(c) To 295°-Diphenylgermanium Oxide.—All diphenyl-germanium oxides are transformed into the 295°-oxide when refluxed briefly in a 40:60 mixture of water–ethanol.

When pure dibromodiphenylgermane is hydrolyzed under acidic (water) as well as alkaline conditions, it gives a white, microcrystalline solid, the high melting (290–295°) diphenyl germanium oxide.

Dayton 7, Ohio

Anodic Reductions. VI. Electrolysis of Benzophenone in Pyridine Solutions between Aluminum Electrodes

By Tsu Tzu Tsai, William E. McEwen and Jacob Kleinberg

The anodic oxidation of aluminum in pyridine solutions of sodium iodide or lithium chloride in the presence of benzophenone gives initial mean valence numbers significantly lower than 3. Reduction products, namely benzhydrol and benzopinacol, are isolated from the anolyte hydrolysate in amounts corresponding to oxidation of aluminum from its measured initial mean valence state to the familiar tripositive state. The ratio of the two reduction products shows a dependence on the nature of the cation of the electrolyte. The same reduction products are obtained from the catholyte hydrolysate when lithium chloride is used as electrolyte and aluminum as cathode. Mechanisms are proposed to account for both anolyte and catholyte products.

It was noted over one hundred years ago by Wöhler and Buff[1] that during the electrolysis of aqueous sodium chloride between aluminum electrodes hydrogen was evolved at the anode and aluminum dissolved with a current efficiency significantly greater than 100% on the assumption of oxidation to the tripositive state. Turrentine[2] also observed the anodic evolution of hydrogen, and proposed that the hydrogen arose from reaction of the solvent water with lower valent (+1 or +2, or both) aluminum formed as a primary anodic oxidation product. Substantial evidence for the anodic generation of lower valent aluminum in anhydrous acetic acid,[3,4] liquid ammonia,[5,6] acetone[7] and ethanol,[4] has also been obtained. Moreover, compelling additional electrochemical evidence for the formation of lower valent aluminum in aqueous salt solutions has recently been reported.[8] Thus, it was shown that when a flowing anolyte consisting of aqueous sodium chloride or nitrate was caused to pass over an aluminum rod serving as anode and then into a solution of an oxidizing agent, e.g., MnO_4^- or Ag^+, contained in a separate vessel, reduction of the oxidant occurred, MnO_4^- to MnO_2 and Ag^+ to Ag°. The occurrence of reduction at a distance from the anode can best be interpreted in terms of a primary anodic oxidation of aluminum to a lower valent state. In none of the investigations cited above could a salt of lower valent aluminum be isolated from solution following electrolysis. However, in every instance in which the anodic current efficiency exceeded 100%, either the solvent itself or some oxidant present in the solvent was reduced.

In view of the fact that in previous work[9-14]

reduction of a variety of organic compounds was effected in pyridine solution by unipositive magnesium anodically generated, and in view of the evidence for lower valent aluminum given above, we decided to investigate the possibility of "anodic reductions" of organic compounds in pyridine solution during the course of electrolysis between aluminum electrodes. The present paper describes the reduction of benzophenone. This compound was chosen because a thorough study has been made of its reduction during electrolysis between magnesium electrodes in pyridine solution.[9] Moreover, it has been shown[15] that the ketyl radical-ion formed as the primary anolyte reduction product in electrolyses between magnesium electrodes is capable of corroding massive magnesium.

Experimental

Materials.—The 10-mm. aluminum rod from which all electrodes were cut was of 99.98% purity and was furnished by the Aluminum Company of America. The sodium iodide was Merck reagent grade, and it was dried at 110° before use. The lithium chloride employed as electrolyte was Baker and Adamson reagent grade. Pyridine, Fisher analytical reagent, was fractionally distilled from sodium and stored over barium oxide. The benzophenone, m.p. 46°, was obtained from Eastman.

Apparatus and Procedure.—The source of direct current was a full-wave mercury tube rectifier, capable of supplying up to 1000 volts. The quantity of electricity passed through the circuit was determined by means of a silver coulometer placed in series with the electrolytic cell. The electrolyses were carried out in a 2-compartment cell with a sintered glass disk separating anode and cathode compartments. The cell was maintained in a constant temperature bath kept at 39.5 ± 0.5°.

The aluminum electrodes were cleaned in 10% sodium hydroxide solution, then washed with distilled water and dried in an oven at 110°. The sodium iodide–pyridine solution

(1) F. Wöhler and H. Buff, Ann., 103, 218 (1857).

(2) J. W. Turrentine, J. Phys. Chem., 12, 448 (1908).

(3) A. W. Davidson and F. Jirik, This Journal, 72, 1700 (1950).

(4) P. Brouillet, I. Epelboin and F. Froment, Compt. rend., 239, 1795 (1954).

(5) M. C. del Boca, Helv. Chem. Acta, 16, 565 (1933).

(6) W. E. Bennett, A. W. Davidson and J. Kleinberg, This Journal, 74, 732 (1952).

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(8) R. Raijola and A. W. Davidson, This Journal, 78, 556 (1956).

(9) M. D. Rausch, W. E. McEwen and J. Kleinberg, ibid., 76, 3622 (1954).

(10) M. D. Rausch, F. D. Popp, W. E. McEwen and J. Kleinberg, J. Org. Chem., 21, 212 (1956).

(11) W. E. McEwen, J. Kleinberg, D. L. Burdick, W. D. Hoffman and J. Y. Yang, This Journal, 78, 4587 (1956).

(12) M. D. Rausch, W. E. McEwen and J. Kleinberg, Chem. Revs., 57, 417 (1957).

(13) J. Y. Yang, W. E. McEwen and J. Kleinberg, This Journal, 80, 4300 (1958).

(14) W. D. Hoffman, W. E. McEwen and J. Kleinberg, Tetrahedron, 5, 293 (1959).

(15) D. L. Burdick, A. V. Santoro, W. E. McEwen and J. Kleinberg, This Journal, 79, 5467 (1957).

was prepared by dissolving 7.5 g. of freshly dried sodium iodide in pyridine and diluting the solution to 100 ml. When lithium chloride was used as electrolyte, a saturated solution was made up. The electrolyte solution was divided equally into the two compartments. The anode compartment invariably contained a weighed amount of benzophenone. In some experiments benzophenone was also added to the cathode compartment. During electrolysis the cell was swept out with pure, dry nitrogen. The conditions of electrolysis (current density, cell voltage and duration) are specified in the appropriate places for the individual experiments. After electrolysis, the electrodes were cleaned with ethanol and distilled water and then dried at 110°.

From the loss in weight of the anode during electrolysis and the quantity of current passed through the cell the *initial mean valence number*, V_i, with which the aluminum entered solution was calculated

$$V_i = \frac{\text{wt. of Ag deposited in coulometer} \times 26.97}{107.88 \times \text{wt. at Al lost from anode}}$$

Isolation of Anolyte Products.—For the sodium iodide–pyridine solutions containing benzophenone an initial current density of 0.005 amp. per cm.^{2} and a cell voltage of 25 v. were employed. During the course of electrolysis the current density was kept approximately constant by manual adjustment until the cell voltage rose to 50 v. Thereafter the voltage was maintained at that value. The catholyte slowly turned blue and a brown color developed in the anolyte solution at the same time that a white precipitate formed.

At the end of a 24-hr. period of electrolysis the anolyte and catholyte were each hydrolyzed with 250 ml. of 30% phosphoric acid and subjected to continuous ether extraction for 24 hr. The ether solution in each case was washed first with 10% sodium carbonate solution, then with 10% sodium sulfite solution, and finally dried over anhydrous calcium chloride. The ether was removed by distillation and the residue dried in a vacuum desiccator and weighed. Each solid was redissolved in a known volume of anhydrous ether and stored for individual determinations of benzhydrol and benzopinacol.

When lithium chloride was employed as electrolyte the current density was maintained at about 0.003 amp. per cm.^{2} and the cell voltage at 130–140 v. After electrolysis the anolyte and catholyte were worked up as described above.

Two 10-ml. aliquots of the ether solution of anolyte material were evaporated to dryness and the residues dried *in vacuo*. One of the residues was dissolved in 5 ml. of glacial acetic acid and to this solution was added 5 ml. of an acetic acid solution 0.06 N in lead tetraacetate and 1 N in potassium acetate. At the same time, a blank and a known synthetic mixture of benzopinacol and benzhydrol were prepared and treated with 5 ml. of the lead tetracetate–potassium acetate solution. The solutions were allowed to stand at room temperature for 2 hr. and then the excess lead tetraacetate was determined by titration with 0.04 N sodium thiosulfate solution of the iodine liberated after the addition of 0.5 g. of potassium iodide, 6 g. of sodium acetate and 100 ml. of water.

The dried residue of the second aliquot was dissolved in sufficient chloroform to make a 10% (by weight) solution and the infrared spectrum was taken. To determine the amount of benzhydrol in the aliquot a calibration curve was constructed in the following manner. A series of ternary mixtures of benzopinacol, benzhydrol and benzophenone was prepared, each mixture containing the amount of benzopinacol determined by the lead tetraacetate titration described above and systematically varied quantities of benzophenone and benzhydrol. The infrared spectrum of each of these mixtures was taken in 10% chloroform solution. The calibration curve was made by plotting the percentage of benzhydrol present in the various mixtures against the height of the absorption peak at 3500 cm.$^{-1}$, which arises from the presence of both benzhydrol and benzopinacol. Since the percentage of the benzopinacol was fixed, the variation of the intensity of the peak was attributed to variation in benzhydrol content. The percentage of benzhydrol in the anolyte aliquot was determined by use of the calibration curve. As a check of the values obtained for benzopinacol and benzhydrol, synthetic mixtures of the appropriate quantities of the two compounds plus benzophenone were prepared and their infrared spectra taken in

10% chloroform solution. In each case the spectrum of the anolyte solution was virtually identical with that of the synthetic mixture. The results for various electrolyses are given in Tables I and II.

ANODIC BEHAVIOR OF ALUMINUM IN PYRIDINE SOLUTIONS CONTAINING BENZOPHENONE

Expt.	Electrolyte	Duration of electrolysis, hr.	Initial anodic current density, amp./cm.^{2}	Cell voltage, v.	V_i
1	0.5 m NaI	24	0.005	25–50	2.76
2	0.5 m NaI	24	.005	25–50	2.69
3	0.5 m NaI	20	.005	25–50	2.64
4	Satd. LiCl^a	24	.003	130–140	2.18
5	Satd. LiCl	24	.003	130–140	2.36
6	Satd. LiCl	15	.003	130–140	2.33
7	Satd. LiCl + 0.06 m AlCl$_3$^{a}	20	.003	130–140	2.64

^{a} Catholyte also contained benzophenone; in all other experiments only the anolyte contained benzophenone.

TABLE II

PRODUCTS ISOLATED FROM ANOLYTE FOLLOWING ANODIC OXIDATION OF ALUMINUM IN PYRIDINE SOLUTIONS CONTAINING BENZOPHENONE

Expt.	Benzophenone, g.	Ag deposited, g.	Al dissolved, g.	Benzopinacol found, g.	Benzhydrol found, g.	Yield, %—Benzopinacol	Benzhydrol
1	4.2429	2.5141	0.2283	0.084	0.139	22 5	74 5
2	4.6798	3.2326	.3008	.135	.203	21.4	63.8
3	4.3264	3.0913	.2924	.150	.248	20 1	69.1
4	4.1106	1.3247	.1517	.457	.163	53.8	38.4
5	3.6474	0.7925	.0847	.181	.095	48.7	51.2
6	4.000	0.8287	.0890	.264	.070	65.0	34.5
7	4.000	1.5058	.1426	.225	.062	64.5	35.4

The percentage yields of benzopinacol and benzhydrol were calculated on the basis that these compounds arose from reduction of benzophenone by lower valent aluminum anodically generated. Since the reduction of benzophenone to benzopinacol represents a one-electron reduction, and benzophenone to benzhydrol a two-electron reduction, the following equations were employed to calculate the theoretical yields of the two reduction products

$$\text{theor. yield of benzopinacol} = (3 - V_i) \times \frac{\text{g. of Al dissolved}}{26.97} \times \frac{\text{mol. wt. of benzopinacol}}{2}$$

$$\text{theor. yield of benzhydrol} = (3 - V_i) \times \frac{\text{g. of Al dissolved}}{26.97} \times \frac{\text{mol. wt. of benzhydrol}}{2}$$

Isolation of Catholyte Products.—In experiments 4 and 7 benzhydrol and benzopinacol produced in the catholyte from reduction of benzophenone were determined in the manner as described above in the treatment of anolyte. The results are given in Table III, where the theoretical yields

TABLE III

PRODUCTS ISOLATED FROM THE CATHOLYTE FOLLOWING ELECTROLYSES BETWEEN ALUMINUM ELECTRODES OF PYRIDINE SOLUTIONS CONTAINING BENZOPHENONE

Expt.	Benzophenone added, g.	Benzopinacol found, g.	Benzhydrol found, g.	Yield, %—Benzopinacol	Benzhydrol
4	4.1020	0.743	0.685	32.8	60.6
7	4.0000	.863	.530	33.7	41.4

are based on the number of coulombs of electricity passed through the cell.

In experiments where no benzophenone was present in the catholyte, appreciable quantities of 4,4'-dipyridyl were isolated from the catholyte by a procedure described previously.[9]

Control and Corrosion Experiments.—Electrolyses were carried out with a saturated solution of lithium chloride in pyridine between aluminum electrodes in the absence of benzophenone. The V_i-values observed were 3.00, 3.06 and 2.97 in runs of varying duration. In contrast to these results, when 0.5 m sodium iodide was the electrolyte V_i-values of 2.46, 2.40 and 2.47 were obtained in electrolyses of 24-hr. duration. Attempts to isolate reduction products from the anolyte in the latter experiments were unsuccessful. However, following the electrolysis in which the V_i was 2.40, 3.000 g. of benzophenone was added to the anolyte and the mixture was stirred for 24 hr. After the usual workup of the mixture, 68 mg. of benzopinacol was found to be present by lead tetraacetate titration. An infrared spectrum of a chloroform solution of the organic material isolated from the mixture gave no conclusive evidence for the presence of benzhydrol.

After electrolysis of pyridine solutions containing benzophenone and either sodium iodide or lithium chloride, neither the anolyte nor the catholyte was capable of corroding massive aluminum. However, the anolyte following electrolysis generally did attack massive magnesium appreciably. For example, after an electrolysis of 24-hr. duration in which the electrolyte was 0.5 m sodium iodide, the amount of benzophenone originally in the anolyte 4.000 g. and the V_i 2.48, a pure magnesium rod placed in the mixture lost 25.1 mg. in a 24-hr. period. On the other hand, the catholyte, which also contained benzophenone, was without effect on massive magnesium.
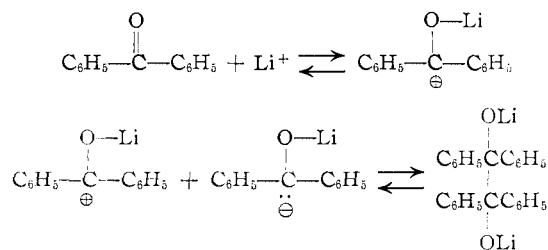
Discussion

The anodic oxidation of aluminum in either sodium iodide–pyridine or lithium chloride–pyridine solutions in the presence of benzophenone gives V_i values significantly lower than the normal value of 3 (Table I). Furthermore, reduction products of benzophenone, namely benzhydrol and benzopinacol, are obtained (after hydrolysis) in amounts substantially corresponding to those expected from oxidation of dissolved aluminum from its initial mean valence number to the common tripositive state by the benzophenone.

Since no evidence was found that the reduction products were formed by the action of some reducing species migrating from the catholyte, reduction in the anolyte presumably occurs by the action of lower valent aluminum anodically generated. In view of the electronic configuration of the aluminum atom and the results of previous investigations of the anodic oxidation of aluminum and other metals,[8,16–18] it seems reasonable to suggest that unipositive aluminum is formed as the primary anodic process. The observed V_i-values then arise as a consequence of the relative rates of a number of competing reactions: (1) oxidation of the unipositive aluminum by loss of electrons in a stepwise manner to the anode, and (2) oxidation of lower valent aluminum (Al^+, Al^{2+}) by benzophenone. The formation of both unipositive aluminum (a two-electron reducing agent) and bipositive aluminum (a one-electron reducing agent) accounts for the production in the anolyte of the conjugate bases of benzhydrol and benzopinacol, respectively. It is of interest to compare this result with that obtained in a similar electrolysis in

which magnesium functioned as the anode,[9] where the only "anodic reduction" product was benzopinacol. In the latter system the only reducing agent which can be generated anodically is unipositive magnesium, a one-electron agent.

The relative quantities of benzhydrol and benzopinacol formed in the anolyte are influenced by the nature of the electrolyte (Table II). With sodium iodide as electrolyte benzhydrol is produced in 64–75% yield and benzopinacol in 20–23% yield. However, with lithium chloride as electrolyte the yield of benzhydrol is lowered to 34–51% and that of benzopinacol raised to 49–65%. This striking change may be explained in either of two ways: (1) The relative amount of reduction of benzophenone by bipositive aluminum is increased in the presence of lithium ion. (2) Lithium ion catalyzes the condensation of the conjugate base of benzhydrol with benzophenone to yield pinacolate ion. Inasmuch as the lithium ion is a much stronger complex former than sodium ion, and since it is difficult to propose a reason why the nature of the cation should influence the relative amount of reduction by uni- or bipositive aluminum, the second explanation appears to be preferable. Specifically, lithium ion functions as a Lewis acid catalyst as shown in the equations for condensation

$$
C_6H_5\!-\!\overset{\displaystyle O}{\overset{\|}{C}}\!-\!C_6H_5 + Li^+ \rightleftharpoons C_6H_5\!-\!\overset{\displaystyle O\!-\!Li}{\underset{\ominus}{\overset{|}{C}}}\!-\!C_6H_5
$$

$$
C_6H_5\!-\!\overset{\displaystyle O\!-\!Li}{\underset{\oplus}{\overset{|}{C}}}\!-\!C_6H_5 + C_6H_5\!-\!\overset{\displaystyle O\!-\!Li}{\underset{\ominus}{\overset{|}{\underset{\cdot\cdot}{C}}}}\!-\!C_6H_5 \rightleftharpoons \begin{array}{c} OLi \\ | \\ C_6H_5CC_6H_5 \\ | \\ C_6H_5CC_6H_5 \\ | \\ OLi \end{array}
$$

It should not be inferred from the equations shown that the bond between lithium and oxygen is a purely covalent one. It is worthy of note that a second strong Lewis acid, namely the tripositive aluminum ion, is continually being generated in the anolyte in all electrolyses. However, its concentration at all times is small compared to that of either sodium or lithium ion.[19]

Evidence that the condensation of the conjugate base of a benzhydrol with a diaryl ketone is promoted by the presence of a metallic ion of high charge density has been obtained in our laboratory.[20] Thus, when 4,4'-dimethylbenzophenone is reduced at a magnesium cathode in sodium iodide–pyridine solution the sole product (after hydrolysis) is 4,4'-dimethylbenzhydrol. However, if during electrolytic reduction magnesium iodide is present in the catholyte, substantial amounts of the pinacol, tetra-p-tolylethylene glycol, as well as 4,4'-dimethylbenzhydrol and a trace of 2-pyridyl-di-p-tolylcarbinol, are formed. The probable mechanism of the formation of the latter compound has been given previously.[15]

The fact that a mixture of benzhydrol and benzopinacol is obtained from the catholyte hydrolysate

(16) D. J. Royer, J. Kleinberg and A. W. Davidson, J. Inorg. and Nucl. Chem.., **4**, 115 (1957).

(17) J. H. Greenblatt, J. Electrochem. Soc., **103**, 539 (1956).

(18) D. V. Kokouliva and B. N. Kabanov, Dokl. Akad. Nauk SSSR, **112**, 692 (1957).

(19) It is not entirely out of the qestion that the benzopinacol formed even when sodium iodide is used as electrolyte arises at least in part by a condensation mechanism analogous to that shown above, with tripositive aluminum functioning as the Lewis acid catalyst.

(20) D. L. Burdick, Ph.D. Thesis, University of Kansas, 1957.

when a solution of benzophenone in pyridine containing lithium chloride is electrolyzed between aluminum electrodes is explainable on the same basis as cited above.

It was noted that the anolyte following electrolysis of solutions of benzophenone between aluminum electrodes was incapable of corroding massive aluminum but did attack a magnesium rod. This behavior, in our opinion, is merely a reflection of the difference in reactivity of the two metals toward the ketyl radical-ion (the precursor of the pinacolate ion) generated in the anolyte by the action of bipositive aluminum on benzophenone. The fact that neither magnesium nor aluminum is attacked by the catholyte after electrolysis is consistent with our interpretation of the mechanism for the formation of pinacol in the catholyte, provided the assumption is made that lithium pinacolate is not dissociated appreciably. Evidence for the small degree of disssociation of this salt has been obtained by magnetic susceptibility measurements.[21,22]

The one puzzling feature of the investigation was the fact that V_i-values for aluminum substantially lower than 3 were obtained in sodium iodide–pyridine solutions in the absence of benzophenone. Attempts were made to isolate a salt of lower valent aluminum but without success.[23] However the anolyte solution following electrolysis possessed reducing power as demonstrated by its ability to reduce benzophenone to the conjugate use of benzopinacol.

(21) S. Sugden and F. L. Allen, *J. Chem. Soc.*, 440 (1936).

(22) E. Müller and W. Janke, *Z. Elektrochem.*, **45**, 380 (1939).

(23) It is of interest that the only lower valent aluminum compound reported to have been isolated in the solid state is AlI. This compound was formed by the use of an electrodeless discharge produced in the vapor of AlI₃ at a temperature below 50° (W. C. Schumb and H. H. Rogers, THIS JOURNAL, **73**. 5806 (1951)).

LAWRENCE, KANSAS

Competitive Inhibition by Substrate during Enzyme Action. Evidence for the Induced-fit Theory[1,2]

BY JOHN A. THOMA AND D. E. KOSHLAND, JR.

The Schardinger dextrins, cyclohexa- and cycloheptaamylose and the internal segments of the starch molecule act as competitive inhibitors of sweet potato beta-amylase. These facts are shown to add support for the induced-fit theory of specificity and to suggest that this new type of competitive inhibition by substrate exists in other enzyme systems.

Introduction

Beta-amylase hydrolyzes only the penultimate linkage of its normal substrate, a linear starch chain. Since the linear portions of the starch can be considered to be a chain of "maltose units," this means that the enzyme has a way of distinguishing the terminal "maltose unit" from all the other "maltose units." This type of subtle distinction is typical of enzymes and hence studies on beta-amylase were performed to clarify the action of this enzyme in particular and the specificity pattern of enzymes in general.

The terminal maltose unit differs from the internal maltose units by the presence of an unsubstituted hydroxyl at the C4 position. It would be desirable, therefore, to test the binding affinity of compounds which had maltose units but no free C4 hydroxyl. Accordingly, cyclohexa- and cycloheptaamylose, which are molecules in this category, were investigated and found to be competitive inhibitors.
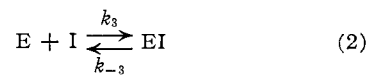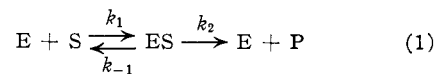
This ability of the cycloamyloses to form complexes with beta-amylase suggested that binding of the internal segments of starch chains would occur. Such "competitive inhibition" by the internal segments would be obscured in a kinetic treatment of hydrolysis because the inhibitor is

a part of the substrate itself. The *relative* amount of inhibition, however, is a function of the chain length of the substrate and variation of polymer length could provide evidence that such inhibition occurs.

These facts can be shown to be inconsistent with a template-type specificity pattern[3] but to be readily explainable by an induced-fit specificity theory[4] of enzyme action.

Theoretical

Inhibition by Internal Segments of a Polymer Chain.—The conventional equations for competitive inhibition are

$$E + S \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ES \overset{k_2}{\longrightarrow} E + P \qquad (1)$$

$$E + I \underset{k_{-3}}{\overset{k_3}{\rightleftharpoons}} EI \qquad (2)$$

$$K_m = \frac{k_{-1} + k_2}{k_1} \qquad (3)$$

$$K_i = \frac{k_{-3}}{k_3} \qquad (4)$$

$$\frac{1}{v} = \frac{1}{V_m} \left[1 + \frac{K_m}{(S)} \left(1 + \frac{(I)}{K_i} \right) \right] \qquad (5)$$

Inhibition by internal segments of a homogeneous polymeric chain cannot be demonstrated with

(3) E. Fischer, *Ber.*, **27**, 2985 (1894).

(4) D. E. Koshland, Jr., *Proc. Natl. Acad. Sci., U. S.*, **44**, 98 (1958)