The resulting potassium salt (III) accepted one proton upon potentiometric titration with aqueous acid. *Anal.* Calcd. for $K_4B_{20}H_{18}\cdot 2H_2O$: H_2O, 8.44; B, 50.7; K/B, 0.200; equiv. wt., 427; mol. wt., 427. Found: H_2O, 8.3; B, 50.5; K/B, 0.200; equiv. wt., 432; mol. wt., 435. Addition of tetramethylammonium ion to an acidified solution of III produced a salt identical with that obtained directly from I. The $B_{20}H_{19}^{-3}$ ion exhibits a pK_a of 6.3.

The previously reported[1] isomerization of the "second isomer" of $B_{20}H_{18}^{-2}$ to authentic $B_{20}H_{18}^{-2}$ in aqueous acid was actually an air oxidation (perhaps catalyzed by a trace of ferric ion) of $B_{20}H_{19}^{-3}$ to $B_{20}H_{18}^{-2}$. Thus, a solution of III in 1 *M* mineral acid at 25° was stable indefinitely in a nitrogen atmosphere, while an 18% conversion to $B_{20}H_{18}^{-2}$ was observed after 72 hr. in an oxygen atmosphere. Furthermore, the oxidation of $B_{20}H_{19}^{-3}$ to $B_{20}H_{18}^{-2}$ was accomplished with hydrogen peroxide (42% yield) and ferric ion (68% yield) in acidic aqueous solution.

The B^{11} n.m.r. spectrum of III contained a singlet (area 2) at lowest field, a symmetrical low field doublet (area 2), and a symmetrical high field doublet (area 16). This spectrum is in agreement with that of a $B_{10}H_{10}^{-2}$ ion substituted at one apex. On this basis, III may be formulated as two $B_{10}H_{10}^{-2}$ polyhedra joined by a two-center bond at their apices.[4]

Protonation of $B_{20}H_{18}^{-4}$ to produce $B_{20}H_{19}^{-3}$ may proceed by proton addition to this B–B two-center bond.[4] The B^{11} n.m.r. spectrum of an acidified solution of III is not sufficiently well defined to permit a firm decision to be made on this point. However, the spectra thus far obtained suggest that the acidic proton exists in an unsymmetrical environment. A B–H–B bridge band is observed at 5.40 μ in the infrared spectrum of $B_{20}H_{19}^{-3}$.

Assuming that the proposed structures[4] of $B_{20}H_{18}^{-2}$ and $B_{20}H_{18}^{-4}$ are correct, the oxidation of $B_{20}H_{18}^{-4}$ to $B_{20}H_{18}^{-2}$ in acidic solution requires the intervention of a molecular rearrangement[5] (apex–apex to apex–equatorial interactions).

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(4) A structure first suggested for a then unknown $B_{20}H_{18}^{-4}$ ion by W. N. Lipscomb, *Proc. Natl. Acad. Sci. U. S.*, **47**, 1791 (1961). It was further postulated that a $B_{20}H_{19}^{-3}$ could be formed by protonation of the B–B two-center bond in this $B_{20}H_{18}^{-4}$ and that $B_{20}H_{18}^{-2}$ contained two such bridge bonds, each of which joins two $B_{10}H_{10}^{-2}$ units by apex–equatorial interaction.

(5) Such rearrangements were previously suggested by Kaczmarczyk-Dobrott, and Lipscomb (ref. 2) and were described as polyhedral isomerizations in which apical and equatorial positions in $B_{10}H_{10}^{-2}$ interconvert. Other reaction paths are also available.

(6) (a) Alfred P. Sloan Research Fellow; (b) National Science Foundation Undergraduate Research Assistant, Summer, 1962.

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Neighboring Group Participation in Phosphate Ester Hydrolysis

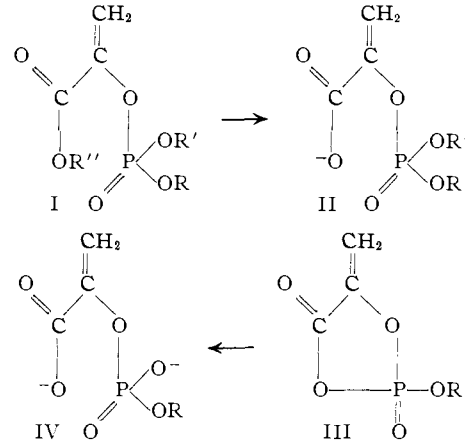
Sir:

We wish to report the rapid hydrolysis of the P,P-dimethyl ester (I, R = R′ = CH_3; R″ = H) to free phosphoenol pyruvate under mildly acidic conditions.

Whereas in bicarbonate buffer (pH 8.0) at 100° this dimethyl ester undergoes quantitative hydrolysis in 6.5 hr. to the P-monomethyl ester[1] (IV, R = CH_3), in initially neutral solution *both* methyl groups are lost at room temperature, the pH falling to 2.5, with hydrolysis to free phosphoenol pyruvate[2] (IV, R = H) being complete within 72 hr.

Both stages of the hydrolysis involve nucleophilic attack on phosphorus since the P,P-diphenyl (I, R = R′ = C_6H_5, R″ = H) and P- methyl, P-phenyl (I, R = CH_3, R′ = C_6H_5, R″ = H) esters also give free phosphoenol pyruvate under these conditions, the latter by way of the monomethyl ester (identified by paper chromatography).

The hydrolysis of the methyl group of IV (R = CH_3) is much faster than that observed with simple dialkyl phosphates under acidic conditions.[5] Moreover, it is complete before detectable hydrolysis of the enol–ester linkage of the product occurs. These observations indicate a reversal of the usual order of relative reactivity of the mono- and dialkyl phosphates under similar conditions,[5,6] even though in this case the monoester is an enol phosphate. We suggest that the neighboring carboxyl group participates in the hydrolysis.[7] One possible mechanism involves nucleophilic attack on phosphorus by carboxylate oxygen.



At least one proton must be associated with the displacement, since the dianion (IV, R = CH_3) is stable at pH 8. This implies that the molecular species displaced is methanol rather than methoxide ion. A concerted displacement is indicated by the specificity of both steps. In each case a methyl group is hydrolyzed preferentially, notwithstanding the fact that enol–ester linkages are usually more labile under acidic conditions.[8] Such selectivity is normally observed in the acid and base-catalyzed hydrolyses of trialkyl and dialkyl phosphate esters bearing vicinal hydroxyl functions.[9,10]

(1) Isolated as the barium salt, having a correct analysis, and consistent n.m.r. and infrared spectra.

(2) Phosphoenol pyruvic acid can be isolated as the monocyclohexylammonium salt in 50% yield. *Anal.* Found: C, 40.7; H, 6.9; N, 5.2. $C_9H_{18}PO_6N$ requires C, 40.5; H, 6.7; N, 5.2. This is superior to previous methods for the synthesis[3] of this ester and we are reporting details of the preparation elsewhere.[4]

(3) F. Cramer and D. Voges, *Chem. Ber.*, **92**, 952 (1959).

(4) V. M. Clark and A. J. Kirby, *Biochim. Biophys. Acta*, in press.

(5) F. H. Westheimer, Special Publication No. 8, The Chemical Society, London, 1957, p. 1; C. A. Vernon, *ibid.*, p. 17.

(6) J. Kumamoto and F. H. Westheimer, *J. Am. Chem. Soc.*, **77**, 2515 (1955).

(7) Significantly the P-methyl, C-ethyl ester (I, R = H, R′ = CH_3, R″ = C_2H_5) is stable in aqueous solution at pH 5.

(8) F. W. Lichtenthaler, *Chem. Rev.*, **61**, 607 (1961).

(9) D. M. Brown in "Advances in Organic Chemistry. Methods and Results," Vol. 3, R. A. Raphael, E. C. Taylor, and H. Wynberg, Ed., Interscience, Publishers, Inc., New York, N. Y., 1963, p. 75.

Here a five membered cyclic intermediate is known to be involved.

Hydrolysis of the cyclic anhydride (III, R = H) can proceed by the attack of a water molecule at phosphorus or at the carbon atom of the carbonyl group. Two of our experiments indicate that the former is more likely. (i) Reversal of the hydrolytic sequence is observed when the dianion (IV, R = H) as the monocyclohexylammonium monopyridinium salt is heated to reflux in methanolic solution. After 5 hr. the starting material had disappeared and comparable amounts of inorganic phosphate and the monomethyl ester (IV, R = CH_3) could then be detected.[11] (ii) Treatment of the monocyclohexylammonium phosphoenol pyruvate with a 10% excess of dicyclohexylcarbodiimide in dry pyridine solution gave a readily hydrolyzed compound which we believe to be the cyclic anhydride (III, R = H). Removal of N,N-dicyclohexyl urea and solvent left a viscous oil having a *single* carbonyl absorption at 1785 cm.$^{-1}$ and P=O and P—O—alkyl bonds at 1290 and 1110 cm.$^{-1}$.[12] Addition of methanol to a pyridine solution of the compound prepared in this way gave immediately the monomethyl ester (IV, R = CH_3)[14] *but no carboxylic ester*.

Addition of an excess of cyclohexylamine to a pyridine solution prepared as before gave the enol phosphoramidate {(IV, $-NH\cdot C_6H_{11}$). *Anal.* Found for the barium salt: C, 29.1; H, 5.12; N, 3.58. $C_9H_{14}PO_5NBa\cdot H_2O$ requires C, 29.1; H, 4.53; N, 3.77.} *but no carboxylic amide*. Thus, the cyclic anhydride appears to be a powerful *phosphorylating* agent. This is in contrast to open-chain acyl phosphates, which are normally acylating agents.[15-17]

However, this behavior is not entirely unexpected, as four-covalent phosphorus in a five-membered ring is known to be exceptionally susceptible to nucleophilic attack.[18,19] The participation of a neighboring carboxyl group has been implicated by Chanley, *et al.*,[11,20] in the hydrolysis of salicyl phosphate near pH 5; this ester, too, is stable at pH 8.5.

Acknowledgment.—The award of a Research Studentship by Gonville and Caius College and of a D.S.I.R. Maintenance Allowance to A. J. K. are gratefully acknowledged, as are the helpful comments of a referee.

(10) The vicinal hydroxyl also catalyzes the removal of the second esterifying group in basic solution. Presumably a neutral (OH) can approach the negatively-charged phosphate residue more effectively than carboxylate anion, removal of a proton taking place after this has occurred.

(11) *Cf.* J. D. Chanley, E. M. Gindler, and H. Sobotka, *J. Am. Chem. Soc.*, **74**, 4347 (1952).

(12) Each of these three absorption bands is at a higher frequency than usual[13] as would be expected for the cyclic structure III.

(13) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," Methuen, London, 1958, pp. 178, 311.

(14) Isolated as the barium salt in 60% yield within 10 min.

(15) F. Lipmann, and N. O. Kaplan, *Ann. Rev. Biochem.*, **18**, 267 (1949).

(16) D. E. Koshland, *J. Am. Chem. Soc.*, **73**, 4103 (1951).

(17) F. Cramer and K.-G. Gärtner, *Chem. Ber.*, **91**, 1562 (1958).

(18) J. R. Cox, R. E. Wall, and F. H. Westheimer, *Chem. Ind.* (London), 929 (1959).

(19) P. C. Haake and F. H. Westheimer, *J. Am. Chem. Soc.*, **83**, 1102 (1961).

(20) J. D. Chanley and E. M. Gindler, *ibid.*, **75**, 4035 (1933).

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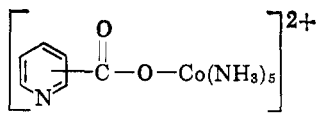
RECEIVED JUNE 24, 1963

Isomeric Pyridinecarboxylates as Bridging Groups in Oxidation–Reduction Reactions. Electron Transfer through Nitrogen

Sir:

Comparison of the rates of reduction of the isomeric pyridinecarboxylatopentaamminecobalt(III) ions



(2-, 3-, 4-)

with Cr(II) indicates that electron transfer may occur through nitrogen, resulting ultimately in reduction of tripositive cobalt bound to the carboxylate group. Like other conjugation-related effects exhibited by pyridine derivatives, this path may be observed for α and γ substituents, but not for β.

The rates of reduction of these carboxylato complexes and of two pyridinedicarboxylato complexes are compared with rates for the corresponding N-methyl derivatives[1] in Table I. For the nonmethylated complexes,

TABLE I

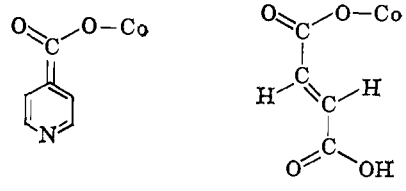
SPECIFIC RATES FOR REDUCTION OF PYRIDINECARBOXYLATOPENTAAMMINECOBALT(III) IONS WITH Cr^{2+}

Ligand	pK_{BH^+}	k_{BH^+} (acid path)	k_B (basic path)	k_{Me} (N-methyl deriv.)
	(l. mole^{-1} sec.$^{-1}$, 25°, μ = 3.0)			
Pyridine-2-carboxylato	4.49	...	2×10^5	0.087
Pyridine-3-carboxylato	4.73	0.11	...	0.13
Pyridine-4-carboxylato	4.79	1.3	1.5×10^3	1.4
Pyridine-2,5-dicarboxylato	<0	...	>200	8
Pyridine-2,6-dicarboxylato	<0	...	>150	...

rates may be expressed as the sum of two terms, pertaining, respectively, to the protonated form of the complex ($HPyCOORo^+$) and to the nonprotonated form (PyCOORo)

$$-[d(Co(III))/dt] = k_{BH^+}(Cr^{2+})(HPyCOORo^+) + k_B(Cr^{2+})(PyCOORo)$$

where k_{BH^+} and k_B, the specific rates for the acidic and basic forms, are evaluated from the dependence of rate on acidity and from K_{BH^+}, the acidity constants of $HPyCOORo^+$. As indicated in Table I, only the basic path was detected for the 2-isomer, even in 3 *M* $HClO_4$. Both paths are observed with the 4-isomer, whereas only the acidic path appears with the 3-isomer, which reacts at a rate comparable to the N-methylated complexes. The marked similarity between the 4-carboxylato complex and the fumarato complex



which is known to undergo reduction by attack on the noncoordinated carboxyl group,[2] strongly suggests that the basic path for reduction of the 4-carboxylato complex is associated also with remote attack by Cr(II), in this case on the nitrogen atom. However, the spectrum of the product (ϵ_{max} 23.6 (410 mμ), 19.5 (579 mμ)), is very similar to that obtained from reduction of the isomeric 3-carboxylato complex (ϵ_{max} 22.6

(1) Cobalt analyses for complexes described (prepared as the perchlorates) were in agreement with indicated formulas. Preparations, as well as analyses, will be described subsequently in a more detailed report.

(2) D. K. Sebera and H. Taube, *J. Am. Chem. Soc.*, **83**, 1785 (1961); R. T. M. Fraser and H. Taube, *ibid.*, **83**, 2239 (1961).