two different ways yielding either the starting material or the isotopic exchanged products. Therefore, the maximum quantum efficiency for the exchange *via* a dimeric intermediate is 0.25. We have shown that the exchange may take place from both the singlet excited state and the triplet state of acetone. The very high quantum efficiency of the exchange from the triplet state in the presence of water may be explained by the formation of a polymeric intermediate such as **2**, while the exchange from the singlet excited state which is not catalyzed by water may be rationalized by the formation of a 1,3-dioxetane intermediate **1** which will dissociate back to acetone under our experimental conditions. The investigation is being continued.

Acknowledgment. The authors wish to acknowledge the National Institutes of Health, Grant No. AM-11,-676, and the National Science Foundation, Grants GP-16,347 and GP-32,278, for the support of this work.

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Hydrolysis and Aminolysis of Metal Ion Activated Esters. Nucleophilic Paths and Properties of the Tetrahedral Intermediate

Sir:

The occurrence of nucleophilic or general base catalyzed paths for hydrolysis of acyl-activated esters or amides is an important question in metal activated

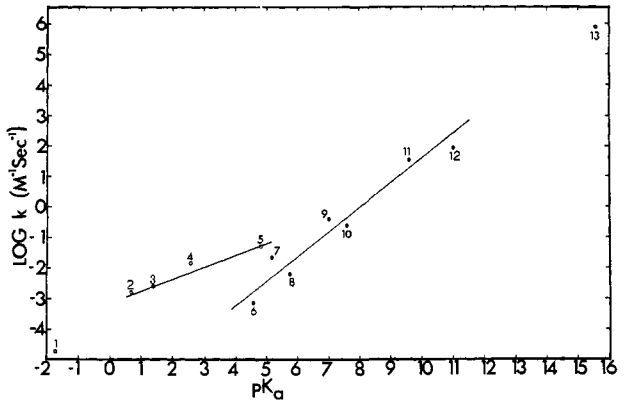
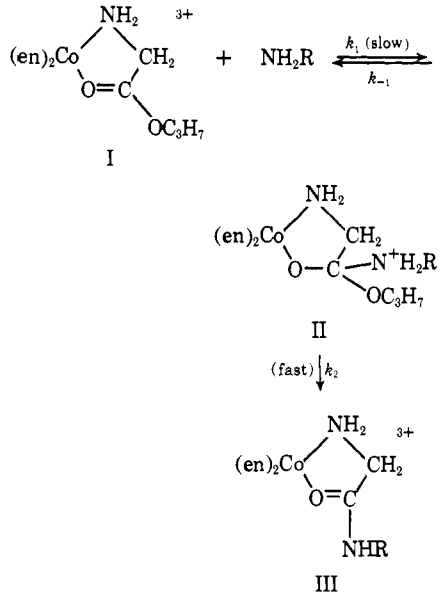


Figure 1. Plot of log k for lysis of $[Co(en)_2(glyOC_3H_7)](ClO_4)_3$ in aqueous solution *vs.* pK_a of nucleophile: 1, water; 2, trichloroacetate; 3, dichloroacetate; 4, chloroacetate; 5, acetate; 6, aniline; 7, pyridine; 8, aminoacetonitrile; 9, imidazole; 10, glycine ethyl ester; 11, ammonia; 12, dimethylamine; 13, hydroxide. β *ca.* 0.4 (oxygen anions), 0.8 (nitrogen bases).

enzymes such as carboxypeptidase A[1] and leucine aminopeptidase,[2] and in serine proteinases.[3] Previously it has been shown that nitrogen bases act as nucleophiles toward the metal ion activated ester I in aqueous solution but the mechanism of catalysis by oxygen bases (Figure 1) was not established although some support for a general base catalyzed role was presented;[4] we now report that acetate ion also acts as a nucleophile toward I. The distinction between the two mechanisms



(1)

occurs in the formation of an anhydride intermediate IV in the nucleophilic path, whereas the general base reaction leads directly to hydrolyzed product V, reaction 2. Although IV is much more rapidly hydrolyzed than I, its presence can be detected by competition experiments.

Rate data and products for the reaction of $[Co(en)_2(GlyOC_3H_7)](ClO_4)_3$ with H_2O, HO^-, NH_2CH_2CN, and $CH_3CO_2^-$ are given in Table I. It is apparent that contributions to the rate of ester disappearance by k_{OAc} and k_N (N = NH_2CH_2CN) determined from the rate law

$$k_{obsd} = k_{H_2O}[H_2O] + k_{OH}[OH^-] + k_N[N] + k_{OAc}[OAc^-]$$

are unchanged by the presence or absence of aminoacetonitrile and acetate, respectively, and that when acetate is absent the $k_N[N]$ contribution is balanced by the amount of $[Co(en)_2(GlyNHCH_2CN)]^{3+}$ found in the products. The latter experiments demonstrate that aminoacetonitrile acts entirely as a nucleophile toward I, and the independence of k_{OAc} and k_N establishes the absence of a $k[AcO^-][N]$ term in the rate law. Furthermore, when both acetate and aminoacetonitrile are present under conditions where $k_{OAc}[AcO^-]$ dominates k_{obsd} (~80%), the amount of $[Co(en)_2(GlyNHCH_2CN)]^{3+}$ formed remains practically unchanged. These results require aminoacetonitrile to compete for the acetate path following the rate-determining step and are consistent with the formation of the anhydride IV. Also they require aminoacetonitrile, HO^-, and H_2O to have essentially the same competition properties for

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Table I. Second-Order Rate Constants and Product Analyses for Reaction of $[Co(en)_2(GlyOC_3H_7)](ClO_4)_3$ with Aminoacetonitrile and Acetate Ion in Aqueous Solution (25.0°, μ = 1.0 $NaClO_4$)

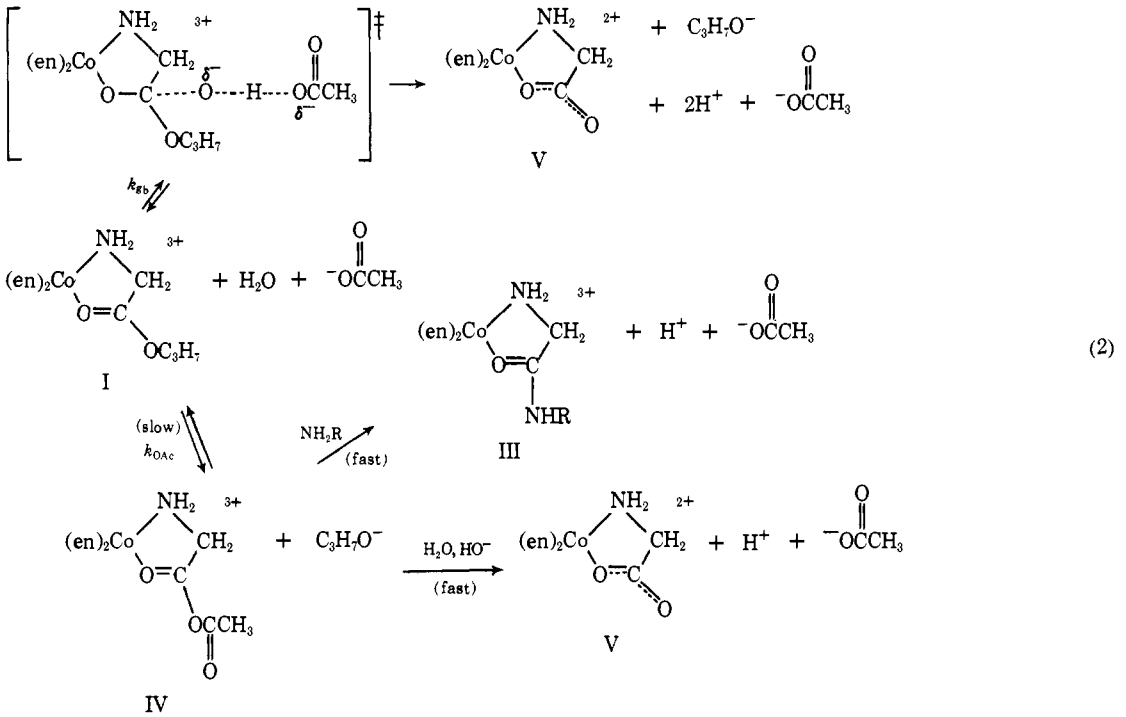
Nucleophile[a]	pH[c]	[Nucleophile],[c] M	$k_{nucleophile}$, M^{-1} sec^{-1} [d]	Isolated products[b]	
AcO^-	4.98–5.19	0.019–0.36 (6)	$5.5 \pm 0.5 \times 10^{-2}$	100% $[Co(en)_2(Gly)]^{2+}$	
NH_2CH_2CN	5.26–5.74	0.007–0.24 (6)	$6.2 \pm 0.7 \times 10^{-3}$	$[Co(en)_2(Gly)]^{2+}$ + $[Co(en)_2(GlyNHCH_2CN]^{3+}$ [g]	
NH_2CH_2CN	5.74 (2)	0.32		76, 74%	24, 26%
NH_2CH_2CN	5.36 (2)	0.07		87, 88%	13, 12%
AcO^- + NH_2CH_2CN	5.34–5.42	0.05–0.10 (AcO^-) (6) 0.19–0.38 (N)	$5.5 \pm 0.5 \times 10^{-2}$ (k_{OAc}) $6 \pm 1 \times 10^{-3}$ (k_N)		
AcO^- + NH_2CH_2CN	5.73, 5.76	0.45 (AcO^-) 0.32 (N)		77, 76%	23, 24%
AcO^- + NH_2CH_2CN	5.31, 5.36	0.39 (AcO^-) 0.07 (N)		86, 86%	14, 14%
H_2O[e]	0–2	55.5 (4)	1.89×10^{-5} (k_{H_2O})	100% $[Co(en)_2(Gly)]^{2+}$	
HO^- [f]	4.1–6.0	2.14×10^{-10}– 1.70×10^{-8} (4)	0.8×10^8 (k_{OH})	100% $[Co(en)_2(Gly)]^{2+}$	

[a] pK_a for aminoacetonitrile determined by pH titration as 5.76 in 1 M $NaClO_4$, 25.0°, pK_a for acetic acid taken as 4.80. [b] Products separated on Dowex 50W × 2 resin using 1–2 M HCl and estimated spectrophotometrically at 487 nm; $[Co(en)_2(GlyNHCH_2CN)]^{3+}$ isolated as $[Co(en)_2(GlyGlyOH)]^{3+}$ due to acid hydrolysis during elution. [c] Numbers in parentheses indicate number of experiments. [d] Calculated using $k_{obsd} = k_{H_2O}[H_2O] + k_{OH}[HO^-] + k_N[N] + k_{OAc}[AcO^-]$. [e] Spectrophotometric data at 487 nm and pH 1 gave $\Delta H^{\pm}$ = 15.4 kcal mol^{-1}, $\Delta S^{\pm}$ = −29 cal mol^{-1} deg^{-1}, for water path, μ = 1.0 (KNO_3). [f] Radiometric data at pH 5 gave $\Delta H^{\pm}$ = 16.9 kcal mol^{-1}, $\Delta S^{\pm}$ = 39 cal mol^{-1} deg^{-1} (corrected for dissociation of H_2O) for the hydroxide path, μ = 1.0 (KNO_3), pK_w (25°) = 13.77. [g] Amounts varied according to acetonitrile concentration.

the anhydride as for the parent ester. If acetate ion were acting as a general base, competition by aminoacetonitrile in this path would be excluded and $[Co(en)_2(GlyNHCH_2CN)]^{3+}$ formation would be substantially reduced. The results of these and similar experiments using other amines and carboxylic acids (Figure 1) imply that *all oxygen and nitrogen bases act as specific nucleophiles rather than as general bases toward acyl-activated esters or amides of the structural type I, irrespective of their basicity toward a proton.*

There has also been a continuing interest in mechanims of aminolysis of esters in aqueous solution particularly with regard to the existence of discrete addition intermediates and whether the addition step k_1, or loss of alcohol k_2, is rate determining.[5,6]

Aminolysis of I (NH_2R = $NH_2CH_2CO_2C_2H_5$) in dimethyl sulfoxide is not concerted and both the rate of formation and decay of II have been observed as separate reactions. This study will be described in detail subsequently,[7] but it is of interest here that at pH 10 in aqueous solution II forms 92 ± 1% III and 7–8% I, while in 0.1 M HCl 25 ± 2% I is regenerated. This establishes that $k_2 > k_{-1}$ in both acidic and alkaline conditions, and it may be deduced that if the inter-



(2)

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mediate II is formed in the aqueous aminolysis reaction *it occurs following the rate-controlling transition state.* Certainly the rate of disappearance of II in aqueous solution is too fast to follow using conventional stopped flow techniques ($t_{1/2} < 10$ msec at 25° in 50% DMSO–water). It is our contention that a similar situation exists for other amines and also for oxygen nucleophiles (Figure 1), with k_1 rate controlling, even though I represents a highly acyl-activated ester containing a "poor" leaving group.

Finally, we note (footnotes *e*, *f* to Table I) that the 10^{11}-fold catalysis of HO^- compared to H_2O is provided entirely by the large increase in $\Delta S^{\ddagger}$. A similar large positive $\Delta S^{\ddagger}$ (14 cal mol^{-1} deg^{-1}) accompanies formation of the intermediate II in dimethyl sulfoxide. These large values suggest that solvation plays an important role in determining the overall rate and differences in rate for such reactions and this question is being examined in more detail.

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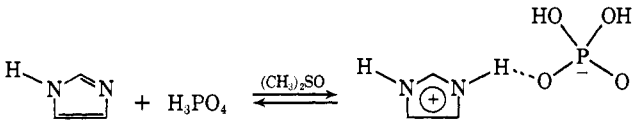
Base Stacking and Hydrogen Bonding in Crystals of Imidazolium Dihydrogen Orthophosphate

Sir:

Nuclear magnetic resonance effects accompanying the titration of imidazole with phosphoric acid in dilute solution in dimethyl sulfoxide have been attributed to a strong hydrogen bonding association.[1]



This hypothesis was, in turn, applied to the interpretation of nmr studies of the active site binding in ribonuclease, leading to a mechanism which involves hydrogen bonding between the imidazolyl side chain of the enzyme's histidyl residue 119 and a substrate phosphate moiety.[1,2] We have prepared the salt, imidazolium dihydrogen orthophosphate, and determined its crystal structure, and our results reveal short, strong (N–H···O–P) hydrogen bonds. Furthermore, we find structural evidence for stacking interactions between the imidazolium rings. This suggests to us that such interactions might occur between imidazolyl side chains in proteins and the purine or pyrimidine bases in nucleic acids.

The salt crystallized spontaneously on evaporation *in vacuo* of a very concentrated, equimolar, aqueous solution of imidazole and phosphoric acid. The structure analysis proved the salt to be anhydrous and confirmed the expected stoichiometry, *viz.*, $(C_3N_2H_5)^+$-$(H_2PO_4)^-$. The colorless, deliquescent crystals are monoclinic[3] with lattice dimensions $a = 8.53 \pm 0.01$ Å, $b = 12.72 \pm 0.02$ Å, $c = 15.93 \pm 0.02$ Å, $\beta = 126.13 \pm 0.06°$ (goniostat measurements, $20 \pm 2°$, λ(Mo Kα) = 0.7107 Å); space group $P2_1/c$ (No. 14); $\rho_{measd} = 1.59$ g cm^{-3} (by flotation), $Z = 8$ formulas per unit cell (two per crystallographically asymmetric unit), and $\rho_{X\text{-}ray} = 1.59$ g cm^{-3}. The crystal structure was solved by heavy atom methods and refined by full-matrix least-squares iteration using 3382 (observed) structure factor magnitudes, which were measured on a four-circle diffractometer (Picker FACS-I) using graphite monochromated Mo Kα X radiation. At an intermediate stage of the refinement, all the hydrogen atoms were located by a difference electron density synthesis and included in the subsequent final refinement which converged with (conventional) $R = 0.046$. Final atomic coordinates are listed in Table I. Observed and calculated structure factor data are listed in Table II.[4]

Table I. Atomic Coordinates (and Least-Squares Inverse-Matrix Estimated Standard Deviations)[a]

Atom	x/a	y/b	z/c
N(11)	18751 (31)	43783 (16)	44154 (15)
C(12)	34828 (41)	42929 (21)	53670 (20)
N(13)	38223 (33)	52045 (18)	58475 (16)
C(14)	23920 (43)	58884 (20)	51942 (22)
C(15)	11540 (39)	53775 (21)	42884 (20)
N(21)	−31674 (30)	3338 (15)	47822 (18)
C(22)	−27397 (33)	6870 (19)	56708 (19)
N(23)	−38152 (28)	15260 (14)	54893 (14)
C(24)	−49804 (41)	17095 (19)	44386 (19)
C(25)	−45593 (42)	9729 (20)	39981 (19)
P(1)	24964 (7)	34331 (4)	16910 (4)
O(11)	20857 (25)	35267 (13)	6378 (12)
O(12)	27986 (31)	44474 (14)	22420 (15)
O(13)	7804 (32)	28072 (18)	15390 (15)
O(14)	43095 (36)	27512 (24)	24297 (18)
P(2)	−11424 (7)	20832 (4)	29686 (4)
O(21)	3128 (23)	27930 (13)	30052 (12)
O(22)	−32212 (21)	22915 (13)	20687 (11)
O(23)	−10384 (24)	22087 (14)	39739 (12)
O(24)	−5461 (24)	9264 (12)	29403 (14)
H(N11)	1341 (60)	3812 (32)	3949 (31)
H(C12)	4378 (58)	3668 (33)	5707 (32)
H(N13)	4984 (57)	5351 (32)	6600 (31)
H(C14)	2318 (48)	6659 (25)	5346 (25)
H(C15)	46 (53)	5637 (31)	3611 (29)
H(N21)	−2701 (48)	−245 (25)	4728 (26)
H(C22)	−1827 (51)	317 (29)	6357 (28)
H(N23)	−3700 (39)	1912 (20)	5987 (21)
H(C24)	−5828 (41)	2273 (21)	4134 (21)
H(C25)	−5240 (54)	750 (30)	3201 (30)
H(O13)	874 (52)	2767 (27)	2119 (28)
H(O14)	5157 (67)	2709 (35)	2269 (34)
H(O23)	−80 (49)	2056 (24)	4459 (26)
H(O24)	−1338 (54)	512 (31)	2838 (29)

[a] $\times 10^5$ for nonhydrogen atoms; $\times 10^4$ for hydrogen atoms.

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(3) At the kind suggestion of a referee, we note that the unit cell that we report in the text, and on which our results and discussion are based, is not the Bravais-reduced cell. The lattice of the latter cell has space group symmetry $P2_1/n$ and dimensions $a_B = 8.53$ Å, $b_B = 12.72$ Å, $c_B = 12.90$ Å, $\beta_B = 93.80°$. The coefficients of the system of transformation equations which gives fractional atomic coordinates in the Bravais-reduced cell from coordinates in our unreduced cell are $10\bar{1}/010/001$.
(4) Observed and calculated structure factor data will appear following these pages in the microfilm edition of this volume of the journal. Single copies may be obtained from the Business Operations Office, Books and Journals Division, American Chemical Society, 1155 Sixteenth St., N.W., Washington, D. C. 20036, by referring to code number JACS-72-4034. Remit check or money order for $3.00 for photocopy or $2.00 for microfiche.