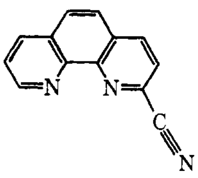
Strongly Catalyzed Ligand–Ligand Reaction within a Mixed Metal Complex

Sir:

Among the largest observed rate accelerations by metal coordination are the increase[1] in base-catalyzed hydration rate of **1** by 10^7 with the Ni^{2+} complex, and 10^9 with Cu^{2+}. Even larger effects were seen[1,2] in metal-catalyzed hydrations of **2**. Although we have found several cases[3] in which metal ions organized, and catalyzed, a reaction between two ligands in a mixed complex, no such ligand–ligand process could be detected[1] with **1**. We now wish to report that in the case of **2** it is indeed possible to get metal-catalyzed attack by a second organic ligand within the mixed complex, and that very large rate increases accompany this process.



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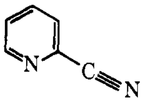

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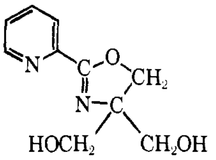
When 10 mmol of **2** in aqueous ethanol is treated with 20 mmol of trishydroxymethylaminomethane (Tris) and 20 mmol of $CuCl_2$, 2-(2′-pyridyl)-4,4-dihydroxymethyl-Δ^2-isoxazoline (**3**) is formed in essentially quantitative yield. The product, mp 146–147°, has the expected nmr, ir, uv, and mass spectra. The same product is formed when Ni^{2+} is substituted for Cu^{2+}. Although in the absence of Tris the metal-catalyzed reactions[1] of **2** afford pyridine-2-carboxamide (**4**), spectroscopic observations show that **3** and not **4** is the exclusive product when $CuCl_2$ is used at 1 mM and Tris is used at 2.5 mM. Under these conditions Cu^{2+} exists as a Tris complex, and attack of the Tris ligand is 10^2 times as fast as attack by water, although the bulk concentration of the latter is over 10^4 times that of the Tris. The amide **4** is completely stable to metal and Tris under these conditions.



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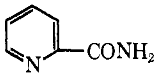

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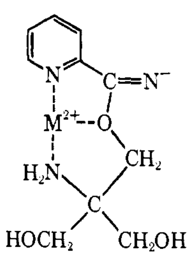
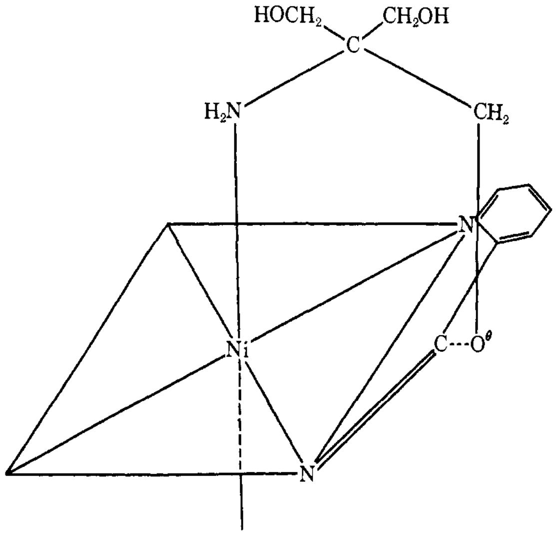
Extensive kinetic studies[4] show that the transition state[5] contains the metal ion, the nitrile **2**, one and only one coordinated Tris, and one and only one OH^-.

Under all conditions related to those described above Tris fails to attack **1**, and in the presence of Ni^{2+} or Cu^{2+} **1** gives only the corresponding carboxamide. The distinction in the behavior of **1** and **2** is the principal piece of evidence which allows us to choose between the two[1] obvious mechanisms for the Tris reaction with **2**. The kinetic law shows that it is an oxygen atom of Tris which attacks a cyano group of **2** in the rate-limiting step, since with hydroxide ion the Tris hydroxyl would be equilibrated with its alkoxide form. Addition of an oxygen of Tris to **2** to form the corresponding imino ester is followed by reaction with the Tris amino group to produce **3**. In mechanism I,[6] the O^- which attacks the cyano group of coordinated **2** comes from the coordination sphere of the metal, and the metal has the function of delivering the nucleophile. In the second general mechanism (II),[6] the metal which is coordinated to **2** acts as a Lewis acid to stabilize the developing N^- in the cyano group as a nucleophile attacks it from an external direction.



mechanism I



mechanism II

Molecular models show that either mechanism I or II (with slight strain) could operate with compound **2**. Mechanism I should operate perfectly well in the case of the phenanthroline compound **1** also, but models show that it is extremely unlikely that mechanism II could operate in this latter case. The strain in the transition state for mechanism II involves a little bending of the bond between the pyridine nitrogen of **2**

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(1) R. Breslow, R. Fairweather, and J. Keana, *J. Amer. Chem. Soc.*, **89**, 2135 (1967).

(2) *Cf.* also K. Sakai, T. Ito, and K. Watanabe, *Bull. Chem. Soc. Jap.*, **40**, 1660 (1967).

(3) R. Breslow and D. Chipman, *J. Amer. Chem. Soc.*, **87**, 4195 (1965); R. Breslow and L. E. Overman, *ibid.*, **92**, 1075 (1970).

(4) Details may be found in the Ph.D. Thesis of M. Schmir, Columbia University, 1969.

(5) From the temperature dependence of the reaction we determine that $\Delta H^{\ddagger} = +13.7 \pm 0.3$ kcal/mol. From the full second-order rate constant expressed as first order in the mixed complex, which we deduce from the known[1] binding constant for **2** with Ni^{2+}, the $\Delta S^{\ddagger} = +23$ eu. For comparison, the attack of hydroxide ion on either **1** or the Ni complex of **1** has a $\Delta H^{\ddagger}$ of +15.1 and 15.7 kcal/mol, respectively.[1] The attack of hydroxide ion on **2** has a $\Delta H^{\ddagger}$ of 15.6 kcal/mol.[1] On the other hand, the $\Delta S^{\ddagger}$ for the alkaline hydration of **1** was −20 eu, while $\Delta S^{\ddagger}$ for the Ni^{2+}-catalyzed hydration of **1** was +14 eu.[1] These very large accelerations by metal ions, includng the present one, are reflected principally in the entropy of activation.

(6) For simplicity these mechanisms are described and shown with the other two OH's of Tris uncoordinated. In each case one additional OH can reach a coordination position of the metal.

and the metal, but in **1** this bending would lead to decoordination of the most basic nitrogen atom in **1**, and it would be very unfavorable for this compound.

It thus seems most likely that mechanism II is involved here, and it is related to the one we had already described[1] for the hydration of **1**. The metal ion serves as a Lewis acid, and the very large catalysis is chiefly associated with a gain in coordination in the transition state for the addition.[7] In addition to this factor, the reaction of Tris with **2** in the presence of metal ions has extra help from the coordination of Tris with the metal, so that the well-known effects of neighboring group participation can operate even when these effects involve the development of a small amount of strain in the transition state.

(7) Either mechanism can account for the finding that the very large acceleration in this reaction is located chiefly in the $\Delta S^{\ddagger}$ part of the activation parameters, since the Tris is already bound to the metal ion in the starting materials and thus loses no further translational freedom in the transition state. The positive value of $\Delta S^{\ddagger}$ must reflect the liberation of solvent molecules in this transition state.

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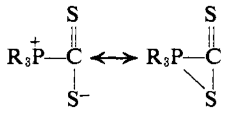
2-Benzylidene-1,3-dithioles. A Remarkably Rapid Wittig Reaction

Sir:

Aliphatic phosphine–carbon disulfide complexes (**1**)



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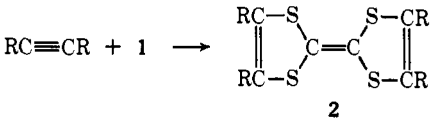
have been known for 90 years,[1] but very few chemical reactions of the complexes have been reported. We wish to report a general reaction of the complexes with acetylenes and aromatic aldehydes.

The adduct of carbon disulfide and tributylphosphine[2] reacted with acetylenes having at least one electron-withdrawing substituent at temperatures as low as −30° as judged by the disappearance of the purple-red color of **1**. Poor yields of bidithioles **2** could be



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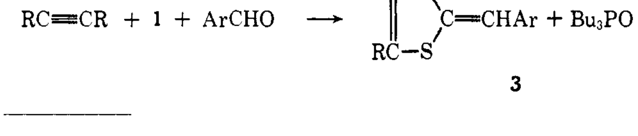
obtained. When aromatic aldehydes were also present, excellent yields of 2-benzylidene-1,3-dithioles (**3**) were obtained.



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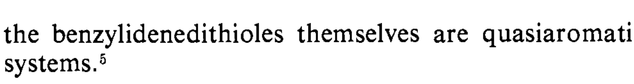
This reaction has proved to be a general one for acetylenes although requisite reaction conditions vary with the acetylene. Aryl acetylenes reacted slowly at room temperature, acetylene reacted at a useful rate at 100° or higher, and electronegatively substituted acetylenes reacted rapidly at 0 to −30°. The rate differences observed with the acetylenes are consistent with the rate-determining reaction being a nucleophilic attack of **1** on the acetylene to give the phosphorane **4**. A subsequent Wittig reaction of **4** with the aromatic aldehyde would complete the reaction.



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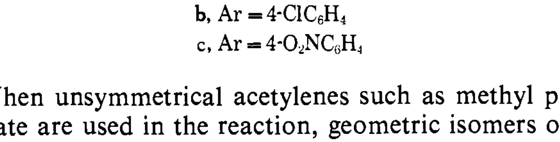
A remarkable feature of the reaction is its rapidity. As methyl propiolate is added to an ethereal solution of benzaldehyde, carbon disulfide, and tributylphosphine at −30°, dimethyl 2-benzylidene-1,3-dithiole-4,5-dicarboxylate precipitates from solution. This reaction is several orders of magnitude faster than other Wittig reactions.[3] Moreover, the ease of reaction of **4** with aldehydes is the type of behavior normally characteristic of the stable, less reactive, resonance-stabilized alkylidene phosphoranes.[3]

A possible explanation of the abnormal reactivity of **4** is that in the zwitterionic structure contributing to **4**, although considerable stabilization of the negative charge by the two adjacent sulfur atoms might be expected,[4] any tendency toward planarity in the dithiole ring would lead to a cyclic 8-π-electron system which would be antiaromatic and destabilized. The negative charge in **4** is removed from the dithiole ring in the transition state leading to the betaine **5**, and a lowered activation energy would be expected. Collapse of **5** to **3** and phosphine oxide should also be rapid because



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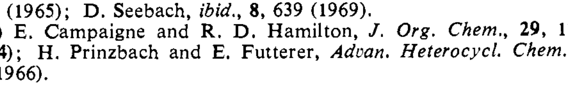
the benzylidenedithioles themselves are quasiaromatic systems.[5]



6a, Ar = 4-pyridyl
b, Ar = 4-ClC$_6$H$_4$
c, Ar = 4-O$_2$NC$_6$H$_4$

When unsymmetrical acetylenes such as methyl propiolate are used in the reaction, geometric isomers of **6** are formed—usually in nearly equal yields. The existence of the two isomers is clearly shown by the two

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(1) A. W. Hofmann, *Ann. Chem. Suppl.*, **1**, 26, 59 (1861); A. Hantzsch and H. Hibbert, *Chem. Ber.*, **40**, 1508 (1907).

(2) W. C. Davies and W. J. Jones, *J. Chem. Soc.*, 33 (1929).

(3) A. Maercker, *Org. React.*, **14**, 270 (1965).

(4) E. J. Corey and D. Seebach, *Angew. Chem., Int. Ed. Engl.*, **4**, 1075 (1965); D. Seebach, *ibid.*, **8**, 639 (1969).

(5) E. Campaigne and R. D. Hamilton, *J. Org. Chem.*, **29**, 1711 (1964); H. Prinzbach and E. Futterer, *Advan. Heterocycl. Chem.*, **7**, 39 (1966).