solute configuration of cobalt(III) β-diketonates[14] are therefore now on a firm basis. The validity of the spectroscopic criteria for chromium tris-β-diketonates has been confirmed by the X-ray analysis of Λ-$(+)_{589}$-*trans*-Cr((+)atc)$_3$[5] and also by our preliminary studies of Δ-$(-)_{589}$-Cr(acac)$_3$ in quasiracemic crystals.

Further, it is noted that the CD bands of $(-)_{546}$-Co(acac)$_3$ at 44,400 and 38,200 cm^{-1} (Figure 1) may be assigned,[11] respectively, to the A_2 and E components of the exciton-split $\pi-\pi^*$ transition, and that the sign of the rotatory power of these bands also predicts[20] the Λ configuration.

Finally, we emphasize several advantages of the method of determining absolute configurations in quasiracemic crystals. This method avoids a full X-ray analysis on a compound whose molecular structure is already known,[21] and it avoids the necessity of completely resolving the compound, a task of considerable difficulty in the case of nonpolar, electrically neutral complexes. Relatively little effort is required in cases where the crystal structure of a suitable racemic crystal has already been determined and, once such a structure is available, the method can be applied to an entire series of isostructural complexes. Our work in this area is continuing.

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(14) The Λ configuration has been (or may be) assigned to the $(-)_{546}$-cis and $(-)_{546}$-trans cobalt(III) complexes with the anions of (+)-hydroxymethylenecamphor,[15,16] (+)-3-acetylcamphor,[13,16,17] (+)- and (−)-hydroxymethylenecarvone,[18] 5-methylhexane-2,4-dione,[19] and 1-phenylbutane-2,4-dione.[11]

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(21) Such an analysis for a crystal of $(-)_{546}$-Co(acac)$_3$ which we have grown would require determination of the coordinates for two independent molecules (44 atoms) since the crystal has space group $P2_1$, $a = 11.31$, $b = 12.47$, $c = 12.50$ Å, $\beta = 101.04°$, $Z \approx 4$.

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Catalysis in Dipolar Aprotic Solvents. A Proton-Relay Mechanism Resembling the Mechanism of Action of Serine Enzymes[1]

Sir:

We are investigating the catalyzed hydrolysis of *p*-nitrophenol acetate (PNA) in dipolar aprotic solvents, and have found that in acetonitrile containing imidazole and benzoate ion, the dominant rate term is first order in substrate, imidazole, and benzoate ion. Crystallographic studies of a number of hydrolytic enzymes indicate that chymotrypsin, trypsin, elastase, subtilisin, and papain have a common mechanism of action involving a proton-relay mechanism.[2] An aspartate carboxyl is hydrogen bonded to an imidazole ring which is in the active site and hydrogen bonded to a serine (cysteine in papain) which functions as the nucleophile in the first step of hydrolysis. It therefore appears that proton transfer accompanies nucleophilic attack by the serine hydroxyl which is therefore expected to be much more nucleophilic than a normal serine hydroxyl. Since the active sites of enzymes would be expected to have solvent properties considerably different from aqueous solutions and may resemble dipolar aprotic solvents containing small amounts of water, our results appear to be of considerable interest.

Our early studies[3] were concerned with catalysis by imidazole. We have demonstrated in a range of dipolar aprotic solvents that hydrolysis of PNA is both first and second order in imidazole.[3,4] Recently, we have investigated the mechanisms of catalysis by mixtures of imidazole (IM) and carboxylate ions in acetonitrile and the results appear to be important in understanding enzyme action and biochemical evolution.

All the studies reported here were carried out by following the appearance of *p*-nitrophenol in acetonitrile at constant salt concentration, $[(n\text{-Bu})_4N^+ClO_4^-] + [(CH_3)_4N^+C_6H_5CO_2^-] = 0.01\ M$, [PNA] is approximately $10^{-4}\ M$, $[H_2O] = 1.0\ M$, and $T = 30.1°$. When imidazole alone is added, the hydrolysis of PNA follows the rate laws in eq 1 and 2.[4] Analysis of k_{obsd} at [IM]

$$v = k_{obsd}[PNA] \quad (1)$$

$$k_{obsd} = k_1[IM] + k_2[IM]^2 \quad (2)$$

$= 0.015$–$0.20\ M$ yields $k_1 = 3.1 \times 10^{-3}\ M^{-1}$ sec^{-1} and $k_2 = 1.3 \times 10^{-2}\ M^{-2}$ sec^{-1}.

When benzoate ion is added, there is marked catalysis,[4] and the infinity point corresponds to complete reaction. With $[C_6H_5CO_2^-] = [C_6H_5CO_2H]$ we find the dependence of k_{obsd} in eq 3 in studies both (1) at

$$k_{obsd} = k_1[IM] + k_2[IM]^2 + k_2[IM][RCO_2^-] \quad (3)$$

constant concentration of imidazole and varied concentrations of benzoate ion ($k_2' = 1.0\ M^{-2}$ sec^{-1}), and (2) at constant concentration of benzoate ion and varied concentrations of imidazole ($k_2' = 1.0\ M^{-2}$ sec^{-1}). Although there may be a term in benzoate ion alone, $k_1'[RCO_2^-]$, it is experimentally indistinguishable from zero in these experiments. Change of $[C_6H_5CO_2^-]/[C_6H_5CO_2H]$ from 10:1 to 1:1 keeping $[C_6H_5CO_2^-]$ constant has a small effect on the rate of hydrolysis of PNA. Preliminary experiments with acetate ion indicate behavior qualitatively similar to benzoate ion.

In the presence of initially added *p*-nitrophenol, there is no significant change in the rate of hydrolysis. Since we are measuring the rate of appearance of *p*-nitrophenol, this result, our other results with imidazole and *N*-methylimidazole, and basicity relations in acetonitrile[5] all indicate that the mode of catalysis represented by k_2' involves the carboxylate ion acting as a general base to abstract a proton from imidazole which func-

(1) Research supported by Grant No. AM-12743 from the National Institute of Arthritis and Metabolic Diseases.

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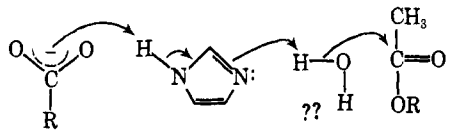
tions either as a nucleophile or as a general base with water as nucleophile (eq 4). The question of water



(4)

involvement has been investigated but a clear answer is not yet possible.

Enzymatic active sites may resemble dipolar aprotic solvents such as acetonitrile with small amounts of water present. The amide structure of the peptide backbone is certainly dipolar and crystallography has demonstrated variable amounts of water in active sites. Consequently, the medium we have studied appears to be a plausible model for the effective medium of an active site. It is striking that k_2' is predominant in this medium at $[C_6H_5CO_2^-]$ approximately 4×10^{-3} M and [IM] approximately 0.1 M and that catalysis by benzoate ions and imidazole is much more effective than benzoate ion alone or imidazole alone. Therefore, catalysis by carboxylate ion and imidazole is a very powerful mode of catalysis even in the absence of the binding, orientation, and proximity effects which are important in enzymatic catalysis.

The effectiveness of this mode of catalysis also has important implications for biochemical evolution. The evolution of proteins as biological catalysts imposes certain limitations on the solvent properties of active sites. To the extent that it is true that active sites must resemble the medium we have investigated, the proton relay mechanism (eq 4) appears to be a particularly effective catalytic mechanism that would have been readily selected in the course of evolution when carboxylate, imidazole, and hydroxyl groups were available as functional groups of proteins.

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Formation and Oxidative Addition Reactions of Five-Coordinate Iridium(I) Complexes

Sir:

While oxidative addition reactions of covalent molecules such as H_2 to low-spin d^8 complexes (notably to iridium(I) complexes of the type $Ir(CO)L_2X$, where L = phosphine or arsine and X = halide) have received considerable attention,[1-5] the reactivity patterns associated with variation of the ligands in such complexes are not yet well understood. Such ligand variations (as well as related variations in ligand concentrations and solvent properties) are especially significant when they are accompanied by changes in the coordination number of the d^8 complex from four to five. We wish to communicate the results of studies which reveal some new effects of this type and which contribute to an understanding of them.

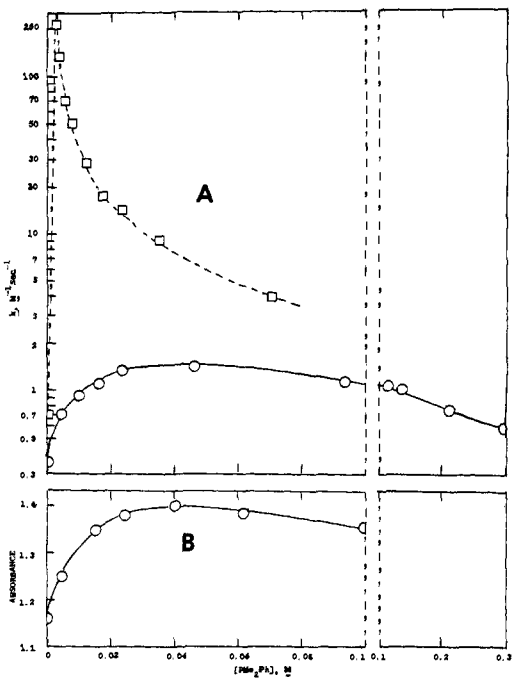

Figure 1. (A) Effect of excess PMe_2Ph on the rate of reaction of $Ir(CO)(PMe_2Ph)_2Cl$ with H_2 at 25°: ○, in chlorobenzene; □, in dimethylformamide. (B) Absorbance change at 362 nm accompanying the addition of PMe_2Ph to a 5.35×10^{-4} M solution of $Ir(CO)(PMe_2Ph)_2Cl$ in chlorobenzene.

Contrary to the behavior of the well-known compound $Ir(CO)(PPh_3)_2Cl$[3,4] which, in solution, is unaffected by the addition of excess PPh_3, we have found that the addition of low concentrations of excess PMe_2Ph (up to 0.04 M) to chlorobenzene solutions of the analogous complex $Ir(CO)(PMe_2Ph)_2Cl$ (**1**) results initially in the reversible association reaction described by eq 1, leading to the formation of the five-coordinate complex, $Ir(CO)(PMe_2Ph)_3Cl$ (**2**).

$$\underset{\mathbf{1}}{Ir(CO)(PMe_2Ph)_2Cl} + PMe_2Ph \underset{}{\overset{K}{\rightleftharpoons}} \underset{\mathbf{2}}{Ir(CO)(PMe_2Ph)_3Cl} \quad (1)$$

Evidence for this equilibrium is provided by the following observations: (1) the spectral changes accompanying the addition of up to 0.04 M PMe_2Ph, corresponding to the disappearance of the 377-nm band of **1** and to increases in absorbance at wavelengths below an isosbestic point at 365 nm and above another isosbestic at 394 nm; (2) the isolation from solutions containing excess PMe_2Ph of the pure solid compound $Ir(CO)(PMe_2Ph)_3Cl$ which has been fully characterized spectrally and by elemental analysis (ν_{CO} = 1885 *vs.* 1960 cm^{-1} for **1**) and whose structure is now being determined by X-ray diffraction; (3) the increased rate of reaction with H_2 accompanying the addition of up to 0.04 M PMe_2Ph. The reaction with H_2 under these conditions yields the previously characterized complex,[6] $Ir(CO)(PMe_2Ph)_3H_2^+$, in accord with eq 2. The spectral and reactivity changes, both depicted in Figure 1, parallel each other and quantitatively fit the equilibrium described by eq 1 yielding the values 2×10^{-2} M^{-1} for the equilibrium constant K and

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