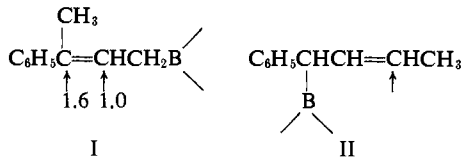
under the methyl protons. It was, therefore, 1-*p*-tolyl-1,3-propanediol diacetate (bp 131° (2 mm)).

Similarly, metalation and subsequent hydroboration of 1-phenylbut-2-ene[5] gave after acetylation in 60% yield (bp 100–110° (1 mm)) the mixture of the two diacetates of the diastereoisomeric 1-phenylbutane-1,3-diols and less than 10% of other distillable products. The isomers (3:4 ratio) were separated by glpc. The first isomer showed the benzylic proton at δ 5.81 (t, J = 7 Hz), the other proton α to acetate at 5.0 (q, J = 6 Hz), a methyl at 1.20 (d, J = 6 Hz), and the protons of the two acetoxy groups at 1.93 (s) and 1.96 (s); the corresponding signals for the diastereoisomer were at 5.76 (t, J = 7 Hz), 4.76 (q, J = 6 Hz), 1.20 (d, J = 6 Hz), 1.96 (s), and 2.0 (s).

A mixture of positional isomers was obtained only in the reaction with 3-phenylbut-1-ene.[6] The products in the last reaction consisted of 3-phenylbutane-1,3-diol and the diastereoisomeric 3-phenylbutane-1,2-diols in a 1.6:1 ratio. Acetylation of the mixture of diols gave a mixture (bp 130–140° (2 mm)) of a monoacetate of the 1,3-diol and diacetates of the 1,2-diols. The monoacetate showed the methyl α to the hydroxyl group at δ 1.5 (s), the methylene α to the acetoxy group at 4.06 (t, J = 6 Hz), the other methylene at 2.13 (m), and the acetoxy protons at 1.66 (s). The 1,2-diacetates showed three protons α to acetoxy groups, six protons of the acetoxy groups, and a methyl as a doublet. The pmr was not well resolved, since the diastereoisomers were not separated. All the compounds showed correct elemental analyses. The separations were performed by glpc on a 5 m × 1/4 in. column of 15% diethylene glycol succinate on Chromosorb W.

The reaction of phenylallyllithium with borane takes place either at the 1 or the 3 position of the allylic system to give a four-coordinated boron complex. It is possible that this complex transfers a hydride ion to excess borane present in the solution, forming a borohydride ion and an allylic borane. This allylborane, or the initial complex, is hydroborated in a regiospecific[7] manner to give predominantly the product with the two boron atoms in the molecule separated by three carbon atoms.

The attachment of the first boron atom to the phenylallyllithium system probably did not occur at the carbon next to the phenyl group. The collapse ratio during the protonation[8] of the phenylallylic anion was reported to be 2.4:1 for the 3 and 1 positions, respectively. The reaction of the anion with borane is less exothermic than protonation (and perhaps also reversible) and should give a larger amount of the more stable conjugated product than protonation. This was supported by the reaction of phenylallyllithium with trimethyl borate, that gave cinnamyl alcohol after oxidation of the product with hydrogen peroxide. The reaction of borane with the lithium derivative obtained from 3-phenylbut-1-ene should also give the allylic borane I in the first step, since even protonation has shown in this case a collapse ratio[6] of 40:1 in favor of the conjugated product. The second boron atom has a choice between a secondary and tertiary carbon and the last was preferred, contrarily to what is observed generally during hydroborations.[4] The first introduced boron



atom is certainly responsible for this effect. The position of the introduction of the first boron atom into 1-phenyl-3-methylallyllithium is less certain. Stabilization of the charge by the phenyl and of the double bond by the methyl group[6] will favor attack at the benzylic position. Further attack by borane of the possible intermediate II occurs almost entirely at only one of the two secondary carbons, the one further from the first boron atom.

The following procedure was used. Allylbenzene (2 g) was added to 23 ml of 1.6 *M* butyllithium in ether; the solution was left overnight[9] at room temperature and then added dropwise to 50 ml of a cooled solution (ice) of 2 *M* borane in THF. The solution was stirred for 5 hr, excess diborane decomposed slowly with 40 ml of water, and the product was oxidized by 40 ml of NaOH (3 *N*), dropwise addition of 40 ml of hydrogen peroxide, and subsequent stirring for 3 hr. Extraction of the product from the mixture (saturated with K_2CO_3) with three portions of 30 ml of ether and acetylation overnight with 16 ml of acetic anhydride–pyridine (1:1) gave 2.6 g of the diacetate, bp 125° (0.5 mm).

A reaction of ethyllithium with diborane was reported by Schlesinger and Brown to give lithium borohydride.[10] Recently a number of base-catalyzed reactions of borane were observed and were assumed to proceed *via* carbanions.[11]

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A Model for Alcohol Dehydrogenase. The Zinc Ion Catalyzed Reduction of 1,10-Phenanthroline-2-carboxaldehyde by *N*-Propyl-1,4-dihydronicotinamide

Sir:

Zinc ion is essential for the catalytic activity of horse liver alcohol dehydrogenase;[1-4] one zinc ion appears to be present[5-7] at each of the two active sites of the enzyme. The most likely location of the metal ion within the active site is at or near the binding sites of the nico-

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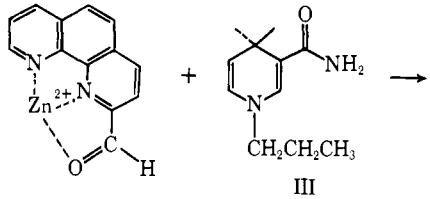
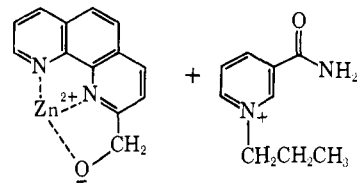
tinamide moiety of the coenzyme NAD^+ and the aliphatic alcohol and aldehyde substrates.[5-9] Although no direct proof of the coordination of the functional groups of the substrates to the enzymic zinc ion exists, several investigators have suggested that such interactions could efficiently catalyze hydride transfer between coenzyme and substrate by polarizing the carbonyl of aldehyde substrates and by facilitating deprotonation of the hydroxyl group of alcohol substrates.[10-12]

In the present communication, we wish to report that zinc ion efficiently catalyzes the reduction of 1,10-phenanthroline-2-carboxaldehyde (I) to 1,10-phenanthroline-2-carbinol (II) by *N*-propyl-1,4-dihydronicotinamide (III) in acetonitrile at 25° (eq 1). This is the first "model" reaction which supports the catalytic function of the enzymic metal ion indicated above as well as the first example of the reduction of an aldehyde by an NADH analog in a nonenzymic system.[13-15]



Zn^{2+}–I

III



(1)

Zn^{2+}–II

The Zn^{2+}–I complex was chosen for study since 1,10-phenanthroline derivatives generally have a high affinity for zinc ion and construction of molecular models of the complex indicated that the carbonyl group of the aldehyde could coordinate to the metal ion. This latter interaction is possibly analogous to the suggested coordination of the aldehyde to the enzymic zinc in the reactive enzyme–NADH–aldehyde ternary complex. The zinc ion catalyzed reaction between I and III was carried out in anhydrous acetonitrile instead of water since the true substrates for alcohol dehydrogenase are the unhydrated aldehydes and not their hydrated or aldehydrol forms.[16] In aqueous acetonitrile, the Zn^{2+}–I complex exists predominantly in the hydrated form.

One inherent disadvantage of this system is that the zinc ion may promote reduction of the aldehyde by an indirect electronic effect through the aromatic ring system in addition to interacting directly with the carbonyl group. The relative importance of these two possibilities has not yet been determined for the *o*-phenanthroline system.[17] However, the zinc ion catalyzed reduction of pyridine-2-carboxaldehyde and pyridine-4-carboxaldehyde by tetraethylammonium borohydride in acetonitrile has been investigated and the rate of reduction of the Zn^{2+}– pyridine-2-carboxaldehyde complex is at least 100 times greater than that of the Zn^{2+}–pyridine-4-carboxaldehyde complex.[18] These results indicate that the sole mode of zinc ion catalysis of pyridine-2-carboxaldehyde cannot be an electronic effect exerted by the metal ion through the aromatic pyridine ring but must involve a direct interaction of the metal with the carbonyl. By analogy, the zinc ion catalysis of the reduction of 1,10-phenanthroline-2-carboxaldehyde (I) by *N*-propyl-1,4-dihydronicotinamide (III) is probably not only due to an electronic effect generated by the metal ion through the *o*-phenanthroline system but most likely also involves direct interaction or proximity of the metal to the carbonyl to a significant extent.

The reaction indicated in eq 1 can be readily assayed spectrophotometrically either by following the loss of the characteristic dihydronicotinamide spectrum of III at 350 mμ upon oxidation or by measuring the conversion of Zn^{2+}–I to Zn^{2+}–II at 292 and 272.5 mμ. Since Zn^{2+}–I absorbs more intensely than Zn^{2+}–II at 292 mμ, the reduction of Zn^{2+}–I to yield Zn^{2+}–II is characterized by a net decrease of absorption at this wavelength; on the other hand, the greater absorption of Zn^{2+}–II at 272.5 mμ relative to Zn^{2+}–I results in a net increase of absorption at this wavelength as the reaction proceeds. The reaction was generally studied at 25° in acetonitrile with Zn^{2+}, I, and III present at concentrations of 10×10^{-5}, 5×10^{-5}, and 5×10^{-5} *M*, respectively. Under these conditions, the yield of the Zn^{2+}–II complex was greater than 80% as measured spectrophotometrically. No reduction of 1,10-phenanthroline-2-carboxaldehyde (I) by *N*-propyl-1,4-dihydronicotinamide (III) can be observed in the absence of zinc ion.

The second-order rate constant for the reduction of Zn^{2+}–I by III at 25° in acetonitrile is $19 \pm 4\ M^{-1}\ min^{-1}$. The rate of the reaction is the same, within experimental error, when dihydroquinone is present at comparable concentrations to the Zn^{2+}–I complex. Since dihydroquinone generally affects free-radical reactions,[14] the reduction of the Zn^{2+}–I complex by III most likely proceeds by a hydride transfer mechanism.

Confirmation that the primary product in the reaction was the Zn^{2+}–II complex came from product analysis of the reaction mixture by ultraviolet, infrared, and mass spectrometry as well as paper chromatography. For product analysis, 250-ml reaction mixtures, con-

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(17) These effects could be distinguished if the reduction of an electronically equivalent isomer of I was studied in which the aldehyde function was remote from the zinc ion. If direct interaction of the carbonyl with the metal ion was the essential feature of the catalysis, the rate of reduction of the isomeric aldehyde would be considerably slower. This experiment has not yet been performed since it is not readily apparent which of the chelated isomeric 1,10-phenanthroline aldehydes would be electronically equivalent to the Zn^{2+}–I complex and none of these aldehydes, other than the isomer synthesized here, are presently available.
(18) The zinc ion catalyzed reduction of pyridine-2-carboxaldehyde, unlike the pyridine-4-carboxaldehyde, is too rapid to study by conventional mixing techniques. As a result, only a lower limit can be presented for this rate ratio. Further studies of the zinc ion catalyzed reduction of pyridine-2-carboxaldehyde, as well as 1,10-phenanthroline-2-carboxaldehyde, by tetraethylammonium borohydride are being undertaken using stopped-flow techniques.

taining concentrations of reactants comparable to those used to estimate the yield of the reaction spectrophotometrically, were prepared and allowed to proceed to completion. The product was isolated by removing the acetonitrile, dissolving the residue in chloroform, and extracting with an aqueous zinc chloride solution. After enough EDTA was added to the aqueous phase to chelate all the zinc ion present, the product was reextracted into chloroform. The chloroform solution was then dried over sodium sulfate and evaporated to dryness. The residue yielded ultraviolet and infrared spectra that were very similar to those of an authentic sample of 1,10-phenanthroline-2-carbinol. When part of the residue was dissolved in an ethanolic solution of dimedone and chromatographed on Whatman No. 3M paper using isopropyl alcohol–water–trichloroacetic acid–ammonia (75 ml:25 ml:5 g:0.2 ml) as the solvent system, a spot indistinguishable from an authentic sample of 1,10-phenanthroline-2-carbinol was obtained.

The mass spectra of the residue and that of independently synthesized 1,10-phenanthroline-2-carbinol (II) were very similar and consistent with the calculated composition $C_{13}H_{10}N_2O$ for II. Each spectrum possessed the intense and characteristic molecular ion peak at *m/e* 210 as well as an isotope peak at *m/e* 211 that was 14.5% as intense as the molecular ion peak.[19]

As further proof that II was the product and in order to investigate if the reaction proceeded by direct hydrogen transfer, 1-propyl-4,4-dideuterionicotinamide (86% isotopically pure by nuclear magnetic resonance) was used as the reductant in place of the corresponding dihydronicotinamide. The product was then isolated as indicated above. An intense molecular ion peak at *m/e* 211, corresponding to monodeuterated 1,10-phenanthroline-2-carbinol ($C_{13}H_9DN_2O$) and accounting for 70% of the product, was observed when the mass spectrum of the reaction product was obtained at the approximate appearance potential of the P − 1 (*m/e* 209) peak of undeuterated 1,10-phenanthroline-2-carbinol. These results provide further evidence that II is the primary product of the reduction. They also demonstrate that II is formed by direct hydrogen transfer from III to the carbonyl carbon of Zn^{2+}–I. Even though direct hydrogen transfer is very likely in the absence of any readily exchangeable hydrogens in anhydrous acetonitrile, its demonstration is essential if this this system is to be considered an appropriate model for the alcohol dehydrogenase reaction.[20,21]

In summary, the zinc ion catalysis of the reaction between 1,10-phenanthroline-2-carboxaldehyde and *N*-propyl-1,4-dihydronicotinamide strongly suggests that either coordination or, at the least, proximity to a metal ion is a feasible and efficient method for activation of a carbonyl group for reduction. The catalytic efficiency of the zinc ion must be significant since (a) no reaction could be detected in the absence of the metal ion and (b) 1,10-phenanthroline-2-carboxaldehyde is the first aldehyde to be reduced by a dihydronicotinamide in a nonenzymic system. Although the present experiments cannot be considered proof that zinc ion serves a similar catalytic function in alcohol dehydrogenase, they certainly strengthen the view that coordination or proximity of the carbonyl to the zinc ion could be a very important feature of the enzymic catalysis.

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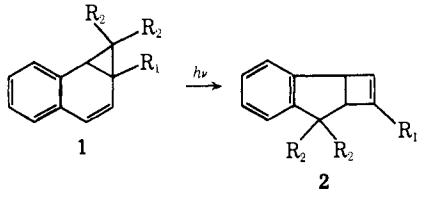
Intermediacy of a 1,2-Benzotropilidene in the Photochemical Rearrangement of a Benzonorcaradiene to a Benzobicyclo[3.2.0]hepta-2,6-diene

Sir:

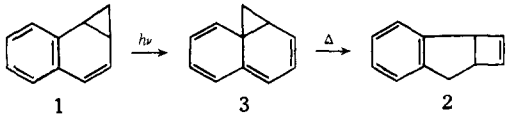
The photochemical rearrangement of the benzonorcaradiene moiety **1** to the benzobicyclo[3.2.0]hepta-2,-6-diene skeleton **2** has been noted by several groups.[1]



a, $R_1 = R_2 = H$
b, $R_1 = CO_2CH_3$; $R_2 = H$

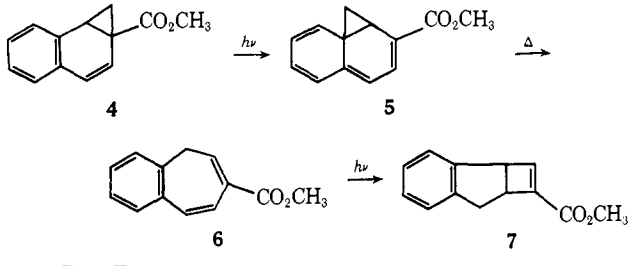
One mechanism for this conversion involves the intermediacy of **3** which undergoes thermal rearrangement to **2** (Scheme I). A second possible mechanism for

Scheme I. The One-Photon Route for the Benzonorcaradiene to Benzobicyclo[3.2.0]hepta-2,6-diene Conversion



this process is a two-photon sequence wherein diene **6** is a direct precursor of **7** (Scheme II).[1d] While

Scheme II. The Two-Photon Route for the Benzonorcaradiene to Benzobicyclo[3.2.0]hepta-2,6-diene Conversion



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