Kinetics and Mechanism of Oxidation of Glycine, Alanine, and Threonine by Fluoride Coordinated Bismuth(V) in Aqueous $HClO_4$–HF Medium

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Abstract

The kinetics of oxidation of amino acids viz. glycine, alanine, and threonine with bismuth(V) in $HClO_4$–HF medium have been studied. The kinetics of the oxidation of all these amino acids exhibit similar rate laws. The second-order rate constants were calculated to be 2.04×10^{-2} dm^3 mol^{-1} and 2.72×10^{-2} dm^3 mol^{-1} s^{-1} for glycine and alanine, respectively, at 35°C and 5.9×10^{-2} dm^3 mol^{-1} s^{-1} for threonine at 25°C. All the possible reactive species of both bismuth(V) and amino acids have been discussed and a most probable kinetic model in each reaction has been envisaged.

Introduction

The oxidation of amino acids by various oxidants studied [1–3] extensively yields aldehydes as the product in most of the reactions. However, nitriles are reportedly formed with chloramine T[2]. Sodium bismuthate has frequently been employed in synthetic organic [5] and analytical chemistry [6]. Burstein and Wright [7] prepared aqueous solutions of Bi^V in a mixture of HF and $HClO_4$, whereas, aqueous Bi^V solutions in $HClO_4$ were reported by Ford–Smith et al. [8].

The mode of oxidation of amino acids is not only biochemically important but also helps in better understanding of their reducing properties in solutions. This prompted us to undertake the title study from three viewpoints.

First, bismuth(V) employed in solid-state frequently in organic syntheses does not tell the nature of the oxidant and, also, its solution properties. Second, α-keto acids reported [3] to be the intermediates in the oxidation of amino acids are important to decide the pathways in the reaction mechanism. Third, the reported [8] solubility of solid bismuthate in $HClO_4$ can help in better speciation of fluoro-bismuth(V) species in aqueous $HClO_4$–HF mixture.

Experimental

Material

Sodium bismuthate (A. R. Riedel) was the source of bismuth(V), and bismuth(III) was obtained from BDH AnalaR grade Bi_2O_3. Perchloric acid and hydrofluoric acid were of A. R. Riedel quality. Bismuth(V) solutions were stored in Teflon vessels. Stoppered Teflon flasks were employed for the reaction mixture. All other chemicals

International Journal of Chemical Kinetics, Vol. 26, 577–585 (1994)
 CCC 0538-8066/94/050577-09

were either of AnalaR grade or G. R. Merck quality and used as supplied. Doubly distilled water was used, second distillation was from alkaline permanganate solution in an all glass still.

Bismuth(V) Solution

The requisite quantity of solid sodium bismuthate was digested in an aqueous mixture of 1.0 mol dm^{-3} $HClO_4$ and 1.5 mol dm^{-3} HF for ca. 15 min that yielded a transparent bismuth(V) solution. The solution was standardized iodometrically [9] (see later) and exhibited no change in its titre value even after ca. 2 h if the solutions were kept at refrigerated temperature (ca. 5°C). However, fresh solutions were always prepared and employed when required.

The tests for hydrogen peroxide were negative but the solution indicated that presence of the large quantities of bismuth(III) as an impurity in bismuthate sample or bismuth(III) was appearing in the solution via reduction of bismuth(V) by H_2O during digestion of the sample in aqueous $HClO_4$–HF mixture.

Our efforts to prepare bismuth(V) solution in $HClO_4$ were not successful and a suspension of bismuth(III) always resulted in the addition of the solid bismuthate into $HClO_4$.

Iodometric Determination of Bismuth(V)

Aliquots of the reaction mixture were mixed with 0.01 mol dm^{-3} KI and then pH of the mixture was adjusted to 2–3 by adding the calculated amounts of NaOH. A slight turbidity appears at this pH and that can be considered to be an indicator of achieving the requisite pH of the mixture. EDTA solution (0.01 mol dm^{-3}) was added and the liberated iodine was titrated against sodium thiosulphate solution using starch as an indicator.

Kinetic Procedure

Reactions were carried out in a thermostatted water-bath at (35 ± 0.1)°C in glycine and alanine and (25 ± 0.1)°C in threonine reactions unless where stated otherwise. The reaction mixture containing bismuth(V) and other reaction components, respectively, were taken in stoppered Erlenmeyer flasks immersed in a water-bath to attain the desired temperature. A known aliquot of preequilibrated solution of amino acids was added to initiate the reaction and the starting time was recorded when the pipettee was half empty. Aliquot samples (5 or 10 cm^3) were periodically withdrawn for iodometric analysis of Bi^V. Since bismuth(V) solutions were not free [7] from bismuth(III), the latter did not affect the rate of the reaction.

Initial rates (k_i) were calculated employing plane mirror method [10]. Pseudo-first-order plots were also made where amino acid concentrations were more than 10-fold concentration of the oxidant. Second-order plots were made wherever reaction conditions permitted. Triplicate rate measurements were in agreement to within ± 8%.

Stoichiometry and Product Analysis

The reactions with an excess of amino acids over bismuth(V) in $HClO_4$–HF mixture

were allowed to occur in a thermostatted water-bath for ca. 3 h and the absence of bismuth(V) was ensured by iodometric test. The solution of 2,4-dinitrophenyl hydrazine in 2.0 mol dm^{-3} HCl was added to the reaction mixture and then the mixture was left overnight at refrigerated temperature. An orange-yellow precipitate obtained in the mixture was centrifused, washed with ice cold HCl solution and then air dried.

^1H NMR of the hydrazone derivative in $CDCl_3$ in glycine displayed a pair of doublets at 7.9d (J = 9 Hz) and 9.11d (J = 2 Hz) for two protons and a third proton showed double doublet at 8.7dd (J = 1.2 Hz). The olefinic methylene protons indicated a singlet at 7.37. In case of alanine, an upfield doublet at 2.2d (J = 6 Hz) for olefinic methyl and a quartet at 7.7 (J = 6 Hz) for methylene protons appeared. Aromatic protons displayed typical 1,2,4-splitting pattern at 8.04 (J = 9 Hz), 8.77 double doublet (J = 9, 2 Hz), and 9.24 (J = 2 Hz) signals. The reaction mixture also indicated though slightly the presence of nitrile by $FeCl_3$ and NH_2OH test. Therefore, the reaction mixtures of gylcine and alanine respectively yielded aldehydes predominantly with significantly lesser amounts of nitriles. However, nitriles were identified in threonine as represented by eq. (1).

(1)

$$RCH(NH_3)COOH + 2Bi(V) \longrightarrow R{-}CN + CO_2 + NH_3 + 2Bi(III) + 5H^+ + NH_3$$

where $R = CH_3 - CH(OH)$

Bismuth(V) Dependence

The concentration of bismuth(V) was varied at fixed concentrations of other reaction ingredients. A plot of initial rate (k_i) vs. [Bi(V)] yields a straight line passing through the origin conforming first-order with respect to bismuth(V). Pseudo-first-order rate constants (k') were independent of the initial $[Bi^V]$. Second-order plots of $\log[Bi(V)]_t/[AA]_t$ or $\log[AA]_t/[Bi(V)]_t$ vs. time (t) in the reactions of glycine and alanine respectively (where AA is for amino acids) were also made. The second order rate constants from these plots were in agreement with the rate constants calculated from the initial rates and the pseudo-first-order rate constants, respectively (Table I).

The stoichiometric second-order plots in the reaction of threonine of $\log(2a - x)/(b - x)$ vs. time (t) (where $a = [Thr]_0$; $b = [Bi^V]_0$ and 'x' is Bi^V at any time t) were also made (Fig. 1). The agreement of the second-order rate constants with the rate constants calculated from the initial rates (Table I) also indirectly supports the observed stoichiometry in the threonine-bismuth(V) reaction.

Amino Acid Dependence

The concentration of the amino acids were also varied at fixed concentrations of other reaction components. The plots of initial rates (k_i) vs AA yielded straight lines passing through the origin indicating unit order with respect to each amino acid (Table I).

TABLE I. Rate constants for the reactions of amino acids by bismuth(V) in $HClO_4$–HF mixtures. $[H^+] = 1.0$ mol dm^{-3}, $[HF] = 1.5$ mol dm^{-3}.

10^2[Glycine], mol dm^{-3}	1.0	1.0	1.0	1.0	1.0	2.0	4.0	6.0
10^3[Bi(V)], mol dm^{-3}	2.1	3.1	4.1	5.3	10.3	2.0	2.0	2.0
10^7(ir), mol dm^{-3} s^{-1}	1.1	1.8	2.4	3.1	5.7	2.3	4.2	6.3
$10^4k'$, s^{-1}	–	–	–	–	–	1.1	2.1	3.0
10^3k_{exp} dm^3 mol^{-1} s^{-1}	5.3	5.3	5.2	5.3	5.0	5.5	5.3	5.1
10^3k_{cal} dm^3 mol^{-1} s^{-1}	5.1	5.7	5.8	5.8	5.5	5.6	5.1	5.2
10^3[Alanine], mol dm^{-3}	1.0	1.0	1.0	1.0	5.0	15.0	25.0	35.0
10^3[Bi(V)], mol dm^{-3}	2.2	3.3	4.4	5.4	2.0	2.0	2.0	2.0
10^7(ir), mol dm^{-3} s^{-1}	2.3	3.7	5.0	6.4	1.2	3.1	5.7	7.7
$10^4k'$, s^{-1}	–	–	–	–	–	–	2.7	3.6
10^2k_{exp} dm^3 mol^{-1} s^{-1}	1.2	1.1	1.2	1.1	1.2	1.1	1.1	1.0
10^2k_{cal} dm^3 mol^{-1} s^{-1}	1.1	1.1	1.2	1.2	1.2	1.0	1.1	1.1
10^3[Threonine], mol dm^{-3}	5.0	5.0	5.0	5.0	5.0	5.0	10.0	15.0
10^3[Bi(V)], mol dm^{-3}	1.3	2.6	3.8	5.1	8.8	2.1	2.1	2.1
10^7(ir), mol dm^{-3} s^{-1}	5.0	9.2	14.0	19.2	33.0	7.3	14.0	23.3
$10^4k'$, s^{-1}	–	–	–	–	–	–	7.3	11.1
10^2k_{exp} dm^3 mol^{-1} s^{-1}	7.5	7.2	7.8	7.3	7.9	7.8	7.3	7.7
10^2k_{cal} dm^3 mol^{-1} s^{-1}	7.9	7.2	7.3	7.5	7.6	6.9	6.9	7.3

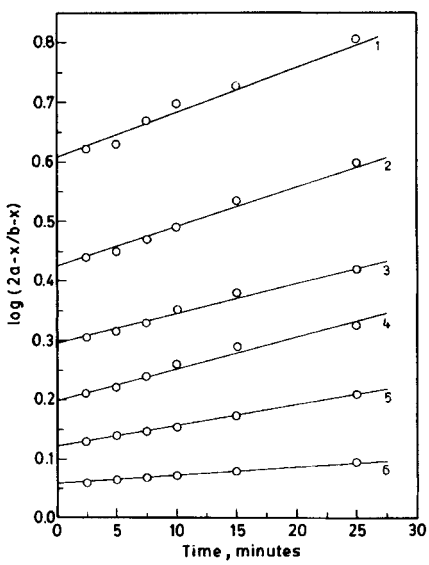


Figure 1. Second-order plots [Threonine] = 5.0×10^{-3} mol dm^{-3}; $[HClO_4] = 1.0$ mol dm^{-3}; [HF] = 1.5 mol dm^{-3}; Temp = 25°C; [Bi(v)] = (1), 2.55×10^{-3} mol dm^{-3}; (2) 3.80×10^{-3} mol dm^{-3}; (3) 5.1×10^{-3} mol dm^{-3}; (4) 6.37×10^{-3} mol dm^{-3}; (5) 7.5×10^{-3} mol dm^{-3}; and (6) 8.75×10^{-3} mol dm^{-3}.

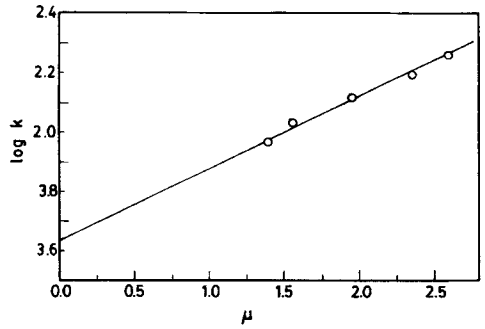


Figure 2. Ionic strength dependence [Bi(v)] = 2.0×10^{-3} mol dm^{-3}; [Glycine] = 1.0×10^{-3} mol dm^{-3}; [$HClO_4$] = 1.0 mol dm^{-3}; [HF] = 1.5 mol dm^{-3}; and Temp = 35°C.

Hydrogen Ion Dependence

Hydrogen ion concentration was varied at constant concentrations of amino acids, bismuth(V), and ionic strength, the latter was maintained constant, employing lithium perchlorate. The rate decreases with increasing hydrogen ion concentration in all these reactions.

Ionic Strength Dependence

Ionic strength was varied from 1.0 to 2.6 mol dm^{-3} employing lithium perchlorate at fixed concentrations of other reaction components. The rate increases with increasing ionic strength in case of glycine and alanine but remains unchanged in case of threonine.

Since the ionic strength is beyond the range of Bronsted–Jerrum equation, the plot of log(k) vs. ionic strength (I) yields a straight line. (Fig. 2)

Such a linearity ascribes to a reaction between neutral molecules or a neutral molecule and ion. The rate of the reaction remains unchanged with the variation of [HF] (0.0–2.0 mol dm^{-3}), [NaF] (5.0–30) $\times 10^{-3}$ mol dm^{-3} and [Bi(III)] (2.5–10) $\times 10^{-3}$ mol dm^{-3}, respectively. This rules out any equilibrium involving bismuth(III) and preceded by the rate limiting step.

Discussion

The kinetic results of the title study correspond to a common mechanism. Also, the chemical transformations of the functional groups in amino acids hardly bring any distortion in the inert hydrocarbon chain. The amino acids species in aqueous solution are pH dependent and are governed by equilibria (3) [11].

(3)
$$\begin{array}{ccccc} R'-CH-COOH & \overset{-H^+}{\rightleftharpoons} & R'-CH-COO^- & \overset{-H^+}{\rightleftharpoons} & R'-CH-COO^- \\ | & & | & & | \\ {}^+NH_3 & & {}^+NH_3 & & NH_2 \end{array}$$

where, R′ = H, $-CH_3$, $-CH_3-CH(OH)$ are for glycine, alanine, and threonine, respectively.

However, the hydrogen ion concentration employed in these reactions in view of the pK's of amino acids indicate that the cationic form of the amino acids should be the predominant amino acid species.

Since bismuth(V) is transparent in u.v. and visible region, no spectral information can be ascertained about the oxidant species in aqueous $HClO_4$–HF mixture. The fluoro hydroxo species of Bi^V of the type $BiF_x\ OH)_6^-$ are reported [7] on the known pattern [12,13] of fluoro species of As^V and Sb^V. Since fluoride ion does not affect the rate, either all the fluoro species of Bi^V are of similar reactivity or an ultimate fluoride saturated Bi^V species is formed in the solution. If Sb^V complexes in HCl medium [14,15] are any guide, Bi^V in aqueous $HClO_4$HF mixture might be in the form of BiF_6^-. Since $SbCl_6^-$ hydrolyses slowly, BiF_6^- hydrolysis must be much slower [16]. An earlier report [8] related to the dissolution of bismuthate in $HClO_4$ was also repeated but the mixture always yielded Bi^{III} instead of Bi^V perchlorate.

Hydrogen ion dependence is considered to be relevant to the mechanism particularly in view of a dipolar or a cationic nature of amino acid. $HBiF_6$ as in equilibrium(4) has earlier been reported [17] to be the reactive species of bismuth(V). Therefore, the observed hydrogen ion dependence accounts for the reactivity of both $HBiF_6$ and BiF_6^- species.

$$BiF_6^- + H^+ \overset{K_P}{\rightleftharpoons} HBiF_6 \tag{4}$$

Considering BiF_6^-, $HBiF_6$, and the cationic form of amino acids to be the reactive species, a plausible reaction mechanism consisting of steps (4) to (6) can be envisaged.

$$BiF_6^- + AA^+ \overset{K_1'}{\rightleftharpoons} C_1 \xrightarrow{k_1'} \text{Products} \tag{5}$$

$$HBiF_6 + AA^+ \overset{K_2'}{\rightleftharpoons} C_2 \xrightarrow{k_2'} \text{Products} \tag{6}$$

where AA^+ is the cationic form of the amino acids, C_1 and C_2 are the intermediate complexes with small equilibrium constants. Such intermediate complexes are not unique in view of the reported amino acid complexes with Os(VIII) [18], Fe(II) [19], and $Fe(ON)_6^{4-}$ [20]. Thus, the loss of Bi^V through the redox decomposition of these complexes leads to the rate law (7) or (8).

$$-d[\text{Bi(V)}]/dt = \frac{k_1'K_1' + k_2'K_2'K_P\,[H^+]}{1 + K_P\,[H^+]}[\text{Bi(V)}]_T\cdot[AA^+]_T \tag{7}$$

or

$$k' = \frac{k_1'K_1' + k_2'K_2'K_P\,[H^+]}{1 + K_P\,[H^+]} \tag{8}$$

where $[\text{Bi(V)}]_T$ and $[AA]_T$ are the gross analytical concentrations of fluoro-bismuth(V) and amino acid species, respectively. Since the equilibrium constants K_1' and K_2' are small, the rate law (8) is further reduced to (9)

$$k = \frac{k_1 + k_2K_P\,[H^+]}{1 + K_P\,[H^+]} \tag{9}$$

where $k_1 = k_1'K_1', k_2 = k_2'K_2'$, and k is an observed second-order rate constant. Since, $K_P[H^+] > 1$, rate eq. (9) further reduces to (10) (K_P is supposed to be ≥ 10 $dm^3\ mol^{-1}$ in view of the hydrogen bonding).

$$k = k_2 + \frac{k_1}{K_P\,[H^+]} \tag{10}$$

A plot of k vs. $[H^+]^{-1}$ from eq. (10) yielded a straight line with nonzero intercept (Fig. 3), k_2 and k_1/K_P were evaluated from the intercept and gradient, respectively. The values of k_2 to be 2.0, 3.0, and 6.5 $dm^3\ mol^{-1}\ s^{-1}$ in case of glycine and, 5.5, 9.0, and 12.2 $dm^3\ mol^{-1}\ s^{-1}$ in case of alanine have been evaluated at 35, 40, and 45°C, respectively. In case of threonine k_2 was calculated to be 3.2, 5.5, and 8.6 $dm^3\ mol^{-1}\ s^{-1}$ at 25, 30, and 35°C, respectively. Similarly, k_1/K_P to be 1.9, 2.4, and 3.3 s^{-1} in case of glycine and 2.2, 2.5, and 3.3 s^{-1} in case of alanine were evaluated at 35, 40, and 45°C, respectively. However, k_1/K_P were evaluated to be 3.5, 8.6, and 9.6 s^{-1} at 25, 30, and 35°C, respectively, in case of threonine. These values of k_1/K_P and k_2 were substituted in the rate eq. (10) and the calculated rate constants (k_{cal}) were in agreement with the experimental values (k_{exp}) (Table I) demonstrating the best correlation of a linear relationship.

A chemically rational interpretation even in absence of activity coefficient data for these complex systems appears tempting if zwitterion is considered to be the reactive form of amino acids. Therefore, the following reaction mechanism can be envisaged:

(11) $$\mathrm{R'{-}CH(NH_3^+){-}COOH} \overset{K'}{\rightleftharpoons} \mathrm{R'{-}CH(NH_3^+){-}COO^-} + \mathrm{H^+}$$

(12) $$\mathrm{R'{-}CH(NH_3^+){-}COOH} + \mathrm{BiF_6^-} \xrightarrow{k''_1} \text{Products}$$

(13) $$\mathrm{R'{-}CH(NH_3^+){-}COO^-} + \mathrm{BiF_6^-} \xrightarrow{k''_2} \text{Products}$$

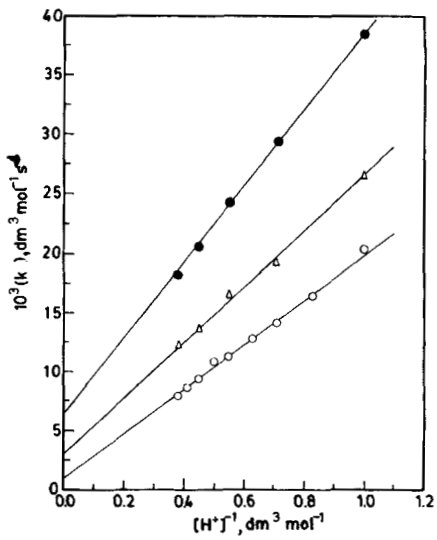


Figure 3. Plot of k vs. $1/[H^+][Bi(v)] = 2.2 \times 10^{-3}$ mol dm^{-3}; [Glycine] $= 1.0 \times 10^{-3}$ mol dm^{-3}; [HF] – 1.5 mol dm^{-3}, Temp = ○, 35°C; △, 40°C; and •, 45°C.

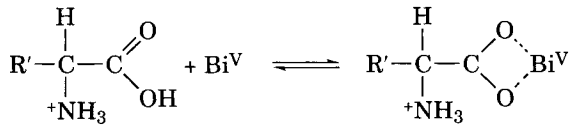
This leads to the rate law (14) or (15)

$$\frac{-d[\mathrm{Bi(V)}]}{dt} = \left(k_1'' + \frac{k_2'' K'}{[\mathrm{H^+}]}\right)[\mathrm{BiF_6^-}]_T[AA]_T \tag{14}$$

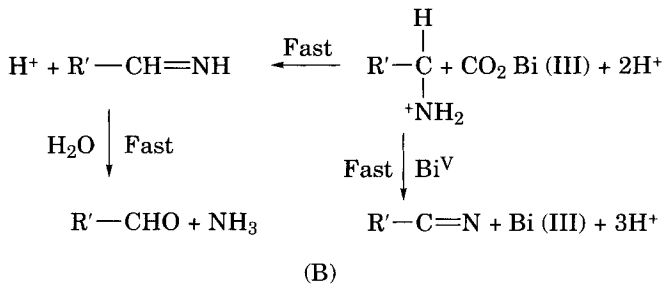
or

$$k'' = k_1'' + \frac{k_2'' K'}{[\mathrm{H^+}]} \tag{15}$$

The rate law (15) like eq. (10) also accounts for the observed hydrogen ion dependence. However, these two kinetic proposals are indistinguishable. Also the comparative reactivity pattern of these amino acids does not help in making this distinction. Nevertheless, the following Scheme I accounts for the stoichiometric and kinetic results:



(A)



(B)

Scheme I

The path (A) yields aldehyde in case of glycine and alanine but nitrile is exclusively obtained in case of threonine.

The intermediate R′–CH = $^+NH_2$ formed in two electron transfer step rearranges to imine which either hydrolyzes to an aldehyde or further undergoes oxidation to nitrile. Probably hydroxyl group on β-carbon in threonine makes this difference.

Bibliography

[1] B.T. Gowda and D.S. Mahadevappa, *J. Chem. Soc. Perkin Trans.*, **2,** 323 (1983); M.S. Ramachandran and T.S. Vivekanandan, *Bull. Chem. Soc. Japan,* **60,** 3397 (1987); R.C. Acharya, N.K. Saran, S.R. Rao, and H.N. Das, *Int. J. Chem. Kinet.*, **14,** 143 (1982); R.N. Mehrotra, R.C. Kapoor, and S.K. Vajpai, *J. Chem. Soc. Dalton Trans.*, 999 (1984).

[2] M.S. Ramachandran, T.S. Vivekanandan, and R. Nithyanandan, *J. Chem. Soc. Perkin Trans. II,* 1507 (1985).

[3] M.A. Beg and Kamaluddin, *Acta Chimica,* **86,** 65 (1975); *Ind. J. Chem,* **13,** 1167 (1975).

[4] I. Pinto. B.S. Sherigara, and H.V.K. Udupa, *Bull. Chem. Soc. Jpn,* **63,** 3625 (1990).

[5] L.P. Fieser and M. Fieser, *Reagents for Organic Synthesis,* Wiley, New York, 1967, p. 1045; C.J.R. Adderley and F.R. Hewgill, *J. Chem. Soc. C,* 2770 (1968).

[6] A. A. Goryonov and L. L. Sveshnikova, *Zh. Neorg. Khim.*, **6,** 1543 (1961).
[7] G. T. Burstein and G. A. Wright, *Nature* (London), **221,** 169 (1969).
[8] M. H. Ford-Smith and J. J. Habeeb, *J. Chem. Soc. Dalton Trans.,* 461 (1973).
[9] K. M. Inani, Seema Agrawal, P. D. Sharma, and Y. K. Gupta, *Ind. J. Chem.,* **29A,** 927 (1990).
[10] M. Latshaw, *J. Am. Chem. Soc.,* **47,** 793 (1925).
[11] A. R. Kemble and H. A. Macpherson, *Biochem. J.,* **56,** 548 (1954).
[12] L. Kolditz and W. Ronseh, *Z. Anorg. Allg. Chem.,* **293,** 168 (1957).
[13] L. Kolditz and D. Sarrack, *Z. Anorg. Allg. Chem.,* **293,** 132 (1957).
[14] H. M. Newmann and R. W. Ramette, *J. Am. Chem. Soc.,* **78,** 1848 (1956).
[15] S. B. Willis and H. M. Newmann, *J. Am. Chem. Soc.,* **91,** 2924 (1969).
[16] J. L. Dawson and J. Wilkinson, *J. Inorg. Nucl. Chem.,* **32,** 501 (1970).
[17] K. M. Inani, P. D. Sharma, and Y. K. Gupta, *J. Chem. Soc. Dalton Trans.,* 2571 (1985).
[18] J. Nyilasi, P. Somogyi, and Nagy, *Ken. Poly.,* **78,** 407 (1972); *idem; Acta Chim. Acad. Sci. Hung.,* **75,** 405 (1973).
[19] A. Albert, *Biochem. J.,* **47,** 531 (1950).
[20] W. U. Malik and N. Aslam, *Ind. J. Chem.,* **8,** 736 (1970).

Received September 15, 1992
Accepted March 18, 1993