obtained in this or any other study. It can even be argued that the A factor of less than 10^{13} points to a closed structure for the activated complex.

Thermochemical considerations[1] show that the isomerizations of 1-methylcyclopropene to 2-butyne, 1,3-butadiene, and 1,2-butadiene are exothermic by 23.5, 32.3, and 19.4 kcal/mole, respectively, but this order does not correlate with the importance of the formation of these products in the pyrolysis.

The diradical mechanism can be applied to this system to give the following possibilities.
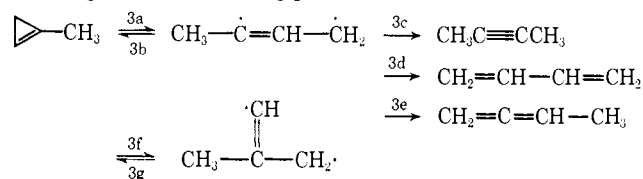
The diradical that is formed in step 3f has no simple alternative except to return to 1-methylcyclopropene.

All the observed products can be explained by pathways which originate in the linear diradical formed in step 3a. It is interesting that 1,2-butadiene is the only product that can be formed in two distinct ways. One of these involves a 1,4-hydrogen shift over a double bond, while the other requires a 1,2-hydrogen shift across a double bond. Neither process seems sterically simple. Both 2-butyne and 1,3-butadiene are formed by 1,2-hydrogen shifts in the diradical. 1,3-Butadiene is a less important product (than 2-butyne) although its formation requires the migration of one of three equally possible hydrogen atoms in the methyl group in 1-methylcyclopropene. A clear understanding of the stereochemistry of the diradical may serve to explain these peculiarities.

Pyruvate Dimerization Catalyzed by Nickel(II) and Zinc(II). I. Equilibrium with Nickel(II) and Zinc(II)[1]
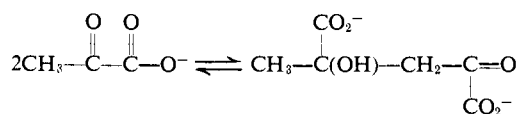
D. E. Tallman and D. L. Leussing

Contribution from the Department of Chemistry, Ohio State University, Columbus, Ohio 43210. Received April 7, 1969

Abstract: Dimerized pyruvic acid, $HO_2CCOCH_2C(OH)(CH_3)CO_2H$, behaves as a dibasic acid: $pK_{1a} = 1.73$, $pK_{2a} = 3.72$. The dianion forms 1:1 and 2:1 complexes with both Ni(II) (log β_1 1.50, log β_2 2.80) and Zn(II) (log β_1 1.72, log β_2 3.00). The stabilities are of the order observed with bidentate oxygen donors. Comparison with model ligands suggests that the predominant mode of chelation involves the hydroxyl and carboxyl groups attached to the asymmetric carbon.

There has been considerable interest in recent years in the metal ion promotion of nucleophilic organic reactions.[2-5] This interest is partially attributed to the possible relationship of these reactions to analogous enzymatic processes. An understanding of the factors that determine the effectiveness of various metal ions and the mechanisms by which the metal ions function to accelerate a given reaction in these model systems should prove to be a valuable asset for the elucidation of the role of metal ions in metal-ion-activated enzyme systems.

The metal-ion promotion of pyruvate dimerization has been known for many years.[6,7] However, there ap-

pears to be no quantitative information on the kinetics of this reaction or on the nature and stability of the metal complexes of dimeric pyruvate. In order to understand the kinetics of this interesting reaction, it is necessary to have a complete description of the reaction solution in terms of all species present under a given set of conditions. The present investigation was undertaken to determine the acid dissociation constants of monomeric and dimeric pyruvic acid and the stabilities of the various complexes of monomeric and dimeric pyruvate with Ni(II) and Zn(II).

Experimental Section

Dimer-free sodium pyruvate was supplied by the Sigma Chemical Co. and was stored at 0.5°. Analysis by ion exchange of Na+ for H+ followed by titration with NaOH indicated a purity of 99.6 $\pm$ 0.1% calculated as $NaC_3H_3O_3$. Recrystallization from water gave no significant change in purity. Because sodium pyruvate solutions slowly dimerize upon prolonged standing, stock solutions were prepared immediately before use.

Stock solutions of metal chlorides were prepared and standardized according to accepted methods.

Solutions containing pyruvate dimer were prepared immediately before use by adding an aliquot of 0.01 M potassium cyanide solution as catalyst to an aliquot of 1.00 M sodium pyruvate solution and diluting to an accurately known volume after dimerization equilibrium was attained. The time required for the establishment of equilibrium under these conditions was determined spec-

(1) This research has been supported by a grant from the National Science Foundation.

(2) M. Bender, Advances in Chemistry Series, No. 37, American Chemical Society, Washington, D. C., 1963, p 19.

(3) M. Jones, Advances in Chemistry Series, No. 49, American Chemical Society, Washington, D. C., 1965, p 153.

(4) J. Halpern, *Ann. Rev. Phys. Chem.*, 16, 103 (1965).

(5) J. Halpern, *Chem. Eng. News*, 44 (45), 68 (1966).

(6) L. Wolff, *Ann. Chem.*, 305, 154 (1899).
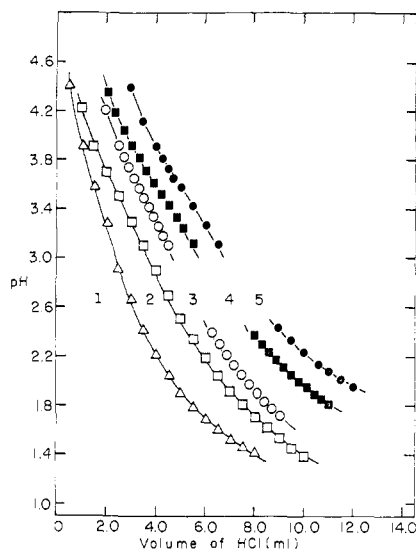
(7) A. W. K. DeJong, *Rec. Trav. Chim.*, 20, 81 (1901).

Figure 1. Comparison of experimental titration points and calculated titration curves for the H^+-pyruvate–pyruvate dimer system. Initial conditions for curves 1–5 are given in the order initial volume (ml), monomer concentration (M), dimer concentration (M), HCl concentration (M): (1) 25.00, 0.0239, 0.0373, 0.4008; (2) 10.00, 0.0958, 0.1491, 0.4008; (3) 10.00, 0.0961, 0.1500, 0.4008; (4) 25.00, 0.0480, 0.0750, 0.4008; (5) 25.00, 0.0240, 0.0375, 0.2004. The solid lines are curves calculated using the accepted values of the acid dissociation constants describing the system. To facilitate presentation of the plots, curves 3 and 4 have been shifted to the right by 1.000 ml, and curve 5 has been shifted to the right by 2.000 ml.

trophotometrically to be 100 min after cyanide addition. Changes in the monomer–dimer ratio after dilution were found to be negligible within 45 min. The equilibrium composition of a monomer–dimer stock solution was obtained from its pmr spectrum at 60 Mc.[8] From the ratio of the area of the methyl peak of monomeric pyruvate (P^-) at 50 cps to the area of the methyl peak of dimeric pyruvate (D^-) at 109 cps, the value of the dimerization constant, K_d, was calculated to be 6.5, in excellent agreement with earlier results.[8]

$$2P^- \underset{}{\overset{K_d}{\rightleftharpoons}} D^{2-}$$
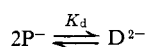
sults.[8] The formation of higher polymers was considered negligible under these conditions since the ratio of the dimer methyl peak area to the dimer methylene peak area was found to be 3:2. The formation of higher polymers would give rise to lower methyl to methylene ratios.[8]

All experiments were run at 25.0°. The ionic strength was maintained constant at 1.0 M by the addition of NaCl. A Corning Model 12 pH meter and a Radiometer Type GK 2021C glass–calomel combination electrode were used for the measurement of pa_H. The system was standardized against the National Bureau of Standards phosphate and tartrate buffers. The absorption measurements were obtained using a Cary 14 spectrophotometer equipped with a thermostated cell holder. Nuclear magnetic resonance spectra were obtained using a Varian A-60 spectrometer.

The pK_a[9] of pyruvic acid at an ionic strength of 1.0 M, 25°, was determined potentiometrically to have a value of 2.105 ± 0.013.

The formation constants of the metal–pyruvate complexes were evaluated spectrophotometrically at the 315-mμ band of pyruvate. Solutions containing various ratios of pyruvate ion, metal ion, and hydrogen ion were prepared, and the absorbance of each solution was recorded as a function of time. The absorbance–time curves were then extrapolated back to the time of mixing the solutions, the extrapolations seldom amounting to more than 0.01–0.02 absorbance unit. The observed decrease in absorbance of the solu-

tions is due to the dimerization of pyruvate promoted by the metal ions. The total pyruvate level was varied from 0.025 to 0.50 M, total metal was varied from 0.075 to 0.125 M, and the range of total hydrogen ion concentration was 6×10^{-4} to 6×10^{-3} M. Mass balance relationships were set up as follows.

$$M_{tot} = [M^{2+}] + [MP^+] + [MP_2] \tag{1}$$

$$P_{tot} = [P^-] + [MP^+] + 2[MP_2] + [HP] \tag{2}$$

$$H_{tot} = [H^+] + [HP] - [OH^-] \tag{3}$$

The total quantities on the left-hand side of eq 1–3 are known from the compositions of the solutions. Equilibrium was invoked by replacing the terms for the associated species on the right-hand side by their formation constants. Since the acidity constant of pyruvic acid has been evaluated in separate experiments, the only unknown constants in each set of experiments were the formation constants of the metal–pyruvate complexes. Hydrogen ion concentration on the right-hand side of eq 3 was obtained using the empirically determined relationship pH = $1.014pa_H + 0.042$. Initial values are assumed for the stability constants of the metal–pyruvate complexes, β_{1p} and β_{2p}, and for the molar extinction coefficients of these complexes, ϵ_{MP} and ϵ_{MP_2}. Therefore, a theoretical absorbance (A), corresponding to each experimentally observed absorbance, can be calculated from the equation

$$A = (\epsilon_P[P^-] + \epsilon_{HP}[HP] + \epsilon_{MP}[MP^+] + \epsilon_{MP_2}[MP_2])l$$

where the extinction coefficients of pyruvate and pyruvic acid, ϵ_P and ϵ_{HP}, have been obtained in separate experiments, and l is the length of the spectrophotometric cell. The four constants, β_{1P}, β_{2P}, ϵ_{MP}, and ϵ_{MP_2}, were systematically varied and the best set of constants giving the minimum sum of the squares of the residuals, U, defined by

$$U = \sum_i (A_{theor\ i} - A_{obsd\ i})^2$$

was obtained using a pitmapping technique.[10,11] The standard deviation of 14 points for the Ni(II) system was 0.012 absorbance unit; the standard deviation of 15 points for the Zn(II) system was 0.009 absorbance unit.

The acid dissociation constants of dimerized pyruvic acid were obtained from potentiometric titrations with standard hydrochloric acid of dimerized solutions. These dimerized solutions had compositions lying in the range 0.02–0.10 M in monomeric pyruvate and 0.03–0.15 M in dimeric pyruvate. Proton magnetic resonance showed that lactone formation in the acidified dimer solutions[6,8] was negligible as long as titration times were kept under 20 min. A check was made at the end of each titration by preparing a new solution identical in composition with the last point of the titration and comparing its pH with the pH obtained from the last titration point. In all cases the pH readings agreed to within 0.025 pH unit. The following mass balance relationships apply at each titration point.

$$H_{tot} = [H^+] + [HP] + [HD^-] + 2[H_2D] - [OH^-] \tag{4}$$

$$P_{tot} = [P^-] + [HP] \tag{5}$$

$$D_{tot} = [D^{2-}] + [HD^-] + [H_2D] \tag{6}$$

The total quantities on the left-hand side of eq 4–6 are readily calculated at each point on the titration curve and, invoking equilibrium, the terms for the associated species on the right-hand side can be replaced in terms of the corresponding acid dissociation constants, a_H, P^-, and D^{2-}. The dissociation constant of pyruvic acid is known and the unknown acid dissociation constants for dimeric pyruvic acid were obtained using a curve-fitting procedure where the sum of (pH$_{calcd}$ – pH$_{obsd}$)^2 was minimized.[12] The agreement between the theoretical curves calculated using the "best" constants and the experimentally observed curves is illustrated in Figure 1.

The potentiometric titration technique was employed for the evaluation of the metal–dimer stability constants. The determination of these constants was complicated by the changes in the

(8) D. L. Leussing and C. K. Stanfield, J. Am. Chem. Soc., 86, 2805 (1964).

(9) The acidity constants in this paper are reported as: $K_a = a_H \cdot ([B]/[HB])$ where a_H is the activity of hydrogen ion as determined from the pH measurement and the remaining species are expressed as concentrations.

(10) L. G. Sillen, Acta Chem. Scand., 16, 159 (1962).

(11) N. Ingri and L. G. Sillen, ibid., 16, 173 (1962).

(12) D. L. Leussing and D. C. Shultz, J. Am. Chem. Soc., 86, 4846 (1964).

Table I. Summary of Equilibrium Constants Describing the Nickel(II)- and Zinc(II)-Pyruvate-γ-Methyl-γ-hydroxy-α-ketoglutarate Systems ($25°$, $\mu = 1.0$)

Proton Equilibria	
Pyruvate monomer	Pyruvate dimer
$pK_{a,P} = 2.105 \pm 0.013$	$pK_{1D} = 1.73 \pm 0.04$
	$pK_{2D} = 3.72 \pm 0.03$

	Log β_{1P}	Log β_{2P}	Log $K_{ex,P}{}^a$	Log β_{1D}	Log β_{2D}	Log $K_{ex,D}{}^a$
			Equilibria Involving Metal Ions			
Ni(II)	0.883 ± 0.014	0.948 ± 0.032	-1.23	1.50 ± 0.08	2.80 ± 0.30	-2.22
Zn(II)	1.16 ± 0.02	2.00 ± 0.03	-0.95	1.72 ± 0.06	2.98 ± 0.20	-2.00

^{a} $K_{ex,L}$ is defined for $M^{2+} + HL \rightleftharpoons ML + H^+$.

pyruvate and dimer concentrations brought about by the presence of metal ions. These changes in solution composition were much too rapid and appreciable to be neglected and often resulted in precipitation of the slightly soluble metal–dimer salt. To circumvent these problems, a batchwise titration procedure was adopted in which each point on a titration curve represented a single experiment. A typical titration point was made by diluting an aliquot of the monomer–dimer stock solution to the desired concentration and adding an accurately measured volume of standard hydrochloric acid from a buret. An aliquot of standard metal solution was then added to the titration solution, and the pH was recorded as a function of time. The pH was extrapolated back to the time of metal addition, the extrapolations seldom amounting to more than 0.015 pH unit. A titration curve was obtained from a series of such points in which only the volume of added hydrochloric acid was varied.

Assuming initially that the formation of mixed ligand complexes and the formation of tris-dimer complexes are negligible, the following four mass balance equations can be written for each titration point.

$$H_{tot} = [H^+] + [HP] + [HD^-] + 2[H_2D] - [OH^-] \quad (7)$$

$$P_{tot} = [P^-] + [HP] + [MP^+] + 2[MP_2] \quad (8)$$

$$D_{tot} = [D^{2-}] + [HD^-] +$$
$$[H_2D] + [MD] + 2[MD_2{}^{2-}] \quad (9)$$

$$M_{tot} = [M^{2+}] + [MP^+] +$$
$$[MP_2] + [MD] + [MD_2{}^{2-}] \quad (10)$$

Again the total quantities on the left-hand side are known at each titration point and the terms for the associated species on the right-hand side can be replaced by terms containing the corresponding acidity constants, stability constants, a_H, M^{2+}, P^-, and D^{2-}. The acid dissociation constants of monomeric and dimeric pyruvic acid and the stability constants of the metal–pyruvate complexes had been evaluated separately, and the unknown constants for the metal complexes of dimeric pyruvate were obtained by minimizing the pH differences between calculated and observed titration curves. In Figure 2, comparison of the theoretical titration curves computed using the calculated values of the constants with the experimental points reveals the good agreement which has been achieved.

Results and Discussion

The acid dissociation constants and the stability constants which have been evaluated in this study are reported in Table I. The standard deviations assigned to the constants do not represent deviations from the "true" values of the constants since the correlations between all the constants applying to the systems were not studied. The assigned uncertainties do reflect how well the reported values of the constants reproduce the experimentally observed results.

The metal–pyruvate stability constants obtained spectrophotometrically in this investigation are in reasonable agreement with values of the constants obtained potentiometrically by Leussing and Shultz.[12] Also shown in Table I are the proton replacement constants for the reaction

$$M^{2+} + CH_3COCO_2H \overset{K_{ex}}{\rightleftharpoons} CH_3COCO_2M^+ + H^+$$
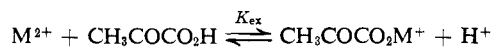
where $\log K_{ex} = \log \beta_{1p} - pK_{a,P}$.

It is usually observed that complex stabilities for related ligand systems parallel the proton affinities of the ligands. Therefore, the constants describing the replacement of a proton from related ligands by a given metal ion are expected to have approximately the same
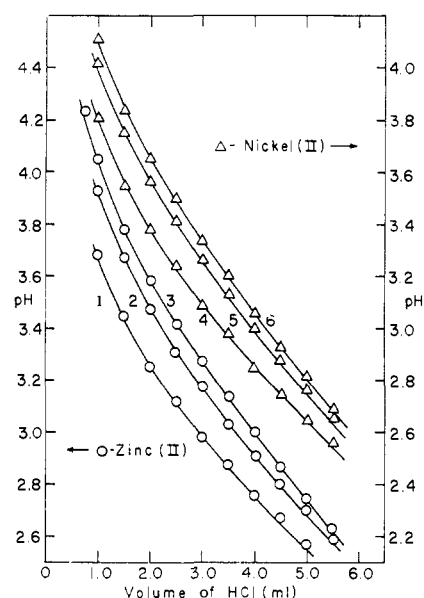
Figure 2. Comparison of experimental titration points and calculated titration curves for the Ni(II)- and Zn(II)-pyruvate-pyruvate dimer systems. Titrant: 0.2002 M HCl; solution titrated: 25.0 ml of 0.02407 M pyruvate monomer, 0.03763 M, pyruvate dimer. After addition of titrant, the following aliquots of metal were added: (1) 5.00 ml of 0.6275 M Zn(II); (2) 5.00 ml of 0.3137 M Zn(II); (3) 4.00 ml of 0.2510 M Zn(II); (4) 5.00 ml of 0.6320 M Ni(II); (5) 5.00 ml of 0.3160 M Ni(II); (6) 4.00 ml of 0.2528 M Ni(II). The solid lines are curves calculated using the accepted values of the constants describing the system.

value. The Zn(II) exchange constant for pyruvic acid is considerably greater than that for propionic acid, log $K_{ex} = -3.7$. This means that the stability of the metal–pyruvate complex is greater than is to be expected on the basis of ligand basicity alone. This enhancement of the metal–pyruvate complex stabilities may be at least partially if not completely attributable to the ability of pyruvate to form a five-membered chelate ring with the metal ion.
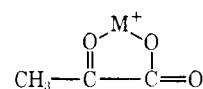
The values of pK_a for the two carboxylate groups of pyruvate dimer in Table I are comparable to values reported for acids which are similar to the dimer in structure. The α-keto end of the dimer structurally resembles the corresponding end of α-ketoglutaric acid ($pK_{1a} = 1.9pK_{2a} = 4.56$)[13] whereas the opposite end of the dimer is related to lactic acid ($pK_a = 3.74$),[14] the α-hydrogen of lactic acid being replaced by $-CH_2COCO_2^-$. It is interesting to note that the replacement of the α hydrogen of lactic acid by $-CH_2COCO_2^-$ has little effect on the acidity of the lactate carboxylate group. A similar effect is observed when a methyl hydrogen of acetic acid ($pK_a = 4.53$)[14] is replaced by $-CH_2COCO_2^-$ to give α-ketoglutaric acid. There do not appear to be very significant inductive or electrostatic effects for $-CH_2COCO_2^-$.

(13) O. R. Buzzelli, Masters Thesis, The Ohio State University, 1966.
(14) L. G. Sillen and A. E. Martell, "Stability Constants of Metal Ion Complexes," 2nd ed, The Chemical Society, London, 1964.

The dimer dianion was found to form 1:1 and 2:1 complexes with both Ni(II) and Zn(II), and the stabilities of the complexes (Table I) are of the order observed with bidentate oxygen donors.[14]

The values of log $K_{ex,D}$ are similar to those calculated for lactic acid[14] (-1.9) rather than monohydrogen α-ketoglutarate (-3.3) or monohydrogen glutarate (-3.4). This suggests that chelate structure A predominates over B and C.
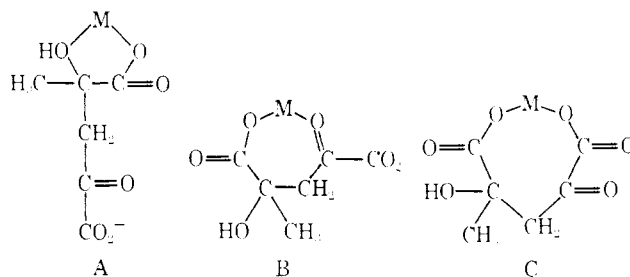
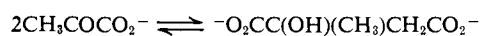# Pyruvate Dimerization Catalyzed by Nickel(II) and Zinc(II). II. Kinetics[1]

D. E. Tallman and D. L. Leussing

Contribution from the Department of Chemistry, Ohio State University, Columbus, Ohio 43210. Received April 7, 1969

Abstract: Ni(II) and Zn(II) catalyze pyruvate dimerization *via* a two-step reaction: enolate formation of complexed pyruvate followed by addition of a second pyruvate to the complexed enolate (carbanion). Proton loss from complexed pyruvate shows general base catalysis with water catalysis comprising the predominant path in the dilute acetate buffers employed. The rate of water-catalyzed proton removal is somewhat faster with Ni(II) than with Zn(II), but the reverse order of metal ion activity appears to hold for the addition reaction. This reactivity pattern can be ascribed to the differences in metal ion–enolate bond strengths with perhaps the ability of Zn(II) to form a less sterically constrained mixed complex contributing to a faster rate of addition. An approach is presented for correcting spectrophotometric rate data for time-dependent apparent deviations from Beer's law caused by changes in species distribution.

The catalytic effect of metal ions on pyruvate dimerization has been long known,[2] and metal ion catalysis in other condensation-type reactions has also been reported[3-6] but little quantitative information regarding the mode of metal ion activity appears to be available. Thus, a study of metal ion effects in pyruvate dimerization would provide pertinent information regarding an important class of reactions. Pyruvate dimerization can be conveniently followed spectrophotometrically because the intensity of absorption for the 315-mμ n $\rightarrow$ π^* transition of the carbonyl group de-

$$2CH_3COCO_2^- \rightleftharpoons ^-O_2CC(OH)(CH_3)CH_2CO_2^-$$

creases by a factor of approximately 2 as two pyruvate ions (P$^-$) form one γ-methyl-σhydroxy-γ-ketoglutarate ion (D^{2-}). The recently completed study of the equilibrium properties of the Ni(II) and Zn(II) pyruvate monomer–dimer systems[7] permits the evaluation of the extinction coefficients for the dimeric species, and therefore an analysis of spectrophotometric rate data becomes possible.

The calculation of rate constants for systems such as the present, which contain labile metal ions and reacting ligands in comparable concentrations, in general, is complicated by changes in the distribution of product and reactant species as the reaction proceeds. These concentration changes not only cause time-dependent variations in the rate law terms, but, if reactant or product species have different extinction coefficients, apparent time-dependent deviations from Beer's law are introduced into a rate function derived from spectrophotometric results. The availability of high-speed computers now makes it possible to easily correct for

(1) This project was supported by a grant from the National Science Foundation.
(2) L. Wolff, *Ann. Chem.*, **260**, 126 (1890); **305**, 154 (1899).
(3) M. L. Bender, "Reactions of Coordinated Ligands," Advances in Chemistry Series, No. 37, American Chemical Society, Washington D. C., 1963, Chapter 2.
(4) L. Benoiton, M. Winitz, R. F. Colman, M. Birnbaum, and J. P. Greenstein, *J. Am. Chem. Soc.*, **81**, 1726 (1959).
(5) P. N. Gordan, *J. Org. Chem.*, **22**, 1006 (1957).
(6) D. A. Fraser, R. W. Hall, and A. L. J. Raum, *J. Appl. Chem.*, **7**, 676 (1957); D. A. Fraser, R. W. Hall, P. A. Jenkins, and A. L. J. Raum, *ibid.*, **7**, 689 (1957).

(7) D. E. Tallman and D. L. Leussing, *J. Am. Chem. Soc.*, **91**, 6253 (1969).