appears reasonable that the mechanism whereby pyridine prevents complete substitution of $POCl_3$ to R_3PO involves an effective reduction in Grignard reagent concentration, probably by association with RMgX. The suggestion that phosphonic acids may be produced in better yield by using larger proportions of pyridine at lower temperatures[5] may be valid, but not because of blocking Cl atoms in $POCl_3$. Work has been started in this Laboratory to study quantitatively the effect of bases on Grignard reactions involving $POCl_3$ and related compounds.

The work with pyridine and α-picoline indicates that $POCl_3$ probably does not form quaternary salts with any pyridine bases. Actually, compounds have been isolated between $POCl_3$ and acids such as SO_3[17] and $SnCl_4$.[18] In light of the results obtained with pyridine bases, formula I, may be considered a more likely structure than formula II. An incidental result of the present work is that doubt is cast on the postulated reaction mechanism in a recent paper,[19] which requires quaternary compound formation between $POCl_3$ and a pyrazine derivative.

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COMMUNICATIONS TO THE EDITOR

THE NATURE OF THE XANTHINE OXIDASE FACTOR

Sir:

A factor(s) in liver residue and soy flour which increases the level of liver and intestinal xanthine oxidase when fed to weanling rats has been described by Westerfeld and Richert.[1,2,3,4] An excellent assay for this factor utilizing rat intestine also has been described by these authors.[5] However, the nature and mode of action of this substance(s) is unknown.

During the course of fractionation studies on liver residue it was found that the xanthine oxidase factor(s) could be partially liberated by autoclaving in water. The activity of the extracts so obtained was found to be dialyzable and stable to severe acid or alkaline treatment.

When liver residue or extracts from liver residue were ashed, the activity, surprisingly enough, was found to be unaltered. The inorganic material so obtained, when assayed spectrographically,[6] was found to contain many elements among which were Al, Sb, Ba, B, Cr, Co, Pb, Mo, Ni, Ag, Sn, Ti, V and Zn. The more "common" elements such as K, P, Na, Cu, Fe, Si, Mg and Mn were also present. In addition, the activity of liver residue or its ash could be replaced by including a supplement of Hoagland's A-Z solution[7] in the diet of rats. Further investigation with single salt supplements revealed that the ingestion of molybdate ion is responsible for the increased xanthine oxidase levels.

The addition of as little as 1 mg. of sodium molybdate/kg. diet or the injection of 10γ subcutaneously gave values for xanthine oxidase equal to that obtained when 10% liver residue was fed. Table I shows some typical data. Preliminary studies indicate that no other element is able to replace molybdenum and the highly specific nature of this effect is therefore apparent.

TABLE I

EFFECT OF LIVER RESIDUE, LIVER RESIDUE FRACTIONS AND MOLYBDATE ION ON RAT INTESTINAL XANTHINE OXIDASE VALUES

Supplement added to basal diet/kg.	Average X. O. value, c.mm.O_2 uptake/unit time/unit wgt. of intestine
None	4.4
10% liver residue (LR)	25.6
Liver residue extract (LRE) ≏16% LR	32.0
Ash of LR ≏ 10% LR	28.2
Ash of LRE ≏ 20% LR	26.9
Dialyzed LRE ≏ 20% LR	5.1
Sodium molybdate, 1 mg.	23.5

To our knowledge, this represents the first report suggesting an *in vivo* role for molybdate in an animal enzyme system. The possible importance of this finding on the role of molybdenum in animal nutrition is of course obvious. Studies are now in progress to elucidate the precise role of molybdenum on the activity of xanthine oxidase.

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RECEIVED JANUARY 21, 1953

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