Kinetics and Mechanism of the Dehydrofluorination of 2,3-Bis(N,N-difluoramino)butane[1]

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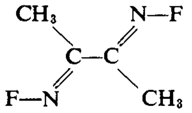
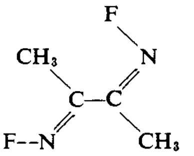
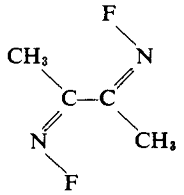
Abstract: A mechanistic scheme has been developed for the dehydrofluorination of 2,3-bis(N,N-difluoramino)-butane (I) in diglyme–water (30:70) at 50°. It has been shown that the loss of hydrogen fluoride from I is only slightly slower than loss of a second molecule of hydrogen fluoride from the intermediate to give the final products, the three *syn,anti* isomers of 2,3-bis(N-fluorimino)butane (II). The predicted monodehydrofluorination intermediates, the *syn* and *anti* isomers of 2-N,N-difluoramino-3-N-fluoriminobutane (III), have been observed kinetically and have been isolated and identified. Rate constants have been derived for the individual dehydrofluorination steps for all isomers involved. Activation parameters for the dehydrofluorination of I have also been determined.

Although the mechanism of dehydrohalogenation across carbon–carbon bonds has been studied extensively,[2] the elimination of hydrogen halide across carbon–nitrogen bonds has received considerably less attention. Several N-iod-[3], brom-[4], chlor-,[5] and fluoramines[6] are known. The base-catalyzed dehydrohalogenation of primary and secondary chloramines and fluoramines, giving aldimines, nitriles, or ketimines, occurs readily and is of some synthetic utility.[5,7] The only available kinetic data for dehydrohalogenation across a carbon–nitrogen bond are for the base-catalyzed elimination of hydrogen chloride from benzalchlorimines, X-C_6H_4—CH=NCl, in alcoholic solvents.[8]

We have now examined in detail the elimination of hydrogen fluoride across a carbon–nitrogen single bond. The kinetics and mechanism of dehydrofluorination of 2,3-bis(N,N-difluoramino)butane (I) in aqueous solution have been studied. In the presence of base, I readily loses two molecules of hydrogen fluoride to yield 2,3-bis(N-fluorimino)butane (II). The dehydrofluorination product exists in three separable *syn,anti* geometric forms for which the configurations have been established.[9]


syn,syn
IIa


syn,anti
IIb


anti,anti
IIc

The rate of dehydrofluorination in aqueous medium is not affected by the presence of added acid; the reaction is general-base catalyzed. In the aqueous system employed in the present work, the solvent water acts as the base and the kinetics are pseudo-first-order.

2,3-Bis(N,N-difluoramino)butane (I) has two diastereoisomers which are readily separated by gas chromatography. The first isomer to be eluted is arbitrarily labeled Ia, the second Ib. The stereochemistry of the diastereoisomers is not known. In the present work, the dehydrofluorination of isomer Ia has been studied in detail since only for this diastereoisomer could the starting material, intermediates, and products be well resolved by gas chromatography, thus permitting reliable determination of the reaction kinetics.

Results and Discussion

Dehydrofluorination of Ia. By means of an extraction–gas chromatographic technique, the kinetics and mechanism of the dehydrofluorination of 2,3-bis(N,-N-difluoramino)butane (I) to 2,3-bis(N-fluorimino)-butane (II) in diglyme–water (30:70) have been studied in detail. Figure 1 illustrates the concentration–time dependence of the various substances observed during the course of the reaction. There are two transient peaks, labeled IIIa and b, which are not present initially, but which build up and then eventually disappear during the course of the reaction. The diimine product, 2,3-bis(N-fluorimino)butane (II), exists in three *syn, anti* geometric forms for which the configurations have been determined.[9] These geometric isomers (IIa, b, and c by retention time) are formed in the ratio 73.6 (±2%):22.6(±4%):3.8(±21%)(IIa:IIb:IIc). The isomers, produced in 86% yield, are stable under the reaction conditions. Although the observed hydrogen ion infinity titers were always within a few per cent of the

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(1) This work was supported by the Office of Naval Research, Contract Nonr 3760(00).

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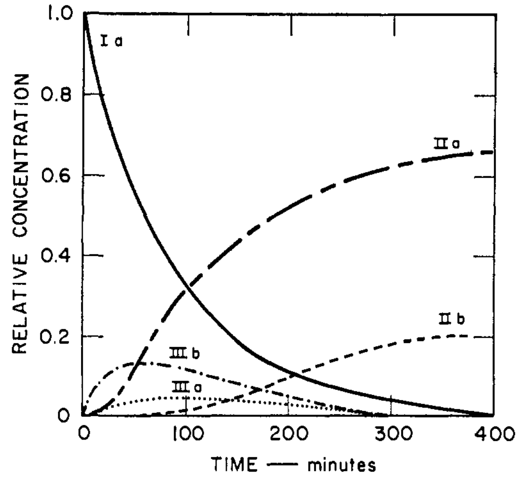


Figure 1. Concentration-time curves for dehydrofluorination of Ia in 30% aqueous diglyme, 50°. Ia is 2,3-bis(N,N-difluoramino)-butane. IIa and b are geometric isomers of the product, 2,3-bis-(N-fluorimino)butane. Isomer IIc does not appear on this scale. IIIa and b are the monodehydrofluorination intermediates.

theoretical value, preliminary vpc evidence indicated the presence of small quantities of low molecular weight material at the end of the reaction. Consequently, total decomposition rate constants (k_{Ia}) have been corrected for 86% dehydrofluorination in the present calculations. This correction does not affect the kinetics, provided the decomposition is a first-order process.

Data for the dehydrofluorination of Ia show that when 50% of the total amount of IIa has been produced, 68% of Ia has disappeared. After correcting the initial amount of Ia for 14% decomposition, it is still found that 63% Ia has disappeared owing to dehydrofluorination when half of the IIa has appeared. The Ia disappears with an average observed rate constant (k_{Ia}) of 1.95×10^{-4} sec^{-1} (±4%), following linear first-order kinetics from 0 to 90% reaction (Figure 2). After an initial induction period, the observed rate of appearance of IIa ($k_{\mathrm{IIa}} = 1.13 \times 10^{-4}$ sec^{-1}, ± 7%) also exhibits first-order kinetics from 25 to 90% reaction. The rate plot for production of hydrogen ion shows a distinct break after approximately 60% reaction. The kinetics for hydrogen ion production are complicated because this species is produced in many different reactions.

This kinetic behavior is consistent with a reaction sequence in which the rate of loss of the second molecule of hydrogen fluoride to yield product is not significantly faster than the rate of loss of the first molecule of hydrogen fluoride from Ia. The transient peaks observed by gas chromatography then correspond to the *syn* and *anti* monodehydrofluorination intermediates. Ia loses one molecule of hydrogen fluoride, giving rise to both geometric isomers of 2-N,N-difluoramino-3-N-fluoriminobutane (III). The initial dehydrofluorination step is not reversible. If it were, isomerization should occur between the diastereoisomers of I. The gas chromatograms clearly show that starting with either diastereoisomer, the other isomer is never produced during the reaction. Since the diastereoisomers of I do not isomerize under the reaction conditions, the monodehydrofluorination intermediates do not return to starting material; consequently, they do

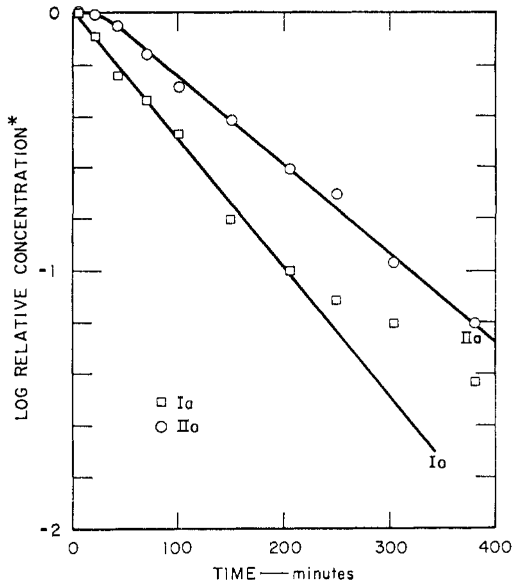
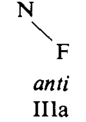


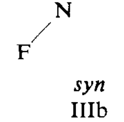
Figure 2. Observed rates of disappearance of Ia and appearance of IIa in 30% aqueous diglyme, 50°. *Relative concentration of Ia = $(\mathrm{Ia})_t/(\mathrm{Ia})_0$; $k_{\mathrm{obsd}}^{\mathrm{Ia}} = 1.95 \times 10^{-4}$ sec^{-1}. Relative concentration of IIa = $[(\mathrm{IIa})_\infty - (\mathrm{IIa}_t)]/(\mathrm{IIa})_\infty$; $k_{\mathrm{obsd}}^{\mathrm{IIa}} = 1.13 \times 10^{-4}$ sec^{-1}.

possess and retain a definite *syn,anti* geometry. The *syn* intermediate then loses an additional molecule of hydrogen fluoride to produce the *syn,syn* (IIa) and *syn,anti* (IIb) diimine products while the *anti* intermediate gives rise to the *syn,anti* (IIb) and *anti,anti* (IIc) geometric products.

Small quantities of both intermediates have been isolated, and they have been shown to be the monodehydrofluorination intermediates proposed in the above reaction scheme. When IIIb was redissolved in a 30% aqueous diglyme mixture at 50°, IIa and b were produced in the ratio 24.2 (±6%) to 1 and IIa was formed with a rate constant of 2.96×10^{-4} sec^{-1} (±12%). Upon similar treatment of IIIa, only production of the most abundant product, IIb, could be observed; the concentration of IIc was too low to be detected. Since intermediate IIIb was found to produce the *syn,syn* and *syn,anti* isomeric products, it was assigned the *syn* configuration. Similarly, the *anti* geometry has been assigned to intermediate IIIa.



anti
IIIa



syn
IIIb

From the ratio of the geometric isomers produced in a kinetic run of Ia (IIa:IIb:IIc::73.6:22.6:3.8) and the ratio of isomers formed from intermediate IIIb (IIa:IIb::24.2:1) under the same reaction conditions, it is possible to determine the relative rates of dehydrofluorination of the intermediates to give the various isomeric products. These values appear in parentheses in Figure 3 for a diglyme-water (30:70) solvent mixture at 50°. It follows that 77 ± 2% of the dehydrofluorination reaction proceeds through intermediate IIIb and 23 ± 2% through IIIa.

From the measured rate constant for disappearance of intermediate IIIb ($k_3 = 2.96 \times 10^{-4}$ sec^{-1}, ±12%), absolute values can be assigned to k_4, k_5, and k_6. The total rate constant ($k_1 + k_2$) for dehydrofluorination of Ia (1.68×10^{-4} sec^{-1}, ±8%) is taken to be equal to 86% of the observed value for the total destruction of Ia ($k_{\text{Ia}} = 1.95 \times 10^{-4}$ sec^{-1}). The constant k_1 is then 77% of the total dehydrofluorination rate. The values for these various rate constants are summarized in Table I.

Table I. Rate Constants for Dehydrofluorination of Ia in 30% Aqueous Diglyme, 50°

Rate constant[a] × 10^5 sec^{-1}		± error
k_1	12.8	1.3
k_2	4.0	0.5
k_3	29.6	3.4
k_4	1.2	0.3
k_5	26.0	3.6
k_6	5.0	1.1

[a] Assignments refer to Figure 3.

The destruction of intermediate IIIb is only some 2.4 times faster than its formation [$(k_3 + k_4)/k_1 = 2.4$ ± 22%]. This rate ratio predicts that the maximum concentration of IIIb relative to the initial concentration of Ia will be 0.22 (±34%) and that this maximum will occur after 81 min (±50%). Assuming extraction and vpc response characteristics for IIIb (and IIIa) similar to those of Ia or II, the observed maximum concentration of IIIb, relative to the initial concentration of Ia actually decomposing through IIIb, was always approximately 0.2, occurring sometime between 50 and 85 min.

The disappearance of intermediate IIIa is 7.8 times faster than its formation [$(k_5 + k_6)/k_2 = 7.8$ ±24%]. From this ratio, the relative maximum concentration of IIIa is calculated as 0.10 (±60%), occurring after 126 min (±60%) of reaction. Although the values for the minor peak of IIIa are not especially reliable owing to overlap with the major peak of IIa on the vpc, the observed maximum concentration of IIIa (0.16), relative to the initial concentration of Ia decomposing through intermediate IIIa, was within experimental error of the predicted value. This maximum occurred sometime between 110 and 160 min. IIIa always reached a maximum concentration after IIIb, and its relative concentration was always apparently less than that of intermediate IIIb.

The rate for the observed formation of IIa from Ia can be calculated from k_1 and k_3. The resulting rate constant (1.19×10^{-4} sec^{-1}) is in excellent agreement with the measured value (1.13×10^{-4} sec^{-1}). The calculated rate exhibits an induction period similar to that seen experimentally.

If it is assumed that Ia only undergoes dehydrofluorination, k_1 becomes 1.5×10^{-4} sec^{-1}; k_3, k_4, k_5, and k_6 remain unchanged. The predicted maximum concentration of intermediate IIIb becomes 0.25, occurring at 77 min. The calculated rate constant for the observed formation of IIa is then 1.35×10^{-4} sec^{-1}. The agreement between these calculated values and the observed values is not as good as the agreement between the values calculated assuming 86% dehydrofluorination and the observed values, indicating that some decomposition of Ia other than dehydrofluorination does take place.

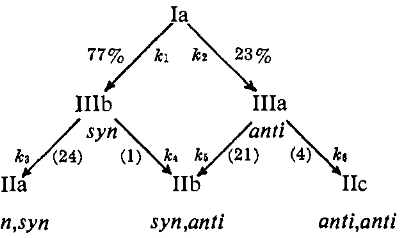


Figure 3. Dehydrofluorination scheme for Ia in 30% aqueous diglyme, 50°.

Activation Parameters. The decomposition of Ia was examined briefly in diglyme–water (30:70) at 75°. The dehydrofluorinated products were formed in the ratio 72.1:23.1:4.8::IIa:IIb:IIc, in approximately 78% yield. Assuming the ratio of products arising through IIIb is the same at 75° as found at 50°, the relative rates of k_3, k_4, k_5, and k_6 appear to have remained unchanged between 50 and 75°. At the higher temperature, 75% of the dehydrofluorination of Ia proceeds through IIIb and 25% through IIIa. After correcting the observed rate constant for disappearance of Ia ($k_{\text{Ia}} = 1.26 \times 10^{-3}$ sec^{-1}) for 78% dehydrofluorination, a value of 7.38×10^{-4} sec^{-1} is obtained for k_1 and 2.44×10^{-4} sec^{-1} for k_2 at 75°. The activation parameters calculated for the dehydrofluorination (k_1 and k_2) of Ia in 30% aqueous diglyme are given in Table II.

Table II. Activation Parameters for the Dehydrofluorination of Ia in 30% Aqueous Diglyme

Rate constant	$\Delta H^{\ddagger}$, kcal/mole	$\Delta F^{\ddagger}$, kcal/mole	$\Delta S^{\ddagger}$, eu
k_1	15.0	24.7	−30.2
k_2	15.5	25.5	−30.9

Activation energies for the base-catalyzed, concerted elimination of hydrogen halides across carbon–carbon bonds in alcoholic solvents are usually 5–10 kcal/mole higher than those observed in the present work.[2a,b] The corresponding entropies of activation are negative, usually falling in the range of −1 to −10 eu. These eliminations do not go through carbanion intermediates,[2c] but are concerted. However, in the 2-phenylethyl system,[2a] the ρ was found to increase from +2.07 for the elimination of hydrogen iodide to +3.12 for hydrogen fluoride, indicating an increase in carbanionic character at the β-carbon in the transition state of the latter reactions. By choice of appropriate compounds, the elimination of hydrogen fluoride across a carbon–carbon bond can involve a true carbanion intermediate. Under similar reaction conditions, the activation energies are generally higher in these stepwise eliminations than in the concerted ones mentioned above, and the entropies of activation become positive.[2e–g]

Kinetic studies on the base-catalyzed loss of hydrogen chloride from benzalchlorimines in alcoholic solvents indicate that this reaction is a concerted elimination.[8] The activation energies are a few kcal/mole higher than those observed in the present work; the entropies are negative, and ρ is approximately +2.

The loss of the first molecule of hydrogen fluoride from Ia in aqueous solution is most likely a concerted elimination. The lack of isomerization between the diastereoisomers of I is evidence against a typical carbanion mechanism for the elimination. The negative entropies of activation, indicating a loss in degrees of freedom in the transition state, are not consistent with a stepwise carbanion mechanism, but they do suggest a concerted elimination. In addition, compound Ia would not be expected to be acidic enough to ionize in a simple acid–base reaction in water. However, dehydrofluorination of Ia is quite rapid for such a reaction involving water as a base, again indicating that the loss of hydrogen fluoride from Ia must be a concerted elimination.

The negative entropies of activation for dehydrofluorination of Ia are rather large compared to typical values for dehydrohalogenation. Steric factors alone probably do not account for this. The entropy of hydration of a fluoride ion is considerably more negative than those for the other halide ions because solvation is more important for ions of large charge to ionic radius ratios.[10] It is quite probable that the large negative entropies of activation reflect such hydration at the incipient fluoride ion in Ia. This would be consistent with a concerted mechanism in which both the hydrogen–carbon and the fluorine–nitrogen bonds are breaking in the transition state. In the uncatalyzed hydrolysis of benzyl fluoride in water–acetone (90:10), for example, the enthalpy of activation is 19.1 kcal/mole and the entropy of activation is -29.1 eu at 50°.[11] This large, negative entropy most likely is due to hydration of the incipient ions in the transition state.

Dehydrofluorination of Ib. The mechanistic scheme developed for the dehydrofluorination of Ia also describes the dehydrofluorination of the other diastereoisomer, Ib. In the latter case, the two observed transient intermediates were shown to be IIIa and b by comparison of vpc retention times with authentic samples. The isomeric dehydrofluorination products from Ib in 30% aqueous diglyme at 50° were obtained in approximately 80% yield, in the over-all ratio of IIa: IIb:IIc::84.6:13.6:1.8. Assuming the ratio of products from intermediate IIIb reported above (IIa:IIb:: 24.2:1), it is found that the ratio of products arising from IIIa (IIb:IIc:: 5.6:1) for this diastereoisomer is in good agreement with that ratio found for the Ia isomer (IIb:IIc::5.2:1). This supports the relative rate assignment of k_3, k_4, k_5, and k_6. For Ib, 88% of the dehydrofluorination reaction proceeds through intermediate IIIb and 12% through IIIa. The rate of disappearance of Ib could not be measured accurately because of overlap of Ib and IIIa on the gas chromatograph. However, the average observed rate constant for production of IIa from Ib (1.23×10^{-4} sec^{-1}) is not very different from the value for production of IIa from Ia (1.13×10^{-4} sec^{-1}). Since both diastereoisomers have the same value of k_3, they both must have nearly the same values of k_1 to give similar constants for production of IIa. If the values of k_1 are arbitrarily chosen to be the same, k_2 for Ib then becomes 1.8×10^{-5} sec^{-1}. The similarity in dehydrofluorination rate constants for the two diastereoisomers of I undoubtedly reflects the similarity in steric requirements for the two compounds.

Experimental Section

2,3-Bis(N,N-difluoramino)butane (I). This compound was prepared by the gas-phase addition of tetrafluorohydrazine to 2-butene.[6c,7] Since samples of the neat liquid have been known to explode, compound I was stored as a 50% solution in methylene chloride. The material was recovered by cautiously distilling off the excess solvent. The 2,3-bis(N,N-difluoramino)butane [bp 109°; 50–51° (93 mm)] in the residue was a mixture of two diastereoisomers which were separated and purified by gas chromatography (15% didecyl phthalate on 80–100 AW Chromosorb P DMCS, 10 ft × $^3/_8$ in. Al, 100°, 111 cc He/min). The first isomer to be eluted was labeled Ia, the second isomer Ib. All mixtures were approximately 46% Ia and 54% Ib prior to separation. The stereochemistry of the diastereoisomers has not been determined.

2-N,N-Difluoramino-3-N-fluoriminobutane (III). The dehydrofluorination of Ia (1.6×10^{-2} *M*) in 250 ml of a 30% aqueous diglyme (diethylene glycol dimethyl ether) solution at 50° was quenched after 45 min of reaction by pouring onto ice. The organic substances were extracted repeatedly with mixed hexanes and the combined organic extracts were dried over sodium sulfate. The excess solvent was removed by distillation and the two isomers of III were separated by gas chromatography (20% didecyl phthalate on 42–60 chrom FB, 5 ft × 0.25 in. Al, 76°, 50 cc He/min). The first intermediate to be eluted was labeled IIIa, the second IIIb. Milligram quantities of both intermediates, contaminated only with II, were isolated.

The infrared spectrum of the intermediate isolated in the largest amount, IIIb, showed certain similarities to the infrared spectra of both starting material and dehydrofluorination products. Although the sample contained 84% IIIb, 10% IIa, and 6% IIb, the small contributions due to the impurities were easily accounted for from known spectra. The IIIb infrared spectrum exhibited an absorption band in the carbon–nitrogen double bond region (1650 cm^{-1}, w) which was less intense and at a higher frequency than any of the carbon–nitrogen double bond absorptions in the conjugated isomeric products (IIa, 1600 cm^{-1}, s; IIb, 1640 cm^{-1}, m, 1620 cm^{-1}, m, sh; IIc, 1630 cm^{-1}, w).

Kinetic Studies. All dehydrofluorination studies were performed in Teflon FEP, 16-oz, narrow-mouth bottles. The kinetics were followed by vpc analysis of reaction aliquots with time. Rate constants for disappearance of starting material and appearance of product were obtained directly from the slopes of plots of the logarithm of the relative concentration, log (counts$_t$/counts$_0$) and log [(counts$_\infty$ − counts$_t$)/counts$_\infty$], respectively, *vs.* time. Distribution coefficients for Ia, Ib, IIa, and IIb between 30% aqueous diglyme (15.0 ml) and both mixed hexanes and benzene (2.0 ml) were measured. Within experimental error, the distributions of IIa and IIb between 30% aqueous diglyme and benzene were found to be identical, and that of isomer IIc was assumed to be the same. The distribution of Ia, Ib, and IIa between mixed hexanes and 30% aqueous diglyme was found to be independent of hydrofluoric acid in the aqueous phase in concentrations corresponding to zero, half, and complete dehydrofluorination in a kinetic experiment. The vpc response characteristics for both diastereoisomers of I and all isomers of II were also determined. The three geometric isomers of II had identical vpc response characteristics, thus permitting reliable determination of the product yield for the dehydrofluorination reaction. All experiments were performed in duplicate.

Dehydrofluorination of I. To initiate reaction, a 0.3-g sample of Ia or Ib of known weight dissolved in 3.0 ml of diglyme (diethylene glycol dimethyl ether) was added to a mixture of 75 ml of diglyme and 175 ml of water (30% diglyme to enhance solubility; 8×10^{-3} *M* I; 246 ml total volume at 50.1°) maintained at either 50.1 or 75.2°. Aliquots (15.0 ml) were withdrawn with time and extracted with 2.0 ml of benzene or mixed hexanes and a few grams of ice. The organic extracts were then analyzed directly by gas chromatography (20% didecyl phthalate on 42–60 Chromosorb FB, 5 ft × 0.25 in. Al, 76°, 50 cc of He/min).

When mixed hexanes were employed as extraction solvent, only product isomers IIa and IIb were recovered from the reaction mixture. When the more polar solvent, benzene, was used, all three isomers were recovered. Because of solvent tailing, however, the kinetics for disappearance of I could not be measured accurately when benzene was employed. The kinetic data for appear-

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ance of IIa for the two extraction solvents are in excellent agreement.

Dehydrofluorination of IIIa. A sample (60% IIIa, 40% IIa) containing approximately 1 mg of IIIa dissolved in diglyme was added to an aqueous diglyme mixture maintained at 50°, resulting in 12 ml of a 30% aqueous diglyme solution which was approximately 6×10^{-4} *M* IIIa. At 0 and 100% reaction, 5.0-ml aliquots were withdrawn and extracted with 0.7 ml of benzene. The aqueous extracts were analyzed for developing hydrofluoric acid content by titration with standard sodium hydroxide solution; the organic extracts were analyzed directly by vpc for organic product. Only production of one organic product, the most abundant geometric isomer, IIb, was observed. The concentration of IIc was too low to be detected. The amount of the impurity, IIa, did not increase during the course of the reaction.

Dehydrofluorination of IIIb. When the diglyme sample (91% IIIb, 9% IIa) containing approximately 3 mg of IIIb was added to an aqueous diglyme mixture maintained at 50°, 20 ml of a 30% aqueous diglyme solution, which was approximately 1.1×10^{-3} *M* IIIb, was obtained. After 0, ~75, and 100% reaction, 5.0-ml aliquots were withdrawn and extracted with 0.7 ml of benzene. Again the aqueous phase was titrated with standard sodium hydroxide solution for developing acidity, and the organic phase was analyzed by vpc for organic product. The only observable products were hydrofluoric acid and the two geometric isomers, IIa and IIb. The total yield of organic product was at least 90%. The final ratio of IIa to IIb, corrected for the initial amount of IIa, was 24.2 (±6%) to 1. The integrated rate constant for decomposition of IIIb was 2.96×10^{-4} sec^{-1}; this value was actually used for k_3. The measured value for production of IIa from IIIb was 3.42×10^{-4} sec^{-1}, while the corresponding rate constant for hydrogen ion production was 2.4×10^{-4} sec^{-1}. When 73% of IIIb had disappeared, 78% of IIa and from 64 to 67% of the hydrogen ion had appeared. These percentages, and consequently the rate constants, are in very good agreement, considering the accuracy of the determinations for the small sample employed.

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Metal-Catalyzed Hydration of Phenanthroline Nitrile[1]

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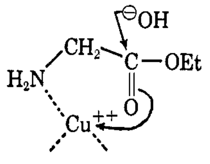
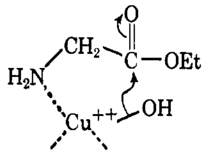
Abstract: The hydration of 2-cyano-1,10-phenanthroline to the corresponding amide is strongly promoted by metal ions such as Cu^{2+}, Ni^{2+}, and Zn^{2+}; with Ni^{2+}, the reaction is first order in metal–substrate complex and first order in hydroxide ion. The second-order rate constant for the Ni^{2+}-catalyzed process is 10^7 that for the alkaline hydration in the absence of metal; the entire acceleration is accounted for by the change in $\Delta S^{\ddagger}$. With Cu^{2+}, the acceleration by metal is of the order of 10^9. Studies with nucleophiles other than hydroxide ion show that the mechanism of metal-catalyzed addition to the nitrile probably involves external attack, with the metal acting as a general acid, rather than the kinetically equivalent attack by nucleophile from the metal coordination sphere. The hydrolysis of the product amide to the carboxylic acid shows much weaker metal catalysis. The contrast between these two hydrolysis reactions is perhaps related to the "rack" mechanism which has been proposed for some enzymatic processes.

The metal-catalyzed hydrolysis of coordinating substrates is a subject of continued interest.[4] Such processes represent attractive models for the catalytic role of metals in some enzymatic hydrolyses,[5] but they also pose interesting mechanistic problems. For instance, the well-known[6] hydrolysis of glycine ethyl ester, catalyzed by Cu^{2+}, is first order in metal, substrate, and hydroxide ion.[7] Two kinetically equivalent mechanisms can be considered for such a process: (a) attack by external hydroxide ion with the metal serving to stabilize the developing carbonyl anion, or (b) attack on the carbonyl group by metal-bound hydroxide ion.



a



b

The two processes cannot be distinguished by simple kinetic tests (their transition states differ only in the position of one proton). Busch has shown[8] that when an intermediate related to mechanism a is prepared, using Co^{3+}, it will hydrolyze according to mechanism a; however, as he points out, this does not show that mechanism a is in fact followed except in this special case.

For a variety of reasons we decided to study the metal-catalyzed reactions of 2-cyano-1,10-phenanthroline (I). This substrate has the advantage that it should be strongly and completely bound to various metal ions, and that the cyano group is in a well-defined position within a metal complex, near the metal, but for reasons

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(4) *Cf.*, M. L. Bender, "Reactions of Coordinated Ligands," Advances in Chemistry Series, No. 37, American Chemical Society, Washington, D. C., 1963, Chapter 2.

(5) For a review of metal-activated enzymes, see B. L. Vallee, "The Enzymes," 2nd ed, P. D. Boyer, H. Lardy, and K. Myrbäck, Ed., Academic Press Inc., New York, N. Y., 1960, Chapter 5.

(6) M. L. Bender and B. W. Turnquest, *J. Am. Chem. Soc.*, **79**, 1889 (1957).

(7) D. Chipman, Ph.D. Thesis, Columbia University, 1965.

(8) M. D. Alexander and D. H. Busch, *J. Am. Chem. Soc.*, **88**, 1130 (1966).