysis rate constants were calculated by expressions  $k_{-1} = k_1/K_1$ ,  $k'_{-1} = k'_1 K_b/K_1$ .

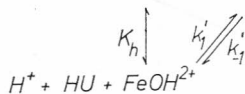
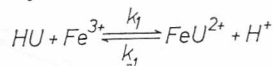
<sup>e</sup> At 0.1 M ionic strength and 20 °C (lit. 17).

<sup>f</sup> Kinetically determined under the same experimental conditions.

### Kinetics

The three first order observable processes in the reaction of hydroxyurea with iron(III) ion are illustrated in Figure 5. After the complex is formed it decomposes through the stages which involve redox processes and which are rather complicated. This paper deals with the first reaction. Figure 6 shows that a dependence of  $k_{\text{obs}}$  on the total iron(III) concentration at constant H<sup>+</sup> ion concentration is linear. The calculated value of  $K_1$  from this kinetic data agrees well with that obtained from equilibrium measurements (see Table). The acid dependence shown in Figure 7 is similar to that observed for the complexation of a series of mono(hydroxyamato)iron(III)

complexes, suggesting the parallel path mechanism which is well known and typical of many ligation reactions of ferric ions. The reaction path which would involve interaction of iron(III) ion with hydroxyureato anion,  $U^-$ , may be ruled out by the same arguments as presented before.<sup>5</sup> Thus, the reaction by which the iron(III) and hydroxyurea form the mono(hydroxyureato)iron(III) complex may be described by the Scheme:



$$K_1 = \frac{k_1}{k_{-1}} \quad (4)$$

$$K_1' = \frac{k'_1}{k'_{-1}} \quad (5)$$

When iron(III) is present in a molar excess over hydroxyurea and when  $[H^+] \gg K_h$ ,  $K_h = 1.0 \times 10^{-3}$  M at 2.0 M ionic strength, 25 °C,<sup>19</sup> the observed rate constant is defined by eq. (6).

$$k_{obs} = (k_1 + k'_1 \frac{K_h}{[H^+]}) [Fe]_{tot} + k_{-1} [H^+] + k'_{-1} \quad (6)$$

Equation (6) requires a linear dependence of  $k_{obs}$  on the total iron(III) concentration at constant proton concentration, as shown in Figure 6. In addition, eq. (6) requires a three parameter function when the system goes in an

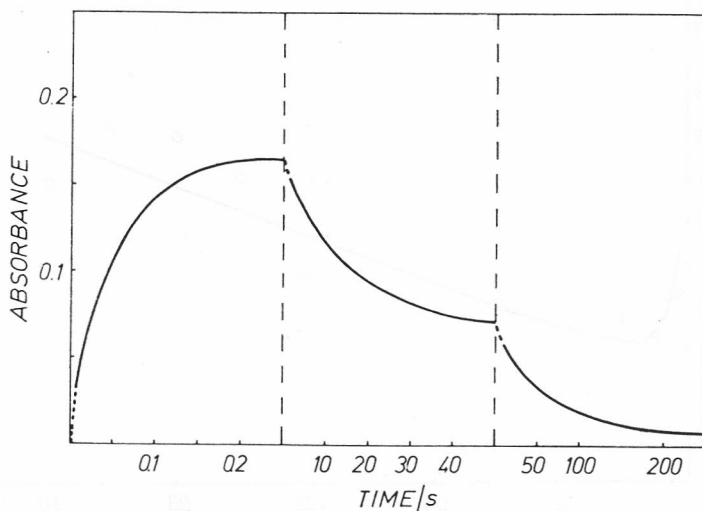


Figure 5. Illustration of the three first order observable processes in the reaction of hydroxyurea with iron(III) ion. Conditions:  $[Fe(III)]_{tot} = 2 \times 10^{-2}$ ,  $[HU]_{tot} = 1 \times 10^{-3}$ ,  $I = 2.0$  M ( $HClO_4/NaClO_4$ ), 25 °C,  $\lambda = 560$  nm,  $[HClO_4] = 0.05$ .



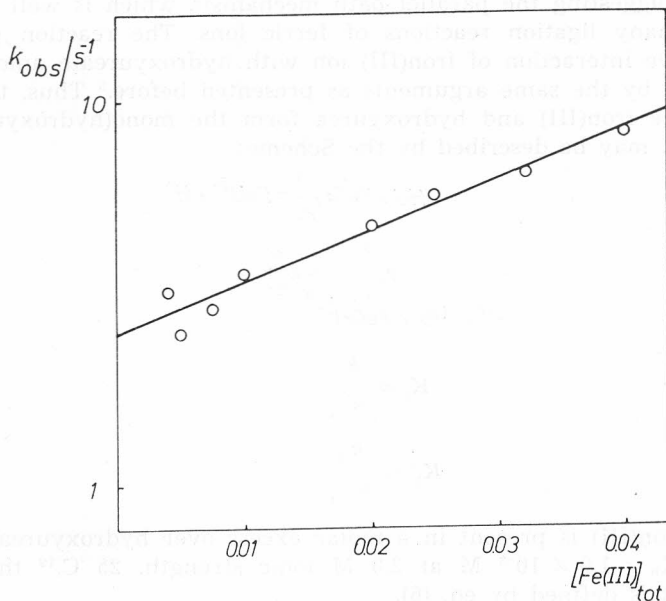


Figure 6. Observed first order rate constants for the formation of mono(hydroxyureato)iron(III) complex plotted as a function of the total iron(III) concentration. Conditions:  $[\text{HU}] = 5 \times 10^{-4}$ ,  $\lambda = 560 \text{ nm}$ ,  $25^\circ\text{C}$ ,  $I = 2.0 \text{ M}$  ( $\text{NaClO}_4/\text{HClO}_4$ ),  $[\text{HClO}_4] = 0.05$ .

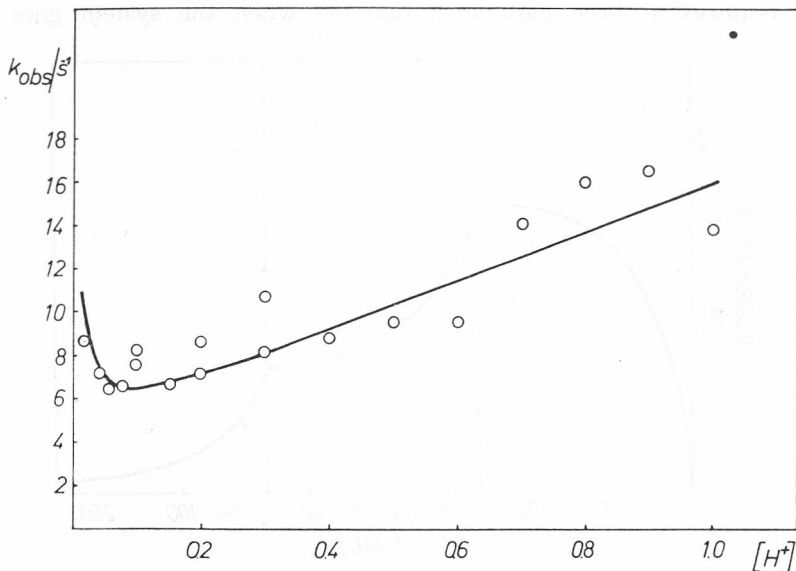


Figure 7. Plot of  $k_{\text{obs}}$  vs.  $[\text{H}^+]$  for the mono(hydroxyureato)iron(III) complex formation reaction at  $25^\circ\text{C}$ . The solid line represents a least square fit of the data to eq. (7). Conditions:  $[\text{Fe(III)}]_{\text{tot}} = 2 \times 10^{-2}$ ,  $[\text{HU}] = 1 \times 10^{-3}$ , ( $\bullet$ ), and  $5 \times 10^{-4}$  ( $\circ$ ).

equilibrium (Figure 7). The non-linear least square procedure was applied to refine the parameters of rearranged eq. (6) into eq. (7) using the formation kinetic data points and spectrophotometrically determined  $K_1$  value.

$$k_{\text{obs}} = (k_1 + k'_1 \frac{K_h}{[H^+]}) [\text{Fe}]_{\text{tot}} + \frac{k_1 [H^+] + k'_1 \cdot K_h}{K_1} \quad (7)$$

Similarity of the kinetic expressions of the interaction of ferric ion with hydroxyurea and the other monohydroxamic acids allowed us to test the reaction mechanism by the already used kinetic relationship.<sup>5</sup> In Figure 8 kinetic data for hydroxyurea are plotted together with the data for different monohydroxamic acids taken from references 5. and 9. The linear relationship between  $\ln k'_{-1}$  and  $\ln k_{-1}$  is usually interpreted to mean that the acid-independent ( $k'_{-1}$ ) and acid-dependent path ( $k_{-1}$ ) of the hydrolysis exhibit a similar mechanism which is, in addition, common to all the complexes studied in a particular series. Therefore, on the basis of this plot it is reasonable to suppose a common reaction mechanism for all monohydroxamic acids including hydroxyurea. Obviously, this is in disagreement with the conclusion presented above, based on the equilibrium data, where a different mode of coordination has been proposed.

Two possible modes of coordination of HU with iron(III) ion are depicted by formulas IV and V, in which cases a stable five-membered ring may be

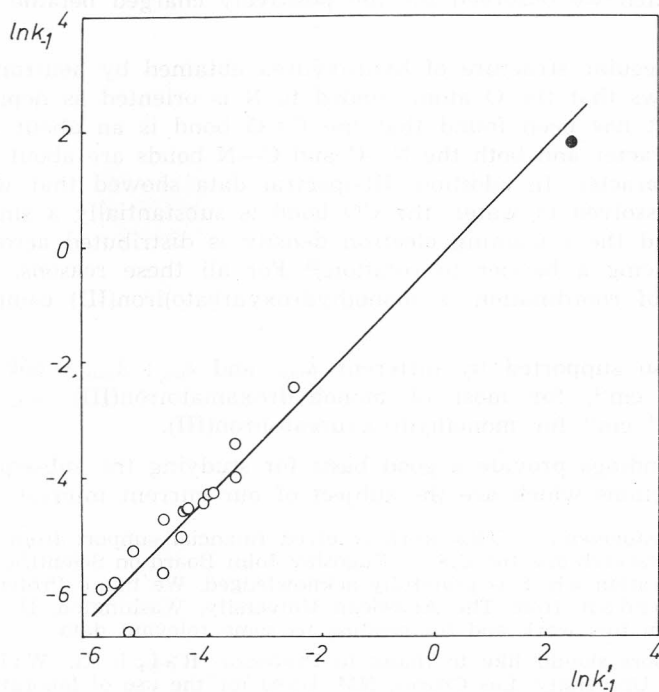
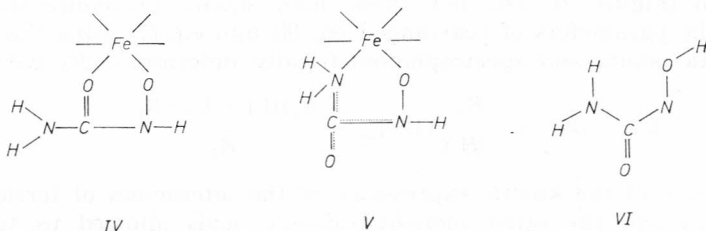


Figure 8. Plot of  $\ln k'_{-1}$  vs.  $\ln k_{-1}$ . The data marked by (○) were collected from the Crumbliss *et al.* papers, (●) values for the mono(hydroxyureato)iron(III) complex.



formed. If structure V is effective, one might expect that the hydroxyurea data point (●) should lie outside the line in Figure 8. However, several factors may be invoked to explain the position of the obtained point. This point lies on the line, but outside the region of other data points of most hydroxamateiron(III) complexes for which structure IV has been proposed. The explanation may be that structure V enhances the rate in both acid catalyzed and spontaneous hydrolysis by approximately the same factor, thus ensuring the same slope for the hydroxyureatoiron(III) complex as for other complexes.

Furthermore, the position of the HU data point on the line requires the same intercept as other hydroxamateiron(III) complexes. According to the Asher and Deutch explanation<sup>20</sup>, the dominant factor for the intercept is the net charge of the complex which is the same for structures IV and V. Asher and Deutsch demonstrated that positively charged ligands lie below the line, which we observed for the positively charged betaine hydroxamic acid.<sup>21</sup>

The molecular structure of hydroxyurea obtained by neutron diffraction analysis shows that the O atom bonded to N is oriented as depicted in formula VI.<sup>22</sup> It has been found that the C=O bond is an about 80% double bond in character and both the N—C and C—N bonds are about 10% double bonds in character. In addition, IR-spectral data showed that when hydroxyurea is dissolved in water, the CO bond is substantially a single bond in character and the remaining electron density is distributed across N—C—N bonds producing a barrier to rotation.<sup>22</sup> For all these reasons, structure V as a mode of coordination in mono(hydroxyureato)iron(III) complex is preferred.

It is also supported by different  $\lambda_{\max}$  and  $\epsilon_{\max}$ ;  $\lambda_{\max} \sim 500$  nm,  $\epsilon_{\max} \sim 1000$  M<sup>-1</sup> cm<sup>-1</sup>, for most of monohydroxamateiron(III);  $\lambda_{\max} = 560$  nm,  $\epsilon_{560} = 400$  M<sup>-1</sup> cm<sup>-1</sup> for mono(hydroxyureato)iron(III).

These findings provide a good basis for studying the subsequent decomposition reactions which are the subject of our current interest.

*Acknowledgement.* — This work received financial support from the Croatian Council for Research and the U.S. — Yugoslav Joint Board on Scientific and Technological Cooperation which is gratefully acknowledged. We thank Professor Nancy Rowan Gordon from The American University, Washington, D. C., USA, for her interest in this work and for sending us some relevant data.

The authors should like to thank to Professor Ralph G. Wilkins (New Mexico State University, Las Cruces, NM, USA) for the use of laboratory facilities.

## REFERENCES

1. J. B. Neilands, *Microbial Iron Transport Compounds (Siderochrome)* in *Inorganic Biochemistry*, G. Eichhorn Ed., Elsevier, New York, 1973, p. 167.
2. J. B. Neilands Ed., *Microbial Iron Metabolism*, Academic Press, New York, 1974.
3. H. Kehl Ed., *Biology and Chemistry of Hydroxamic Acids*, Karger, New York, 1982.
4. K. N. Raymond and T. P. Tufano in *The Biological Chemistry of Iron*, H. B. Dunford *et al.* Eds., D. Reidel Publishing.
5. B. Monzyk and A. L. Crumbliss, *J. Amer. Chem. Soc.* **101** (1979) 6203.
6. M. Biruš, Z. Bradić, N. Kujundžić, and M. Pribanić, *Inorg. Chim. Acta* **55** (1980) 65.
7. S. A. Kazmi and J. V. Mc Ardle, *J. Inorg. Biochem.* **15** (1981) 153; and references therein.
8. T. P. Tufano and K. N. Raymond, *J. Amer. Chem. Soc.* **103** (1981) 6617.
9. C. P. Brink and A. L. Crumbliss, *Inorg. Chem.* **23** (1984) 4708.
10. M. Biruš, Z. Bradić, N. Kujundžić, and M. Pribanić, *Inorg. Chem.* **23** (1984) 2170.
11. L. L. Fish and A. L. Crumbliss, *Inorg. Chem.* **24** (1985) 2198; and references therein.
12. M. Biruš, Z. Bradić, G. Krznarić, N. Kujundžić, M. Pribanić, P. C. Wilkins, and R. G. Wilkins, *Inorg. Chem.* **26** (1987) 1000, and references therein.
13. B. Stearns, K. A. Losee, and J. Bernstein, *J. Med. Pharm. Chem.* **6** (1963) 201.
14. C. W. Young, G. Schochetman, S. Hodas, and M. E. Balis, *Cancer Res.* **27** (1967) 535.
15. V. S. Sharma and D. L. Leussing, *Talanta* **18** (1971) 1137.
16. H. A. Benessi and J. H. Hildebrand, *J. Amer. Chem. Soc.* **71** (1949) 2703.
17. R. Berger and H. P. Fritz, *Z. Naturforsch.* **27b** (1972) 608.
18. M. Biruš, G. Krznarić, M. Pribanić, and S. Uršić, *J. Chem. Res. (S)* (1985) 4; *(M)* (1985) 147–171.
19. R. M. Milburn and W. C. Vosburgh, *J. Amer. Chem. Soc.* **77** (1955) 1352.
20. L. E. Asher and E. Deutsch, *Inorg. Chem.* **12** (1973) 1774.
21. M. Biruš, G. Krznarić, N. Kujundžić, and M. Pribanić, *Croat. Chem. Acta*, submitted for publication.
22. W. E. Thiessen, H. A. Levy, and B. D. Flaig, *Acta Cryst.* **B34** (1978) 2495.
23. G. R. Parker and J. D. Korp, *J. Pharm. Sci.* **67** (1978) 239.

## SAŽETAK

**Kompleksacija željeza(III) sa hidroksiureom u vodenoj otopini perklorne kiseline**

A. Bedrica, M. Biruš, N. Kujundžić i M. Pribanić

Željezo(III) i hidroksiurea stvaraju mono(hidroksiureato)željezo(III) kompleks. Na 25 °C i u kiseloj otopini ionske jakosti  $I = 2,0$  ( $\text{HClO}_4/\text{NaClO}_4$ ) ravnotežni kvocijent stvaranja kompleksa iznosi  $K_1 = 1,4$ , a konstante brzine stvaranja jesu:  $k_1 = 16,8 \text{ M}^{-1} \text{ s}^{-1}$  iz  $\text{Fe}^{3+}$  i  $k'_1 = 5450 \text{ M}^{-1} \text{ s}^{-1}$  iz  $\text{FeOH}^{2+}$ . Analogne konstante brzina reakcija za povratnu reakciju hidrolize su  $k_{-1} = 11,8 \text{ M}^{-1} \text{ s}^{-1}$  i  $k'_{-1} = 6,3 \text{ s}^{-1}$ .