material with $K = 0.082$ was isolated, it was found to be the desired nonadecapeptide V. Redistribution of V in 2-butanol/0.5% trichloroacetic acid for 214 transfers gave a band with $K = 0.58$.

Quantitative amino acid analysis of the 24-hour hydrolysate of V by both the chromatographic procedure[13] and the paper-fluorodinitrobenzene method[14] gave this composition in molar ratios: $Ser_{1.8}Tyr_{1.0}Met_{1.1}Glu_{1.0}His_{1.1}Phe_{1.1}Arg_{3.1}Try_{1.0}Gly_{2.0}Lys_{2.9}Pro_{2.2}Val_{1.0}$. Tyrosine and tryptophan were determined by a spectrophotometric method.[15] Digestion of V successively with trypsin, chymotrypsin and leucine aminopeptidase produced the expected constituent amino acids by quantitative analysis.[14] NH_2-terminal amino acid analysis by the fluorodinitrobenzene procedure[14,16] disclosed serine as the NH_2-terminal residue, with traces of glutamic acid and lysine.

The synthetic nonadecapeptide,[17] according to the results of bioassay by the *in vitro* adrenal method,[18] had an ACTH activity of 31 U.S.P. units per mg. Estimation of ACTH activity by the usual adrenal ascorbic acid depletion procedure[19] gave a potency[20] of 29 U.S.P. units per mg. A single dose of 0.1 microgram of the peptide caused a change in melanophore index in hypophysectomized *Rana pipiens*[21] from 1+ to 3+ within one hour, an MSH potency comparable to that of the native adrenocorticotropins.[22]

[13] D. H. Spackman, W. H. Stein and S. Moore, *Anal. Chem.*, **30**, 1190 (1958).

[14] A. L. Levy, *Nature*, **174**, 126 (1954).

[15] T. W. Goodwin and R. A. Morton, *Biochem. J.*, **40**, 628 (1946).

[16] F. Sanger, *ibid.*, **39**, 507 (1945).

[17] A glutaminyl analog of the nonadecapeptide also has been synthesized by similar routes and its ACTH activity was found to be lower than that of the parent peptide.

[18] M. Saffran and A. V. Schally, *Endocrinology*, **56**, 523 (1955); C. Rerup, *Acta Endocrin.*, **29**, 83 (1958).

[19] M. A. Sayers, G. Sayers and L. A. Woodbury, *Endocrinology*, **42**, 379 (1949).

[20] We wish to thank Drs. M. Pabst and M. Speeter of the Upjohn Company for the assay data.

[21] L. T. Hogben and D. Slome, *Proc. Roy. Soc.*, **B108**, 10 (1931).

[22] C. H. Li, *Laboratory Investigation*, **8**, 574 (1959).

[23] This work was supported in part by a grant (RG2907) from the United States Public Health Service of the National Institutes of Health, and a grant from the Albert and Mary Lasker Foundation, New York.

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CONDUCTANCES OF SOME LANTHANIDE COBALTICYANIDES IN DIOXANE-WATER: A RE-ASSESSMENT

Sir:

The conductances of four lanthanide cobalticyanides in water and in 10% and 20% dioxane-water at 25° have been measured by Atkinson[1] and the corresponding Λ_0 and K values evaluated by the method of Shedlovsky.[2] For $LaCo(CN)_6$ in water, the given answers are $\Lambda_0 = 168.36$ and $K = 3.835 \times 10^{-4}$ but while the former is in excellent agreement with a previous estimate,[3] K is much higher than that which James and Monk[3] obtained by the method of Davies,[4] which makes use of the limiting forms of the equations of Onsager and Debye and Hückel

$$\Lambda_i = \Lambda_0 - S(c_i\,\Lambda/\Lambda_i)^{1/2} \qquad (1)$$

$$-\log f_i = A z_i^2 I^{1/2} \qquad (2)$$

S and A are numerical constants[5] under given physical conditions, Λ_i is the equivalent conductance for an equivalent ionic concentration c_i and I is the ionic strength ($= 3c_i$ here). These equations are solved by applying successive approximations to (1) till Λ_i is constant, taking $\Lambda_i = \Lambda_0$ on the right-hand side for a start. Some of the data of Atkinson have been recalculated along these lines and are summarized by the table where c is in equivs./l.; the original Λ_0 values were used.

DISSOCIATION CONSTANTS DERIVED BY THE METHOD OF DAVIES ($K \times 10^4$)

$10^2c^{1/2}$	0.50	1.0	1.5	2.0	2.5	3.0
$LaCo(CN)_6$ in water	1.25	1.64	1.73	1.75	1.67	1.72
$LaCo(CN)_6$ in 10% dioxane	0.43	0.55	0.59	0.59	0.59	0.55
$LaCo(CN)_6$ in 20% dioxane	0.25	0.28	0.27	0.22	0.19	0.16
$NdCo(CN)_6$ in water	0.36	0.53	0.61	0.64	0.71	0.70

Considering firstly the figures for $LaCo(CN)_6$ in water (with omission of that at $c^{1/2} = 0.005$—it is a common feature of conductance that measurements below $c^{1/2} = 0.01$ are often too low, probably because of adsorption effects), the average of $K = 1.70 \times 10^{-4}$ is in good accord with the result of James and Monk,[3] namely, 1.73×10^{-4}. The most likely explanation why Atkinson's answer is so much higher is that Shedlovsky's method,[2] which was devised for 1:1 electrolytes, needs a slight modification when applied to higher valent symmetrical electrolytes since for 3:3 types

$$K = c_i^2 f_i^2/3(c - c_i) \qquad (3)$$

and the appropriate plot is $1/\Lambda S'(z)$ against $c\Lambda f_i^2 S'(z)/3\Lambda_0^2$, where $S'(z)$ is a special function.[2] By dividing the original answer by the extra factor of 3, one does in fact find an answer reasonably close to the average of the Table.

The value for 10% dioxane is also now of the same order as James[6] obtained for the very similar system of $LaFe(CN)_6$ in 9.67% dioxane, namely, $K = 0.76 \times 10^{-4}$ ($\Lambda_0 = 138.0$). On the other hand it is to be seen that consistent results cannot be obtained with $\Lambda_0 = 116.6$ for $LaCo(CN)_6$ in 20% dioxane although the average for $c^{1/2} = 0.01$ and 0.015 of 0.27×10^{-4} is in general agreement with $K = 0.26 \times 10^{-4}$ obtained[6] for $LaFe(CN)_6$ in 18.1% dioxane. It would be possible to remove the drift by increasing Λ_0 but K would then be $<0.15 \times 10^{-4}$.

The position is much less satisfactory when the other results of Atkinson are analyzed by the present method. This is illustrated by the results for

[1] G. Atkinson, THIS JOURNAL, **82**, 818 (1960).

[2] T. Shedlovsky, *J. Franklin Inst.*, **225**, 739 (1938).

[3] J. C. James and C. B. Monk, *Trans. Faraday Soc.*, **46**, 1041 (1950).

[4] E. C. Righellato and C. W. Davies, *ibid.*, **26**, 592 (1930); C. W. Davies and J. C. James, *Proc. Royal Soc.*, **195A**, 116 (1948).

[5] H. S. Harned and B. B. Owen, "The Physical Chemistry of Electrolytic Solutions," Reinhold Publ. Corp., New York, N. Y., 1958.

[6] J. C. James, *J. Chem. Soc.*, 1094 (1950).

$NdCo(CN)_6$ in water for K increases steadily as c increases. Since the results for $LaCo(CN)_6$ and for[4] $LaFe(CN)_6$ in water do not show this drift, and since Λ_0 is well established, it can only be assumed that the fault is of an experimental nature.

With regard to the plotting procedures of Shedlovsky[2] and the analogous one of Fuoss and Kraus[7], the conclusions drawn may be in error even when using the correct expressions if the measurements are faulty. Accordingly a good check is to calculate K for each measurement and this may be done by use of

$$c_i = c\Lambda S'(z)/\Lambda_0 = c\Lambda/\Lambda_0 F'(z) \qquad (4)$$

where $F'(z)$ is the special Fuoss–Kraus function,[7] together with equations (2) and (3).

Finally, by analogy with the K values of a number of lanthanide sulfates, which also have been evaluated from conductances in water,[8] and which are all around $pK = 3.65$, one would expect to find only small differences among the pKs of the lanthanide cobtalticyanides in a given solvent.

[7] R. M. Fuoss and C. A. Kraus, THIS JOURNAL, 55, 476 (1933).

[8] F. H. Spedding and S. Jaffe, *ibid.*, 76, 882 (1954).

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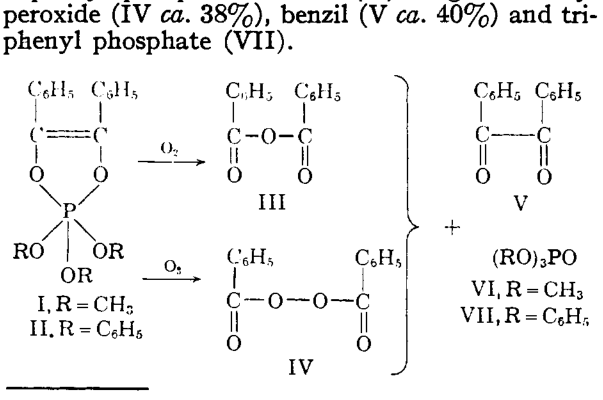
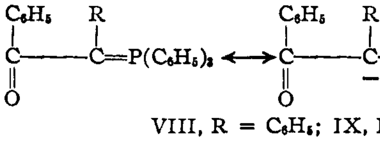
THE REACTION OF PHOSPHORANE DERIVATIVES WITH OZONE. BENZIL-TRIALKYL PHOSPHITE ADDUCTS AND PHOSPHINEACYLMETHYLENES[1]

Sir:

We have described[2] the formation of benzoic anhydride (III, *ca.* 30%), benzil (V, *ca.* 67%) and trimethyl phosphate (VI, *ca.* 94%) in the reaction of oxygen with the crystalline 1:1 adduct (I) derived from benzil and trimethyl phosphite. The reaction was carried out in benzene solution at room temperature, for five days. We wish to report now the rapid conversion of the adduct I into benzoyl peroxide (IV, *ca.* 50%), benzil (V, *ca.* 30%) and trimethyl phosphate (VI, nearly quantitative yield) by *ozone* in hexane solution at −70°. *Ozone* reacted rapidly with the benzil-triphenyl phosphite adduct[2] (II) to give benzoyl peroxide (IV *ca.* 38%), benzil (V *ca.* 40%) and triphenyl phosphate (VII).



A second type of phosphorane derivative,[3] the relatively stable triphenylphosphineacylmethylenes (VIII and IX), have been found to react very rapidly with ozone, in methylene chloride at −70°. VIII gave benzil (V, 80%), benzoyl peroxide (IV, 14%) and triphenylphosphine oxide (XI, 90%). IX yielded phenylglyoxal (X, 88% as 2,4-dinitrophenylosazone, m.p. 296–298°) and triphenylphosphine oxide (XI, 96%).[4]



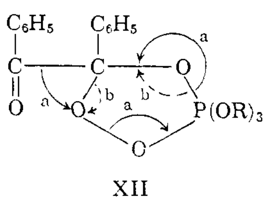
$$C_6H_5\text{–}\underset{\|}{\overset{}{C}}(=O)\text{–}C(R)=P(C_6H_5)_3 \longleftrightarrow C_6H_5\text{–}C(=O)\text{–}\overset{-}{C}(R)\text{–}\overset{+}{P}(C_6H_5)_3$$

VIII, R = C_6H_5; IX, R = H

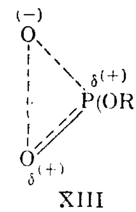
The ratio of benzoyl peroxide (IV) to benzil (V), in the reaction of ozone with adduct I decreases as the polarity of the solvent and the temperature are increased: 37% of IV and 52% of V were formed in methylene chloride at −70°. In methylene chloride at room temperature, the yield of IV was 14% and that of V was 60%; in addition, some benzoic anhydride (III, 11%) was obtained under these conditions. Under the conditions of the ozonization, neither adduct (I) nor ylide (VIII) reacted appreciably with pure oxygen[5] or with benzoyl peroxide; benzil was not attacked by ozone.

The reactions with ozone were carried out under anhydrous conditions and the composition of the reaction mixture was ascertained by comparisons of the infrared spectra with those of authentic mixtures. In addition, peroxidic material was determined by the iodimetric method,[6] and all the products were isolated.

We have suggested[2,7] that the "phosphinemethylene secondary ozonide" XII is an intermediate in the reaction of oxygen with the adducts I and II. Possible modes of decomposition of the ozonide XII to: (a) benzoic anhydride plus phosphate ester, or (b) benzil plus a peroxidic phosphate ester XIII are shown below. XIII is the phosphorus analog of Criegee's "zwitterion"[6] and should decompose into molecular oxygen plus a phosphate ester, for instance through dimerization.



XII



XIII

The reaction of the adducts I and II with *ozone* could involve the "perozonide" XIV (or a five-membered equivalent). Possible decompositions of XIV to: (a) benzoic anhydride[8] plus the peroxidic

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[1] Acknowledgment is made to the Donors of the Petroleum Research Fund administered by the American Chemical Society for partial support of this Research (Grant 286-A) and to the National Cancer Institute of the National Institutes of Health (Grant CY-4769).

[2] F. Ramirez, R. B. Mitra and N. B. Desai, THIS JOURNAL, 82, 2651 (1960).

[3] F. Ramirez and S. Dershowitz, *J. Org. Chem.*, 22, 41 (1957): *cf.* footnote 1.

[4] The formation of olefins from this type of compound and peracetic acid has just been reported (D. B. Denney and L. C. Smith, THIS JOURNAL, 82, 2396 (1960)).

[5] Some reactive phosphinemethylenes are converted to dimeric olefins by molecular oxygen (H. J. Bestmann, *Angew. Chem.*, 72, 34 (1960).

[6] P. Bailey, *Chem. Revs.*, 58, 925 (1958).

[7] F. Ramirez and N. B. Desai, THIS JOURNAL, 82, 2652 (1960).

[8] For anhydride formation in ozonization see ref. 6, pp. 951 and 964.